Cosmetic Science and Technology Series/Volume 20

Antiperspirants and Deodorants

Second Edition, Revised and Expanded

edited by
Karl Laden

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Antiperspirants and Deodorants

COSMETIC SCIENCE AND TECHNOLOGY

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Consultant
Technology Transfer and New Product Development
Haifa, Israel



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About the Series

The Cosmetic Science and Technology series was conceived to permit discussion of a broad range of current knowledge and theories of cosmetic science and technology. The series is made up of books written either by a single author or edited volumes with a number of contributors. Authorities from industry, academia, and government from all over the world are participating in writing these books.

The aim of the series is to cover the many facets of cosmetic science and technology. Topics are drawn from a wide spectrum of disciplines ranging from chemistry, physics, biochemistry, analytical and consumer evaluations to safety, efficacy, toxicity, and regulatory questions. Organic, inorganic, physical and polymer chemistry, emulsion technology, microbiology, dermatology, and toxicology all play a role in cosmetic science.

There is little commonality in the scientific methods, processes, and formulations required for the wide variety of cosmetic and toiletries manufactured. Products range from hair-, oral-, and skin-care preparations to lipsticks, nail polishes and extenders, deodorants, body powders and aerosols, to over-the-counter products, such as antiperspirants, dandruff treatments, antimicrobial soaps, acne and sunscreen products.

Cosmetics and toiletries represent a highly diversified field involving many subsections of science and ''art.'' Indeed, even in these days of high technology, ''art'' and intuition continue to play an important part in the development and evaluation of formulations and the selection of raw materials. There is a move towards more sophisticated scientific methodologies in the fields of claim substantiation, safety testing, product evaluation, and chemical analyses, as well as a better understanding of the properties of skin and hair.

Emphasis in the Cosmetic Science and Technology series is placed on reporting the current status of cosmetic technology and science in addition to

historical reviews. The series has grown to twenty books dealing with the constantly changing technologies and trends in the cosmetic industry, including globalization. Several of the books have been translated into Japanese and Chinese. Contributions range from highly sophisticated and scientific treaties, to primers, practical applications, and pragmatic presentations. Authors are encouraged to present their own concepts, as well as established theories. Contributors have been asked not to shy away from fields that are still in a state of transition, or to hesitate to present detailed discussions of their own work. Altogether, we intend to develop in this series a collection of critical surveys and ideas covering diverse phases of the cosmetic industry.

The second edition of *Antiperspirants and Deodorants* is the twentieth book published in the Cosmetic Science and Technology series. Since the publication of the first edition of *Antiperspirants and Deodorants* by Karl Laden and Carl Felger ten years ago, there have been significant changes in both the marketplace and technology. New product forms, new regulations on a global scale, and changing consumer expectations and perceptions have significantly altered this business. Examples include the widespread use of volatile and non-volatile silicones that has allowed the development of new product forms, such as anhydrous roll-on products, and the utilization of a new gelling agent, dibenzylidene sorbitol, in the formulation of clear antiperspirant sticks.

This book represents a major departure from the first edition and significantly expands the book's scope. Two chapters dealing with the formulation aspects of the various types of antiperspirant and deodorant products sold worldwide have been added. Another innovative approach is two new chapters on the changing technology trends as illustrated by the extensive patent literature covering this field. As the author illustrates, relying on scientific literature alone gives an incomplete picture of what happens in the ''real world'' and it is the volume and intricacy of the patents that provide a real clue to the new trends in this field.

I want to thank all the contributors for taking part in this project and particularly the editor, Dr. Karl Laden, for developing a new approach to this greatly expanded second edition of *Antiperspirants and Deodorants.* Special recognition is also due to Sandra Beberman and the editorial staff at Marcel Dekker, Inc. In addition, I would like to thank my wife Eva, without whose constant support and editorial help I would never have undertaken this project.

Eric Jungermann, Ph.D.

Preface

It has been 10 years since the first edition of *Antiperspirants and Deodorants* was published. In the intervening years, there have been many significant new developments in terms of ingredients, packaging, and products. In addition, a considerable number of changes have occurred in areas that directly affect the industry, such as new regulatory issues, safety and toxicological questions, information concerning skin micro-organisms, odor generation, and sweat gland physiology.

This second edition of *Antiperspirants and Deodorants* has been written with a view toward updating the interested reader on the latest technology impacting on this major Health and Beauty Aid (HBA) category.

Antiperspirants and deodorants represent one of the largest of the HBA product categories. The proportion of adult consumers regularly using these products is over 90% in the United States. Their frequency of daily use and total dollar sales ($1.5 billion/year in the U.S.) is exceeded only by that of toothpastes. Antiperspirants and deodorants are also the most diverse HBA product category in terms of product forms available to the consumer. Products are sold as aerosols, pump sprays, squeeze sprays, sticks, cream dispensers, roll-ons, and dabbers. Within each packaging form, a whole array of very different types of formulations is also offered. Sticks, for example, can be suspensoid solid formulations, clear sticks, soft solid sticks, soft clear gel sticks, and so forth. Further broadening the range of products is the fact that each of these forms is available as both an antiperspirant and a deodorant.

Antiperspirants can be defined as products that reduce the amount of perspiration generated (usually in the underarm area). Deodorants are products that reduce underarm odor. While the consumer and some marketers use the terms interchangeably, they represent two distinct and separate functions. Antiperspirants fight wetness, deodorants fight odor. While antiperspirant

products usually also provide odor control, many deodorants only provide odor control and do not reduce wetness.

The U.S. market is the most developed (and mature) for antiperspirant and deodorant products. However, both categories also enjoy considerable growth and success on an international level. In many of these markets, the preferred product forms and attributes differ significantly from those found in the U.S. and even from neighboring countries. It is this diversity and vitality of the antiperspirant and deodorant market that makes the subject interesting and challenging for the researcher, formulator, and marketer.

It is hoped that this second edition will offer considerable new information to all those whose work impacts on this major HBA category.

To that end, it has been completely rewritten and updated. Five entirely new chapters have been introduced that will increase the value of the book to a broader range of technical and nontechnical people working in the field. In addition, previously existing chapters have been expanded to cover fields that were not covered in the first edition.

Among the major changes introduced in the second edition are:

1. Two new chapters relating to antiperspirant and deodorant formulations. These chapters are intended for nontechnical readers (marketing, advertising, sales) as well as scientists unfamiliar with the field of antiperspirant and deodorant formulations. They offer a guide to understanding the ingredients used in these products and the purposes they serve.
2. Two new chapters reviewing antiperspirant and deodorant patent technologies in the 1990s. Taken together, these two chapters offer insight into the technological fields being pursued, and which companies are doing the work.
3. The chemistry behind higher-efficacy aluminum and zirconium/aluminum salts (commonly called activated ACH and activated ZAG salts) is reviewed for the first time. Also included is a new and thorough review of the chemistry of aluminum/zirconium and zirconium/aluminum glycine complexes. This is the first such chapter in this field.
4. The chapter covering the function and structure of the human eccrine sweat gland has been completely rewritten and updated, with an entirely new section covering the apocrine sweat glands.
5. The chapter on regulatory issues has been rewritten with an expanded emphasis on international issues.
6. Information concerning the microbiology of the axilla and the odors

produced has been condensed into a single chapter and updated to reflect the major changes occurring in these fields.

7. The chapters dealing with the clinical evaluation of antiperspirants and deodorants have also been combined into a single chapter and updated to reflect current testing procedures.
8. The chapter covering deodorant ingredients has been completely rewritten to include the large number of new materials and new approaches currently available for achieving odor control.
9. The safety issues involved in the use of antiperspirants has been updated and includes a review of information available concerning aluminum exposure and Alzheimer's disease.

I am indebted to all the contributing authors for their efforts in preparing their manuscripts and in meeting the various deadlines imposed upon them. Without their cooperation and excellent submissions this volume would never have been published.

I would also like to thank my wife, Judy, for encouraging me to take on this project. At times I wondered if it was a wise decision, but in the end, she was right. Thanks to my assistant, Pat Eaton, for following up on a variety of details and sometimes serving to nudge certain authors. I am indebted to Alpa Cosmetics for the occasional use I made of their office facilities and to Harry Brand for being a true friend since my Aliyah to Israel.

This book is dedicated to the memory of some of my mentors and colleagues who guided and assisted me during my career in this industry: Raymond Reed, William Mueller, John Menkart, Phillip Sokel, and Carl Felger.

Karl Laden

Contents

About the Series *iii*
Preface *v*
Contributors *xi*

1. Antiperspirants and Deodorants: History of Major HBA Market 1
   Karl Laden

2. Structure and Function of Human Sweat Glands 17
   Paul M. Quinton, Hugh Y. Elder, D. McEwan Jenkinson, and Douglas L. Bovell

3. Axillary Odor Determination, Formation, and Control 59
   John N. Labows, John T. Reilly, James J. Leyden, and George Preti

4. Chemistry of Aluminum Chlorohydrate and Activated Aluminum Chlorohydrates 83
   John J. Fitzgerald and Allan H. Rosenberg

5. Chemistry of Aluminum-Zirconium-Glycine (AZG) Complexes 137
   Allan H. Rosenberg and John J. Fitzgerald

6. Deodorant Ingredients 169
   Stephen A. Makin and Michael R. Lowry

7. Safety of Antiperspirant Salts 215
   Ronald J. Wulf

8. A Guide to Understanding Antiperspirant Formulations 233
Christopher J. C. Edwards and Anthony K. Mills

9. A Guide to Understanding Deodorant Formulations 259
Stephen Hazell

10. Regulations of Underarm Antiperspirants and Deodorants 283
David C. Steinberg

11. Clinical Evaluation of Antiperspirants and Deodorants 305
John E. Wild, James P. Bowman, and Linda P. Oddo

12. Antiperspirant Technology Trends from the Patent Literature 327
Karl Laden

13. Deodorant Technology Trends from the Patent Literature 357
Karl Laden

Index *383*

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1

Antiperspirants and Deodorants: History of Major HBA Market

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I. INTRODUCTION

The marketing of products specifically made for controlling underarm wetness and odor only began slightly over 100 years ago. The first product in this category, Mum deodorant, was brought out in 1888 (1). Starting from products that were reportedly first used mainly by people in the entertainment field, antiperspirants and deodorants have grown to be one of the largest Health & Beauty Aids (HBA) product categories in the United States. Toothpaste is the only HBA product enjoying more frequent use by a larger segment of the public, although consumer sales in both categories are about the same, $1.5 billion. This overview of the history of antiperspirant and deodorant products (AP&D) will attempt to analyze what technologies, packaging developments, materials, and social changes influenced this growth. It has certainly not grown at a steady rate. In the first 50 years U.S. product sales grew to $20 million a year. In the last 50 years, product sales have grown to over $1.5 billion a year.

The range of antiperspirant and deodorant packaging forms and types of formulations currently being offered the consumer is probably greater than for any other HBA category. It includes aerosols, pump sprays, squeeze sprays, creams, roll-ons, suspension roll-ons, deodorant sticks, antiperspirant solids, clear solids, soft solids, gels, and pads.

The first commercial product for specific underarm use was Mum de-

odorant, a waxy base containing zinc oxide, a weak antimicrobial agent. One hundred and ten years later, the Mum brand name still exists as a trademark of Bristol-Myers. The first commercial antiperspirant appeared in 1903 under the brand name Everdry (2). It was an aqueous alcoholic solution of aluminum chloride. The product was applied by wetting a cotton ball with the product and dabbing it under the arms. It is interesting to note that current deodorant products are considerably more efficacious than the original zinc oxide deodorant, while antiperspirant products are probably less efficacious than the original aqueous aluminum chloride. While no efficacy measurements were done on those early products, current testing would suggest efficacy in the 60% to 70% range, while modern antiperspirant products inhibit sweating between 30% and 55%.

One might think that inhibition of sweating by 50% does not seem a very useful level of efficacy. Going out in a rain storm with an umbrella with 50% holes in it will hardly keep you dry. However, people do not measure antiperspirant efficacy by percent reduction in sweating. The consumer is more interested in whether sweating is sufficiently reduced that sweat won't wet through to their clothing. Wetting through to clothing usually depends on the type and fit of clothes being worn, the rate of sweating, and the rate at which sweat is evaporating from the underarm area. Because of these variables, it is not surprising that a consumer's ability to evaluate product efficacy is not very precise. Therefore, depending on how the above factors interrelate, sometimes a 20% reduction in the amount of sweat is sufficient to prevent wetness breakthrough, while there may be other times when a 70% reduction is not enough.

II. GROWTH OF MARKET

The growth of the antiperspirant and deodorant industry in the United States has outpaced many other Western countries. Not only are the numbers of people who use antiperspirants and deodorants on a regular basis far different from country to country, but so are the men-women split and the product application preferences (see Table 1). In the United States, aerosol antiperspirant and deodorant users account for less than 20% of the market; in the United Kingdom, it is over 80%. In Germany over 25% of the AP&D product sales are pump sprays; in the U.S. and France, this form almost doesn't exist. Germany sells over 20% of its AP&Ds in a roll-on package; in neighboring France the figure is less than 1%, and in Sweden it is over 70%. The form that completely dominates the most developed AP&D market (the United States) is the stick. This includes deodorant sticks, antiperspirant solids, soft solids, and

Table 1 Product Form Preference and Number of Users

	% Product sales by form						
	U.S.	U.K.	France	Germany	Italy	Holland	Spain
Aerosols	16.0	79.9	79.1	36.2	37.0	41.5	56.0
Roll-ons	12.7	14.7	0.2	22.0	2.2	30.7	17.7
Sticks/solids	52.8	5.1	17.5	9.5	17.8	10.6	17.2
Pumps	—	0.1	1.0	26.8	30.5	11.8	4.5
Gels	12.5	—	—	—	—	—	—
Soft solids	5.0	—	—	—	—	—	—
Creams	0.7	0.2	2.2	5.5	12.5	5.4	4.6
	% Adults using AP&Ds						
	92	85	63	70	—	—	—

Table 2 Sales of AP&Ds in Europe

	U.K.	Germany	France	Italy
Sales (US$) $\times 10^6$	485	483	367	99
Population (18–65) $\times 10^6$	38.0	57.6	37.9	39.7
Per capita (18–65) AP&D expenditures US$	12.7	8.4	9.7	2.5

gels (the latter two are not stick products but are dispensed from packages resembling the stick format). Taken together, this product form accounts for almost 70% of U.S. AP&D sales. In not a single European country do these stick forms account for more than 22% of the market. Finally, while the population of the United Kingdom and France are approximately equal (58 million), the expenditures on AP&Ds in the United Kingdom are about 30% higher (see Table 2).

Since each packaging form has its own distinct application aesthetics, one can only conjecture why certain packaging forms have gained acceptance in different countries. In this chapter, the author will attempt to trace the growth of AP&Ds in the U.S. market with a special view toward identifying how application aesthetics affected product acceptance.

III. EARLY PRODUCTS

The first antiperspirant products were aqueous alcoholic solutions of aluminum chloride. It is not difficult to identify the negative attributes of these early

products. You applied them with a wetted cotton ball, so you had to wash your hand after each application. They felt wet and cold. They dried rather slowly and went through a very sticky phase during the drying process. They irritated the skin and damaged clothing. In spite of all these highly negative attributes, they did reduce perspiration and help stop odor. These benefits were important enough that within several years of their introduction, one product, Odo-Ro-No, became so successful, it began to advertise nationally in 1914 (3). The first scientific report on the efficacy of aluminum chloride as an antiperspirant appeared in 1916 in the Journal of the American Medical Association (4). While noting its efficacy in reducing perspiration, the article also cautioned about its irritancy in causing burning, stinging, and redness.

In the early 1930s, with the introduction of Arrid Cream, the first major improvement in product form occurred (5). The product used aluminum sulfate as the active ingredient incorporated into a cream base. This offered the consumer a product that was much more cosmetic in appearance than the simple solutions of aluminum chloride, and probably slightly less irritating. It simplified application under the arm and dried faster with less stickiness. It was also less effective.

Cream antiperspirant products quickly began to replace the simple solutions and even gained acceptance over cream deodorants. For almost 20 years, creams represented essentially the only antiperspirant form available, and by the mid-1940s was reported to control 88% of the category. The advertising slogan ''Don't be half safe, use Arrid to be sure'' became very well known. (The ''Use Arrid to be sure'' slogan from the 1940s should not be confused with the 1980s' ''Raise your hand if you're Sure'' slogan promoting the Sure line of antiperspirants.) By 1945, Arrid Cream controlled about 34% of the $30 million antiperspirant market (6). With the later development of newer packaging forms, cream antiperspirants have been greatly reduced in popularity in the United States (it now represents about 1% of the category). However, some 65 years after it was first introduced, Arrid continues to be the leading cream antiperspirant in the United States.

IV. IRRITANCY AND CLOTHING DAMAGE

A considerable amount of work was done in trying to reduce the irritancy and clothing damage caused by antiperspirant salts. This usually involved additives to reduce the acidity and protect garments from damage. Alum and borax were early materials tried (7). Less acidic salts such as aluminum formate (8) and the phosphates were also reported (9). For many years urea was the mate-

rial of choice to buffer the acidity (10). This plus other amino compounds often helped reduce the irritation and clothing damage, but never completely solved the problem.

Initial attempts to prepare less acidic or partially neutralized salts of aluminum chloride were mostly unsuccessful because simple partial neutralization led to the formation of insoluble precipitates, gels, or colloids of aluminum hydroxides. It wasn't until the 1940s that partially neutralized aluminum hydroxy chlorides began to be described and their use in antiperspirants proposed (11–14). The use of 5/6 basic aluminum chlorohydroxide as the antiperspirant ingredient of choice began in 1947 (15). A 1949 patent covering some specific formulations with this ingredient was subsequently rejected (16).

It is the view of the author that the introduction of aluminum chlorohydroxide represented the technology breakthrough responsible for the subsequent rapid growth of this category. It probably represents the single most important ingredient development in the antiperspirant field. It offered formulators and product users a major improvement. Instead of formulations with relatively acidic pHs that were modified with buffering materials such as urea and amines, formulators could work with an antiperspirant salt solution that had a pH of 4 to 5. The 5/6 basic salt was considerably less irritating to the skin, so that not only could more people use antiperspirant products without irritation but even daily use was not a problem for most consumers. In addition, a great many of the issues relating to clothing damage from antiperspirant salts were dramatically reduced. On the negative side, this new antiperspirant salt was considerably less effective as an antiperspirant. However, the positive attributes far outweighed this reduction in efficacy. The history of this category contains several other instances where the popularity of less effective products replaced more effective ones based on other attributes.

In spite of the very large reduction in irritancy and clothing damage offered by aluminum chlorohydroxide over the more acidic salts, even this material is not completely free of these problems (17,18). While specific data are not available, it is common for significant numbers (up to 10%) of users to occasionally experience stinging, itching, redness, and soreness. The severity of these reactions is usually at a very low level and does not always occur with every application. In addition, instances of clothing damage and color changes still occur. In many cases these reactions lead consumers to change brands or switch to using non-aluminum-containing deodorant products. Thus the development of even milder products continues to be a challenge. Recently some marketers have focused on skin mildness as a key attribute of their product. Some brand names that convey mildness such as Vaseline Intensive Care, Dove, and Nivea have recently introduced AP&D lines. (Vaseline Intensive

Care claims "Tough on perspiration, easy on your skin" while Dove's antiperspirants claim "1/4 moisturizing cream" in their formulas.)

V. NEW PACKAGING FORMS

If the first 50 years of new-product development in the AP&D industry culminated in the introduction of aluminum chlorohydroxide in the late 1940s, then the most recent 50 years can be divided into two distinct development periods. The mid-1940s until the early 1960s saw the introduction of virtually all of the application forms now on the market. During this period, deodorant pads, the squeeze bottle, roll-ons, sticks, pump sprays, and aerosols were developed. Since then, all new products have been essentially formulation rather than packaging developments. Let me hasten to add that this does not mean that significant design and functionality improvements were not added to the packaging forms mentioned above. This includes better-designed and functional stick and solid containers, larger ball roll-ons, improved pumps, better squeeze spray containers, and new designs for soft solid and gel dispensers. However, since the early 1960s most of the new product advancements have been based on creative formulations and new ingredients rather than new applicators and packaging improvements.

The development of plastics during World War II led to the introduction of plastic bottles in the 1940s and a new antiperspirant applicator based on the old Venturi glass bottle–rubber bulb perfume atomizer. The product was a squeeze bottle spray atomizer for dispensing antiperspirants and deodorants. The best-known product in this form was called Stoppette (19). Because the spray concept worked on a Venturi principle, the formulations delivered from this package had to be low-viscosity, often aqueous alcoholic solutions. The sprays developed from these early packages were often coarse, wet, cold, and sticky. Overapplication also caused the product to run down the sides of your body. In many ways it had many of the same negatives as the original aqueous alcoholic solutions applied with a cotton ball. However, these types of products achieved a modest (albeit short-lived) degree of consumer acceptance in the United States. The one outstanding advantage of this product form over all other AP&Ds marketed at the time was that it could applied without using your fingers. The acceptance of this product form by many consumers over more cosmetically aesthetic creams demonstrated the strong negative feelings that many consumers had about applying a product to their underarm area with their fingers. In fact, subsequent to the squeeze spray, the one feature

every new antiperspirant or deodorant form has in common is that it does not need to be rubbed in with your fingers.

In the late 1940s, a new technology was introduced for writing instruments. It involved applying ink to a paper using a liquid ink supply which was transferred to the paper by means of a rolling ball. The ballpoint pen was an immediate success. Borrowing from this new technology, the scientists at Bristol-Myers thought this might also be a convenient way to apply cosmetic formulations to the skin, particularly antiperspirants. In 1952 they introduced the first roll-on antiperspirant into test market (2). Called Roulette, the product failed because of technical problems with the ball and fitment. Three years later they brought out an improved version called Ban, whose success sparked the growth of the roll-on form of application for antiperspirants. Within 5 years, sales of roll-on AP&Ds greatly exceeded that of creams, and the squeeze spray applicator was almost gone from the U.S. market. Forty years later the roll-on form of application continues to be popular, accounting for almost 13% of U.S. sales with considerably greater popularity in many European markets (e.g., Germany, 22%; Holland, 30%; Scandinavian countries, about 50%).

The success of roll-ons is not difficult to understand taking into consideration the product attributes. Like squeeze bottles, the product could be applied without having to rub it under your arms with your fingers. However, unlike squeeze sprays, formulations did not have to be low-viscosity aqueous alcoholic products. Higher-viscosity liquid emulsions combined with more controlled and even application gave the formulator leeway to prepare products with considerably better aesthetic properties. These included more even application, no dripping down the side of your body, products that were less cold and sticky during drying, and more elegant cosmetic feeling to the overall application. By the early 1960s, AP&D sales in the United States had grown to over $100 million. While less acidic AP salts and new, easier application forms were important in stimulating this growth, the author believes other factors were also at play. Prominent among these was changing social awareness.

VI. SOCIAL AWARENESS

Over 2000 years ago, the Roman poet Ovid warned young people not to let a ''goat find its way underneath your arms'' (20). Despite this warning, the actual use of underarm products for controlling odor and wetness did not really begin to grow rapidly until the 1950s. Certainly, advertising (particu-

larly television) played an important role in generating greater awareness of this category of products. Lifebuoy deodorant soap, with its well-known radio commercials promising to stop B.O. (body odor), was one forerunner to these.

However, something else was also happening. Workers were moving from factory jobs involving some degree of physical labor to office jobs. This change in working environment sparked a greater concern for hygienic issues such as perspiration and odor. The acceptance of wetness and odor that might have existed among people working in a factory environment no longer seemed acceptable in a business office. This growing social awareness of odor and wetness was merely reinforced by television advertising and new AP&D products. Pretty soon, wetness and odor were socially unacceptable in both white-collar and blue-collar environments. In recent years, with the emphasis on physical fitness, it is interesting that wetness and odor when exercising or doing hard physical labor has taken on, in many instances, almost a macho image. However, under almost any other social or work-related circumstance, it is considered offensive.

In addition to greater social awareness, antiperspirant and deodorant product sales increased because of greater year-round usage. Sweating can be stimulated in many different ways, including physical effort, heat, and emotional stimulation. In the early years many people considered antiperspirants as hot-weather products. While the advent of air-conditioned workplaces and homes might have been expected to result in declining antiperspirant and deodorant sales, this did not occur. Instead there was a growing awareness, promoted through advertising, of emotional stress as a stimulant for sweating. In addition, the rapidity with which emotional stress can bring about sweating and the quantity of sweat generated are considerably greater than those produced by temperature alone.

This realization meant that even people working and living in air-conditioned environments still had need for antiperspirant and deodorant products. In reality, it did not take a lot of convincing to make the consumer aware of emotional sweating. Phrases like "nervous sweating" and situations depicting embarrassing or stressful situations became commonplace in advertising for antiperspirant and deodorant products. An early print advertisement for Arrid explained it quite clearly. "There are two kinds of perspiration, physical and emotional. Physical comes from work and exercise; emotional from excitement and tension. Even in a tender moment, a sudden gush of emotional perspiration can embarrass you." Soon these products lost their seasonality, and year-round usage became the norm.

VII. AEROSOLS

Aerosol deodorant products came into the market in the late 1950s. They were based on technology generated in the U.S. Army for spraying insecticides. The first major brand name was Right Guard. Initially the product was believed to have antiperspirant properties because of the presence of zinc phenol sulfonate in the formula. When the zinc salt was shown to be devoid of antiperspirant activity, the product was sold as strictly a deodorant (with hexachlorophene as the primary deodorant ingredient). The aerosol format for underarm application was an immediate success. Not only did many roll-on and cream users switch to aerosols, but the aerosol form began to attract many men into the category who previously did not use underarm products. While Right Guard was not strictly positioned for men, the name, fragrance, and the product's association to Gillette certainly gave it a "for men" image.

Adding to the number of men who began using deodorants in the 1950s was another new product form, stick deodorants. Old Spice stick (clearly a male brand) pointed out its advantages over earlier product forms with its claims. "No more runny liquid, sticky cream, messy fingers." In 1958 Mennen introduced its Speed Stick for men. It was the first of the gel sticks based on glycols rather than alcohol, and dispensed from an oval swivel-up container.

In the 5 years from 1962 to 1967 the AP&D category doubled, from $100 million to $200 million a year. Much of this growth was stimulated by the new aerosol form. Aerosol products soon overtook roll-ons as the preferred product form. It was positioned for general family use, and the fact that it further removed the application process from the underarm area was captured by the Right Guard advertising slogan, "Nothing touches you but the spray itself." One can only speculate on what attracted consumers to the form. Certainly it was fast and easy to apply. Its light, fine mist deposited evenly, and because of its high alcohol content the product dried quickly without stickiness (although with a distinct amount of cooling compared to roll-ons). However, none of the original aerosol products afforded the consumer any protection against wetness. This meant that a considerable number of consumers were switching from roll-on antiperspirants, which reduced sweating by about 40%, to aerosol deodorants, which did not reduce sweating at all. Whether this suggests that the other attributes of the aerosol product form outweighed the efficacy advantages of creams and roll-ons is unknown. It also may have indicated the poor perception of many consumers in judging product efficacy. For many, perhaps odor control was really all they needed.

The race to produce the first successful aerosol antiperspirant was won by the Carter-Wallace Co. with their introduction of Arrid Extra Dry about 5 years after the aerosol deodorants came to market. Carter solved the corrosion and clogging problem incurred with earlier aerosol formulations containing aluminum salts by suspending aluminum chlorohydroxide in an anhydrous emolient and dispensing the suspension under relatively high propellant pressure. Aerosol antiperspirants quickly overcame aerosol deodorants in popularity while the whole market continued to grow (by 1970, the U.S. market reached $300 million a year, with aerosol antiperspirants accounting for 45% and deodorants for 30%). This trend toward the aerosol form continued to strengthen, so that a few years later, aerosols represented over 80% of the AP&D market with aerosol antiperspirants outselling deodorants 3:1.

The fact that aerosol antiperspirants quickly replaced aerosol deodorants in popularity might seem to suggest that in spite of what was said above, when other things are equal (i.e., both products being aerosols), consumers will opt for antiwetness efficacy. However, a number of observations cast some uncertainty about the conclusion. The first is that aerosol deodorants and aerosol antiperspirants are very different in the application aesthetics. The deodorants being high-alcohol-containing products produced a definite cooling effect on the skin and could cause stinging on shaved or mildly irritated skin. Since the aerosol antiperspirants contained no alcohol, the spray tended to reach the skin feeling warmer. Once on the skin, the antiperspirants gave the sensation of drying almost immediately, since only the dry-feeling emollient oil and particulate antiperspirant salt residue remained on the skin. With deodorant aerosols, a significant amount of alcohol was deposited on the skin which produced a cool, wet feeling that took a few moments to dry.

It can be argued that the consumer trend for aerosol antiperspirants was based as much on its application aesthetics as on its antiperspirant efficacy. It must be remembered that the early aerosol antiperspirants were not very effective, reducing perspiration only 20% to 25%. Certainly consumers to whom efficacy was important and who were able to judge product effectiveness would have stayed with the roll-ons, which reduced sweating around 40%. One can only assume that the consumers who gave up roll-ons for aerosols were either poor judges of product efficacy or gave greater importance to product aesthetics.

VIII. AEROSOLS UNDER ATTACK

Starting in the 1970s, a series of events slowly began eroding the confidence of the U.S. consumer in aerosols in general and AP&D aerosols in particular.

It began with the introduction into the market of aerosol antiperspirants based on aluminum/zirconium salts. The conversion from aluminum chorohydrate to the aluminum/zirconium salt significantly increased the efficacy of these products. The Sure brand, which contained an aluminum/zirconium salt, even encouraged consumers to use Sure under one arm and their regular brand (containing an aluminum salt) under their other arm, and ''Let your body tell you which AP spray keeps it drier.'' Arrid XX claimed their aluminum/zirconium aerosol kept you ''50% drier'' than an aluminum spray. The aluminum/zirconium salts had already found widespread use in other antiperspirant product forms to boost their efficacy.

In testing its own aluminum/zirconium aerosol product before entering the market, Gillette discovered some lung abnormalities in long-term animal inhalation studies. These results were brought to the attention of the Food and Drug Administration (FDA), which subsequently banned the use of aluminum/zirconium salts in AP aerosols (21). This unfavorable publicity was the first of four events to affect consumer attitudes concerning aerosol AP&Ds. In most cases these types of unfavorable publicity stemming from governmental regulations had multiple negative effects: first, when the announcement is made that the FDA was studying the situation; again usually many months if not years later, when the government announces the results of its evaluation (in this case an announced ban); and yet again when the ban actually takes effect (often 1 to 2 years later).

The second series of adverse news for aerosols in general were the publications by Molina and Rowland (22). The results of their experiments suggested that chlorofluorocarbons in aerosol propellents were depleting stratospheric ozone levels which are essential for filtering harmful UV rays from reaching the surface of the earth. While highly controversial at first, these results plus the experiments of others, eventually led to a ban on the use of most chlorofluorocarbon propellants in aerosols (23).

Adding further to consumer concerns about using aerosol antiperspirants was the announcemtnt by the FDA advisory panel on antiperspirants that it was asking for further review of the long-term safety of aluminum-containing aerosols (24). All of these events essentially took place in the mid to late 1970s. Coming into the foreground at the same time was a growing consumer awareness of environmental issues and safety. It is reasonable to imagine that many consumers did not distinguish between the specific issues involved in each of the above cases, but rather came away with an overall concern with using aerosols in general, and aerosol antiperspirants in particular. It did not matter that by the end of the 1970s and early 1980s aluminum/zirconium salts were no longer being used in any aerosol antiperspirants, that chlorofluoro-

carbons had been replaced by hydrocarbons as the propellants, and that the FDA advisory panel had ruled that aluminum-containing antiperspirant aerosols were safe and effective (25). The damage to consumer confidence in aerosol AP&Ds had already been done. (Companies that were weak or did not compete in the aerosol segment of the AP&D business even encouraged this flight from aerosols. "Get off the can and get on the stick," said a Mennen advertisement.) In 1974, about 82% of all AP&D sales in the United States were aerosol products; just 8 years later, the figure had fallen to 32%. In the past a technologically new product form was always the reason for the decline of an older form (e.g., roll-ons replaced creams; aerosols replaced roll-ons). However, this time the aerosol segment of the AP&D market declined because of consumer concerns with the form as opposed to enchantment with a new product. It is interesting to note that in the United Kingdom, where many of the FDA-related safety issues were not as prominent, the aerosol form has maintained its dominance of the AP&D category. (Over 80% of AP&Ds sold in the United Kingdom are aerosols. This figure is almost the same as that found in the United States in the early 1970s, before aerosols came under attack.)

IX. SUSPENSION ROLL-ONS AND SOLIDS

During the period when aerosols started their decline in popularity, several new products began to appear which, rather than being based on unique packaging forms, were dependent on new formulation expertise and new raw materials. Aerosol antiperspirant formulators had already discovered the benefit of replacing some or all of the emollient oils originally used in these products with new raw materials called cyclomethicones. The volatility, low heat of vaporization, and good feel of these materials made them excellent candidates for use in aerosols. They decreased the greasy after-feel because they evaporated off the skin. The low heat of vaporization meant that they did not produce a cooling, wet sensation during evaporation. Unlike the emollients previously used, they did not contribute to garment staining and they improved the antiperspirant efficacy of aerosols by not interfering with the dissolution and action of the aluminum chlorohydrate.

These cyclomethicone compounds were to become a key component of almost all the new product formulations that benefited from the decline in aerosols. If the discovery of aluminum chlorohydrate represented the single most important active ingredient for the growth of the AP&D category, then volatile silicones are the most important nonactive ingredients contributing to

the development of new products in this category (26). One might reason that if the U.S. consumer liked the feel of an antiperspirant aerosol but was becoming concerned with the method of application (spraying), why not apply the same type of formulation without spraying it on. The new suspension roll-ons introduced in the late 1970s (Dry Idea being the first) did just that.

These products essentially represented an aerosol concentrate, modified so as to be applicable from a roll-on container. The high concentration of cyclomethicone in these roll-ons gave them a dry feel and left little residue. However, the major product formulation that gained from the decline in aerosols was the antiperspirant solid (called solids to distinguish them from stick deodorants). Packaged in containers that resembled the antiperspirant and deodorant sticks first introduced in the 1950s, they differed dramatically in formulation. Unlike the old antiperspirant sticks, which relied on waxy mixtures, or deodorants, which were glycol gels, the new solids were essentially an antiperspirant aerosol concentrate modified into a stick form. They contained high levels of cyclomethicones with active ingredient and suspending agent (just like an aerosol) plus added components to solidify the mixture. It is not surprising that given the U.S. consumer's liking for the feel of an aerosol antiperspirant, they would choose products to use in its place that offered the same type of aesthetics (or, as P&G's new Sure solid advertised in the late 1970s, "the dry feel of a spray").

X. SOFT SOLIDS AND GELS

The trend toward high concentrations of cyclomethicones in AP formulations continued with the newer product formulations called soft solids and gels. The soft solids resembled the formulation approach of both the suspension roll-ons and the solids, except that the consistency of the suspended antiperspirant salt in cyclomethicone was adjusted to a cream. The gels made use of a new silicone polymer to form a clear microemulsion type of gel structure. The only new product form that deviated from the high-silicone, dry-feel-formulating approach was the clear solids. The requirement of clarity in a rigid stick form necessitated a radical change in the formulation of these types of products (27). They used an acid-stable dibenzylidene sorbitol gelling agent with a propylene glycol soluble antiperspirant. The aesthetics of this type of formulation were considerably different from all of the above high-silicone formulations. They were stickier and slower drying. It is therefore not surprising that these clear solids have not gained wide market acceptance. (A more complete

description of the formulations of the various types of antiperspirant and deodorant products can be found in Chapters 8 and 9.)

The 1990s has seen a trend toward formulating all of the above type products so as to reduce the appearance of visible residues on both the skin and clothing. While virtually every formulator and user of high-silicone-based antiperspirant formulations had observed the white-appearing residue those products left behind on the skin, it took almost 10 years before companies began addressing this deficiency. What makes this particularly intriguing is that the solution to this whitening problem is something any experienced formulator could have achieved quite easily had he thought or been asked to do it. Such an observation makes one wonder whether there are yet other product negatives that lend themselves to easy formulation fixes.

One may note that this review of the history of the AP&D product category has made little mention of active ingredients aside from aluminum chlorohydroxide. Actually, considerable progress has been made in the development of new active ingredients. These include controlled particle size and controlled particle-shaped antiperspirant powders, more acidic (and more active) forms of aluminum chlorohydroxides, glycol-soluble aluminum salts, aluminum/zirconium salts, and the more recent development of high-efficacy activated aluminum and aluminum/zirconium salts. The chemistry of these salts is reviewed elsewhere in this book (Chaps. 4 and 5). These newer and more active antiperspirant salts, while offering the consumer and marketer real product advantages, seldom played a significant role in developing new product forms or affecting the direction of growth of the category.

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3

Axillary Odor Determination, Formation, and Control

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I. INTRODUCTION

Research on the formation and control of axillary malodors has led to the identification of specific steroids and acids which represent this unique body odor. The characterization of secretions of the underarm and the skin bacteria involved in odor formation have resulted in a comprehensive picture of the environment of the underarm. Standard odor control mechanisms such as use of antimicrobials and antiperspirant salts to reduce bacterial action or substantive fragrances to mask odors are still the commercial methods for reducing an individual's body odor. However, there is the potential for using our new understanding of the axillary chemistry to develop new methods of odor con-

trol. In addition, the normal axillary odorants may be involved in human olfactory communication by affecting the physiological states of others. These topics will be explored in this chapter.

Research on the origin and characterization of axillary odors has been primarily from two laboratories; Monell Chemical Senses Center in Philadelphia, and the laboratories of Professor D. B. Gower, currently of King's College London, which focused on the presence and metabolism of androst-16-enes. Extensive reviews have been published on studies from these laboratories (1–7).

II. AXILLARY SECRETIONS

Significant variations in both the total number of bacteria and the composition of the bacterial flora exist for different body regions, reflecting differences in the amount of water and nutrients available to support bacterial growth (8). The human axilla provides an ideal combination of ecological factors for bacterial growth. The anatomy of the axilla produces a semioccluded environment that minimizes evaporation of water needed for bacterial growth. The rich supply of eccrine sweat glands, which provide water, amino acids, electrolytes, and minerals; apocrine sweat glands, which secrete a substance rich in protein and lipid; and sebaceous glands, which produce a mixture of lipids, contribute substrates that support bacterial proliferation.

The apoeccrine gland has been characterized in the axilla and shown to develop from the eccrine gland. This gland, as well as the apocrine gland, develops at puberty and responds to both cholinergic and adrenergic stimulation. It is as numerous as the eccrine and apocrine glands, and is capable of sustained fluid secretion greater than the eccrine gland and may contribute substantial moisture to the axillary environment (9).

Of additional interest is the presence of steroid components of the apocrine secretions, which serve as possible precursors for formation of malodors. Two androgen steroid sulfates, dehydroepiandrosterone (DHA) and androsterone, have been characterized in the secretion as well as steroid conjugates, such as androstenol sulfate and glycosides, which serve as bacterial substrates (10,11). Proteins are present in the secretion, and several enzyme activities have been detected in excised apocrine glands, including β-glucuronidase, 3-α-hydroxy-steroid dehydrogenase, 4-ene-5α-reductase, and esterases which can metabolize steroid precursors. Protein/acid complexes have also been identified which on dissociation release characteristic ''sweaty axillary malodorants'' (see page 67).

III. BACTERIOLOGY

The bacterial flora of human skin is a relatively simple one, consisting of aerobic cocci of the Micrococcaceae family, aerobic diphtheroids, primarily *Corynebacterium* species; anaerobic diphtheroids of the genus *Propionibacterium;* yeast from the genus *Pityrosporum;* and occasional Gram-negative species. The axilla supports one of the highest densities of bacteria on human skin and, because of the semioccluded anatomy, is relatively less prone to environmental contamination. Organisms recovered from the axilla are therefore representative of the indigenous flora of skin. Quantitative and qualitative changes in the bacterial flora, specifically the aerobic cocci and diphtheroids, have been correlated with differences in the quality of axillary odor (see below).

In a study of 205 subjects employing quantitative techniques, the axillary flora were found to consist of a stable population of aerobic and anaerobic organisms with the total number ranging from 5×10^5 to 10^6 organisms/cm^2 (12). The day-to-day variation was minimal, with a coefficient of variation of 13%. Axillary hairs were found to have extremely low numbers of bacteria and were not viewed as a significant aspect of axillary bacteria. Comparison of the axillary flora in terms of right- and left-handedness did not reveal any significant differences, nor did a comparison of the right versus the left axillary flora within subjects. Males and females had similar numbers of bacteria; significant compositional differences were found.

In a classical study, *Staphylococcus aureus, S. epidermidis,* coryneforms, M. *juteus,* and Gram-negative bacteria were isolated from cultures made from a small number of subjects ($n = 20$). When these organisms were incubated with apocrine sweat, malodor was produced only with the Gram-positive organisms (13). Coagulase-negative cocci and coryneforms were the dominant organisms recovered in another group ($n = 29$) (14). In a study designed to determine the effects of topical antibacterial agents on the flora of the axilla and the production of odor, aerobic coagulase-negative cocci and coryneform bacteria were found to be the most abundant organisms (15). The number of bacteria recovered from the axilla was of the order of 10^6 organisms/cm^2.

Two distinct types of axillary flora have been described—a flora dominated by lipophilic diphtheroids (85% of the flora), and a flora dominated by coagulase-negative cocci (16). In experimental manipulation of the cutaneous flora, excessive hydration favors proliferation of coryneform bacteria, and for this reason, a major factor determining the composition of the axillary flora may be a difference in eccrine sweating (17). Another report found 70% of the axillary flora to be coryneforms and concluded that these organisms were

predominantly *Corynebacterium* species (18). However, it was also reported that the axillary flora was dominated by coryneforms and that the majority (78%) were nonlipophilic in nature (19). In a comprehensive study involving 163 males and 122 females, it was found that the axillary flora was dominated by aerobic cocci or by coryneforms (20). In this series, 64% of the males had an axillary flora dominated by coryneforms, and 27% had a coccal flora. This ratio was reversed in the females. The predominant genus found in the axillary coryneforms was *Corynebacterium* (83%), with 5% *Brevibacterium* and 12% other coryneforms. In those with a coryneform-dominated flora a mean of 10^6 coryneforms/cm^2 was recovered, compared to a fivefold lower density in those with a coccal-dominated flora.

Studies in our laboratories showed that all subjects had Micrococcaceae recovered from the axillae. The most frequently recovered was *Staphylococcus epidermidis* species (51%); *Staphylococcus saprophyticus* was recovered from 29%, while *S. aureus* was found in only 10% (12). Differences in other studies may be explained by population and/or climate. Aerobic diphtheroids or coryneforms were frequently recovered and classified as aerobic diphtheroids belonging to two genera—*Corynebacterium* and *Brevibacterium.* The aerobic diphtheroids that do not require lipid (large-colony diphtheroids) have not been as well characterized, but those recovered from the axilla also appear to belong to *Corynebacterium* (21). Significant differences in the carriage rate of lipophilic diphtheroids (*Corynebacterium lipophilicus* is the proposed name for this species) were found in males and females. Males had a carriage rate of 85%, compared to 66% for females (12). However, the mean number of these organisms, when present, was the same for males and females. The large-colony diphtheroids were found in 26% of males and 25% of females, and the mean number of these bacteria, when present, was the same for both sexes. Higher numbers of diphtheroids, i.e., 10^6 to $10^7/cm^2$, have been found (19).

The association of odor with bacteria in vivo has been confirmed in a more extensive study involving a European population where odor-positive coryneforms were all species of *C. xerosis* (22,23). Further studies also showed that the axillary pH of 6.0 was the optimum pH for the coryneforms. Axillary extracts from low odor formers gave strong axillary odor on incubation with coryneforms, suggesting that odor differences may not be in quality of apocrine secretion but in the makeup of the bacterial population. However, in other studies, with a North American population, the lipophilic diphtheroid strains identified in the axillae were found to be distinctly different from both *C. bovis* and *C. xerosis,* though the latter has been found in populations of elderly in institutional settings and those with poor hygiene (21).

IV. AXILLARY STEROIDS

A. Characterization of Axillary Steroids

Studies directed at the elucidation of axillary secretions and their odors initially focused on determining the type, abundance, and origin of the androst-16-enes. These studies paralleled work on the analysis of the same compounds in boar saliva, where they are important for sexual communication with the sow, and in boar fat, where it was necessary to quantitate the off-odor, i.e., "boar taint odor," due to a combination of androstenone and skatole. In 1945, Prelog et al. commented on the intense urine/perspirationlike odor of the androst-16-ene ketones, particularly 5a-androst-16-en-3-one (androstenone) (24). These initial organoleptic observations coupled with the identification of these volatile steroids in the axillary region have prompted many investigators to assume that volatile steroids were the predominant odorants in the axillae.

Initially it was necessary to use the techniques of isotope dilution mass spectroscopy using deuterated steroids and radioimmunoassay (RIA) because of the low levels and low odor thresholds of the δ-16-androstenes. Using mass spectrometry, Gower was the first to detect androstenone in the axilla and later with RIA could show significant differences between males (range 12 to 1134 pmol/24 h or 3 to 310 ng) and females (13 to 39 pmol/24 h or 3.5 to 11 ng) (25). There was some variation among individuals on a retest over a 2- to 3-day period; however, there were no differences with handedness, and no relationship to age among adults (26).

Androstenol was detected on axillary pads in 1974 (27). In a 1976 study the ratio of androstenone to testosterone in the plasma was reported as 1:1.4, while in the axilla it was 10:1 (28). This is suggestive of selective excretion of at least a close precursor of androstenone in apocrine secretion. Androstenone has also been detected in samples of human saliva and adipose tissue. Androstenone was detected in axillary hair (0.1 to 100 ng/mg), while androstadienone was at a higher concentration than androstenone in all subjects (29). Subsequent studies have also detected all five androstenes in apocrine secretion (30).

In another study, axillary secretions were collected on cotton pads worn overnight in the underarm. Following extraction and then removal of steroid sulfates, analysis by gas chromatography–mass spectrometry (GC-MS) using multiple ion monitoring was sensitive enough to detect all the androstene steroids, including androstenone (molecular ion = 272), androstadienone (270), β-androstenol, α-androstenol (274), and androstadienol (272) (1). The results

of an analysis of 10 male subjects showed that the levels of androstadienone are higher than androstenone and that both steroids are present in those individuals with higher odor ratings.

B. Metabolism of Androstenes: Urinous/Musk Odors

Androst-16-enes can be formed from pregnenolone using enzyme preparations from boar testes or adrenals, or sow ovaries. Subsequent studies show this also occurs in human testis (31). The steroid sequence involves the formation of androstadienol and its subsequent modification to androstadienone, androstenone, and further reduction to α- or β-androstenol. Initial experiments involving lipophilic diphtheroids and selected steroid substrates showed the hydrolysis and oxidation of 3β-sulfates and the oxidation of 3α-sulfates. Thus, the sulfates of androstadienol, pregnenolone, and DHA, all with β geometry, are converted to the corresponding 3-keto derivatives. 3α-Androstenol, but not its sulfate, is converted to androstenone (1).

Further reports have examined steroid transformations by axillary coryneforms and *C. xerosis* in particular (22,23,31,32). Odor-positive aerobic coryneform species converted both androstadienone and androstadienol to androstenone and 3α-androstenol. The odor-negative and *Micrococcus* species could only bring about the latter reaction. In all cases, no androst-16-enes were observed to be formed from testosterone, pregnenolone, DHA, or any non-androst-16-ene precursor (33). Subsequent to this report it has been determined that androsterone sulphate (AS) is converted into androsta-4,16-dien-3-one and androst-16-enyl-3-sulfate into androstenone, both odorous steroids, with an axillary Coryneform isolate (32). AS metabolism also led to formation of androst-16-en-3-ols. The above studies confirm the previously proposed scheme (Fig. 1) (1). This involves the initial and necessary secretion of a conjugate of androstadienol (or androsterone or other non-δ-16-androstene) to begin the metabolic sequence. All subsequent enzyme reactions are available from the odor-positive bacteria or extracellular enzymes in apocrine secretion. Further studies supporting this scheme, based on enzyme inhibitors, are described in the section on odor control.

V. AXILLARY ACIDS

A. Characterization of Axillary Acids

The descriptors used for axillary odors include sweaty, acid, musty-damp, and/or hircine (goatlike). Previous analyses had shown the presence of isoval-

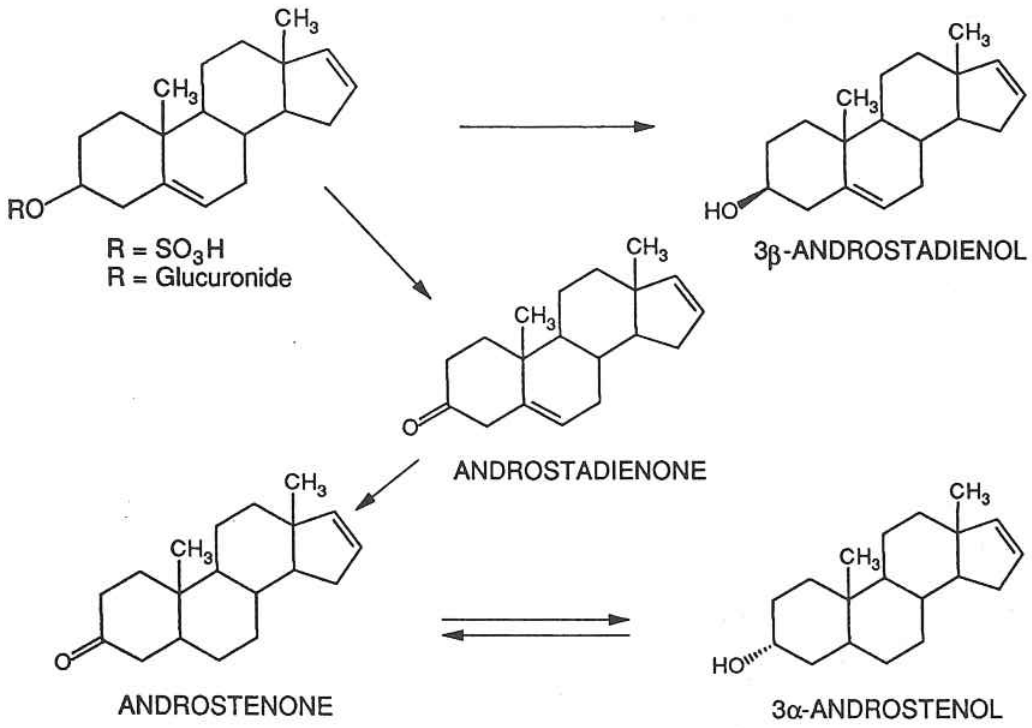


Figure 1 Formation of odorous steroids from conjugates of androstadienol.

eric acid and similar short-chain acids in axillary secretions (1). Subsequent studies, which sought the compound responsible for the characteristic axillary odor, employed both an odor panel and ''smell chromatography'' (33). Olfactory comparison of the chromatographically separated odors from six male subjects with the original concentrated extracts identified a region in the chromatogram that had characteristic axillary odor. This region did not correspond to either volatile steroids or short-chain acids in retention time. Analysis of these components by GC-MS showed an array of C-6 to C-11 straight-chain, branched-chain, and unsaturated acids. The largest was (E)-3-methyl-2-hexenoic acid (Table 1).

Confirmation of the structure of the major characteristic odor component, (E)-3-methyl-2-hexenoic acid (E3M2H), was based on mass spectral, infrared, and NMR data as well as synthesis. It was distinguished from the (Z)-cis isomer, which is also present as a minor component in the axillary extracts (33). In terms of relative abundance, the C_6 to C_{11} organic acids, particularly E3M2H, are present in far greater concentrations than androstenone: ~357 ng/μL extract of E3M2H vs. ~ 0.5 ng/μL extract of androstenone. Combined female axillary extracts have also been examined (34). In female

Table 1 Acids Characterized in Axillary Secretions

Straight-chain	Methyl-branched	Ethyl-branched
Hexanoic	2-Methyl Hexanoic	2-Ethyl Hexanoic
Heptanoic	*3-Methyl Hexenoic*	4-Ethyl Pentanoic
Octanoic	3-Methyl Hexanoic	*4-Ethyl Heptanoic*
Octenoic	2-Methyl Heptanoic	4-Ethyl Octanoic
Nonanoic	2-Methyl Octanoic	4-Ethyl Nonanoic
Nonenoic	2-Methyl Nonanoic	4-Ethyl Decanoic
Decanoic	2-Methyl Decanoic	
Undecanoic		

samples, the straight-chain acids were present in greater relative abundance than E3M2H; further, no androstenone was seen in female extracts. Androstenol was present, albeit in far lower concentration than E3M2H or the other acids: ~ 150 ng/μL extract of E3M2H vs. ~ 3.5 ng/μL extract androstenol. The *Z*-isomer of E3M2H is also present in each gender, although in different relative abundance: 10:1 (*E*:*Z*) in males; 16:1 (*E*:*Z*) in females.

In addition, 7-octenoic acid is also present and represents a compound with a high odor impact. The ''goat acid,'' 4-ethyl-heptanoic acid, was also identified as one of the acids. This had been previously characterized as a doe attractant and the main odor constituent of the sebaceous gland secretion of the mature male goat during breeding season (35). This compound also shows a mixed reaction to men while being disagreeable to women; a specific anosmia exists in humans as well as a low odor threshold (Table 2) (36).

E3M2H was once thought to characterize the odor of patients suffering from schizophrenia, since it was first identified in their whole body sweat, but was later found in normal individuals (37,38). E3M2H has an odor characteristic of human axillary sweat. Although E3M2H is a major analytical component of the characteristic axillary odor in males, a number of components are necessary for the complete axillary ''bouquet.'' In addition, studies from both our laboratory and another documented both the presence of a specific anosmia for both isomers of E3M2H, and an olfactory threshold for the E-isomer that is within an order of magnitude of that for androstenone (39,40). Consequently, the strength and quality of the odor produced in the axillae appear to be related to the axillary bacterial populations and perhaps the concentrations of E3M2H present, but further, rigorous organoleptic studies must confirm this.

B. Metabolic Formation of Axillary Acid Odorants

Early studies on the role of bacteria in generating axillary odor demonstrated that apocrine sweat was sterile and odorless, and that odor was produced by axillary microorganisms acting on apocrine sweat (13). Sterile eccrine sweat produced no odor when incubated with bacteria. Numerous studies now demonstrate that a decrease in axillary odor correlates with a decrease in axillary coryneforms (12,41).

In studies comparing the axillary flora of those with a strong disagreeable axillary odor to those with a ''sweaty'' odor, significant quantitative and qualitative differences were found. Those with a strong unpleasant odor had a significantly higher number of bacteria—$10^6/cm^2$, compared to $10^5/cm^2$ (12). More striking, however, were the marked differences in the composition of the flora. Every subject with a strong axillary odor had lipophilic diphtheroids present in high numbers. The geometric mean count was 810,000, compared to a 55% prevalence with a mean of 53,000 in those with a sweaty odor. These results suggested that lipophilic diphtheroids (*C. lipophilicus*) were responsible for generating the most offensive notes. In further studies, sterile odorless apocrine sweat was placed on the forearms of volunteers and subsequently incubated with aerobic cocci, coryneform bacteria, and Gram-negative organisms. Typical strong axillary odors were produced only when lipophilic and large-colony corynebacteria were incubated with apocrine sweat. A sweaty, isovaleric acid type of odor was produced by micrococci and Gram-negative bacteria.

Recent studies have demonstrated that the water-soluble components of apocrine secretion contain E3M2H and other constituents of the characteristic axillary odor bouquet bound to nonvolatile molecules (42). These odorants can be released by base hydrolysis (5% NaOH) or by incubation with axillary bacteria. Separation and hydrolysis (by NaOH or enzymes) of the proteins found in apocrine secretions have demonstrated that E3M2H is carried to the skin surface bound to two proteins, designated apocrine secretion odor binding proteins 1 and 2 (ASOB1 and 2). ASOB1 and ASOB2 have apparent molecular weights of 45 and 26 kDa, respectively, by sodium dodecylsulfate-polyacrylamide gel electrophoresis (SDS-PAGE) (43,44). Antisera to each of these proteins were prepared using purified proteins pooled from several male donors. The antisera (mixture of antibodies) were employed to detect by Western blotting the electrophoretically separated proteins by antibodies, the proteins in male and female apocrine secretions as well as in a variety of other body fluids (e.g., tears, forehead and areaolar sweat, submaxillary and parotid saliva,

urine, ear wax, serum, and nasal secretions) from males. All except urine showed the presence of these proteins. The male and female apocrine secretion proteins were qualitatively similar (45). Structure determination of ASOB2 showed that the primary amino acid sequence of ASOB2 is identical to that of apolipoprotein D (apoD), and in situ hybridization using an antisense oligonucleotide probe for apoD mRNA demonstrated that the site of expression for the apoD is the apocrine gland.

ApoD is a member of the a-2μ microglobulin superfamily of proteins (also known as lipocalins). The role of plasma apoD is not known, nor is its ligand(s). E3M2H is the first in vivo ligand identified for apoD, as it appears in apocrine secretion. There is a 2:1 molar ratio of E3M2H to apocrine apoD.

VI. ODOR COMMUNICATION

A. Axilla as Source of Primer Pheromones

Studies with rodents have demonstrated that reproductive behavior is modulated by odors. The effects of female odors on males include puberty acceleration, hormonal surge, and odor production; male odors can induce estrus or block pregnancy. Female odors can advance or delay the cycle of competing females, thus inducing estrous synchrony (46). These are examples of primer pheromonal effects which result in internal metabolic responses, and differ from releaser effects which result in overt immediate behavioral changes and have been reviewed elsewhere (3,47). Although the popular press has romanticized the involvement of releaser effects in human sexual interactions, these effects are inherently more difficult to demonstrate because the responses to odor are confounded by other sensory inputs and by the context in which the odor is presented. No releaser pheromone effects have been demonstrated in humans.

There is evidence that the human axilla is a source of ''odorants'' which act as primer pheromones. This conjecture is based on the physiology and anatomy of the axillae and its similarity to other mammalian systems which produce odorants that induce a physiological change. Indirectly, both the sebaceous and apocrine glands are secondary sexual characteristics and fully develop during puberty. This results in a distinct change in body odors, particularly in the axillary and scalp regions. The apocrine glands, androgen target organs, are analogous to the apocrine/sebaceous glands in other mammals, and could be considered as the human scent gland (2,3).

B. Effects on Menstrual Synchrony

The anecdotal observations of synchrony among women living in college dormitories has been confirmed in several experiments (for review see 2,48). Though there has been some controversy surrounding these results, it is generally accepted that synchrony, although not occurring in all cases, is a real phenomenon and represents a potential human pheromonal effect (49,50). In an initial investigation of this phenomenon, Russell demonstrated that axillary odors could affect menstrual synchrony (51). In a more extensive, double-blind study, axillary odors were collected from throughout the cycle of four donor women and were combined into 10 extracts each representing 3-day periods of a ''synthetic'' 30-day menstrual cycle. The extracts from the appropriate phase were placed on the upper lips of female recipients for three consecutive menstrual cycles. Their cycles were found to approach the cycle of the donor after the third menses (52).

A similar protocol of axillary extract application was used in an experiment when male axillary secretions were placed on women who had a history of unusually long or short cycles. These recipients showed a statistically significant change in their cycle length toward the normal length (29.5 + 3 days) after 12 weeks' exposure to male extracts (53). In both cases, it is possible to use an objective measure, change in cycle length, rather than the subjective measures, e.g., ''attraction,'' ''arousal,'' ''submissive,'' used to define the releaser effects. Results, reported in a preliminary fashion, from another laboratory suggest that females who received axillary secretions from donor females collected during the follicular phase experienced a shortening of their menstrual cycles. There was a lengthening of the cycle for females who received secretions collected during the ovulatory phase (54).

These above studies present compelling evidence that human axillary extracts contain components that act as primer pheromones which alter menstrual cycle length and timing. When considered together with the chemical studies described, which demonstrate that a major axillary odorant is carried to the skin surface by apolipoprotein D, these results suggest a remarkable similarity between the human axilla and nonhuman mammalian odor sources used in chemical signaling. In the hamster, house mouse, and possibly the pig, chemical signals that modify endocrinology and behavior are carried by similar proteins referred to as lipocalins (3).

These results also suggest that an analytical examination of axillary extracts from females during the menstrual cycle might reveal marked differences in axillary constituents. In one analysis of the steroid content of the extracts, it could be demonstrated that androstenol concentrations varied over

the cycle and peaked at the midfollicular phase (55). Several of the acidic components, which constitute the characteristic axillary odors, have been isolated and analyzed by GC-MS from the follicular and ovulatory phases of the menstrual cycle. High levels of n-C7, C8, and C10 acids as well as subnanogram levels of E3M2H are found in follicular phase. E3M2H levels increased significantly, and concentrations of normal acids remained constant or decreased in the ovulatory phase (56).

Quantification of each donor's axillary flora indicated no difference in the number of micrococci (*Staphylococcus epidermidis* and *S. saprrophyticus*) in either cycle phase. However, differences were found in the population of LDs with significantly greater amounts of LDs, found in the ovulatory phase. The increased levels of E3M2H in the ovulatory phase may be due to changes in the number of LD bacteria, which are associated with stronger-smelling axillary secretions.

C. Involvement of Vomeronasal Organ

In many animals, the sensory receptors for some pheromones are a specialized group of neurons located in the vomeronasal organ (VNO), or ''Jacobson's organ,'' which is in the nose. Numerous recent reports have suggested that humans possess a functioning VNO and that activation of the organ is possible with certain chemosensory cues or ''vomeropherins'' (57,58). Openings to this putative structure are on either side of the nasal septum, about 1 cm from the opening of the nasal cavity. Vomeropherins are steroidal in structure and are alleged to be isolated from human skin or are synthetic analogs of skin-derived steroids; several of these steroids resemble androstenol and androstenone in structure. In addition, two naturally occurring vomeropherins are reported to be androsta-4,16-diene-3-one (androstadienone, from males, is identical to one of axillary steroids and ''excites'' female VNO) and estra-1,3,5(10),16-tetra en-3-o1 (estratetraneol, from females, ''excites'' male VNO) (59). Vomeropherins, in ''proportions that are trade secrets'' have been incorporated in Realm fragrances.

Vomeropherins are alleged to be human pheromones because they ''stimulate'' the human VNO. People did not report smelling anything during administration of vomeropherins, suggesting that olfactory receptors were not stimulated. Electrical responses, equivalent to generator potentials, were recorded from the putative VNO of humans (58,60). These responses differed with the type of chemical cue used and the gender of the subject. One should be cautious in interpreting the origin of these responses since explanations other than activation of ''pheromone receptors'' are possible. Further, many

of the steroid compounds being employed as ''synthetic vomeropherins'' in these experiments closely resemble naturally occurring estrogen, androgen, and progestin hormones. Thus, since actual steroid hormones have not been used in control studies, one can speculate that metabolic enzyme systems in the nose altered the vomeropherin structures to become an active steroid hormone (47,61).

VII. OLFACTORY PERCEPTION

A. Body Odors and Specific Anosmia

In psychological experiments dealing with odor perception, the absolute threshold (the lowest concentration perceived) can be used to determine the relative sensitivity of individuals. For most odorants, i.e., floral, a bell-shaped distribution is observed for individual thresholds across a large population. However, for many odorants associated with the human body there is a bimodal distribution with individuals being either sensitive or insensitive to the odor. This phenomenon is known as ''specific anosmia,'' and such anosmias have been characterized for odors representing fishy, sweaty, spermous, urinous, and musky (62–63). These represent five of the more than 30 suggested anosmias, some of which relate to specific fragrance classifications (64).

Table 2 shows the odor sources, a representative chemical, and the percentage of the population which show those specific anosmias which are directly related to human odors. Though there are other anosmias such as carvone, the urinous and sweaty odors from the above list represent some of the highest percentages found. These data show that in many situations individuals do not perceive or are insensitive to and thus may not respond to

Table 2 Specific Anosmias Related to Body Odors

			Anosmia	
Odor source	Odorant	Primary odor	%	Threshold
Axilla	Androstenone	Urinous	46–50	0.18 ppb
	Androstenol	Musky	12	6.2 ppb
	E-3-methylhex-2-enoic	Sweaty	11	14 ppb
	4-Ethylheptanoic	Hircine	16	1.8 ppb
Axilla/foot	Isovaleric acid	Sweaty	3	1 ppm
Uremic breath	Trimethylamine	Fishy	6	
Semen	1-Pyrroline	Spermous	16	

human odors in the same manner (62–65). This has implications on any studies on malodor masking by odor panels if the panel has not been prescreened for the relevant anosmias. The association of human body odors with the odors of both natural and synthetic fragrance components has been detailed in the publications of Jellinek (66).

B. Perception of Androstenone and E3M2H

Other interesting olfactory effects include the induction of odor perception with androstenone and cross-adaptation with both androstenone and E3M2H. Two of the laboratories studying the olfactory properties of androstenone have reported incidences of the investigators who were originally anosmic to this material to have acquired the ability to detect it. A controlled study showed that individuals exposed to androstenone three times per day over a 6-week period became osmic to it with a substantial increase in threshold for 10 of 20 subjects (4,67). Several compounds similar in structure and/or odor to axillary malodorants have been tested for their ability to modify their perception (68–71). The ethyl esters of E3M2H were tested for their potential to reduce perception of the malodor E3M2H. The protocol involved the alternate presentation of ester and malodor, and an odor intensity assessment of E3M2H. If an individual is first adapted to the ethyl esters, the perception of E3M2H is reduced (68).

Androstenone has been reported to have both a urinous and musk component to its odor, with the latter experienced by those who are less sensitive. Interestingly there is a third group, which does not detect this material at any concentration (63). Attempts to use a musk compound, galaxolide, to adapt and therefore reduce the odor intensity of androstenone were unsuccessful. This is in accord with the lack of correlation of galaxolide and androstenone anosmics in men or with threshold data, although women anosmics to both were more than four times as frequent as expected (65). Exposure over time (twice a week for 8 weeks) to a compound with different structure but similar odor, same anosmia profile, and stereochemistry, *cis*-4-(4′-t-butylcyclohexyl)-4-methyl-2-pentanone (pemenone), produced a reduction in threshold to androstenone (69) (see Ref. 2 for discussion of androstenone analogs). Another alicyclic compound, 4-(4′,4′-dimethylcyclo-hexyl)-2-methylcyclohexanone, also cross-adapted androstenone (70). In other experiments androstanone cross-adapted androstenone, and a significant but weaker cross adaptation was found for an odorless analog, 3-methylidene-androstane, to androstanone but not androstenone (71). All of these molecules share the urinous-sweaty odor

note. These approaches offer some rationale for designing molecules for specific malodors, but require a better understanding of this phenomenon.

VIII. ODOR CONTROL

The various methods for axillary odor control have been reviewed in the previous edition of this book, and only additional approaches will be described here (72). There are several basic approaches for odor control, all of which take advantage of the knowledge of the compounds responsible for the malodor and the mechanism of odor formation. These include antibacterials and antiperspirants to control bacterial growth, fragrances created specifically to blend/mask with the malodors, and methods to extend fragrance delivery through encapsulation or fragrance precursors (profragrances) which can utilize either pH changes on skin or bacterial enzymes for prolonged fragrance delivery.

A. Antibacterial

The primary method for odor control has been the use of antiperspirants, usually aluminum salts, i.e., aluminum chlorhydrate, which are known to physically penetrate and block the sweat pores. This reduces the presence of moisture and nutrients provided by glandular secretions which control bacterial growth and ultimately the bacterial metabolism of the axillary secretions. Al salts can also act as antibacterials and can reduce the pH below the optimum for bacterial metabolism. The properties of aluminum salts have been extensively reviewed (73).

At present, the antibacterials triclosan and trichlorocarbanilide, which are stable, substantive to the skin, and safe, are used in deodorants and deodorant soap (72). The latter are believed to act through interaction with cell membranes and interference with the uptake of cell nutrients. Triclosan was shown to be effective in specifically reducing axillary bacteria during a 6-month usage study. Specific components of fragrance oils have shown some antibacterial activity but are 100 to 1000× less effective than the antibacterials used in deodorant soaps. The drawbacks of the above approaches are individual sensitivity, the reduction in effectiveness of antimicrobials that sometimes occurs because of the delivery system, and the indiscriminate effects on all bacteria. The use of the aluminum salts and chloroantibacterials also has some negative effects in the context of environmental and personal safety that may lead to

their replacement, as was the case for hexachlorophene. Alternative approaches involving fragrance delivery or enzyme inhibition offer future opportunities.

B. Odor-Neutralizing/Masking

$NaHCO_3$ is still a popular active ingredient in deodorants and can be formulated into all delivery forms including aerosols. It is effective in neutralizing the acidic components such as E3M2H once they are formed. However, the bicarbonate might be expected to keep the axilla basic and actually facilitate the enzyme reactions.

Fragrance has been used to counter malodorants either by overpowering the malodorants or by odor masking (74,75). The use of selected compounds tested against the acid and steroid malodorants can result in effective odor masking (76). Deo-fragrances have been developed which blend with the axillary malodorants to give an overall acceptable odor. In any deodorant, the fragrance level is limited to one daily application, but the potential for odor development is continual. Two deodorants introduced in the United States have utilized starch-encapsulated fragrances which are released by moisture. Thus, sweat produced by stress or exercise causes the coating to be solubilized and additional fragrance to be released. In another case the fragrance is reencapsulated for later release (77,77a). Sulfhydryl agents, such as N-ethylmaleimide, have been suggested as effective in neutralizing axillary odor which was generated in vitro from axillary secretions and microorganisms and also for preventing buildup of odor on fabrics (78).

A direct reduction in the perception of the odorants that cause axillary odor can be achieved through techniques of cross-adaptation, the decrease in perceptual sensitivity to one odor after exposure to another. Recent studies, referred to in VII.B, demonstrate that exposure to the ethyl esters of E- and Z-3M2H and its higher and lower homologs can reduce the perception of the axillary odorants by 66% (68,70). While all the esters tried demonstrated efficacy, maximum reduction in perception was achieved with the ester that was structurally the most similar to the E3M2H, its ethyl ester. Molecular modeling studies suggested that the greater lipid solubility of the ethyl esters allowed them to have greater access to the olfactory receptors than the acids. Consequently, pleasant-smelling ethyl esters appear to have potential for reducing the perception of all malodors featuring organic acid malodorants.

C. Bacterial Metabolism

Another approach has been to control the metabolism of odor formation, particularly the chemical/enzymatic reactions that take place. These reactions

can be modified by materials which specifically inhibit the hydrolysis and/or oxidation reaction of the precursor steroid glucuronides or sulfates or protein/acid complex.

In axillary studies, it was shown that in general "high odor formers" had both aryl sulfatase and glucuronidase activity compared with the "low odor formers." In in vitro experiments, inhibitors could be tested against these specific enzymes. Zn and Cu ions and hexametaphosphate were all effective against both enzymes, while δ-glucarolactone inhibited β-glucuronidase (79,79a). Apocrine secretion incubated with either the above enzymes or the diphtheroid bacteria generated the expected odor, which could be controlled by glucarolactone or Zn glycinate. These inhibitors have also been shown to be effective as deodorants in vivo. Zn^{2+} is not an effective antibacterial and thus is acting primarily as an inhibitor. To take advantage of the useful properties of Zn^{2+}, an effective delivery system has been developed (80). This involves coating zinc oxide on nylon particles, producing a "hybrid powder" which overcomes the drawbacks of zinc oxide powder. This material provides zinc for complexing acids and enzyme inhibition and is effective against both foot and axillary odors. An aromatic ester of a phenol, such as phenoxy-2-benzoyl-benzoate, has been suggested as an esterase inhibitor which on release of phenol would also act as an antibacterial (81).

The findings demonstrating that an important axillary malodorant appears on the skin surface bound to a protein suggest the possibility that axillary bacteria, adapted for hydrolyzing proteins, can be "fooled" by presenting them with an excess of a compound with amide and ester bonds. This experiment was tried using the amide ester of alanine-11-undecenoic acid, which on incubation with axillary bacteria released undecenoic acid an antibacterial (82).

D. Fragrance Precursors

This metabolic approach can also be used to generate fragrance materials by providing alternate substrates for bacterial enzymes. This profragrance approach involves the hydrolysis of esters (83), orthoesters, ketals/acetals (84–86a), amino acid/ether derivatives (87), or vinyl ethers to form a perfume alcohol and either an acid or aldehyde/ketone to mask axillary malodors. The esters provide substrate for bacterial lipases while the acid-sensitive derivatives are hydrolyzed through an expected acidic pH change on the skin following application from a basic deodorant. Acetals, which were combinations of fragrance alcohols and aldehydes/ketones, were prepared and their hydrolysis was studied at slightly acidic pH values. Those that had the appropriate hydro-

lysis rate were suggested as profragrance materials, though this was not demonstrated in vivo (88). Esters, including sulfates, sulfonates, and phosphates, can serve as precursors for use in deodorants to mask axillary malodor. It was demonstrated with several of the esters that hydrolysis occurred with axillary bacteria through detection of the corresponding alcohols both in vitro and in vivo on T-shirts (89). Hydrolysis of an amino acid ether derivative such as phenylethyl-o-serine was reported to occur with an amino acid lyase from the bacteria (90). An amide complex of a simple amino acid and undecenoic acid was hydrolyzed by axillary bacteria, and effective in reducing malodor through the antibacterial effects of the acid, as mentioned above (91).

In analogy to the metabolism of androstenol sulfate or glycoside to the odorous androstenone by axillary bacteria, it was demonstrated that fragrance glycosides (or glucosides) such as phenethyl galactoside, an acetal combining phenyl ethanol and galactose, can be hydrolyzed with or without a galactosidase to the perfume alcohol (85,86). This same reaction was demonstrated with skin bacteria with a preference for beta-glycosides.

Other patented chemicals used for control of axillary odor include the antibacterials chlorhexidine gluconate, hexylcaine, farnesol, Hyamine (a quaternary nitrogen compound), and polyhexamethylene biguanide-HCl. Antibodies have been made to axillary bacteria and claimed to be effective. An adhesive deodorant tape with cyclodextrin for odor absorption has been proposed. Biochemical approaches have included interference with bacterial adhesion using polysaccharides (88).

IX. CONCLUSIONS

The bacterial distribution in the axilla has been well characterized and related to the formation of specific axillary odors. The latter have been classified as acid or steroid materials that can be found in incubations of the bacteria and apocrine secretion as well as detected in in vivo extracts. Malodor reduction with sulfhydryl agents suggest that other unidentified odorants may be present. Knowledge of the mechanism of odor formation provides a rationale for both direct and indirect approaches to control or mask malodor. The use of fragrance precursors to generate fragrance materials over time could both mimic and mask the malodorants on the same time scale. These odorants also provide interesting odor perception phenomena for study of odor cross-adaptation, anosmia, induction, age and sex differences, and pheromonal communication.

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6
Deodorant Ingredients

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I. INTRODUCTION

Bodily odors may originate from a number of sources including the oral cavity, scalp, crotch, and feet. Arguably the most characteristic and stigmatized of these is, however, axillary odor. The often offensive nature of axillary odor has been recognized for thousands of years, as have approaches for its counteraction. The ancient Egyptians placed balls of incense-flavored porridge in the axilla, and deodorant body rubs were made of ostrich egg and tortoise shell roasted with gallnut from a tamarisk tree (1). Following the advent of soap, the most basic of hygiene measures were found to be effective at causing an immediate diminution of odor. The need for counteractive measures over and above this was, however, prompted by the inability of large sections of society to adopt a personal hygiene regimen. It also became recognized that in a significant proportion of individuals, washing alone only prevents the buildup of perceivable odor for a finite time. This period may be drastically reduced in situations where apocrine sweat production is increased (2). For these reasons many individuals require ''protection'' from the buildup of axillary odor, usually by means of an externally applied product.

The first attempts at odor counteraction involved the use of fragrant oils. This approach has continued to the present day where an overwhelming majority of axillary deodorants contain fragrance. Indeed, for many deodorant body sprays this represents their *raison d'être*. The use of fragrances increased

markedly during the 18th century and represented essentially the only counteractive strategy available until the latter part of the 19th century. It was in 1888 that the first axillary deodorant became commercially available, a waxy cream marketed under the name Mum and containing zinc oxide, an agent that has subsequently found widespread use (3).

In the years following the launch of Mum a wide range of compounds were claimed to be of benefit and were incorporated into axillary deodorants. However, formulators were hampered by a poor understanding of odor formation. From the work of Killian and Panzarella (4) and Shelley et al. (5), it became evident that the bacterial microflora in the axilla played a primary role in the biogenesis of axillary odor. Consequently, the vast majority of subsequent attempts at providing improved deodorancy utilized antimicrobial agents, the rationale being that by decreasing the bacterial numbers present in the axilla, the biogenesis of odor could be decreased. The popularity of such an approach has continued to the present day and currently represents the most widespread strategy for inhibiting odor formation.

As understanding of the microbiology of the axilla has progressed, so has knowledge of the physiology and biochemistry of these organisms. Consequently, there have been an increasing number of attempts to modify the biotransformational pathways leading to odor formation without affecting, to any significant extent, the bacterial microflora. Although the exact mechanisms of odor formation continue to be points of contention, the last 5 to 10 years has seen a marked increase in the numbers of such attempts.

Finally, improvements in the understanding of fragrance components and their deodorizing effects have allowed perfumers to formulate increasingly effective ''deo-perfumes.'' Such attempts have been complemented by the identification and characterization of many of the components of axillary odor.

Although deodorants for personal use may include those for the hair and whole body as well as feminine hygiene products, the following discussions will focus on agents for application to the axilla. This is primarily because of the context of this chapter but also because of all bodily odors, axillary malodor is perhaps the most recognizable, most stigmatized, and most researched.

For the purposes of this review, the ingredients used to obtain deodorancy benefits will be discussed under three main headings:

Inhibitors of odor generation
Odor counteractants
Fragrances and modifiers of odor perception

II. INHIBITORS OF ODOR GENERATION

It is now widely acknowledged that the compounds primarily responsible for axillary odor are formed from odorless precursors present in underarm secretions and, more specifically, apocrine sweat (see Labows *et al.*, Chap. 3). This being the case, perhaps the most fundamental approach to deodorancy is to prevent the formation of these odorous compounds. The majority of workers in the field would agree that the bacteria present in the axilla are largely responsible for the biotransformations leading to odorous compounds, and consequently the earliest and most widespread strategy aimed at the inhibition of odor formation has involved the use of antimicrobials (6).

A number of studies have suggested that there is an association between the overall bacterial numbers present in the axilla and odour (7). The aim of antimicrobial application is therefore to decrease the bacterial numbers such that the transformation of nonodorous to odorous compounds is noticeably diminished. A number of studies have shown such an approach to be effective, i.e., a marked decrease in the axillary microflora population density resulting in a statistically significant decrease in odor intensity (2,8,9). In recent years, however, the widespread use of this approach has been criticized for a number of reasons, some of which will be discussed in the following sections.

There has thus been a general consensus within the cosmetics industry that a decrease in the indiscriminate use of antimicrobials in personal care products is desirable from both a consumer and an environmental perspective. For this reason, the past two decades have seen an increasing number of attempts to target, in more subtle ways, the metabolic pathways responsible for odor formation. The aim has been to provide superior deodorancy while leaving the natural axillary microflora, at least in terms of viability, intact.

In the following section both antimicrobial and nonantimicrobial routes will be discussed. It should be noted that the history of early antimicrobial use in deodorants has received excellent reviews elsewhere (3). In the following discussions the focus will therefore be upon agents widely used in recent years, along with an account of the technological advances in this field.

A. Antimicrobial Agents

As early as 1934 it was suggested that bacteria were at least partly responsible for the formation of axillary odour (3). With this in mind deodorant manufacturers of the day tended to include a wide range of antimicrobial compound in their products. Indeed the first commercially available product contained zinc oxide, a compound possessing weak antibacterial activity. Such agents

as benzoic acid, chloramine T, chlorothymol, formaldehyde, hexamine, oxyquinoline sulfate, sodium perborate, and cresylic acid were widely used in deodorant bar soaps and axillary deodorants. The incorporation of these agents was undertaken with little understanding of the routes to odor formation and in many cases was restricted by the fact that they were, from a cosmetics standpoint, far from ideal (3).

A major step in the understanding of the formation of axillary odor occurred toward the end of the 1940s and beginning of the 1950s, when Killian and Panzarella (4) and Shelley *et al.* (2) presented evidence for the role of bacteria in odor formation. As a logical extension of this finding, it was also shown that use of a topical antimicrobial, hexachlorophene, could significantly retard the development of axillary odor.

Hexachlorophene was discovered in 1941 and launched onto the market in 1948. It represented one of the first effective, cosmetically acceptable antimicrobials of its time, and its efficacy was widely exploited in bars soaps, antiseptics, and axillary deodorants, to name a few. With the success of this compound the deodorant industry began to investigate a range of topical antimicrobials, both established and novel, with renewed vigor. Antimicrobials developed subsequent to hexachlorophene included bithional, 3,3′,4′5-tetrachlorosalicylanilide (TCSA), tribromsalan, and thiram. Bithional, TCSA, and thiram were included in deodorant bar soaps and found some use in axillary deodorants (10). Triclocarban (3,4,4′-trichlorocarbanilide; TCC) was developed around this time and found use in deodorant bar soaps. The 1950s also saw the development of a number of antibacterial cationic agents which found widespread use as disinfectants, antiseptics, and later, axillary deodorants. Some of the antibiotics of the time, including chlortetracycline, tyrothricin, and neomycin, were also proposed for use as axillary deodorants (11,12).

Many of the agents developed subsequent to hexachlorophene were subject to concerns about safety. Bithional, TCSA, and thiram were found to produce photosensitivity reactions and contact sensitivity, and the use of antibiotics was limited by their cost and concerns about resistance. By the late 1960s reservations about the toxicological profile of hexachlorophene had been voiced in a number of quarters. In a well-publicized case the inclusion of 6% hexachlorophene in a baby powder caused a number of fatalities and prompted the FDA to effectively ban the over-the-counter sale of products containing hexachlorophene ($> 0.1\%$) in 1972 (3).

Coincidental with the demise of hexachlorophene was the development of a novel antimicrobial agent, triclosan (2,4,4′-trichloro-2′-hydroxydiphenyl ether), possessing potent inhibitory effects against a wide range of microorganisms (14). This compound, marketed under the trade name Irgasan DP300 as

a topical antimicrobial, subsequently found widespread use in axillary deodorants as well as a wide range of medicinal and cosmetic products. Indeed, of all the compounds developed prior to hexachlorophene's withdrawal, only triclosan, TCC, and a range of cationic surfactants continue to find widespread use in the personal products arena.

In the following section an account of these and newer, novel agents claimed to be of benefit in terms of axillary deodorancy will be discussed.

1. Triclosan

Triclosan (2,4,4′-trichloro-2′-hydroxydiphenyl ether, Irgasan DP300; Fig. 1) is a synthetic, nonionic antibacterial agent developed by Ciba Geigy in the late 1960s (14,15). This lipophilic compound is active against a wide range of Gram-positive and Gram-negative organisms (a notable exception being pseudomonads) and has marked activity against microorganisms present in the axilla including *Staphylococcus epidermidis* and a range of corynebacteria. It is bacteriostatic at lower concentrations and its mode of action is thought to involve perturbation of the cytoplasmic membrane (16). It has been the subject of numerous toxicological studies and has undergone extensive testing both *in vitro* and *in vivo* (for a review see (17)). Skin irritation or sensitization have been reported in only a handful of cases despite the compound's inclusion in a myriad of personal care products (17). Recent work has suggested that this compound possesses anti-inflammatory activity (18).

Triclosan has been used in a vast array of medicinal and cosmetic preparations for application to the skin and, more recently, has found use in dentifrices, where it has inhibitory effects against dental plaque (19). Its use in deodorants has been promoted for some time, and it is now one of the most widely used antimicrobials in body sprays and axillary deodorants, typically at concentrations from 0.15% to 0.3% (w/v).

Workers at Ciba Geigy showed that use of a product containing triclosan (0.1% or 0.2%) reduced both the number of bacteria present in the axilla and

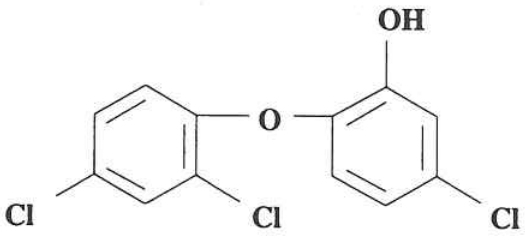


Figure 1 Triclosan.

the production of malodor (9). Baxter and Reed (20) also demonstrated the benefit of triclosan (0.1% w/v in ethanol) when compared to ethanol alone. Although these authors failed to see a corresponding decrease in bacterial numbers, enumeration of bacteria was *via* a contact pad method—a technique likely to prove inaccurate when used in the axilla (21). In a more recent study, again by workers from Ciba Geigy, use of ethanolic sprays containing 0.2% (w/v) triclosan were shown to cause a decrease in total numbers of organisms over and above that of ethanol alone, in both the short term (up to 9 hours) and long term (up to 6 months) (8).

2. *Triclocarban*

Triclocarban (3,4,4′-trichlorocarbanilide, TCC; Fig. 2) is a bisphenol bactericide that has selective activity against Gram-positive organisms, against which it is growth inhibitory. Its use increased significantly after the demise of hexachlorophene, especially in deodorant soaps, where it continues to find widespread use. Its use in axillary deodorants has been limited.

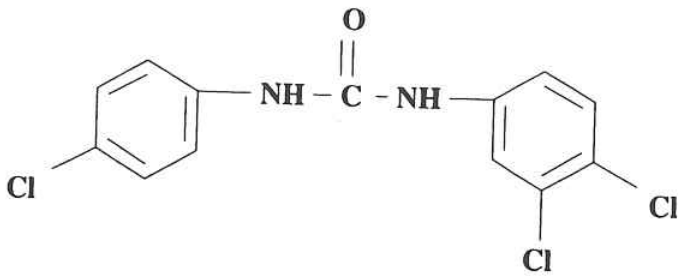


Figure 2 Triclocarban.

3. *Cationic Agents*

The majority of cationic agents used for their antimicrobial activity fall within the group known as quaternary ammonium compounds, also known as QACs, or quats. These are organically substituted ammonium compounds and include such agents as cetyltrimethylammonium bromide, cetylpyridinium chloride, benzethonium chloride, and benzalkonium chloride (22).

These are highly active molecules with bactericidal activity against Gram-positive organisms at concentrations as low as 1:200,000. Gram-negative organisms tend to be more resistant. They are generally well tolerated and have found widespread use in surgical scrubs, hand-washing preparations, antiseptics, and disinfectants, often in combination with biguanides such as

chlorhexidine. They are most effective at neutral or slightly alkaline pHs, and their efficacy is markedly decreased in the presence of organic matter and anionic surfactants. They have been utilized in axillary deodorants and although their action is thought to be primarily due to their antibacterial effects, it has been claimed that certain cationics can cause an immediate diminution of odor *via* complex formation, presumably with volatile fatty acids (VFAs). This has been the case with soyaethyl morpholinium ethosulfate (Forestall, Imperial Chemical Industries), a cationic surfactant that has been promoted for use in axillary deodorants (23). Other cationic surfactants proposed for use as deodorant actives include the quinolone derivative dequalinium chloride, methylbenzethonium chloride, laurylpyridinium chloride, and domiphen bromide (6).

Combinations of an acyl-N-betaine and an alkyl-N,N-dimethylamine oxide or alkyl-N,N-dihydroxyethylamine have been claimed to protect from the formation of body odor for extended periods (24,25), and bisquaternary ammonium derivatives have been claimed to be growth inhibitory for odor-causing bacteria (26). Carboxymethyl cellulose (27) and alginate derivatives (28) of quaternary ammonium compounds have been claimed to provide superior deodorancy, and combinations of alkyldimethylbenzalkonium chloride with amphoteric and anionic surfactants have recently been claimed to offer deodorancy benefits (29).

The biguanide family of bactericides has been dominated by the bisbiguanide chlorhexidine (Fig. 3). Chlorhexidine base is not readily soluble in water and therefore the freely soluble salts, acetate, gluconate, and hydrochloride, are widely used. It is a potent bactericide, having a greater activity against Gram-positive than Gram-negative species. Maximal activity is exhibited at pH 7 to 8, where it exists exclusively as the dication compound. It has found widespread use in antiseptics, hand-washing preparations, irrigation solutions, and axillary deodorants.

Studies examining the effect of wash preparations containing 2% or 4% (w/v) chlorhexidine digluconate (HibiPrep and HibiClens, respectively) have shown significant reductions in the total bacterial load, including lipophilic

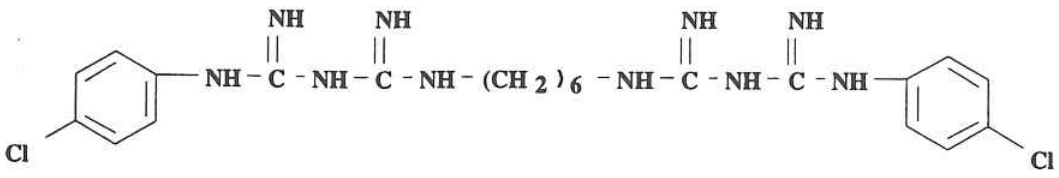


Figure 3 Chlorhexidine.

diphtheroids, present in the axilla (30,31). In a study in which bacteria from the axilla or perineum were translocated on the forearm, chlorhexidine (in 70% v/v isopropanol) was shown to be effective at markedly reducing bacterial numbers and was substantive to skin, presumably due to electrostatic interactions (32). The presence of chlorhexidine in axillary deodorants, in an ethanolic base, was also shown to reduce axillary malodor (relative to ethanol alone) after 24 hours (20).

The antimicrobial activity of chlorhexidine, a bisbiguanide, exceeds that of monomeric biguanides, and this has stimulated the development of polymeric biguanides containing repeating biguanide groups linked by hexamethylene chains. One such polyhexamethylene biguanide (PHMB), consisting of a range of polymer lengths, is marketed under the tradename Cosmocil CQ (Zeneca) and has been claimed to offer deodorancy benefits when applied to the axillae (33,34).

4. Metal Salts

A wide range of aluminum and aluminum/zirconium salts are used as active ingredients in antiperspirants, and their actions are discussed in some detail in other chapters. Although many have potent effects on the eccrine gland, antiperspirants salts also act as effective deodorants. This efficacy is probably *via* two distinct mechanisms. First, it is possible that bacterial growth is retarded due to a decrease in the amount of water present (from eccrine sweat); second, the antiperspirant aluminium salts *per se* have a potent antimicrobial action, resulting in a marked decrease in the axillary microflora (2,35–38). To claim activity as an antiperspirant, the concentration of active ingredient must be sufficient to achieve a 20% reduction in sweat production in 50% of a given population (FDA definition). Levels below those needed to give any discernible effect on eccrine sweat production may, however, still be antimicrobial (39) and can thus have a deodorizing effect. For this reason a number of manufacturers have utilized low levels of aluminum, claiming deodorancy only for their products.

Other heavy metals, such as zinc, copper, and silver, are known to possess antibacterial properties; the zinc salts in particular have found widespread use in axillary deodorants. It is claimed that a primary mechanism of deodorancy is by salt formation with volatile fatty acids. It is likely, however, that their antibacterial properties also have some effects on the axillary microflora. Zinc oxide has been shown to have weak antimicrobial action (40), and zinc phenolsulfonate (Fig. 4) has been widely used for its astringent and antimicrobial activity and continues to be the subject of a number of patents (41,42).

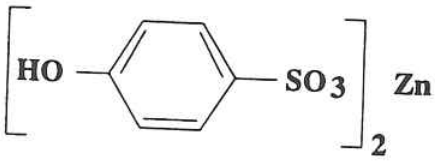


Figure 4 Zinc phenosulfonate.

The use of zinc phenolsulfonate as a deodorant active is discussed further in a later section of this chapter.

5. Carboxylic Acid Derivatives and Glycerides

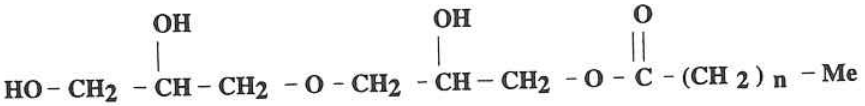
Within recent years a formidable range of carboxylic acids, carboxylic acid derivatives, and glycerides have been patented for use in deodorant compositions, the majority of these originating from Beiersdorf.

Wool wax, or wool fat, is the grease extracted from sheep's wool and consists mainly of fatty acid esters of cholesterol, lanosterol, fatty acid esters of higher alcohols, and free alcohols and fatty acids. The acidic components of this are together termed wool wax acids (WWAs) and have been claimed to offer deodorancy benefits (43). Certain specific WWAs such as α-hydroxy acids, or mixtures thereof, have been claimed for use in deodorant formulations (44), and combinations of WWAs with monocarboxylic acids (preferably unbranched) have been the subject of recent patents (45).

Monocarboxylic acid esters of di- or triglycerols (in particular diglycerol monocaprate, diglycerol monolaurate, diglycerol monolaurate, and triglycerol monomyristate (Fig. 5) have been promoted as antibacterials for both axillary (46) and foot odor (47). A certain number of these have found use in commercially available products. In the treatment of axillary odor they have also been used in combination with WWAs (48).

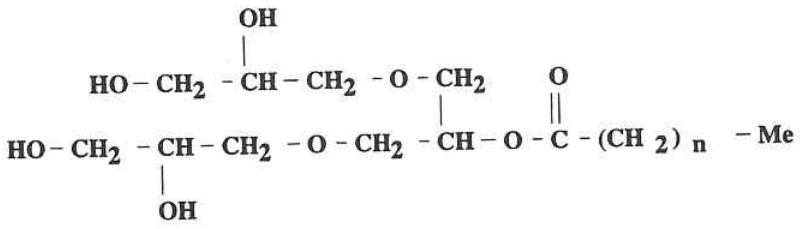
Combinations of mono-, di-, or triglyceryl monoesters with phenyl or phenoxy alcohols has been claimed effective at decreasing the bacterial numbers in the axilla, as well as being of possible benefit in the treatment of superinfections of the skin (49). Interestingly, glycerin monoalkyl *ethers* have also been the subject of a recent patent, where they are claimed to offer selective activity against odor-forming organisms (50).

The bactericidal effects of free fatty acids have been known for some time, C_{12} (lauric acid) possessing maximal activity (51,52). In patent from 1994 it was claimed that lauric acid, in combination with one or more C_6–C_{20} unbranched fatty acid (*e.g.*, caproic, caprylic, capric, myristic, palmitic, or stearic acids), exhibited growth-inhibitory activity against *Corynebacterium*



Diglycerol monocarboxylic acid esters: Diglycerol monocaprate, n=8

Diglycerol monolaurate, n=10



Triglycerol monocarboxylic acid esters: Triglycerol monolaurate, n=10

Triglycerol monomyristate, n=12

Figure 5 Glycerol fatty acid esters.

xerosis (53). A number of monoglycerol carboxylic esters have also been claimed to offer improved deodorancy. Glycerol monolaurate has been long known to possess antimicrobial properties (54), and this agent has found limited use, both alone and in combination with other agents, in axillary deodorants (55,56). Glycerol monocaprate and monocaprylate have been the subject of a range of patents and claimed to be of benefit either alone (57) or in combination with lanolin (wool fat) (58) or lauric acid (59) (when combined with another unbranched monocarboxylic such as caproic, caprylic, pelargonic, palmitic, or stearic acids).

The antimicrobial action of dicarboxylic acids has also been known for some time and within recent years this group of compounds, often in combination with other active agents, have been the subject of a number of patents.

Saturated α,ω-dicarboxylic acids (HOOC—$(CH_2)_n$—COOH, where n = 1–8) either alone (60) or in combination with wool wax acids (61) or monocarboxylic acid esters of mono-, di-, or triglycerol have been claimed to give rise to improved deodorancy *via* inhibitory activity against coryneforms (62,63).

Very recently, alkyne-, alkadiyne-, and/or alkatriynecarboxylic acids have been claimed to "decrease body odour caused by skin bacteria without inhibiting the growth of the normal skin flora" (64). Agents covered in this patent include dec-9-ynoic acid, heptadec-9-ynoic acid, and octadeca-6,12,-diynoic acid. Mixtures of mono-, di-, or triglycerol monocarboxylic acid esters; mono-, di-, or triglycerol dicarboxylic acid monoesters; and dialkylacetic acids such as 2-butyl octanoic and 2-butyl decanoic acids have been claimed to be of benefit in terms of deodorancy as well as in the treatment of a large number of skin diseases (65). A recent patent has claimed that a number of aryl or diaryl 2-acetoxyethanoic acids (*e.g.*, phenyl 2-acetoxyethanoic acid [O-acetyl mandelic acid]) have antibacterial activity against a range of microorganisms and were "effective in preventing the formation of axillary foul odour" (66).

A large number of other compounds and combinations continue to appear in the patent literature. A range of fatty acid esters of sucrose have also been demonstrated to possess antimicrobial activity (67) and have recently been claimed to provide deodorancy benefits, the manufacturers presenting evidence that a number of these compounds have selective activity against *C. xerosis* and *C. minutissimum* (68,68a). Acyl lactylates have also been claimed to provide deodorancy benefits (69).

6. *Farnesol*

Farnesol (3,7,11-trimethyldodeca-2,6,10-trienol; Fig. 6) is an acyclic sesquiterpene present in a wide range of fragrant oils and has been used in perfumery for some considerable time. The nature-identical compound has been synthesized and is used in axillary deodorants, primarily for its antimicrobial properties (70). It has been claimed that 0.3% (w/v) inhibits the growth of *S. epidermidis, S. aureus*, and a corynebacteria isolate, and the manufacturer (Dragoco) has presented clinical data suggesting that the deodorancy effect is comparable

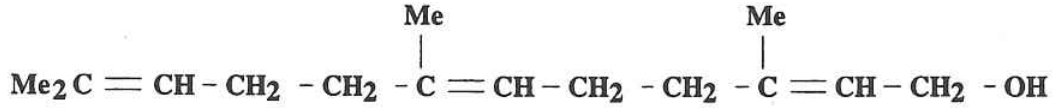


Figure 6 Farnesol.

to that of triclosan. It has also been claimed that this compound has a "selective action" against odor-forming bacteria. It is noted, however, that *S. epidermidis* and corynebacteria together constitute >95% of the organisms present in the axilla (32,71).

This agent has also been formulated in a compound mixture containing glyceryl monolaurate (11% w/v) and phenoxyethanol (53% v/v) (HGQ, Farnesol Plus), which is claimed to possess synergistic antibacterial activity. This mixture was tested against a total of 30 axillary corynebacterial isolates and found to be active against 77% of strains at concentrations of 0.3% and below (55). Sniff-test data suggested that its deodorant efficacy was comparable to that of triclosan (55). Its biological degradability *in vitro* suggested that any residues released into the environment would have less ecological impact than other antibacterial compounds, namely triclosan (55).

7. *Usnic Acid*

Usnic acid (2,6-diacetyl-7,9-dihydroxy-8,9b-dimethyl-1,3(2H,9bH)-dibenzofurandione; Fig. 7) is a secondary metabolite of lichen, first isolated from *Usnea barbata*. This benzofuran derivative occurs as two optical isomers, the dextrorotatory form being substantially more active than the levorotatory form. It possesses analgesic and antipyretic properties (72) and has been shown to have activity against a wide range of bacteria and fungi, including *S. epidermidis and S. aureus* (73). It appears to have little activity against Gram-negative organisms (73). Although this compound has been known for some time, its use has been limited by its poor solubility in commonly used solvents (< 0.01% w/v in water, 0.02% w/v in ethanol). One of the first attempts at producing a water-soluble complex utilized triethanolamine (GD Deo-active Substantive K1149; Orissa Drebing GmbH), and this complex was claimed to degrade on contact with acids on the skin surface, giving rise to a fine dispersion of free usnic acid (74). More recently, Cosmetochem has

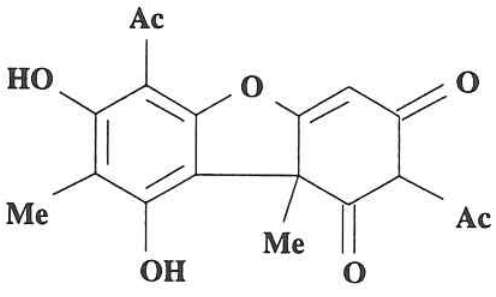


Figure 7 Usnic acid.

derived an amine complex which has improved solubility and retains its activity (Deo-Usnate). Deo-Usnate contains 4.4% to 5% (w/v) usnic acid and has been used in axillary deodorants, usually at a concentration of 0.3% to 1.0% (v/v). It has been claimed that a number of fragrance components, including cinnamyl acetate, eugenol, and isoeugenol, are also able to solubilize usnic acid and thus facilitate its formulation (75).

8. Eugenol

Eugenol (4-allyl-2-methoxyphenol; Fig. 8) is a chief constituent of oil of cloves and has strong antibacterial activity (76). It has been used infrequently in deodorant products, primarily because of its strong and characteristic odor, but also because of skin tolerability.

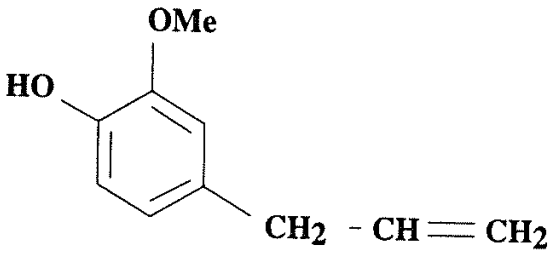


Figure 8 Eugenol.

9. Aliphatic Alcohols and Glycols

One of the most widely used vehicles for deodorant products and body sprays is ethanol, which has well-documented antimicrobial activity (77). The presence of water is essential for activity, with concentrations between 60% (v/v) and 95% (v/v) ethanol being bactericidal (77). In axillary deodorants and body sprays, however, the use of > 95% ethanol is also effective, presumably because of the presence of moisture on the skin surface. Isopropyl alcohol (propan-2-ol) has slightly greater bactericidal activity but is more toxic than ethanol (77). More recently 3,7-dimethlyoctan-1-ol has been claimed for use in axillary deodorants (78).

Glycols have been used for some time in deodorant products, primarily as carrier fluids. Distinct from these properties, however, many glycols have antimicrobial activities (79). For this reason, propylene glycol and dipropylene glycol have been utilized in axillary deodorants for their antimicrobial action (80). A glycerol ether, 3-[(2-ethylhexyl)oxy]-1,2 propandiol (Sensiva SC50) has been claimed to provide a range of benefits, one of which is synergy with

ethanol. Although it has found limited use in products, benefits of this proposed synergy have not been widely researched.

10. Miscellaneous Antimicrobial Agents

A range of esters have been claimed to possess antimicrobial activity, the antimicrobial moiety being generated after hydrolysis of the agent by microbially derived esterases. In a patent from 1987 it was claimed that aromatic acid esters of a phenol or aromatic alcohol had antimicrobial effects (81), and in a subsequent patent phenyl or benzyl benzoyloxybenzoates were claimed to inhibit the growth of esterase-producing microorganisms (82). In both cases it was suggested that the active antimicrobial moeity was only generated after hydrolysis of the parent compound, in the case of a specific example, 4-benzoyloxybenzoate, these moeties being benzoic acid, 4-hydroxybenzoic acid, and benzyl alcohol (82).

Ethylenediaminetetra-acetic acid (EDTA) is a strong chelating agent and will form complexes with many metals. This compound has found widespread use as a preservative and has been included in a range of axillary deodorants. Any inhibitory effect is likely due to chelation of metals of importance for bacterial growth. Recently, a range of chelators have been suggested to have synergistic activity with such agents as triclosan and QACs (83).

A range of antibiotics, including nisin, epidermin, duramycin, and ancovenin, have been suggested to be useful when incorporated into cosmetic deodorants (84), and such agents as tetracaine and naphazoline, better known for their physiological effects on humans, have been claimed to be effective in decreasing the number of odor-forming bacteria present in the axilla (85). In addition, a number of older agents continue to be promoted for use in axillary deodorants including tetrabromocresol (Deodorant Richter) and dichlorophene (Preventol GD). Their use in commercially available products is minimal.

It has recently been reported that there is in human skin a naturally occurring antibiotic peptide which possesses potent antimicrobial action against Gram-negative and, to a lesser extent, Gram-positive organisms (86). This peptide has recently been the subject of a patent application, the inventors claiming that this peptide can "inhibit . . . odour-causing micro-organisms without altering the normal skin flora" (87).

There are a wide range of vegetable extracts (either crude or refined) claimed to be of benefit when used in axillary deodorants (88). The mechanism of action of the majority of these agents is poorly defined. However, it is likely that an antimicrobial effect is at least in part responsible for their claimed effects. Examples include mixtures of citrus fruit seed extracts (89), chitosan

(90) (marketed as Hydagen CMF), ferulic acid, and Deoderm, a combination of oak gall and witch hazel extracts.

B. Non Antimicrobial Agents

Concerns about the widespread use of topical antimicrobials have been voiced for a number of years. In the 1950s and 1960s these concerns tended to focus upon the toxicological profiles of the agents commonly employed, resulting in the withdrawal of a number of compounds from the market, the most notable being hexachlorophene (13). In recent years, however, it has been recognized that the antimicrobials commonly employed as axillary deodorants have excellent safety profiles and have undergone extensive testing both *in vitro* and *in vivo* (17). It is for this reason that the focus has tended to shift toward the long-term effects these agents may have on the microbial consortia they aim to control, and the possible consequences these may have for the host.

It has been generally acknowledged that the commensal flora on the skin offers some protection from colonization by pathogenic microorganisms. This being the case, it has been argued that disruption or modification of this "skin shield" may predispose to opportunistic infections (71). Furthermore, disruption *via* long-term exposure to antimicrobial agents may exert a selective pressure, giving rise to relatively resistant subpopulations of bacteria. It has even been hypothesized that if resistance mechanisms were to involve efflux of the active agent, transfer of such a mechanism to organisms of clinical importance would be a major cause for concern. Distinct from these hypotheses are the ever-present concerns about the release of antimicrobial residues into the environment (*e.g.*, triclosan). Indeed, such concerns have effectively precluded the widespread use of these agents in some European countries.

For these reasons there have been very real demands for effective nonantimicrobial routes to underarm deodorancy. A number of approaches have thus attempted to interfere with the biotransformational steps leading to the production of odorous compounds; the following section will discuss the ingredients associated with such approaches. To understand these strategies, some knowledge of the proposed mechanisms of odor production is required and will be briefly discussed. These accounts are not designed to be exhaustive, rather to enable the reader to appreciate ways in which odor formation pathways may be modified.

1. pH-Modifying Agents and Esterase Inhibitors

One of the first attempts to inhibit enzymatic activity on the skin was prompted by the use of ethyl lactate to prevent the enzymatic cleavage of triglycerides

to free fatty acids, an important stage in the pathogenesis of acne (91). It was proposed that this ester was preferentially hydrolyzed, giving rise to lactic acid, which caused a nonspecific inhibition of esterase activity *via* decreased pH. As it is suspected that esterases play an important role in the formation of axillary odor and the axillary skin tends to be less acidic than that of other regions, cosmetically acceptable pH-modifying agents were sought. From this emerged diethyl tartrate and triethyl citrate (TEC).

Triethyl citrate is the most widely studied of these agents, and the proposed mechanism of action involves preferential hydrolysis (competitive inhibition) by esterases present on the skin surface (the majority of which are probably bacterially derived), giving rise to citric acid. The subsequent reduction in skin pH reversibly reduces the activity of esterases on the surface of the skin, thus inhibiting the formation of odorous compounds. The hydrolysis products are neutralized as a result of the skin's buffering ability, and the enzymes can thus renew their hydrolysis of remaining TEC. Initial results with this compound were encouraging, and a deodorant formulation containing 1% (w/v) TEC was found to be superior to one containing 0.16% triclosan (99% confidence limits) (92). These encouraging results were not, however, supported by later studies. Lukacs *et al.* (93), for example, failed to observe any effect of TEC on odor. In addition, these workers failed to see any effect on cutaneous pH and indeed, observed a correlation between *higher* skin pH and *lower* odor.

More direct routes for altering axillary pH have involved the use of buffers, *e.g.*, a patent for the use of a lactic acid/sodium lactate buffer (94). Any benefits such pH-controlled products may have over nonbuffered products has not, to the authors' knowledge, been the subject of any detailed investigations.

A further example of this approach includes use of a lipophilic derivative of citric acid, which is claimed to markedly inhibit the formation of axillary malodour *in vivo* (95). The authors claim this is by virtue of its phospholipase A_2 inhibition rather than any pH-modifying effect, although the exact mechanism of action is not discussed in detail.

Recently, a number of nonantibacterial esterase inhibitors have been patented for use in deodorants (96,96a). It is claimed that lipid-soluble partial esters of polybasic hydroxycarboxylic acids are more effective inhibitors than many of the short-chain hydroxycarboxylic acid esters. Examples include the citric acid ester of the monoglyceride of hardened tallow fatty acid, and the ester of diacetyltartaric acid with the monoglyceride of hardened tallow fatty acid (96). Esterase inhibition similar to that of the polybasic esters was also observed with esters of aliphatic dicarboxylic acids, including diethyl malonate, diethyl adipate, di-isocetyl azelate, and diethyl glutarate (96a).

2. Inhibition of Odorous Steroid Production

It is now widely acknowledged that odorous 16-androstenes make a significant contribution to the urinous notes associated with axillary malodor (for reviews see Labows *et al.*, this volume; 97, 98) and that these odorants are formed by the metabolism of nonodorous precursors present in apocrine sweat by the axillary microflora. Points of contention are, however, the precise precursors and mechanisms for such biotransformations.

By far the majority of published data substantiate the hypothesis that the odorous steroids 5α-androstenone and androsten-3α/3β-ols are produced from 16-androstadienes by the action of coryneform-derived enzymes (99–101). Although research into these biotransformational pathways has progressed, specific inhibitors of the enzymes involved have not been forthcoming, possibly because of the subtle nature of the biotransformations involved. It is likely that as the details of the biochemistry increase, inhibition of some of these biotransformations may become possible. At present, however, the approaches to the inhibition of odorous steroid production from nonconjugated precursors have been relatively crude (102,103).

A novel mechanism for odorous steroid production was first proposed by Eigen *et al.* (104–106) from Colgate-Palmolive and has recently received some support from other groups (107). This theory proposes that the precursors of the odorous androgen steroids are nonodorous sulfates and glucuronides, and that generation of the free steroids is *via* hydrolysis of these enzymes by bacterial arylsulfatase (AS) and beta-glucuronidase (beta G). In support of this hypothesis, it was found that incubation of apocrine secretions with these two enzymes resulted in malodor formation. In a subsequent publication it was shown that this reaction could be inhibited by the addition of a range of compounds (105). Among those exhibiting inhibitory effects *in vitro* were glucuronolactone, Cu^{2+}, Zn^{2+}, and sodium hexametaphosphate (Sporix). Further investigations utilized a water-soluble zinc salt (zinc glycinate) and determined that the agent was capable of inhibiting both AS and beta-G *in vitro* (108). This agent was found to be relatively substantive to skin and hair. *In vivo* odor evaluation studies suggested that a 4.5% (w/v) solution of zinc glycinate was as effective as 5% (w/v) aluminum chlorohydrate at inhibiting axillary malodor and had a longer-acting action (106,108).

3. Inhibition of Volatile Fatty Acid Production

In addition to odorous steroids it is widely accepted that short- to medium-chain, volatile fatty acids (VFAs) are important components of axillary odor (109,110). Although a vast number of compounds have been identified, it is thought that a primary component of the cocktail is the *trans*-isomer of 3-

methyl-2-hexenoic acid (E-3M2H). It has been found that this compound is transported to the axilla bound to proteins, termed apocrine secretion odor binding protein (ASOB) 1 and ASOB 2, and subsequently identified as apolipoprotein D (111,112). The proposed mechanism of generation of the acid involves hydrolysis of an ester, thioester, or amide linkage by enzymes of bacterial origin, releasing the acid from the protein (113).

In an attempt to exploit such a mechanism, mimics have been designed which would be expected to compete for the binding sites on the bacterial enzymes (113). One such mimic, an alanine derivative of E-3M2H, was transformed to free E-3M2H on incubation with an axillary corynebacterial isolate. It was thus argued that molecules incorporating this link would compete with the E-3M2H-ASOB complex and, if the E-3M2H residue was replaced with a nonodorous or pleasant-smelling compound, the formation of E-3M2H could be inhibited. Furthermore, it was proposed that by forming an acid-alanine-ester compound in which the acid residue is inhibitory, bacterial growth could be retarded. As 10-undecenoic had previously been identified as a component of axillary extracts and possessed antimicrobial properties (114), this compound was coupled to the precursor to form 10-undecenoic-alanine-methyl and 10-undecenoic-alanine-dodecyl esters. These agents exhibited antimicrobial and odor reduction comparable to that of triclosan (1% w/v) (113).

4. *Inhibition of Protein and Amino Acid Biotransformations*

A number of early patents have claimed deodorizing effects with a range of proteinase inhibitors. Proposed mechanisms for any activity are not clear, but a number of patents claim inhibition of odor formation with proteinase inhibitors isolated from fungi (115), animal organs, or vegetables (116,117). More recent patents have proposed a novel protein-precursor mechanism for underarm odor generation (118). Lyon and co-workers from Gillette have claimed that volatile sulfur compounds are responsible for the ''pungent smell characteristic of human axillary odour,'' analogous to the formation of oral malodor (119). The precursors for these compounds are proposed to be of the general formula HOOC—CH(NH_2)—CH_2—S—R (R usually alkyl) and are degraded by the action of pyridoxal dependent enzymes. It is known that such enzymes can be inhibited by a range of compounds, including hydroxylamine, amino acids halogenated at the β carbon, α-methyl amino acids, cycloserine, and pyridoxal phosphate derivatives. *In vitro* testing of aminooxyacetic acid, β-chloroaniline, trifluoroaniline, the α-methyl derivative of S-benzyl cysteine, cycloserine, and pyridoxal showed *in vitro* inhibition of odor formation in the presence of an axillary isolate and apocrine secretions (118). In a subsequent patent (120), O-

acylated serine derivatives of the general formula HOOC—$CH(NH_2)$—CH_2—O—C(O)—R were utilized with the aim of producing nonodorous or pleasantly odorous compounds in preference to the odorous amino acids. In an example of the latter, O-phenylacetyl serine was evaluated *in vitro* for its ability to inhibit odor formation when a bacterial isolate and apocrine secretions were incubated together (120). It is claimed that this compound effectively inhibited malodor formation and that a pleasant honey odor was produced due to the formation of phenylacetic acid.

5. *Inhibitors of Bacterial Adherence*

The adhesion of axillary bacteria to epidermal cells has been investigated with a view to inhibition of this process, thus decreasing the bacterial population density in the axilla. In a relatively early study it was found that glucose and mannose, or oligomers of these sugars, could interfere with the adhesion of axillary isolates to human keratinocytes *ex vivo* (121). In addition, it was found that incorporation of these sugars into an aqueous cleaning preparation resulted in superior removal of odor-causing bacteria. In a similar study it was postulated that epidermal glycolipids provided adhesion motifs for cutaneous staphylococci (122). Adhesion of these bacteria to human corneocytes was inhibited by a number of hydrophobically modified carbohydrates and polysaccharides. This study proposed that incorporation of an unidentified modified carbohydrate into a shower gel formulation could significantly reduce the number of organisms present in the axilla (relative to water). This approach has been the subject of a recent patent (123).

In another study a large number of axillary isolates were subjected to an *in vitro* adhesion assay using differentiated and undifferentiated keratinocytes cultured *in vitro* (124). In agreement with Eigen *et al.* (121), mannose was found to be effective in inhibiting the adhesion process; however, this effect was strain-specific. In addition to mannose, these authors identified a large number of agents capable of consistently inhibiting the adhesion of a range malodor-producing corynebacteria (*C. minitissimum, C. pseudotuberculosis, C. xerosis*, and *C. diphtheriae*). These compounds included N-acetyl-D-glucosamine, galactose, fucose, D-glucuronic acid, a range of glycoproteins (fibronectin), and polysaccharides (alginic acid).

6. *Inhibition of Odors of Nonmicrobial Origin*

A number of patents originating from Procter and Gamble in recent years have proposed that certain malodors are generated in the absence of microorganisms. A number of patents have suggested that "when perspiration from the

axilla or crotch areas is sterilised such that substantially no live bacteria remain to produce malodorous by-products, the perspiration still develops aesthetically objectionable malodour.'' The proposed mechanism involves the reaction of vitamin B_6 (pyridoxine) with (unspecified) components of apocrine sweat, resulting in the formation of odorous compounds (125). In an attempt to inhibit this formation, a number of agents were identified that undergo preferential chemical reaction with the aldehyde form of vitamin B_6. A wide range of nucleophiles, including 1,3-diketones, heterocyclic thiols, primary amines, and heterocyclic disulfides, were claimed to be of use (125–128). For use in the underarm, 2-thiohistidine, phenylhydrazine, canaline, aminoacetic acid, p-methoxyaniline, p-methylaniline, and bis(pyridine)-2,2′-disulfide were cited as specific examples. *In vitro* experiments using artificial eccrine sweat containing pyridoxal phosphate and sterilized apocrine secretions showed that a range of thiols inhibited odor formation and were claimed to be effective deodorant agents. No quantitative data were disclosed, and these agents have not as yet found their way into any commercially available products.

7. *Antibodies*

A limited number of patents have claimed the use of antibodies for the inhibition of odor generation. Any deodorizing action presumably arises from specific binding at sites on the bacterial surface and subsequent inhibition of biotransformations important in odor formation. In an early patent, cows were exposed to a range of antigens *via* a preparation containing killed bacterial cells, including *Staphylococcus epidermidis, Corynebacterium diphtheriae*, and *Corynebacterium acnes* (129). Antibodies were isolated from milk *via* centrifugation and fractionation by column chromatography. The IgG antibodies isolated were claimed to be effective (1% w/w in talc) at combating axillary odor in humans. In a later patent, researchers from Gillette utilized their knowledge of the amino acid β-lyase mechanism (outlined above) to develop monoclonal antibodies (130). Antigen preparations contained *Staphylococcus haemolyticus* cell wall/membrane fragments. After repeated exposure to the antigens, sera of mice were tested (*in vitro*) for the ability to inhibit malodor production (although undisclosed, this was presumably an enzyme inhibition assay utilizing amino acid β-lyase). By fusion of spleen cells with myeloma cells and repeated screening it was possible to select a cell line producing an effective monoclonal antimalodor antibody exclusively.

The incorporation of antibodies into finished products presents many problems, and inactivation by alcohols precludes their use in ethanol-based deodorants. In addition, the regulatory status of products containing antibodies

remains contentious. At present there are no commercially available axillary deodorants containing antibodies.

8. Antioxidants

The oxidation of components of sebum has been proposed as a route for VFA production and there have thus been attempts to inhibit these oxidative steps. Use of α-tocopherol (vitamin E) and ascorbic acid (vitamin C) has been widespread. This is partly due to their inherent antioxidative capabilities, but also because synergistic activity has been observed when these agents are combined with other active agents (131–133). Such synergies have been observed with antimicrobials and with agents such as triethylcitrate (TEC). Indeed, one manufacturer (Henkel) supplies TEC in a ready-mixed form with butylhydroxyltoluene (BHT, Hydagen Deo).

It has also been proposed that lipoxidases (lipoxygenases) are capable of catalyzing the hydroperoxidation of polyunsaturated fatty acids and esters present in sebum, *e.g.*, linoleic acid and its esters. These compounds can further decompose to short- to medium-chain aldehydes, ketones, and acids. A number of patents have therefore claimed the use of lipoxygenase inhibitors including quercetin, hydrazones, esculetin, esters and amides of hydroxybenzoic acid, di- and trihydroxybenzoic acid, and, interestingly, chlorhexidine gluconate (134). A wide range of fragrance ingredients are claimed to possess lipoxidase-inhibitory effects. Indeed, a prerequisite for inclusion in a range of deo-perfumes is the ability to decrease the oxidation of linoleic acid by at least 50% (135). Such agents are discussed in more detail in the Fragrances section of this chapter (Sec. IV).

III. ODOR COUNTERACTANTS

In contrast to the precise attempts at controlling the generation of axillary malodor, the strategies aimed at removing the offensive odors once formed tend to be less specific. The aim of such approaches is to modify or bind the volatile components such that their odor and/or vapor pressure is decreased, ideally to below the olfactory threshold. This has been attempted in a number of ways, and the majority of mechanisms fall into two main categories:

1. Chemical modification/reaction of odor components—*e.g.*, of VFAs to their metal salts
2. Physical binding/entrapment—*i.e.*, adsorption/absorption

In the following section both these approaches will be discussed. It should be noted that although fragrances can influence the vapor pressure of odorous volatiles in the axilla, the action of fragrance is multifaceted and is therefore discussed in a dedicated section later in this chapter.

A. Chemical Modification of Odorous Compounds

There is a large body of literature supporting the hypothesis that many of the compounds responsible for axillary malodor are acidic in nature and thus amenable to reaction with metals to form nonvolatile salts (109). Sodium and potassium bicarbonate have been used for some years as deodorants, their effect probably being attributable to such a mechanism (136). Attempts at formulating these compounds have been hampered by their physical form and solubility characteristics, and novel production methods have been recently proposed to remedy these problems. Precipitation of sodium bicarbonate from a water/methanol mixture has been claimed to give rise to primary acicular particles ~1 to 2 μm in length and possessing surface areas of between 5 and 20 $m^2 g^{-1}$ (137). Coprecipitation with ammonium bicarbonate and subsequent removal of the ammonium salt, by heating under reduced pressure or dissolution, resulted in particles with increased particle and pore size (137,138).

In deodorancy terms the mode of action of such particles is likely to be twofold. First, there may be chemical reaction with acidic components of axillary odor. Second, there will undoubtedly be some adsorption due to the large surface area. Particles coated with maltodextrin were claimed to improve the aesthetics of the finished product, and these encapsulates have been successfully formulated with antiperspirant salts (139). In addition, adsorption of fragrance prior to polymer coating (140) and combination of fragrance in the polymer coating (141) were claimed to result in products whose deodorizing activity is signaled by the release of fragrance.

A range of metal salts and oxides have been used for some time as deodorant ingredients. Their efficacy is thought to be primarily *via* chemical modification of the odorous compounds, although many of the compounds undoubtedly have some antibacterial, antiperspirant, or adsorptive effects (142). Compounds as diverse as cupric sulfate, silver sulfate, potassium permanganate, ferric chloride, sodium hydroxide, sodium hypochlorite, and copper gluconate have been claimed to effectively counteract axillary odor (143). It has also been claimed that both zinc and magnesium hydroxide effectively neutralize 3-methyl-2-hexenoic acid (144), and zinc carbonate has been the subject of a number of patents (145). Zinc salicylate, zinc sulfocarbolate, zinc sulfide, and zinc peroxide found use in early products, and more recently zinc glycinate (146) and zinc pindolate (zinc pyrrolidone carboxylate) (147) have

been claimed for use in deodorants. Of all the zinc compounds, however, zinc oxide and zinc phenolsulfonate (p-hydroxybenzenesulfonic acid zinc salt; ZPS) have been the most widely used in axillary deodorants.

Zinc phenolsulfonate has been used widely in axillary deodorants, being freely soluble in both water and ethanol. Its action is presumably explained by a combination of its antibacterial activity and its ability to react with free volatile fatty acids. It is typically used at a concentration of 2.5% (w/v) and is frequently combined with polyhydric alcohols (41,148). Zinc oxide has been used for some time and possesses mild antibacterial activity, although its primary mode of action is thought to be *via* salt formation with VFAs. In the case of propionic, isovaleric, and caproic acids, such a mechanism has been demonstrated *in vitro*, the proposed reaction being as follows (149,150):

$$2RCOOH + ZnO \longrightarrow (RCOO)_2Zn + H_2O$$

where R = alkyl group.

In formulation terms, zinc oxide is problematic in that it aggregates easily to form amorphous clumps. This leads to major difficulties in terms of manufacture and undesirable sensory attributes. In an attempt to remedy this, Kanda and co-workers developed ''hybrid powders'' containing a uniform coating of zinc oxide on spherical nylon or polyethylene carrier particles (149–152). The physical properties of such powders were dominated by the characteristics of the carrier particles, allowing for improved formulation options. It is claimed the hybrid powders possessed good sensory characteristics and were effective in combating axillary odor. Such technologies have been the subject of patents (153,154); however, it is not known if such preparations have been included in commercially available deodorants.

Hydroxyapatite has been found to be effective at ''quenching'' isovaleric acid *in vitro* (150), and its use in axillary deodorants has been the subject of various patents (155). As was discussed in the previous section, a novel hypothesis for odor generation implicating sulfur-containing amino acids has recently been postulated by workers at Gillette (118). A number of sulfydryl (thiol) reactants have thus been patented for their neutralization potential, *i.e.*, compounds reacting with the S–H bond (156). These include N-ethylmaleimide, diethyl fumarate, di-n-butyl maleate, iodoacetic acid, alginic acid, and dansyl aziridine.

B. Physical Modification of Odorous Compounds

Many attempts have been made to physically adsorb/absorb odorous molecules formed in the axilla with the ultimate goal of immobilizing the odorous

molecules and decreasing the vapor pressure and perceived odor. There tends to be little specificity to such an approach and it is possible that in addition to binding odorous molecules, odor precursors are bound, and odor generation thus inhibited. Indeed, a recent patent has suggested such a mechanism for an acrylate/methacrylate polymer "sponge" (Microsponge) (157). This is claimed to incorporate odor precursors in its interior, the average pore size being sufficiently small to exclude bacteria and thus prevent biotransformations (158).

Although many of the metal oxides and salts described in the previous section will have limited adsorptive capabilities, the agents discussed in the following section are claimed to act primarily as adsorbents/absorbents while remaining, in the majority of cases, chemically inert.

Some of the earliest attempts at odor adsorption involved the use of ion-exchange resins. Thurmon and Ottenstein (159) incorporated carboxylic acid-type ion-exchange resin into an antiperspirant/deodorant formulation and examined the adsorption of a range of compounds (160). Ikai examined the ability of a number of resins to bind fatty acids, ammonia, indole, and a number of bodily odours (161). Application of cationic or anionic exchange resins singly tended to result in a residual "acid or alkaline odour"; however, when they were used in combination, they were claimed to be effective in controlling axillary odor for up to 18 hours. In subsequent years a number of workers have claimed that ion-exchange resins represent effective deodorants but they have not found their way, in any appreciable way, into commercially available products (162,163).

The deodorants industry has showed considerable interest in the zinc salt of ricinoleic acid (*cis*-12-hydroxy-9-octadecenoic acid), a major component of castor oil (164–168). Although antimicrobial effects have been reported (9), such compounds are thought to form, by intramolecular electrostatic interaction, complexes that are capable of incorporating odorous compounds into their structure. Zinc ricinoleate has been available for some time in various forms for use in different types of products. These involve complexes with triethanolamine, propylene glycol, dipropylene glycol, laureth-3, and tetrahydroxypropyl ethylenediamine (168). Although interactions with fragrance components have been noted, they have been used extensively in axillary deodorants and continue to be the subject of a limited number of patents, usually in combination with other active ingredients (169).

Baxter and Reed (20) demonstrated that an ethanolic preparation containing 5.7% (v/v) zinc ricinoleate produced a rapid diminution of odor over and above that of ethanol alone, this benefit persisting for up to 24 hours. More recent work has suggested that zinc ricinoleate can effectively bind iso-

valeric acid and is effective at decreasing mean malodor scores for up to 24 hours (168).

A range of silicones and silicates have been claimed to offer deodorancy benefits. Silica, sodium, magnesium, and calcium silicates have been used for the encapsulation of zeolites, and hollow spherical microparticles comprising calcium or magnesium silicates have been claimed to effectively adsorb axillary odor (170). Sodium silicate has been claimed to offer improved deodorancy (171,172). In a disclosure by L'Oreal, aerogels (highly porous silica complexes) have been claimed to be effective deodorizing agents for axillary odor (173).

The term ''molecular sieves'' encompasses a range of inorganic, crystalline materials with a crystal framework forming a three-dimensional network of pores and cavities. Zeolites, an example of such, are aluminosilicate crystalline materials in which a negatively charged framework exists, the charge being balanced by cations present in the cavities and these cavities accounting for up to 50% of the zeolite's total volume. Due to their high porosity and surface area, zeolities have found widespread use for their adsorptive and catalytic activity (174). In applied settings their characteristics have made them of use in a number of applications including the removal of undesirable volatiles from foods (175). In axillary deodorants zeolites have been claimed to offer deodorant benefits by binding of odorous molecules in the lattice interior of their open structure (176). As they tend to have hydrophilic interiors and thus to adsorb large amounts of water, attempts have also been made at rendering the interior of the lattice more hydrophobic. One result of such an attempt is an ''organophilic'' zeolite (Abscents), claimed by the manufacturer to represent an ''odour eliminating molecular sieve'' (177). Because of their high porosity zeolites have also found use as ''carriers'' for fragrances where they are claimed to result in a prolonged effect (176). In a recent patent the counterions present in a zeolite lattice, typically sodium, were replaced with antibacterial divalent cations, preferably copper, zinc, or silver, and the complex was claimed to provide superior deodorancy when blended with silicone oil or volatile silicone (178).

The cyclodextrins represent a family of cyclic oligosaccharides formed by the action of cyclodextrin glucosyl transferase on starch. They take on a toroidal form, small cylinders with hydrophilic outer surfaces and hydrophobic central cavities (1 to 2 nm diam.) into which smaller molecules can be introduced. They have found widespread use as carriers for smaller organic molecules, and have recently been utilized ''empty'' to remove undesirable compounds from food (179–181). In a similar way to the removal of undesirable compounds from foods, it is claimed that ''empty'' cyclodextrins can bind

odorous molecules or odor precursors, preventing their release (182,183). This approach has been patented in a novel cyclodextrin-containing adhesive tape for application to the axilla (184). Inclusion compounds, ''host-enclosed complexes,'' have also been patented for use in deodorants, where complexed fragrance was claimed to result in sustained perfume release (185,186).

Finally, a diverse range of compounds have been claimed to counteract axillary odor presumably *via* adsorptive/absorptive processes, although in the majority of cases the mechanism of action is not discussed. Amorphous calcium (142) and spangolite analogs have been claimed to offer superior deodorancy, in some cases substantiated by clinical evaluation (187). A number of patents have claimed the use of alum as deodorizing agents for the axilla either alone, where it is claimed to ''suppress perspiration odour and decreases sebum secretion,'' or in combination with other active ingredients such as chlorhexidine (188–191). Recently ammonium alum has been included in commercially available products (192).

IV. FRAGRANCES AND MODIFIERS OF ODOR PERCEPTION

Fragrances have been used for thousands of years for their pleasant olfactory attributes and their effects on mood. In ancient Egypt fragrances were used in religious ceremonies and burials and this era saw, perhaps for the first time, the application of fragrances to the body in the form of fragrant ointments and balms (1,193). The use of fragrance continued through the ages, and there are many examples of the Greeks and Romans using fragrances for personal application. In Europe their use increased markedly during the Renaissance and especially the 17th and 18th centuries, when they were used to mask the lack of personal hygiene. It is now acknowledged, however, that even with a stringent personal hygiene regimen a significant proportion of individuals require protection against the buildup of axillary odor. For this reason fragrances have found widespread use, for both their pleasant bouquets and their odor masking or counteracting capabilities. Fragrances now represent perhaps the most widely used of all deodorant ingredients.

Like any fragrance introduced onto the skin surface, the more volatile components (the ''top notes'') produce an initial burst of olfactory stimuli. After this initial period, typically 15 minutes, there is a period during which the fragrance's characteristics are modified as its composition gradually shifts toward that of the less volatile components, the ''middle'' or ''heart,'' and ''base'' notes. The formulation of a fragrance whose overall balance, or bouquet, is maintained during this sequential volatilization is therefore a primary

goal for the perfumer and one that requires considerable expertise. In the case of axillary deodorants, however, this is not the only factor to be taken into account. This maturation process occurs in the presence of bacterial and skin-derived enzymes, and also in parallel with a gradual increase in the presence of axillary malodorants. Creating a fragrance that will combine with such malodorants and ideally appease them, over prolonged periods and during a sequential shift in the fragrance composition, represents another major challenge for the perfumer.

Fragrances are somewhat unique in that they are formulated from a vast array of odorous materials, both natural and synthetic, to produce the final product. This process cannot be fully explained by simple chemical analysis and thus possesses a certain air of mystique. A comprehensive account of fragrance formulation and malodor counteraction is beyond the scope of this chapter; for more information the reader is directed to one of the many texts available on the subject, *e.g.*, the Haarmann and Reimer Book of Fragrance (194). The following section will provide an introduction to fragrance formulation and malodor control in the context of axillary deodorants and, in addition, give an account of some of the more novel approaches taken in this field.

A. Fragrance Components

A fragrance may conceivably comprise a single raw material, but by far the majority of fragrances comprise many more, often as many as 200. Combining this plethora of materials to create a harmonious and pleasing fragrance which provides certain olfactory stimuli is not a skill completely amenable to a scientific approach, and the experience of a trained perfumer far outweighs any formulation benefits that could be obtained by using a purely chemical approach.

The raw materials used in fragrance formulation are often split into "naturals" and "synthetics," although the distinction is by no means clear-cut. The naturals comprise any materials obtained from natural sources using physical separation techniques such as distillation and extraction. They have been used for centuries and include materials obtained from plants (flowers, seeds, resins, barks, *etc.*) or animals (civet cat, musk deer, *etc.*). The synthetics comprise an ever-expanding group of compounds which includes chemicals first isolated from natural sources and subsequently produced synthetically, and compounds that have never been isolated from nature but have been synthesized in the laboratory. Although the above distinction is widely used, there are a large number of compounds available from either natural or synthetic sources and, consequently, the distinction somewhat blurs.

The descriptors used for raw materials and the fragrances they produce are varied and designed to reflect the subtleties of perfumery. Thus, such phrases as ''citrus, herbal, floral, musk, green, aldehydic, leather, and wood'' are commonly used to describe certain fragrance types. As has been stated, materials are rarely used alone, and a number of ''fragrance concepts'' or ''fragrance families'' have been created. These include floral, Oriental, chypre, lavender, and citrus, all of which are further subdivided to give a vast range of descriptors.

In antiperspirant products fragrance formulation is under some constraints, including acidic pH and the presence of heavy metal ions. Within axillary deodorants, although some allowances have to be made for interactions between active ingredients and fragrance, *e.g.*, zinc salts, the delivery vehicles employed tend to be in general less aggressive. For this reason axillary deodorants do not appear to be dominated by any particular fragrance types.

Many fragrance components have long been known to possess antimicrobial properties (195). Indeed, such agents as farnesol, now primarily used for their antimicrobial actions, were first isolated from fragrance materials. Fundamental research on the antimicrobial effects of natural materials has been undertaken for a number of years and continues to show a wide range of essential oils to have antibacterial effects (196–198). Some of the first attempts to optimize the antibacterial activity of formulated fragrances were undertaken by Haarmann and Reimer and led to the Deo-Safe range of fragrances (199). Workers subsequently attempted to augment the antimicrobial effects of fragrances, and this led to the identification of agents such as farnesol. In an extensive screening of natural oils and synthetic fragrance ingredients Sawano *et al.* (200) recently found a wide range of materials capable of inhibiting the growth of *Arthrobacter* spp., *Corynebacterium* spp., and *Staphylococcus* spp. Oils such as clary sage abs., oakmoss abs., and vetiver oil were claimed to be effective, and a range of synthetic agents including methyl evernate, cedrol, cedral acetate, and aromatic aldehydes were found to be growth-inhibitory. Not surprisingly, farnesol was found to have maximal activity, and other agents, such as geraniol, ethylene brassylate, and a range of macrocyclic musks, were also claimed to possess potent growth-inhibitory activity. Tonalide, galaxolide, and, perhaps surprisingly, 5-α-androst-16-en-3-ol were also claimed to be active (200).

Work in this field, primarily undertaken by the fragrance houses, has produced a range of antibacterial fragrance ingredients which are now available commercially. They have been shown to be effective at inhibiting bacte-

rial growth both *in vitro* (199,200) and *in vivo* (201), and have found widespread use in axillary deodorants.

B. Deodorant Effects

The deodorizing effects of fragrances may be multifaceted. Possibly the most basic, and certainly the most easily explained mechanism, is that of masking. This is an additive process in which the overall character of the malodor is ''overpowered'' or ''covered up'' by a dominant but pleasant aroma, the overall odor intensity increasing. Although this is the most commonly used technique, some care must be taken to ensure that the final character of the fragrance/malodor mixture is a favorable one.

In contrast to simple masking of the malodor it is claimed that certain fragrances are capable of ''incorporating'' a malodorant in such way that the overall character of the fragrance is only complete when this component is present. The successful use of this method is highly dependent upon the formulation technique. Multichannel olfactive blenders, which allow the user to sample an array of odors in various combinations, have been used for fragrance and deodorant formulation (202). By introducing axillary malodor or components thereof into one channel it is claimed that fragrances can be produced which possess a ''void'' that molecules arising from axillary malodor are able to occupy, giving rise to odor diminution.

In contrast to masking or blending, odor counteraction is a process whereby the intensity of malodors is decreased by a fragrance material, which combines with the malodor to give a mixture having a reduced combined odor intensity (203,204). In the context of axillary deodorants, a large number of patents have claimed the use of odor ''counteractants'' giving rise to a range of fragrances termed ''deo-perfumes.'' Such fragrances were pioneered in the 1970s when workers at Unilever found that a number of fragrance ingredients, when combined in a given fashion, were able to consistently provide improved deodorancy. Such deo-perfumes were formulated using a number of given agents from a group divided into six classes:

Class 1:	Phenolic substances, *e.g.*, carvacrol, isoeugenol, and ethyl vanillin
Class 2:	Essential oils, extracts, resins, and ''synthetic oils,'' *e.g.*, geranium and patchouli oils

Class 3:	Aldehydes and ketones, *e.g.*, α-iso-methyl-ionone, β-methyl naphthyl ketone
Class 4:	Polycyclic compounds, *e.g.*, coumarin, methyl cyclopenta-γ-2-benzopyran
Class 5:	Esters, *e.g.*, phenylethyl phenylacetate, diethyl phthalate
Class 6:	Alcohols, *e.g.*, phenylethyl alcohol, dimyrcetol

Individual compounds were only included in the test if they were capable of inhibiting the oxidation of linoleic acid by at least 50% (their lipoxidase-inhibiting capacity; LIC) or were capable of reducing the partial vapor pressure of morpholine over and above that predicted by Raoult's law (the Raoult variance ratio). Initially 65 such agents were identified. Formulation with representatives from a minimum of four of the above classes, along with other constraints, gave rise to perfumes which were capable of providing ''odor reduction values'' that exceeded those of non-deo-perfumes.

Such perfumes were the subject of a vast array of patents, covering applications such as laundry detergents and softeners (205), cleaning agents (206), and products for personal use (135,207,208). They have been used extensively in axillary deodorants, and their success has prompted the development of a range of perfume constituents claimed to have similar effects. Most of the major fragrance houses now produce fragrance materials claimed to have superior deodorizing activity.

In a recent patent an attempt has been made to retain the deodorizing effect of deo-perfumes while removing some of the constraints the original deo-perfumes protocol placed on fragrance formulation (209). Thus, representatives of four of five categories (ethers, salicylates, alcohols, acetate/propionate esters, and methyl aryl ketones) were used to formulate fragrances which were claimed to provide superior deodorancy when compared to fragrances formulated according to the ''original'' deo-perfume formulation rules (209).

Some attempts have been made at influencing the olfactory response once a malodorant reaches nasal receptors. A number of agents have thus been claimed to compete with the malodor receptors in the nose and cause a decrease in the perception of the malodorant. Such approaches have been the subject of patents and are available commercially (210) (Veilex, Bush Boake, and Allen Ltd.). More recent work has examined a phenomenon termed

''cross-adaptation'' whereby the sensitivity to one odorant is decreased after exposure to a different odorant. It was demonstrated that odor magnitude estimates of a 10:1 mixture of (E)- and (Z)-3-methyl-2-hexenoic acid (3M2H), a primary component of axillary malodor, was decreased following adaptation to a mixture of (E)- and (Z)-ethyl esters of 3M2H which possessed a pleasant, fruity odor (211). Such an approach may be expected to decrease the perception of underarm odor and has been the subject of a recent patent (212).

A number of compounds isolated from the human axilla have been postulated to be human pheromones (97,213). These include such compounds as androstenol and androstenone, which possess musk and urinous odors, respectively (97). Mammalian pheromones, including muscone from the musk deer, civetone and skatole from the civet cat, and castoreum from the Canadian beaver, have been incorporated into fragrances for some time (214). Although these agents are used for their fixative and olfactory properties, it has been proposed that many of these agents should be considered as substitutes for androstenol and may thus provide a ''sexual/animal basis for perfumes'' (97). Recently the 16-androstenes have been claimed for use in fragrances, these compounds claimed to be human pheromones and thus being of use in fragrances (215).

C. Fragrance Longevity

Regardless of the mode of action, a fragrance must ideally have a prolonged effect for two reasons. First, the presence of perceivable fragrance is likely to be a consumer cue for deodorancy, and second, the fragrance must be capable of masking or counteracting the axillary malodors over extended periods.

It is recognized that after application to the skin surface there occurs a sequential loss of fragrance components; indeed this fact is fundamental to fragrance formulation. The least volatile components, the base notes, are incorporated to provide longer-lasting fragrance. However, to maintain these base notes at a level that still provides some degree of deodorancy is difficult. Thus, there have been attempts to prolong the action of fragrances in a number of ways, and these will be briefly discussed.

The persistence of a fragrance material depends on a number of factors, *e.g.*, volatility, concentration, and attraction forces between the fragrance material and the base. In ethanolic solution, for example, the ethanol will rapidly volatilize and in the fragrance components remaining there will exist dipole-dipole and hydrogen bond interactions between perfume components. In an

attempt to maximize such interactions and prolong the effect, perfumers use materials of low volatility in their perfumes to improve persistence, a practice commonly referred to as fixation. Fixatives commonly used include musks (nitro-, macro-, and polycyclic) and floral and botanical absolutes. In a recent patent, tonalide, a commonly used musk material, has been claimed to act as a fixative, giving rise to fragrance compositions that have a prolonged effect (216,217).

Encapsulated fragrances have been used for some time and have relatively recently been introduced into deodorant products. A number of fragrance houses produce such encapsulates, and these have been incorporated into a range of commercially available products. Such systems typically contain a starch-encapsulated fragrance which dissolves on eccrine sweating, providing a prolonged effect and ''reminding'' the user that their deodorant product is still active. More sophisticated systems have recently been developed which dissolve in eccrine sweat but lock the perfume back up again in a flexible starch film when perspiration stops, producing multiple bursts of fragrance (218,219).

Any fragrance materials introduced onto the skin surface undergo changes. It is acknowledged that the majority of these alterations are likely to be physical in nature, although in the axilla it has been shown that the presence of an extensive microflora may produce chemical changes giving rise to the production of new odorous entities (220). Such an approach has been exploited in a number of patents. Conversion of O-phenylacetyl serine was claimed to give rise to the fragrance ingredient phenylacetic acid, and was presumably produced by the action of bacterially derived enzymes (120). In a recent patent, the pH of the skin has been exploited to produce prolonged fragrance release (221). A range of acetals or ketals, when delivered to the skin surface *via* an alkaline vehicle, were claimed to undergo hydrolysis prompted by the buffering action of skin (221). In addition, it was shown that bacteria-mediated hydrolysis could occur for the more reactive species even in alkaline conditions (221). This gave rise to the production of agents possessing pleasant odors at some variable time after the fragrance was introduced onto the skin surface.

Recently it has been claimed that the combination of various odiferous alcohols with a range of carboxylic or amino acids gave rise to nonodorous fragrance precursors (222). Thus such agents as geraniol, citronellol, eugenol, borneol, and farnesol, when reacted with acids such as lactic, malic, and ricinoleic acids, were claimed to give rise to compounds that, when introduced into the axilla, would undergo enzymatic transformation, giving rise to a fra-

grant alcohol (222). In this way it was claimed that long-lasting fragrance effects could be achieved.

V. CONCLUDING REMARKS

The search for deodorant ingredients or systems to provide longer-lasting protection against the buildup of malodor is a major activity in the personal care industry. Understanding the mechanisms of axillary odor generation and routes to counteraction remains a primary goal for researchers within both academia and industry. In recent years, the strategies adopted for investigating and remedying the problem of odor generation have become ever more sophisticated, a fact reflected in the scope and depth of patents and publications in this field.

The pivotal role of bacteria in odor formation continues to be acknowledged, and the strategy of interfering with odor formation *via* bacterial kill is still an area of active research. At present the deodorant market is dominated by the use of fragrance and antimicrobials, both of which are of proven value in inhibiting the formation and perception of malodor. For example, an axillary deodorant product typically contains an antibacterial agent, *e.g.*, triclosan, in combination with a fragrance having odor-masking and probably antimicrobial effects, and is formulated in a strongly bactericidal base such as ethanol. The system is thereby designed and optimized for bacterial kill.

Decreasing the number of bacteria present in the axillae is only one way in which odor formation can theoretically be inhibited. Elucidation of the biotransformational/metabolic routes to odor have been a prime focus of attention for a number of researchers in the field, and as a result there have been marked improvements in the understanding of these mechanisms. A number of biochemical ''targets'' have been identified, many of which are amenable to manipulation, and attempts have been made to exploit this knowledge. These have included inhibition and/or exploitation, *e.g.*, the use of ''pro-drugs'' (or ''pro-fragrances''), which are transformed to the active agent only when delivered to the axilla. A large number of patents have been filed that utilize such an approach and which may provide novel routes to deodorancy.

Finally, improvements have been made in determining those characteristics required for fragrance components to counteract odorous molecules. This has led to a range of effective ''deo-perfumes'' which have found extensive use in axillary deodorants. In the future it is likely that improvements in the

understanding of olfaction will create novel ways of altering the perception of the components of axillary odor.

Regardless of the approach taken, the consumer need for protection from malodor will undoubtedly continue, and it can be stated with some confidence that the scientific challenges this area offers, coupled with the size of the deodorants market globally, will continue to provide an incentive for vigorous research into this curious problem.

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7
Safety of Antiperspirant Salts

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I. INTRODUCTION

Aluminum-containing and aluminum/zirconium-containing antiperspirant salts have enjoyed a long history of use by the general public in the reduction and control of axillary perspiration and odor. There is much literature devoted to their chemical description and safety evaluation. Several reviews have been published and the U.S. Food and Drug Administration (FDA) reviewed this class of over-the-counter (OTC) drugs beginning in 1972, which continues to the present time. The subject of this chapter is an overview of this endeavor and several recent workshops, symposia, and reviews which continue to examine the voluminous data and literature attesting to their safety in use. A draft copy of a Toxicological Profile for Aluminum was released in October 1995 by the Agency for Toxic Substances and Disease Registry; Division of Toxicology/Toxicology Information Branch, Atlanta, GA. An updated draft for public comment was recently released, and the comment period ends Feb. 17, 1998.

The profile concludes that the human toxicity potential of aluminum cannot be accurately estimated since a consistent pattern of aluminum-related toxicological effects has yet to be identified. They also conclude that aluminum may be involved in Alzheimer's disease and other neurodegenerative diseases in humans, but that the casual link between aluminum exposure and these diseases is very tenuous (1).

In 1972 the FDA published in the Federal Register a procedure for rules

making for the classification of OTC drugs as generally recognized as safe (GRAS) and/or effective (GRAE) and not misbranded under prescribed, recommended, or suggested conditions of use. The regulation established procedures for categorization of OTC drugs and appointment of advisory review panels of ''qualified experts'' to evaluate safety and efficacy and spell out regulatory definitions of safety, efficacy, benefit-to-risk ratio, combinations, and labeling.

The Antiperspirant Review Panel first convened on March 15, 1974, and had many additional meetings, the last of which was held nearly 4 years later, on Jan. 26, 1978. The review panel performed a comprehensive, thorough review with industry cooperation and participation, which culminated in the publication in the *Federal Register* of proposed (2) and tentative final (3) monographs. The final monograph has not yet been published.

II. INGREDIENT SAFETY—FDA/OTC ADVISORY PANEL REVIEW

A brief overview of the antiperspirant review is being presented to emphasize the regulatory atmosphere, which must be considered when deciding on a course of action or strategy for safety testing of an antiperspirant and/or deodorant product. Although the review panels are advisory to the FDA, there have been instances of the FDA not adopting their recommendations.

Antiperspirants are drugs that have a deodorant component in their activity. Deodorants are cosmetics. A drug is defined in Section 201 (g) (1) of the FDC Act, 21 U.S. Code (USC) 321 (g) (1) as follows:

> The term ''drug'' means . . . articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man . . . and . . . articles (other than food) intended to affect the structure of any function of the body of man . . . and . . . articles intended for use as a component of any (such) articles (4).

A cosmetic is defined in Section 201 (i) of the Federal Food Drug and Cosmetic Act (FDC Act), 21 USC 321 (i) as follows:

> The term ''cosmetic'' means (a) articles intended to be rubbed, poured, sprinkled, or sprayed on, introduced into, or otherwise applied to the human body or any part thereof for cleansing, beautifying, promoting attractiveness, or altering the appearance, and (b) articles for use as a component of any such articles; except that such term shall not include soap.

Antiperspirants are drug products that are also cosmetic products, depending on the claims made. These products, often called ''cosmetic drugs,''

are regulated by the FDA both as drugs and as cosmetics. This is particularly important in complying with labeling requirements.

The terminology ''cosmetic drug'' is also important in considering the safety testing of this product category. These products, often thought of as cosmetics (e.g., antiperspirants as well as sunscreens), are nonprescription drugs and are therefore subject to the drug monographs. They may frequently be cosmetics as well because both cosmetic and drug claims are made in labeling and advertising. If no cosmetic claims are made, these products are regulated only as drugs. It is the intended use or claim which determines whether an article is a drug; thus, foods and cosmetics may also be subject to the drug requirements of the law if health claims are made for them.

When the drug monographs are made final, they will be published in 21 CFR, Part 330 of the Code of Federal Regulations (CFR). A drug product covered by the final monograph system must conform to the conditions of the monograph, or it may not be marketed without an approved New Drug Application (NDA). Manufacturers of antiperspirant drug products should therefore follow developments in the OTC Drug Review very carefully, as they will be required to comply with these monographs as they become final.

Table 1 lists the OTC Antiperspirant Review Panel recommended Category I antiperspirant actives (3). *Aluminum chlorohydrate* has been designated as a *generic* term for the various aluminum chlorohydrate compounds reviewed by the FDA-OTC Review Panel. Since their review indicated that the various aluminum chlorohydrates were similar in properties and that the available submitted toxicity data reviewed by the panel suggested they have identical or very similar toxicities, the panel concluded that their risk potentials were the same. This conclusion was also reached for the *aluminum chlorohydrates* (2). Aluminum chloride and buffered aluminum sulfate currently have more historical interest than wide usage interest (5,6).

The FDA's ultimate purpose was to assure consumers that all OTC drugs on the market are safe, effective, and properly labeled. The review was of active ingredients. Formulated products containing the active ingredients must be tested for safety and efficacy as formulated. It is the responsibility of the manufacturer to ensure safety of the formulated product when a Category I safe and effective active ingredient is used in a formulation (7).

III. SAFETY CONSIDERATIONS

The two most likely routes by which aluminum enters the human body are ingestion and inhalation. No evidence for topical absorption has been reported.

Table 1 Category I[a] antiperspirant active ingredients

Active Ingredient	Concentration	Ratio range Al:Cl	Ratio range Al:Zr
Aluminum chlorohydrate[b]	25% or less concentration (calculated on an anhydrous basis, omitting from the calculation any buffer component present in the compound) of an aerosol and nonaerosol dosage form	2.1 down to but not including 1.9:1	
Aluminum dichlorohydrate[b]	Same as above	1.25 down to and including 0.9:1	
Aluminum sesquichlorohydrate[b]	Same as above	1.9 down to but not including 1.25:1	
Aluminum$_v$ zirconium trichlorohydrate[c]	20% or less concentration (calculted on an anhydrous basis, omitting from the calculation any buffer component present in the compound) of a nonaerosol dosage form	2.1 down to but not including 1.5:1	2.0 up to but not including 6.0:1

Aluminum$_x$ zirconium octachlorohydrate[c]	Same as above	1.5 down to and including 0.9:1	2.0 up to but not including 6.0:1
Aluminum$_x$ zirconium pentachlorohydrate[c]	Same as above	2.1 down to but not including 1.5:1	6.0 up to and including 10.0:1
Aluminum$_x$ zirconium octachlorohydrate[c]	Same as above	1.5 down to and including 0.1:1	6.0 up to and including 10.0:1
Aluminum chloride	15% of less concentration (calculated on the hexahydrate form) of an aqueous solution nonaerosol dosage form		
Aluminum sulfate buffered	8% concentration of aluminum sulfate buffered with 8% concentration of sodium aluminum lactate in a nonaerosol form		

[a] Category I, generally recognized as safe and effective; Category II, not generally recognized as safe and effective; Category III, available data are insufficient to classify as either Category I or Category II.

[b] Complexes with propylene glycol and polyethylene glycol are also Category I.

[c] Complex with glycine is also Category I.

Aluminum compounds are poorly absorbed from the gastrointestinal tract, producing insignificant increases in blood and urine levels. Therefore, it is to be expected that most or all of an orally administered dose would be eliminated in the feces. Also, aluminum inhaled and then ingested due to pulmonary mucociliary clearance and swallowing of the escalated material would be expected to be eliminated in this manner. Experiments in man indicate little danger from ingestions of quantities of aluminum 25 to 30 times those commonly present in the normal diet and environment, which is estimated to be 10 to 100 mg daily. No interference with assimilation of such food components as proteins, carbohydrates, or fats has been reported.

Little more than trace quantities of aluminum have been reported to be absorbed from the respiratory tract. The quantities of aluminum found in the lung are usually attributed to dust in the environment due to the large quantities of aluminum in the soil. Although analytical methods used for detecting trace quantities of aluminum have been criticized as being inadequate for determining the minute quantities of aluminum present in body fluids and tissues, they tend to err on the high side.

A study on human exposure determining the amount of particulate material ($\leq$ 1 μg) from aerosolized aluminum-containing antiperspirant products which may be exposed to the respiratory region during conditions of typical use was submitted to the FDA in 1975. These studies measured the amount of aluminum that reaches the breathing zone; the studies do *not* measure the amount of the ingredient that is absorbed (an amount which is significantly less).

To determine the quantity of aluminum exposed to the nasal or breathing area of man, several experiments were performed and submitted to the Antiperspirant Review Panel in 1974. Determination of (a) the time of spraying and (b) the distance the can is held from the axilla, were used to estimate the quantity of aluminum reaching the breathing area during the use of an aluminum-containing aerosolized antiperspirant. Subjects were instructed to use the product as they would normally in their homes. Data obtained indicate a mean spray time of 1.9 sec and a distance of 5.90 in. from the axilla with 95% confidence limits of 0.78 to 4.65 sec. and 3.25 to 10.75 in. respectively.

To measure the amount of aluminum that would reach the nasal-mouth area where it *might* be inhaled, a mannequin simulated the consumer normal-use position for the product in a small bathroom. The mannequin was placed in a static 6000-L chamber with the aerosol can mounted in fixed positions 6 and 12 in. from the axilla so that the spray could be directed perpendicular to the axilla or at an angle of 10° toward the front of the mannequin. Duration of spray was 2 or 8 sec, simulating the extremes of normal spray time. A

Table 2 Aluminum Deposited in the Facial Area During Laboratory Use of an Aerosol Antiperspirant

Condition of exposure	μg Al/day/in.^{2}	95% confidence limit
Spray nozzle 3'' from axilla face looking forward	0.54	0.39–0.75
Spray nozzle 3'' from axilla face looking forward	0.84	0.58–1.14
Spray nozzle 12'' from axilla face looking forward	1.01	0.72–1.40
Spray nozzle 12'' from axilla face looking toward axilla	2.73	1.96–3.81

respirator device containing a Millipore filter was placed in front of the nasal-mouth area of the mannequin to collect particulate matter reaching this area. The respirator device was attached to a respirator pump which simulated the breathing pattern of a normal resting man at a rate of 12 respirations/min and a tidal volume of approximately 750 mL. Only inhalations were drawn through the filter. Filters were assayed by emission spectroscopy for aluminum. Results indicated no accumulations of aluminum (aluminum was not detected on the filters in quantities any larger than normal background levels, although there was a high probability (95%) of detecting a mean difference between sprayed filters and controls of 7 μg or greater). To assure that the respiratory device was functional, the aluminum-containing antiperspirant was sprayed directly into the face of the mannequin at a distance of 12 in. Results indicate 300 μg (or more) of aluminum on the filter.

Carter-Wallace, Inc., has measured the quantity of aerosolized aluminum-containing products striking the nasal-mouth area in a human-use experiment with 16 human volunteers. Wearing surgical masks to cover nose and mouth areas, the volunteers sprayed an aluminum-containing antiperspirant (3.5% aluminum chlorohydrate) into each axilla for 2 sec daily during 5-day test while breathing normally. Four spray conditions (simulating variable human usage conditions) were evaluated (Table 2). The quantities indicated in Table 2 are of aluminum in μg/in.^{2}/day striking the nose and mouth area (a 1-in.^{2} area corresponds to the approximate area of the filter used in the mannequin respiratory device previously described, and also corresponds reasonably closely to the nasal breathing zone area).

In an attempt to estimate the amounts of aluminum reaching the nasal-mouth area under normal-use conditions in the home, 400 (male and female)

subjects used an aerosolized aluminum-containing antiperspirant one time at home, in the location and manner in which they normally applied an aerosol antiperspirant. They were instructed to wear the paper face mask previously described during the application. The face masks were collected and the aluminum content assayed by emission spectroscopy. Statistical analysis of the data was accomplished. Means and tolerance limits are presented in Table 3. The meaning of the tolerance limits is that 90% of the population has a probability of 0.95 of being within the interval. Again, the aluminum level is expressed as μg/in.^{2}/use.

These experiments, and those described earlier, clearly indicate that the data collected both in the laboratory and in the home under "use" conditions are of the same magnitude in their estimate of the amount of aluminum-containing antiperspirant reaching the breathing zone. Measurements are complicated by the fact that the masks used contain an aluminum background which was *not* subtracted from the data. The mean background for the masks was 0.232 μg of aluminum per square inch, with tolerance limits ranging from 0.135 to 0.80 μg/in.^{2}. It is evident that the values sprayed on the mask by aluminum-containing antiperspirant are extremely low, as they are in the mannequin study. These values are on the order of 1 μg or less in the breathing zone (1 in.^{2}) as compared to a total of dispensed amount of aluminum.

This study, performed in 1975, was on aerosolized formulations sold at that time. Current formulations would deliver considerably less due to the increased particle size of currently supplied aluminum-containing antiperspirant salts (31).

Tipton and co-workers (5), in a series of papers about trace elements in human tissues, reported on the use of emission spectroscopy to measure the concentration and distribution of trace elements, including aluminum. Data were reported for a population of about 250 normal adult cadavers, carefully collected and sampled. A normal cadaver was defined as an individual who

Table 3 Aluminum Deposited in the Facial Area During Aerosol Antiperspirant Home Use (μg Al/use/in.^{2})

		Tolerance limits	
Subjects	*Mean*	*Lower*	*Upper*
Male (n = 199)	0.314	0.161	21.4
Female (n = 201)	0.311	0.157	29.3
Combined (n = 400)	0.314	0.161	18.9
Control (n = 49)	0.232	0.135	0.807

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lung burdens in animals were developed by the Lovelace Inhalation Toxicology Research Institute for the Food and Drug Administration and the Consumer Product Safety Commission. Additional data were developed in the chronic inhalation toxicity study of particulate aluminum chlorohydrate conducted by Becton-Dickinson for the National Institute of Environmental Health Services (NIEHS) (11,12).

The Lovelace Institute studies determined the deposition characteristics and clearance rates for insoluble particulate materials in several mammalian species. These data were incorporated into a computer simulation model which linked the exposure environment, dose to target organ, and biological parameters for a given species. Compartments in the simulation model were designed to correspond to anatomical units, particularly those of the lung, so that deposition characteristics of particles and clearance kinetics following deposition could be determined. The expected consumer exposure to various aerosolized products, including antiperspirants, under simulated human use conditions was also determined. The estimated human lung burden resulting from exposure to aluminum chlorohydrate was 0.6 μg Al/g lung. The simulation model was capable of relating the lung burden of aluminum chlorohydrate achieved in an animal to that estimated to be reached in humans. Furthermore, the model could calculate conditions for experimental exposure which would result in lung burdens in animals 100 times or more than the predicted human lung burdens resulting from typical antiperspirant use (13–15).

In addition to the Lovelace Institute study on aluminum chlorohydrate, a chronic toxicity study on aluminum chlorohydrate was conducted by Becton-Dickinson for NIEHS (16,17). The study employed a more conventional inhalation exposure regimen based on daily exposures of 6 hours per day, 5 days per week for 2 years at three concentration levels—0.25, 2.5, and 25 mg/m^3.

In summary, it may be concluded that the lesions examined in aluminum chlorohydrate–exposed animals are similar to those of foreign body reactions. These are considered to be the response of the normal lung defense mechanisms to inert particulate inhalation. The FDA-OTC Review Panel and the FDA have agreed with this conclusion and classified aluminum chlorohydrate as safe for use in aerosol-formulated products.

Granulomatous lesions have been observed following topical use of the salt sodium zirconium lactate. Granulomatous lesions have been observed in rabbits with this salt. Inhalation exposure in animals has been studied extensively and reviewed by several authors (21,22). The zirconium-containing deodorant sticks recognized as inducing a granulomatous response in the axillae of humans contained the salt sodium zirconium lactate. The zirconium-containing salts, which were declared ''new drugs'' or ''adulterated cosmetic''

products by the FDA in 1977, were aluminum/zirconium complexes and not sodium zirconium lactate, as used in the earlier sticks which produced the axillary granulomas. The aluminum-zirconium complexes have not been shown to induce this response in the axillae (23,24).

Over-the-counter aerosol drug products containing zirconium salts were not considered to be generally recognized as safe (GRAS) antiperspirant drug products because of lack of toxicological data adequate to establish a safe level for human use. It was recognized that certain zirconium compounds have caused human skin granulomas and toxic effects in the lungs and other organs of experimental animals, which led to concern that some zirconium salts, when used as an aerosol, would reach the deep portions of the lungs. Unlike the skin, the lung will not reveal the presence of granulomatous changes until they become advanced and possibly permanent. Adequate evidence could not be presented that zirconium-containing aerosol antiperspirants would not produce hidden lung disease in some users. The FDA issued regulations declaring that aerosol drugs or cosmetic products containing zirconium are new drugs requiring a New Drug Application (21). No NDA has been approved for marketing such a product. No reports of a granulomatous response with *topical use* of the approved aluminum/zirconium salts has been reported.

The various categories of salts—those containing only aluminum salts, those containing only zirconium salts, and those containing both aluminum and zirconium—vary considerably in their chemistry and physical properties. However, the review panel concluded that the skin is relatively impermeable to metallic salts and complexes, and that there was no evidence to suggest that the direct application of antiperspirants to intact skin has been associated with systemic toxic effects (3). Although not in the published literature, the percutaneous dermal toxicity test in animals has been performed for many antiperspirant formulations without reported ill effects (26).

Although antiperspirant ingredients have been associated with, or blamed by some users for, induction of papular or follicular eruptions in the axillae, the OTC review panel observed that the antiperspirant ingredients are not implicated in standard dermatologic texts (3). In current medical thought, these papular or follicular eruptions indigenous to the axillae, e.g., hidradenitis suppurative, Fox-Fordyce disease, and seborrheic dermatitis, are not believed to be caused by antiperspirants.

IV. UNSUBSTANTIATED SAFETY CHALLENGES

The association of aluminum with Alzheimer's disease stems primarily from the findings that aluminum accumulates throughout life in body tissues, includ-

ing brain tissue, in all individuals. Aluminum is ubiquitous. Life on earth developed in a sea of aluminum. Aluminum is the third most abundant chemical element on earth, constituting nearly 8% of the mass of the earth's crust. Air, water, and almost all foods contain measurable amounts of aluminum. It is impossible to avoid exposure to aluminum. Dietary aluminum represents the greatest source of daily exposure. Water and air are minor contributing factors (7,19,20).

In a recent publication on Alzheimer's disease by Pendlebury and Solomon at a CIBA Clinical Symposium (27), the authors summarize aluminum toxicity as follows:

> **Aluminum toxicity**. Instillation of aluminum into the brains of rabbits, cats, and ferrets causes pathologic lesions that resemble the neurofibrillary tangles of Alzheimer disease [AD]. Although molecular studies have confirmed that the aluminum-induced neurofibrillary tangles are composed of aggregates of neuronal neurofilaments, and not hyperphosphorylated tau, recent evidence suggests that aluminum may be a cofactor in processes leading to aberrant tau phosphorylation. Epidemicologic evidence linking aluminum to high-incident foci of dementia in Guam and the Kii peninsula of Japan has been conflicting. At present, aluminum does not appear to play a major etiopathogenic role in AD, and there is no reason to tell people to avoid minor aluminum exposure (deodorants, antacids, aluminum cooking utensils).

In a recent Journal of Toxicology and Environmental Health (28) guest editors Robert A. Yokel and Mori S. Golub report on conclusions from a workshop on research issues in aluminum toxicity with several comments and reviews of the conference issues. They referred to these as themes. The first theme was ''value of cooperation, collaboration, and cross-fertilization among disciplines involved in aluminum research.'' A second theme was the ''growing recognition of aluminum as a systemic toxicant.'' The final theme was the ''promise and problems associated with new methodological developments in the area, such as the use of the Aluminum-26 isotope with accelerator mass spectrometry, the development of microprobe analysis, and the new information on the genetic basis of Alzheimer's disease.'' We should be seeing progress in these areas. In the recently published ''Aluminum in Infants' Health and Nutrition'' edited by P. Zattu and A. C. Alfrey (World Scientific, Singapore, London; January 1998) is a discussion of Aluminum-26 as a biological tracer using accelerator mass spectrometry, by R. Flock and E. Elmore. The scarcity of knowledge on the metabolism of aluminum in the body at physiological levels or the mechanisms by which it can be toxic has been due to the

fact that there is no very sensitive assay for aluminum in very low quantities. Aluminum-26 is the only isotope of aluminum, which is useful for trace work. Aluminum-26 cannot be measured with standard counting techniques. The mid-1980s' development of a new technique, accelerator mass spectrometry (AMS), which was developed to measure rare long-lived radioisotopes such as aluminum-26, should in the near future shed more light on these phenomena. The Department of Physics, Purdue University (West Lafayette, IN) is working in this field. Interesting and exciting data should be forthcoming.

The Cosmetic Toiletries and Fragrance Association (CTFA), in 1993, filed comments with the FDA in response to two citizens' petitions (29) which questioned the use of aluminum and aluminum/zirconium salts in antiperspirant products. After reviewing these two petitions the organization concluded as follows:

1. There are currently in existence sufficient safety data demonstrating that aluminum-containing and aluminum/zirconium-containing OTC antiperspirants are safe, and that they should remain in Category I. No new testing and no additional data are needed to demonstrate the safety of the ingredients.
2. The FDA's Advisory Panel on Antiperspirants conducted a lengthy review of the safety of aluminum and aluminum/zirconium antiperspirants, which included review of numerous acute and subchronic studies. The panel concluded that the ingredients are safe and effective for use by consumers.
3. FDA itself, in its Tentative Final Monograph (TFM) on antiperspirants, reviewed those studies as well as additional long-term inhalation studies, and likewise concluded that the ingredients are safe for OTC use by consumers.
4. After an extensive review similar to that conducted by FDA, other regulatory agencies have also concluded that aluminum- and aluminum/zirconium-containing antiperspirants are safe. Specifically, subsequent to FDA's 1982 TFM, the European Community's Scientific Committee on Cosmetology (SCC) reviewed numerous safety studies on aluminum/zirconium-containing antiperspirants and found the products to be safe.
5. Despite the allegations made in two citizen petitions filed with FDA, there have been no new data that call into question the determinations of safety made by the FDA panel and by FDA itself. Consequently, there is no need for additional data demonstrating the safety of the ingredients.
6. Aluminum is the third most abundant chemical element on earth, and persons are exposed to aluminum in a variety of forms on a daily basis. The level of exposure to aluminum from antiperspirants is small in comparison to the level of exposure from all other sources combined. Furthermore, the level of *exposure* is not of critical importance, from a human safety or public

health standpoint, because the amount of aluminum potentially *absorbed* from antiperspirants (either dermally, by inhalation, or via the olfactory pathway) is even smaller—indeed, negligible.

7. The two citizen petitions advance a number of speculative theories linking exposure to aluminum and Alzheimer's disease have been advanced. There is no convincing evidence that aluminum plays a causative role in Alzheimer's disease.

8. Neurointoxication has occurred only rarely as an industrial disease or as a result of high concentrations of aluminum in fluids used in kidney dialysis. The number of such cases has dwindled worldwide as aluminum has been excluded from dialyzing fluids.

9. Current labeling requirements for aluminum-containing antiperspirant products are adequate. The current label warning requirement—''Avoid excessive inhalation''—has been more than adequate during 20 years of safe market history.

10. The CTFA in summary concludes that ''sufficient safety data [are] in existence to demonstrate that aluminum-containing and aluminum zirconium-containing OTC antiperspirants should remain in Category I (safe and effective). No additional data and no new testing are necessary'' (18).

V. SAFETY TESTING

The CTFA Safety Testing Guidelines is a set of guidelines for antiperspirant/deodorant safety testing. They are available from the CTFA (Suite 800, 1110 Vermont Ave., N.W., Washington, DC 20005). These guidelines were issued on an updated version in 1991. These guidelines address specific topics:

1. Safety substantiation
2. Evaluation of primary skin irritation potential
3. Evaluation of eye irritation potential
4. Evaluation of contact sensitization potential
5. Evaluation of photosensitization potential
6. Evaluation of mucous membrane irritation potential
7. Evaluation of percutaneous toxicity potential
8. Evaluation of oral toxicity potential
9. Evaluation of inhalation toxicity potential
10. Controlled (human) use studies

Note that not all these topics are applicable to all formulated antiperspirant products. A competent toxicologist or an experienced scientific person should be consulted.

These guidelines were prepared by the CTFA Pharmacology/Toxicology Committee in response to industry requests to provide manufacturers of cosmetic, toiletry, and fragrance products with guidance regarding the use of animal and human testing as a means of substantiating the safety of finished products. Safety substantiation is a complex process requiring sound professional judgment in the evaluation of the relevant safety data and information.

No guidelines should be looked at as providing protocols for the conduct of a study, nor should they be looked at as the last definitive word in providing the data and information required for safety substantiation. They are also not intended to be construed as an established minimum of testing for the final marketed product. Rather, the guidelines are intended to identify representative animal and human tests which are useful for substantiating the safety of products, and to guide in the selection and design of appropriate safety testing protocols.

A protocol is prepared in response to a specific objective. A guideline serves only as an outline or framework from which a protocol can be derived. It is the proper conduct of the protocol's objective that establishes a safety document on which acceptable risk evaluation can be accomplished.

The pharmacological principle of dose should be kept in mind when designing a study and preparing a protocol. A demonstration of a dose-response relationship for a toxic effect establishes a better rationale for modification or, for that matter, documentation of an effect.

Some of the tests described in the CTFA guidelines would be inappropriate for particular product categories, and the applicability of a particular test would depend on such factors as the nature and frequency of use of the product, site of application, and nature of ingredients. There may also exist variations of the tests or other relevant and meaningful tests which would be acceptable for judging particular aspects of product safety.

The monographs (proposed and tentative final) address only the safety and efficacy aspects of the *active* ingredients. Since it is the formulated product that will be placed in the marketplace, additional safety studies will be required before a formulated product can be assumed to have sufficient safety and acceptable risk to which consumers can be exposed. It is therefore recommended that safety evaluations be conducted to ensure safety with regard to the potential for irritation and possible contact allergic reaction.

Some of the tests described in the CTFA guidelines would be inappropriate for particular product categories, and the applicability of a particular test would depend on such factors as the nature and frequency of use of the product, site of application, and nature of ingredients. There may also exist variations of the tests or other relevant and meaningful tests which would be acceptable for judging particular aspects of product safety.

Interpretation of guidelines for the safety testing of an antiperspirant/deodorant cosmetic drug is a matter of some variability, with some requiring the bare minimum of safety testing and others requiring extensive data in excess of the studies necessary for an assurance of safety. While this is partially a reflection of preferential priorities and is not directly related to meeting guideline requirements, it does appear that more consideration could be given to more practical use of limited toxicological resources. This could lead to more intelligent use of fewer studies rather than a shotgun approach to safety testing.

The ultimate goal of the safety evaluation is an assurance that a formulation (product) is safe for the expected, recommended, and/or customary conditions of use, as well as under reasonably expected conditions of misuse. Note that not all of these guidelines are applicable to all formulated antiperspirant/deodorant products.

Updated medical literature searches and developments in safety and toxicological evaluation techniques should be followed in order to keep a product in the marketplace under the best of safety assessment know-how. The complaint file can be an excellent and reliable indicator of problems in the marketplace. Additional safety testing and follow-up are ongoing necessities.

VI. SUMMARY

In the book ''Of Acceptable Risk—Science and the Determination of Safety'' prepared by W. W. Lawrence his association with the Committee on Science and Public Policy, National Academy of Sciences, as an Alfred P. Sloan Foundation Resident Fellow in 1973, Dr. Lawrence (30) summarizes well the appropriate and necessary nature of safety evaluation. He states that ''peeled back to their essential nature, all of the many questions about hazards...divide into four lines of investigation.'' In assessing risk, measurements are made in order to:

1. Identify conditions of exposure
2. Identify the adverse effects

3. Relate exposure with effect
4. Estimate overall risk

Answers to these key lines of investigation will ensure marketing of safe products or better products with an *acceptable risk*.

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8

A Guide to Understanding Antiperspirant Formulations

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I. INTRODUCTION

The antiperspirant and deodorant market offers a wider diversity of products than any other section of the personal care industry, with products available on most supermarket shelves around the world. Deodorants are defined as products which reduce axillary malodor, whereas antiperspirants offer both deodorancy and protection against underarm wetness. In the United States the Food and Drug Administration (FDA) further requires that antiperspirants provide at least 20% sweat weight reduction in a standard hot-room test. Given the wide variety of products available, to a newcomer the market seems complex. However, an understanding of the market can be gained from a study of its primary driving forces, namely, the needs of the consumer (which are similar around the world) and the unique feature of this market that the packaging also often forms the product applicator.

First and foremost in the hierarchy of consumer needs is long-lasting control of odor and wetness. Consumers also want their antiperspirants and deodorants to have excellent sensory properties on application and in use, since they use these products daily. Depending on the characteristics of a particular market segment, consumers may prefer products that are smooth on application and feel warm, or which are fresh and quick-drying. Once the product is applied it is often judged by its tactile feel on the skin and its level of deposits, again with acceptability differing by market segment. Also, after

application, the consumer would ideally prefer to be unaware of the product, with the exception of fragrance, which is almost a universal feature of antiperspirant and deodorant products and provides an important cue to long-lasting efficacy. Increasingly, consumers need reassurance that products will not irritate or harm the skin; this need has led to a growing number of ''skin-friendly'' products in some parts of the world.

Individual antiperspirant and deodorant markets around the world are influenced by a number of other important factors including history, economics, the environment, safety, and legislation. For example, where it was historically common practice to apply alcoholic colognes to mask odor, the deodorant market is still dominated by alcoholic deodorants with fresh sensory properties. Here the primary consumer benefit is a combination of odor prevention and fragrance.

Environmentally friendly products are becoming increasingly popular, although the consumer cannot be expected to compromise product performance for environmentally friendly deodorants and antiperspirants. Chlorofluorocarbons (CFCs) were once used widely as aerosol propellants, until the discovery that their accumulation leads to depletion of the ozone layer. Since then they have been replaced worldwide by hydrocarbon and dimethyl ether (DME) alternatives. The CFC environmental issue affected individual markets very differently. Within Europe aerosol formats declined most in the ''greener'' German and Scandinavian markets. In the United States, aerosol antiperspirants were affected simultaneously by CFCs and a safety issue, which led to a ban on the use of zirconium antiperspirant actives in aerosols (1). Today antiperspirant and deodorant sticks dominate the United States market whereas sales of aerosols account for around only 20% of the market. Although the CFC issue had a negative impact on aerosol products for several years, sales of aerosols are now growing or have become stable in many markets around the world (2).

Developments in technology have also made an impact on antiperspirant and deodorant products (3). Since the launch of the first deodorant, Mum, in the late 19th century, followed by the first antiperspirant, Arrid, in the 1930s, there have been four major technology developments:

1. Introduction of aluminum chlorohydrate in 1947 (4), which provided a less acidic antiperspirant active offering better compatibility with skin and clothes
2. Launch of the first roll-on applicator in 1952 (5) (an example of successful technology transfer following the invention of the ballpoint pen)
3. Introduction of the first deodorant aerosol in the 1950s (another ex-

ample of technology transfer from the insecticide sprays developed for the military during World War II); this was followed by the introduction of the first antiperspirant aerosol in the 1960s (6)

4. Development of volatile silicones in the 1970s (7,8), which allowed the formulation of a new generation of "dry" products with high efficacy, excellent sensory properties, and low staining potential

As well as these major technological developments a wide range of other applicators have also been developed including pump sprays, squeeze sprays, sticks, creams, and gels. Often the first new applicator introduced is the one that dominates the market and shapes future developments. This may help to explain why the use of roll-on applicators is widespread in Southeast Asia and stick applicators are popular in countries such as Chile. The differing frequency of usage of applicators around the world is shown in Figure 1.

Aerosols are popular to varying degrees around the world, probably because they are convenient, are easy to use, and deliver excellent performance with the hygienic benefits of a spray. Fragranced all-over bodysprays are particularly popular with younger consumers. In some markets mechanical pump sprays and low-cost squeeze sprays are popular for dispensing alcoholic deodorants; however, the sprays formed have larger droplets, feel wetter on application, and take longer to dry than aerosol sprays because of the reliance on the mechanical delivery of the spray. Aerosol alternative spray formats have so far proven nonviable for suspension antiperspirants because of the unacceptable levels of blockage encountered.

Globally, roll-on and stick applicators are also widely used. Roll-on applicators are able to dispense a wide range of formulations but can suffer from ball-jamming, and some formulations are slow to dry. Roll-ons also tend to be less popular with men because the applicator can trap underarm hair. Stick applicators have become the most popular format in the United States antiperspirant market due to their high efficacy and good application properties. However, unsightly visible deposits can be a problem, and a new class of low-deposit stick applicators have emerged in recent years to combat this problem. Several new and increasingly sophisticated applicators have been developed which dispense new antiperspirant formulations such as gels and soft solids.

A key challenge for manufacturers of antiperspirants and deodorants is to ensure the synergistic combination of a good product with a popular applicator. This challenge has resulted in a wide variety of formulation types: simple solutions which can be contained in and dispensed from aerosols or roll-ons; emulsions which are used in pump sprays, roll-ons, and creams; and nonaqueous suspensions which are used in all formats except pump sprays (9).

The universal feature of the antiperspirant and deodorant market is that

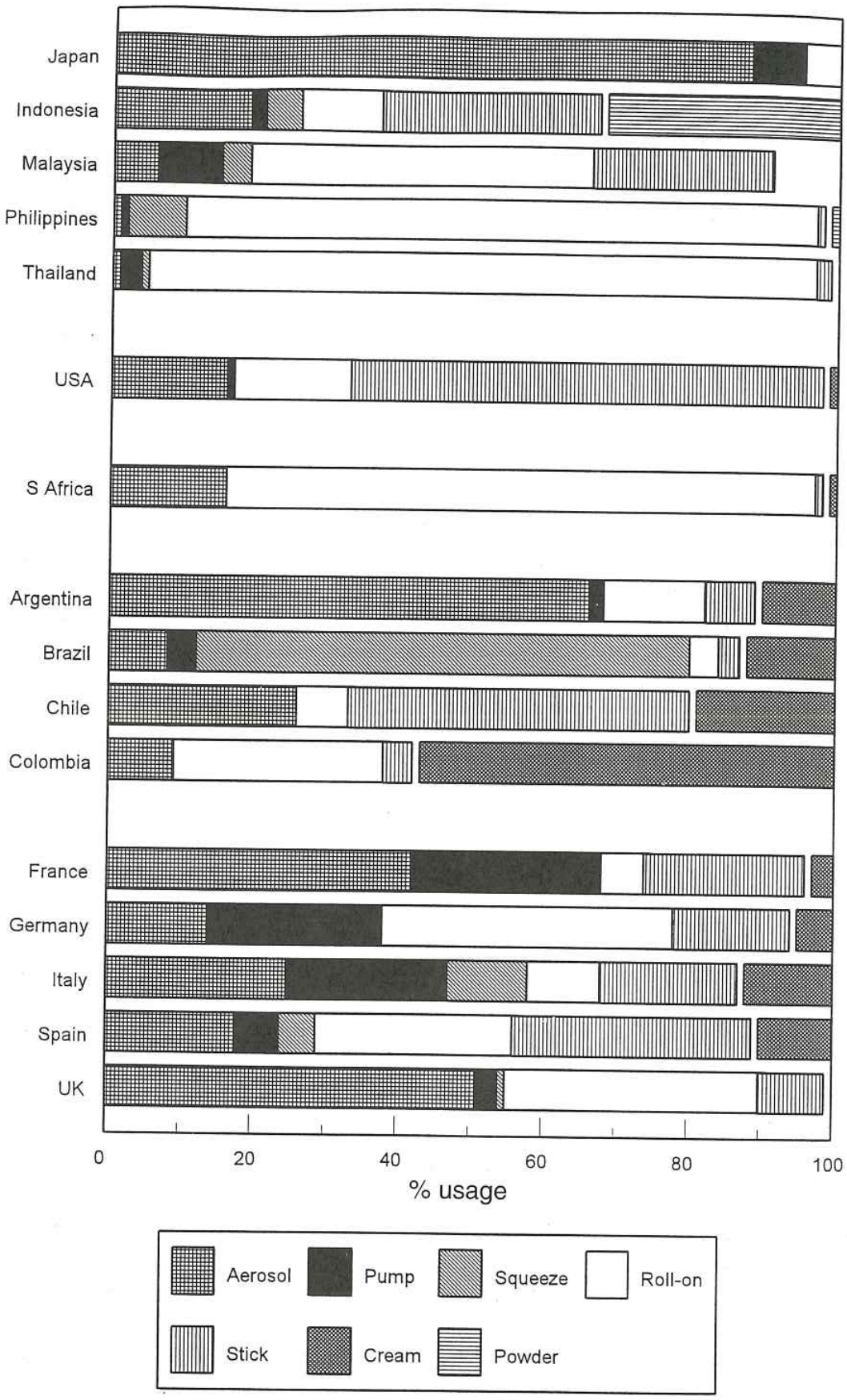


Figure 1 Applicator usage by country.

products must offer the consumer value for money. The highly competitive nature of the market has tended to keep prices low, so control of formulation and packaging costs for the manufacturer is essential. Thus, the formulation scientist must satisfy consumer needs and ensure a high level of compatibility with the chosen applicator at minimum cost.

II. BUILDING BLOCKS OF FORMULATIONS

The physical forms of antiperspirants vary greatly, in part due to the variety of different applicators employed. Given this wide range of forms, from free-flowing liquids to waxy solids, one might expect a survey of formulation technology to be lengthy and complex. However, by studying the constituents of the formulations of almost all antiperspirants, it is possible to identify a common set of building blocks which, when processed appropriately, give rise to each formulation type. The essential building blocks of antiperspirants are:

1. Active ingredients
2. Carrier fluids and aerosol propellants
3. Structurants and emulsifiers
4. Sensory modifiers
5. Fragrances

Active ingredients are materials such as antiperspirant salts which give the products the essential functionality for which the consumer ultimately purchases the product. Active ingredients need to be delivered to the axilla, and therefore are dissolved or suspended in a carrier fluid which usually evaporates from the skin after application of the product. In the case of aerosols a propellant delivers the carrier fluid and active ingredients. A structurant or emulsifier is used to modify the physical characteristics of the carrier fluid, making it compatible with the chosen applicator. Structuring could take the form of a modest increase in viscosity in the case of roll-on applicators, or the formation of a solid matrix for stick applicators. Systems formulated in this way can be relatively unrefined, and thus sensory modifiers are used to improve the skin feel or visual appearance of the product both on application and during wear. Finally, antiperspirants are usually fragranced, although a significant sector exists for unscented products in countries such as the United States. Fragrance plays an essential part in reassuring the user that the product is continuing to function throughout the day.

Ingredients of formulations often have more than one function. Indeed, one of the skills of the formulator is selecting ingredients which perform sev-

eral functions, thus maximizing consumer benefit in the most cost-efficient manner. For example, ethanol is an effective carrier for fragrances and other lipophilic ingredients as well as being quick-drying and an effective deodorant ingredient.

A. Antiperspirant Active Ingredients

There are a number of antiperspirant actives with varying efficacy used to a greater or lesser extent in different formulations (Table 1). The first antiperspirant active, marketed in 1902, was aluminum chloride. To this day aluminum chloride remains the most effective antiperspirant active available (3); however, it is very acidic and thus difficult to formulate, it can cause severe damage to fabrics, and it can irritate the skin. For these reasons, the sulfate salt of aluminum replaced the chloride for a time, although it is less effective. Today aluminum chloride is only used in prescription products for treatment of conditions such as hyperhydrosis. It is not recommended for the formulation of cosmetic antiperspirants.

A major breakthrough in the formulation of antiperspirants came with the introduction of aluminum chlorohydrate, which is significantly less acidic than aluminum chloride (4). This active ingredient is less effective than the chloride salt; however, in practice the loss of efficacy is outweighed by a reduced tendency to damage fabrics and lower skin irritancy, and its relative ease of use in formulations.

Aluminum chlorohydrate is commercially available in a wide range of physical forms including aqueous solutions, which are used in pump sprays, and roll-ons and powders, which are used in aerosols and sticks. For aerosol

Table 1 Antiperspirant Actives

Aluminum chloride
Aluminum sulfate
Aluminum chlorohydrate
''Activated'' aluminum chlorohydrate (AACH)
Aluminum sesquichlorohydrate
Sodium aluminum chlorhydroxy lactate
Aluminum/zirconium tetrachlorohydrex gly (ZAG)
''Activated'' aluminum/zirconium tetrachlorohydrex gly (AZAG)
Aluminum/zirconium tetrachlorohydrate
Aluminum chlorohydrex PG
Aluminum chlorohydrex PEG

applications, in order to prevent valve blockage and to minimize the potentially inhalable fraction below 10 μm, powders with controlled particle size distribution are required. In the United States, the FDA specifies that the inhalable fraction must comprise less than 10% of the total. In contrast, superfine aluminum chlorohydrate powders, where the majority of the particles are smaller than 20 μm, are used in medium-efficacy, low-cost antiperspirant sticks.

So-called ''activated'' aluminum chlorohydrate powders are also widely used and can give up to 50% greater antiperspirant efficacy than the equivalent nonactivated salt. Aluminum chlorohydrate consists of a broad distribution of polymeric species. In dilute solution activation is achieved by thermal aging, which changes the polymer distribution in favor of more active species (10). Subsequent spray-drying ''locks in'' the increased efficacy (10). Activated aluminum chlorohydrate (AACH) loses its efficacy advantage when in solution and therefore is only suitable for use in high-efficacy suspension aerosols or other nonaqueous formulations.

Aluminum sesquichlorohydrate has a lower basicity than the chlorohydrate, and is also available in conventional and activated forms. In its nonactivated form it is useful in the formulation of products based on solutions, due to its solubility in aqueous ethanol, which is often the carrier fluid. Aluminum sesquichlorohydrate is sometimes claimed to have superior efficacy to aluminum chlorohydrate, but the evidence for this is equivocal.

Sodium aluminum chlorhydroxy lactate was first used in sodium stearate–based sticks in the 1950s due to its increased compatibility with soaps. However, its antiperspirant efficacy is low and it is not widely used today.

Aluminum/zirconium salts were developed in the 1970s and give superior efficacy to aluminum chlorohydrate and approximately equivalent efficacy to AACH. Their use in spray products was prohibited in the late 1970s because of fears of toxicity on inhalation, but they remain the active ingredient of choice for high-efficacy antiperspirant sticks, roll-ons, and creams. The simplest aluminum/zirconium salts are the aluminum/zirconium chlorohydrates (ZACH), which are available as powders or aqueous solutions. In solution they are well suited to the formulation of aqueous alcoholic roll-ons. Although these products give relatively high levels of efficacy, they can sting on application, and give rise to color instability if dyes are used to color the solutions. High concentrations of ZACH in solution are also subject to polymerization, resulting in loss of efficacy and an associated increase in viscosity.

Aluminum/zirconium salts can be complexed with several compounds, the most common being aluminum/zirconium chlorohydrex gly (ZAG), which is buffered with glycine to increase pH and improve stability. ZAG and acti-

vated ZAG (AZAG) are available as powders for use in high-efficacy suspension formulations (sticks, roll-ons, and creams). A variety of particle sizes, ranging from ''superultrafine'' to the recently introduced, so-called macrospherical, convey different properties to formulations. Superultrafine grades are widely used in the formulation of suspension sticks as they disperse easily in the formulation during processing and tend not to sediment as the sticks cool. More recently macrospherical actives have been promoted for use in low-residue sticks. Their smooth surface and low surface area:volume ratio, combined with careful control of the refractive index of the rest of the stick matrix, can significantly reduce visible deposits on the skin. If macrospherical actives are used, additional structuring, for example, by the use of colloidal silica, is usually needed in the molten stick matrix to prevent sedimentation.

Aluminum/zirconium-based actives are also available complexed with other agents such as propylene glycol, which improve their solubility in glycol carrier solvents. These complexed actives have recently been used in the formulation of clear antiperspirant sticks which require the active to be dissolved completely in an appropriate carrier fluid (e.g., propylene glycol).

Antiperspirant actives tend to react with other components in formulations due to their acid pH and their tendency to catalyze degradation reactions. Since formulations must meet appropriate standards of stability, particularly with respect to fragrance, special stability modifications of the fragrance may be required. It is also important to ensure that antiperspirant actives contain only low levels of trace metals such as iron, which can cause instability and color formation.

Antiperspirant actives are potentially corrosive to both tin-plate and aluminum aerosol cans and valve components. This is a particular problem with solutions of aluminum chlorohydrate in ethanol or aqueous ethanol. Aerosol antiperspirants containing solutions of aluminum chlorohydrate in aqueous ethanol are therefore not usually marketed. A detailed discussion of the chemistry of antiperspirant actives is given in Chapters 4 and 5 of this volume.

B. Carrier Fluids

Carrier fluids (Table 2) act as solvents or carriers for ingredients in the formulation such as fragrances and antiperspirant actives facilitating delivery of these materials to the axilla. Water was the first carrier fluid to be used in a commercial deodorant and to this day remains the lowest-cost ingredient available to the formulator. Although water is an excellent solvent for antiperspirant actives, it is a poor solvent for lipophilic ingredients such as fragrances, and

Table 2. Carrier Fluids

Water
Ethanol[a]
Cyclomethicone[a]
Isopropyl myristate
Isopropyl palmitate
Propylene glycol[a]
Butylene glycol
Dipropylene glycol[a]

[a]Ingredients with multiple functions.

it feels wet on the skin and is slow to dry. Thus, mixtures of water and ethanol rapidly replaced water as the sole carrier, with the advantage of improved solvency for lipophilic ingredients as well as giving a drier feeling on the skin. Ethanol/water mixtures are used as carrier fluids in antiperspirant roll-ons and pump sprays, and, depending on the ethanol content, it may be necessary to use a solubilizer to dissolve lipophilic ingredients. In the United States ethanol is now classed as a volatile organic compound (VOC) (11), and its use as a carrier fluid is now limited.

Another class of carrier fluids that has revolutionized the formulation of antiperspirants are the cyclomethicones or volatile silicones (7,8). Volatile silicones were first used as carrier fluids in antiperspirant aerosols, but were quickly adopted as the preferred carrier fluid for the formulation of suspension sticks and roll-ons. These fluids, as their name implies, are volatile and yet have a low latent heat of evaporation, leaving the skin feeling warm. Their low surface tension means they spread easily, giving a silky smooth feeling. They are relatively inert when in contact with other components in formulations, they act as good solvents and effective delivery vehicles for active agents and fragrances, and they have a reduced tendency to stain fabrics. Antiperspirant actives are insoluble in volatile silicones, but by using appropriate structuring agents, very effective suspension formulations can be produced. Volatile silicones have to a great extent replaced esters, such as isopropyl myristate and palmitate, as the carrier of choice in suspension formulations. In spite of the advantages of cyclomethicones, they are relatively expensive materials, and isopropyl myristate is still used in low-cost suspension formulations.

Propylene glycol and related glycols are also used as carriers in the formulation of antiperspirants. More recently propylene glycol has been used in transparent antiperspirant sticks (12); however, it tends to be sticky on appli-

cation and, in combination with solubilized antiperspirant actives, the resulting clear sticks can be very tacky. A careful choice of cosolvents and emollients may overcome this drawback.

C. Aerosol Propellants

Antiperspirant aerosols require a liquifiable propellant gas (Table 3) to pressurize the container, dispense the product, and provide additional breakup of the spray droplets through volatilization. Hydrocarbon propellants are typically mixtures of propane, butane, and isobutane and they are usually specified by pressure, so the precise composition of the mixture may vary. Different grades of hydrocarbon propellant are available for use in cosmetic aerosols. These are low in contaminants, such as thiols, which have an unacceptable odor. If it is necessary to lower the overall propellant pressure, pentane can be added to the formulation. However, difficulties related to filling and odor are associated with its use.

Hydrocarbon propellants, which replaced the CFCs, have a much lower liquid density, and therefore suspended solid particles of antiperspirant actives are more likely to sediment (see the following section on structurants). An alternative to hydrocarbon mixture propellants is dimethyl ether (DME), a pure compound. This has similar benefits to hydrocarbons, but it is more miscibile in water and it has a lower odor. As with hydrocarbons, DME is flammable and in this respect presents similar challenges to the formulator. The major disadvantage of DME is its cost relative to other propellants, and it is mainly this factor that has inhibited its wider use as an aerosol propellant for antiperspirants.

Hydrocarbons and DME are both classed as VOCs, so restrictions on their use in a number of countries are increasing (11). Non-VOC propellants, such as hydrofluorocarbons (HFCs), which were developed primarily as refrigerant gases, are now available for use as aerosol propellants. Although HFCs

Table 3. Aerosol Propellants

Propane
Butane
Isobutane
Dimethyl ether
Pentane
Hydrofluorocarbon 134a
Hydrofluorocarbon 152a

are highly volatile, their low photochemical oxidation potentials mean they are not classified as VOCs. HFC 152a is expensive, but in the United States it has been used to reduce the overall VOC content of hydrocarbon-based propellants. It is also used as the sole propellant in some prestige products.

D. Structurants and emulsifiers

1. *Solution Pump Sprays, Roll-ons, and Sticks*

Alcoholic pump sprays require no further structurants as their low viscosity facilitates droplet breakup producing sprays with a desirable dry feel on the skin. The addition of latex-based opacifiers to aqueous alcoholic pump sprays makes them visually resemble emulsions without the use of structurants. An increase in the viscosity of the base formulation is usually needed for roll-ons to control the rate at which product is dispensed by the roll ball. This is generally achieved using cellulosic thickeners such as hydroxy propyl cellulose. Viscosities of 1000 cps (measured using a simple Brookfield viscometer) are usually adequate.

Clear antiperspirant sticks are now available in which the antiperspirant active is dissolved in propylene glycol and gelled with dibenzylidene sorbitol (DBS) (12). These sticks, while being completely clear, tend to be tacky in use and are also prone to instability as DBS degrades to liberate benzaldehyde at low pH. Table 4 gives examples of structurants used in solution formulations.

2. *Emulsion Pump Sprays, Roll-ons, Creams, and Gels*

Solutions of antiperspirant actives can be structured to improve skin feel and ensure effective dispensing from applicators such as pump sprays, roll-ons, and tubes by formulation of emulsions with oils, waxes, and acid-stable, non-salting-out emulsifiers (Table 5). Using this approach, the product rheology can be modified to suit the chosen applicator, while at the same time desirable sensory attributes such as smoothness on application and lack of visible deposits are achieved. Nonionic emulsifiers need to be used due to their improved

Table 4. Structurants for Solution Formulations

Hydroxyl ethyl cellulose
Hydroxy propyl cellulose
Dibenzylidene sorbitol

Table 5. Structurants for Emulsion Formulations

Steareth-2
Steareth-20
Steareth-21
Ceteareth-12
Ceteareth-20
Glyceryl stearate
Cetyl alcohol
Cetearyl alcohol
PEG[a]-20 stearate
Dimethicone copolyol

[a] PEG = polyethylene glycol.

compatibility with antiperspirant salts. In most cases, products are formulated as oil-in-water emulsions with the antiperspirant actives dissolved in the aqueous phase to maximize antiperspirant efficacy. However, water-in-oil emulsions are also used, particularly to form clear gels where the refractive indices of the two phases are matched to achieve transparency. The most commonly used antiperspirant active in emulsion formulations is aluminum chlorohydrate, since obtaining stable emulsions with zirconium salts is more difficult.

A particularly useful class of emulsions which can be made in a range of viscosities suitable for pumpsprays, roll-ons, and creams is formed by a phase inversion process (13,14). Mixtures of nonionic emulsifiers, such as ceteareth-20, glyceryl stearate, steareth-2, or steareth-21, are formulated in a coarse oil-in-water emulsion with oils such as decyl oleate or PPG-15 stearyl ether. The emulsion is heated until its phase inverts and then cooled through a microemulsion phase until it reinverts, forming a very fine oil-in-water emulsion. The waxy materials in the formulation solidify stabilizing an oil-in-water emulsion with a very small droplet size (Fig. 2).

The particles in emulsions of this type are typically less than 300 nm in diameter, and the emulsions are characterized by a bluish hue. The thickness of these emulsions is varied by adding polymeric thickeners or by varying the type and concentration of the nonionic emulsifiers. The key to successful formulation of products of this type is the correct combination of emulsifiers to achieve the phase inversion giving the appropriate hydrophobic/lipophobic balance at ambient temperatures (13,14). Low-viscosity oil-in-water formulations formed in this way containing aluminum chlorohydrate in the aqueous phase are suitable for pump sprays, while formulations with slightly higher

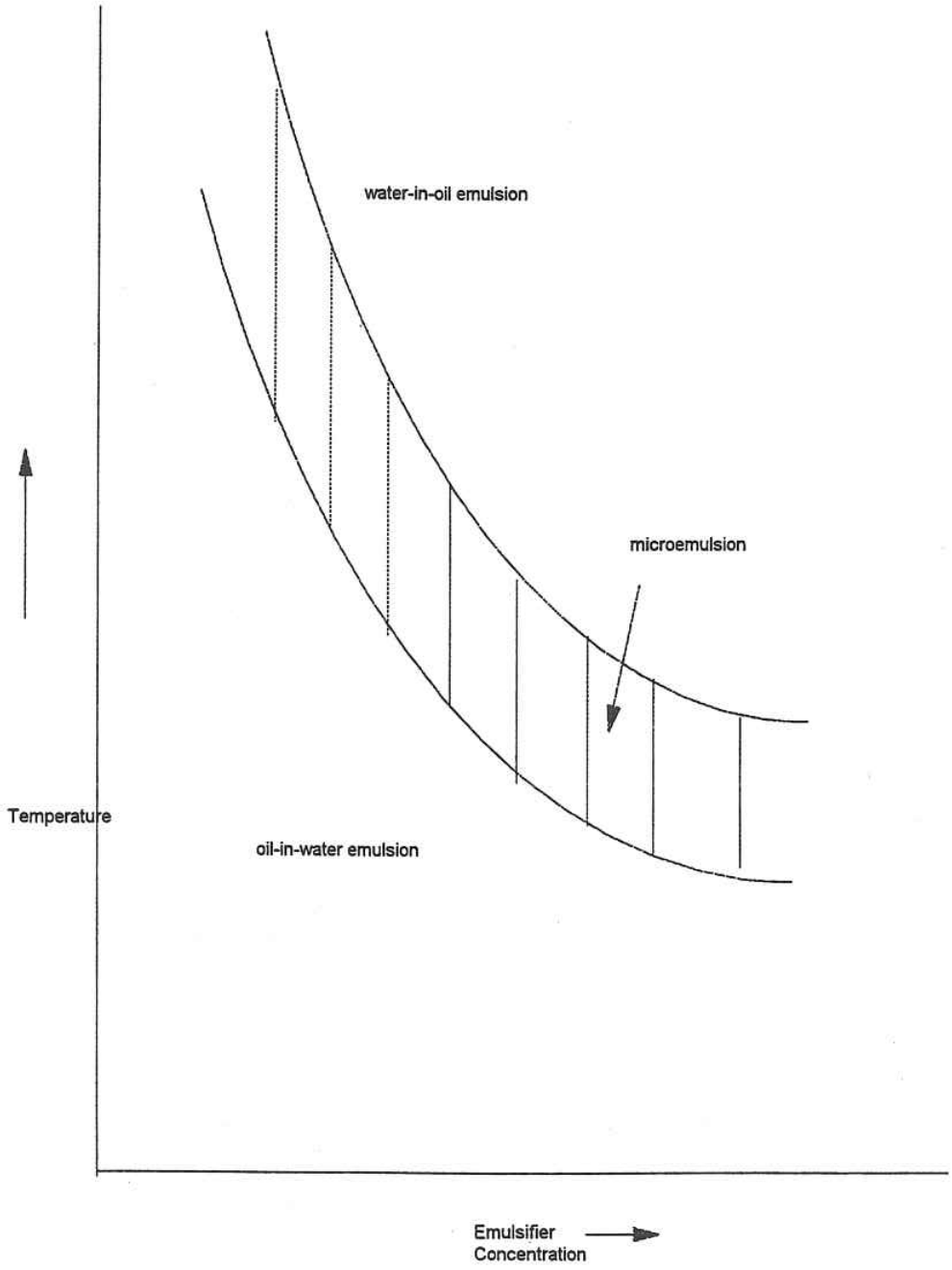


Figure 2 Schematic phase diagram for typical oil-in-water antiperspirant emulsion.

viscosities are more suited to roll-ons. Thickening of the emulsion to form a cream allows use in different applicators, such as domed tubes.

Dimethicone copolyol and mixtures of nonvolatile oils and volatile silicone as the oily external phase are used to produce water-in-oil emulsions. Adjusting the refractive index of the aqueous phase by inclusion of propylene glycol produces transparent formulations. The refractive indices of the two phases in emulsions of this type have different temperature coefficients, so there may be a loss of clarity at extremes of temperature. Clarity will also be lost if the composition of the formulation changes through evaporation. Viscosity can be varied by adjusting the relative phase volumes to produce transparent roll-ons and gels.

3. *Suspension Aerosols, Roll-Ons, Sticks, and Creams*

Suspension formulations are widely used for high-efficacy antiperspirant aerosols, roll-ons, and sticks; since they are nonaqueous, activated antiperspirant salts can be used. To prevent sedimentation in these formulations, the antiperspirant actives and any other powders (such as talc) are suspended in the carrier fluid. In fluid formulations (aerosols or roll-ons) the active powders inevitably sediment with time, and the challenge for the formulator is to slow down this process to ensure that a homogeneous product is dispensed from the applicator. Gentle shaking of the applicator prior to use should resuspend the active powders. Sedimentation of antiperspirant sticks once the stick matrix has solidified is not a problem. However, ensuring that sedimentation does not occur during the manufacturing process is a priority to avoid the production of inhomogeneous sticks.

A range of structurants for suspension formulations are shown in Table 6. Antiperspirant aerosols are generally structured using modified clays including quaternium-18 hectorite or bentonite. The clays themselves need to be structured by the introduction of a small amount of a polar fluid (ethanol or propylene carbonate). In many cases the polar constituents of fragrances will perform this task adequately. The clays are formed from small platelets separated by high-shear mixing, and the polar constituents are introduced to form a ''house of cards'' structure which hinders sedimentation and prevents caking. The amount of clay should be kept to a minimum to help reduce deposits in the axilla. Adequate structuring ensures the active does not ''cake'' on the bottom of the can on standing. Colloidal silica is an excellent structurant for suspension aerosols, but its use in aerosols is restricted due to concerns about toxicity on inhalation. Commercially available prestructured bentone gels are also used in manufacturing.

Table 6. Structurants for Suspension Formulations

Stearyl alcohol
Cetyl alcohol
Hydrogenated castor oil
Synthetic waxes
Paraffin waxes
Hydroxystearic acid
Dibutyl lauroyl glutamide
Alkyl silicone waxes
Quaternium-18 bentonite
Quaternium-18 hectorite
Silica[a]
Propylene carbonate

[a] Ingredients with multiple functions.

Suspension roll-on formulations are similar to antiperspirant aerosol bases, although the preferred active is usually superfine ZAG or AZAG to prevent sedimentation once suspended in cyclomethicone. As with suspension aerosols, structuring is achieved using clays or colloidal silicas, the use of which is not restricted in roll-ons as there are no concerns over inhalation toxicity.

Cyclomethicone is generally the carrier fluid in antiperspirant sticks, and this is structured using waxy materials to form a solid matrix (15). Stearyl alcohol combined with hydrogenated castor oil is miscible in cyclomethicone at high temperatures and is commonly used as a gelling agent for sticks. On cooling, the high-melting-point hydrogenated castor oil crystallizes to form a loose network which then suspends the powders in the formulation while crystallization of the stearyl alcohol solidifies the structure at lower temperatures. Paraffin waxes and synthetic waxes are also used to modify the properties of the stick matrix, and thus obtain the desired balance of aesthetic qualities and stick strength. Low levels of colloidal silica are sometimes used to reduce sedimentation during cooling if the waxes themselves prove inadequate.

Recently, novel structurants including hydroxystearic acid and dibutyl lauroyl glutamide have been developed for use in antiperspirant sticks. These structurants produce low visible deposits on application and confer a translucent appearance to the stick matrix.

Suspension creams can be thought of as thickened roll-on bases or lightly structured sticks. The creams are contained in bespoke packaging forms

that often resemble antiperspirant sticks with domed tops in which an array of slits allows the product to be dispensed. Control of product rheology is therefore critical, and product pack interactions can be particularly complex. Colloidal silica or low levels of waxes (hydrogenated castor oil, stearyl alcohol, or alkyl silicones) are used to thicken nonaqueous suspension creams. The advantage of silica is its relative insensitivity to temperature, although silica-containing products are prone to syneresis and leakage of volatile silicone, which may make them messy to use.

Since structures are so important for both sticks and creams, significant developments of new agents are expected in the future.

E. Sensory Modifiers

The modification of sensory properties of products to improve the feel on the skin and to reduce visible deposits is one of the most important objectives in the formulation of antiperspirants. Many ingredients (Table 7) have been used over the years to achieve these ends, and a complete review of all these agents is beyond the scope of this chapter.

Enhancing the feel of the product on the skin is generally achieved by using emollients, nonvolatile oils, or particulate solids which impart lubricity. Masking visible deposits, primarily due to antiperspirant actives, is achieved by using fluids with high refractive indices which match (as closely as possi-

Table 7. Sensory Modifiers

Cyclomethicone[a]	C7–C14 isoparaffins
Dimethicone	Di-isopropyl adipate
Dimethiconol	Isosorbide laurate
Isopropyl myristate[a]	PPG[b]-14 butyl ether
Isopropyl palmitate[a]	Glycerin
Talc[a]	Hydrogenated polyisobutene
Silica[a]	Polydecene
Polyethylene	Titanium dioxide
Polysaccharides	Phenyl trimethicone
Corn starch	Dioctyl adipate
C12–15 Alcohols benzoate	Hexamethyl disiloxane
PPG-3 myristyl ether	Alcohol[a]
Octyl dodecanol	

[a] Ingredients with multiple functions.
[b] PPG = polypropylene glycol.

ble) the refractive index of the active antiperspirant particles. Some oils (e.g., isopropyl myristate), where the primary function is to act as an emollient, may also contribute to masking deposits. Minimizing the surface area of the active ingredient (and hence minimizing the solid/air interface which scatters light) through the use of macrospherical actives also helps to mask deposits.

As well as improving the feel on the skin or masking deposits, several ingredients perform other functions in the formulation. Silicones are good examples of this (7,8). Cyclomethicones are carrier fluids, but they also impart a unique silky skin feel to products on application. Higher-molecular-weight dimethicone fluids (which are nonvolatile) provide long-lasting benefits in terms of reduced stickiness as well as masking visible deposits. Phenyl trimethicone, an example of a functionalized dimethicone, has the highest refractive index and thus provides the most effective masking of visible deposits. However, expense precludes its use in large quantities.

1. Antiperspirant Aerosols

Antiperspirant aerosols produce powdery deposits which are masked by the inclusion of nonvolatile oils (isopropyl myristate), long-chain alcohols (octyl dodecanol), ethers (PPG -14 butyl ether), or dimethicone fluids. However, the inclusion of oils of this type in aerosol formulations can reduce antiperspirant efficacy and give rise to clothes staining.

2. Antiperspirant Roll-ons

The sensory properties of solution and emulsion roll-ons are largely determined by the carrier fluid/structurant system used. Aqueous alcoholic antiperspirant roll-ons are cooling and fresh on application, although they can sting, particularly after shaving. In contrast, emulsion roll-ons are warmer on application and sting much less, although they can be sticky if the emulsifier and oil combination is not chosen carefully. Low levels of nonvolatile emollients, including isopropyl myristate or propylene glycol, added to solution roll-ons mask visible deposits on drying. The sensory properties of suspension roll-ons are similar to suspension aerosols since their formulations are fundamentally similar. Improvements in roll-ons are usually made in the area of visible deposits which can be decreased by including nonvolatile oils in the formulation, as for aerosols. Reduced efficacy and clothes staining are still potential problems.

3. Antiperspirant Sticks

In antiperspirant sticks cyclomethicone is the carrier fluid of choice. The major disadvantage of antiperspirant sticks is undoubtedly the high level of visible

white deposits left on the skin. As with other applicator forms, ethers (PPG-14 butyl ether) and esters (C12–15 alcohols benzoate, isosorbide laurate, and di-isopropyl adipate) are effective in masking these deposits; however, some esters can result in a greasy feel on the skin. Hydrocarbon fluids including polydecene can be used in suspension formulations of all types to mask deposits, but they tend to impart a ''draggy'' skin feel and are difficult to wash off. When used judiciously in combination with cyclomethicone, these problems can be avoided.

Solid particles play a significant role in the modification of sensory properties of suspension formulations. The simplest example of these is talc, which acts as a structurant (and low-cost filler) while also imparting a dry skin feel. Colloidal silica and corn starch are also used in this manner. Spherical polyethylene particles give a particularly silky feel to formulations due to their lubricity, so these materials have been used extensively in recent years.

Structurants and masking oils in antiperspirant sticks are sometimes difficult to wash off the skin using soap. In such cases nonionic emulsifiers such as C20–40 pareth-10 or C20–40 pareth-40 can be included in the formulation to provide a significant improvement.

4. Gels and Creams

Antiperspirant gels are prone to stickiness, particularly water-in-oil emulsion gels formed using dimethicone copolyol. To reduce the stickiness, low levels of alcohol are often included in the formulation. The sensory properties of emulsion creams depend on the phase structure of the particular blend of surfactants used.

Suspension creams have the advantage of being nontacky, but they have high levels of visible white deposits unless masked by nonvolatile oils ranging from dimethicone fluids to PPG-14 butyl ether and hydrocarbon fluids. The chosen oil must not disrupt the structuring and therefore the stability of suspension cream formulations, which can result in syneresis and leakage of cyclomethicone from the container.

F. Fragrance

Fragrance is a critical part of the sensory makeup of antiperspirants and deodorants. Fragrance performs several functions in an antiperspirant product: during application fragrance helps to turn this relatively mundane act into a pleasant experience; fragrance can play an important role in masking undesirable odors from the product base; and low, persistent levels of fragrance pro-

vide important reassurance of continuing product efficacy. In use, consumers are unlikely to want an overpowering sensation of perfume which could mask fragrances they choose to wear. However, a class of alcoholic deodorant body sprays has been developed where the fragrance forms the primary consumer benefit. Finally, fragrance can provide a significant deodorancy benefit associated with deo-perfume technology (16).

Incorporating fragrance into antiperspirant products is a challenge for the formulator since antiperspirant bases tend to be acidic and often have poor solvent characteristics. Anhydrous suspension formulations also often have a characteristic base odor from the combination of clays and waxes as structurants; these need to be masked effectively by fragrance. Metal ions in antiperspirant actives catalyze the degradation of many fragrance ingredients (17,18), so adequate stability testing during the development process is essential.

III. PUTTING THEORY INTO PRACTICE

The importance of the fundamental building blocks of antiperspirants cannot be overstated. However, it is the successful assembly of these building blocks that ultimately yields the product for the consumer. Example formulations in this section show how the building blocks can be combined to produce different products. The examples are illustrative, and therefore no claim to consumer acceptability, efficacy, or stability is implied.

A. Aerosols

Formulation I (Table 8) is an antiperspirant aerosol with the antiperspirant active aluminum chlorohydrate suspended in cyclomethicone using bentone

Table 8. Formulation I—Antiperspirant Aerosol

Ingredients	% w/w
Aluminum chlorohydrate	10.0
Cyclomethicone	12.0
Quaternium-18 bentonite	0.8
Propylene carbonate	0.6
Fragrance	0.8
Propellant	75.8

(quaternium-18 bentonite) and propylene carbonate as the structurant system. The active could also be AACH to provide additional antiperspirant efficacy, although both forms must have the appropriate particle size distribution for use in aerosols. The propellant is a hydrocarbon, and the product:propellant ratio is approximately 1:4. This is typical of suspension aerosols where the base is more concentrated than that used in alcoholic deodorants or body sprays. Low levels of nonvolatile oils can be added to antiperspirant aerosol formulations to help mask visible deposits, although reduced efficacy is often a consequence.

B. Roll-ons

Formulation II (Table 9) is an example of an aqueous/alcoholic roll-on containing aluminum/zirconium chlorohydrate as the active agent, thickened by hydroxy ethyl cellulose to give optimum dispensing from the roll-on applicator. Low levels of propylene glycol provide emolliency and help prevent jamming of the roller ball. This type of formulation provides high antiperspirant efficacy and on application gives a strong cooling sensation.

A contrast is provided by formulation III (Table 10), which is a simple emulsion roll-on. Ceteareth-20, cetyl alcohol, and glyceryl stearate form the emulsifying system and internal phase of the emulsion. The active ingredient is an aqueous solution of aluminum chlorohydrate, which forms the external phase. Medium levels of efficacy (depending on the amount of active used) are expected of this type of formulation, which is warm and nonstinging on application.

Formulation IV (Table 11) is for a high-efficacy suspension roll-on. The carrier fluid in this case is cyclomethicone (hence the formulation is relatively expensive), and it is structured using quaternium-18 hectorite. The active agent

Table 9. Formulation II—Solution Antiperspirant Roll-on

Ingredients	% w/w
Ethanol	40.0
Water	39.5
Hydroxy ethyl cellulose	0.5
Propylene glycol	1.5
ZACH	17.5
Fragrance	1.0

Table 10. Formulation III—Emulsion Roll-on

Ingredients	% w/w
Aluminum chlorohydrate	15.0
Ceteareth-20	3.0
Cetyl alcohol	2.0
Glyceryl stearate	1.5
Water	77.5
Fragrance	1.0

is ZAG, although ZACH could also be used. For maximum efficacy AZAG is often employed. These formulations are warm and nonsting on application, but tend to leave significant visible white deposits on the skin.

C. Pump Sprays

Formulation V (Table 12) is for a simple aqueous/alcoholic pump spray in which the antiperspirant active is aluminum chlorohydrate. Low levels of cyclomethicone and propylene glycol help to prevent the product drying out in the pump mechanism and retard active crystallization, which leads to blockage. Latex dispersions are sometimes added to the formulation so that it resembles an emulsion. Formulation VI (Table 13) is a true emulsion pump spray which is formed using the phase-inversion process described earlier. The relatively complex emulsifier system ensures the appropriate hydrophobic/lipophobic balance is obtained at room temperature, thus stabilizing the final emulsion. In this case dicaprylyl ether is used to provide emolliency, but other nonvolatile oils could be used.

Table 11. Formulation IV—Suspension Antiperspirant Roll-on

Ingredients	% w/w
Cyclomethicone	67.0
Quaternium-18 hectorite	3.0
Propylene carbonate	1.0
Silica	0.3
ZAG	24.0
Fragrance	1.0

Table 12. Formulation V—Solution Antiperspirant Pump Spray

Ingredients	% w/w
Alcohol	65.0
Aluminum chlorohydrate	15.0
Propylene glycol	3.0
Cyclomethicone	1.0
Water	15.0
Fragrance	1.0

D. Sticks

Formulation VII (Table 14) is for a typical antiperspirant suspension stick. The carrier fluid is cyclomethicone, which is structured using stearyl alcohol and hydrogenated castor oil. A low level of colloidal silica is used to provide structuring during processing and prevent sedimentation of the antiperspirant active before the stick matrix has solidified. As with the suspension roll-on, most types of powdered antiperspirant actives can be used. Ultrafine grades of powders have traditionally been used; however, macrospherical actives in combination with appropriate non-volatile oils are finding increasing popularity in low-residue formulations.

E. Creams and Gels

Formulation VIII (Table 15) is an example of an anhydrous cream in which the carrier fluid is a mixture of cyclomethicone and dimethicone with the non-

Table 13. Formulation VI—Emulsion Antiperspirant Pump Spray

Ingredients	% w/w
Glyceryl stearate	2.25
Ceteareth-20	1.70
Ceteareth-12	0.35
Cetearyl alcohol	0.35
Cetyl palmitate	0.35
Aluminum chlorohydrate	10.00
Water	79.00
Dicaprylyl ether	5.00
Fragrance	1.00

Table 14. Formulation VII—Antiperspirant Stick

Ingredients	% w/w
Cyclomethicone	54.0
AZAG	24.0
Stearyl alcohol	15.0
Hydrogenated castor oil	5.0
Silica	1.0
Fragrance	1.0

volatile oil providing masking of visible deposits. Structuring is achieved using a combination of high-melting-point waxes. The amount of structurant used and hence the hardness of the final product is critical. Talc adds bulk to the formulation and reduces overall cost, and AZAG provides maximum antiperspirant efficacy. Formulation IX (Table 16) is for a similar cream structured with colloidal silica.

Formulation X (Table 17) is an antiperspirant gel made from a solution of ZAG in water and propylene glycol emulsified using a dimethicone copolyol surfactant with cyclomethicone and isostearyl isostearate as the external phase of the emulsion. Optimization of the refractive indices of the two phases of the emulsion yields a transparent product. Loss of water by evaporation or changes in room temperature which produce differential changes in refractive index could cause cloudiness in the product.

IV. A GLIMPSE INTO THE FUTURE

In such a diverse field as the formulation of antiperspirants, predicting future developments is difficult. However, one relative certainty is that consumer

Table 15. Formulation VIII—Wax-Based Antiperspirant Cream

Ingredients	% w/w
Cyclomethicone	37.0
Dimethicone	20.0
AZAG	24.0
Hydrogenated castor oil	7.0
Alkyl silicone wax	5.0
Fragrance	1.0

Table 16. Formulation IX—Silica-Based Antiperspirant Cream

Ingredients	% w/w
Cyclomethicone	46.5
Dimethicone	20.0
AZAG	24.0
Silica	2.0
Talc	6.0
Fragrance	1.0
Propylene carbonate	0.5

needs will not change dramatically. Thus, the importance of efficacy combined with the need for excellent sensory properties on application and in use will remain key objectives for the formulator. Competition in the marketplace is likely to intensify, increasing the demand for excellent formulations at ever decreasing costs. Environmental issues have already had a major impact on the antiperspirant market with the use of CFCs prohibited, the emergence of new legislation on packaging waste, and increased emphasis on air quality. These issues may demand differential regional responses. The recent emergence of a distinct ''skin-friendly'' sector of the market offers scope for consolidation and development of new products offering real benefits to consumers in terms of skin mildness or reduced irritation.

New applicators have historically driven growth in this market and in the future will probably continue to do so. Applicator innovations pose new challenges for the formulator in terms of pack compatibility and controlled delivery of product to the skin. More sophisticated packaging systems, such as those for soft solids and gels, emphasize the product/pack interaction, and

Table 17. Formulation X—Antiperspirant Gel

Ingredients	% w/w
Cyclomethicone	17.0
Dimethicone copolyol	2.0
Isostearyl isostearate	7.5
ZAG	24.0
Propylene glycol	4.0
Water	45.5

the trend to more sophisticated packaging is likely to continue, especially in developed markets.

Considering the fundamental building blocks of any formulation, it is always possible that new antiperspirant actives will emerge. However, the requirements of the FDA and constraints on the testing of new cosmetic materials make this increasingly unlikely. In terms of carrier fluids and propellants, environmental pressures already limit the use of VOCs in some countries, thus accelerating the search for environmentally acceptable alternatives. The fundamental approaches to structuring are unlikely to change, and formulations based on solutions, emulsions, and suspensions are expected to remain the norm for many years. However, new structurants, whether they are used to produce clear or low-deposit sticks or new types of formulation for use in novel applicators, appear to be one of the most fruitful areas for development. Pressure to reduce formulation costs favors multifunctional ingredients and structurants which also deliver desirable sensory attributes.

In summary, the job of the formulator is becoming more demanding as the competition in this market increases, bringing pressure to reduce costs with ever-increasing environmental constraints. New developments are most likely in the areas of novel structurants, improvements to sensory properties, and innovative applicators.

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12

Antiperspirant Technology Trends from the Patent Literature

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I. INTRODUCTION

In many industrial technologies (including antiperspirants and deodorants), reviewing the scientific literature gives an incomplete picture of what is happening in the industry. Much of the new technology gets published only in the patent literature, and only a small amount of that can ever be seen in the new products being sold. This chapter and the following one (dealing with deodorant patents) will attempt to review the technology trends that become apparent from studying the patents issued over an extended period of time. Its purpose is to bring to the attention of scientists working in the field an overview of the patent technology. It is well known that the vast majority of the patents issued are not being used in any current products. However, each new patent issued represents a new finding, deemed important enough by the inventor or his company, to warrant the expense of filing. As such, it represents a potential departure point for the creative scientists to use in their research-and-development activities.

A review of the companies developing the new patent technologies can also offer an insight into the competition. By studying both the number of patents issued and their specific topics, a company can gain knowledge concerning how much effort their competition has expended and in what areas they have been working.

These two chapters are not meant to be a complete review of all patents issued in the 1990s (through June 1997) touching on the antiperspirant and deodorant field. Actually, about 75% of the patents reviewed will be mentioned in these chapters. Many patents disclosing technology only tangentially related to the antiperspirant and deodorant fields are not mentioned. This includes many raw materials whose main application is for another purpose but whose patent also discloses its use in antiperspirants and deodorants.

This author's assignment of the patents into their field of application (e.g., aerosols, roll-ons, etc.) is in some cases arbitrary, especially where the technology disclosed can be used in more than one type of product. In these cases an attempt was made to pick the application field stressed in the patent or choose the field deemed most important. In other cases, all patents relating to specific materials (such as activated antiperspirant salts) or technology (such as long-lasting fragrances) have been reported together irrespective of their field of application. While these arbitrary assignments could have some effect on the absolute numbers shown in the accompanying charts, they are not expected to change the general trends being demonstrated. In many cases the same or very similar patents are filed in different countries. An attempt has been made to list these patents only once, using either the U.S. patent number reference or that of the last country where it was issued or published. The actual name of the company shown on the patent assignment was used in preparing the various tables, irrespective of whether the company is part of a larger conglomerate or has since been acquired by another company.

II. FORMULATED PRODUCTS

A. Sticks and Solids

Patents relating to stick or solid antiperspirants topped the list for most patents issued. This is hardly surprising, taking into account the domination of the stick form of antiperspirant in the U.S. market in the 1990s. A considerable number of these patents focused on clear sticks and on reducing the appearance of residue left by the product (Table 1).

1. Clear Sticks

Most patents in this field focused on the use of dibenzylidene sorbitol with various additives to improve the clarity, stability, and odor. Procter and Gamble (P&G) was issued patents on substituted dibenzylidene alditols having better stability at the acidic pH's produced by the antiperspirant salts (1,2).

Table 1 Stick Patents

Category	No. of patents	Patents by company (more than one)	
Clear sticks	21	Procter & Gamble	19
		Gillette	5
Reduced whitening	8	Bristol-Myers	3
		Chesebrough-Pond's	3
Special additives	13	Helene Curtis	3
		Mennen	3
Gel and miscellaneous	12	Unilever	3
		Dow Corning	4
Processing and packaging	4	Other (Companies and private inventors with one patent)	15

Compounds disclosed included substituted derivatives such as di (m-fluoro) dibenzylidene sorbitol.

Thickeners such as hydroxyalkyl cellulose and/or chelating agents have been reported to improve stability (3). By lowering the dibenzylidene sorbitol levels to 1.5% or lower, the clarity and odor of the stick are greatly improved. The hardness of the stick is maintained by the addition of the hydroxyalkyl cellulose, and the color is improved by the addition of the chelating agent.

Mennen discloses the use of guanidine compounds, such as guanidine carbonate, as stabilizing agents (4). Bristol-Myers proposes using weakly basic organic nitrogen compounds such as urea to prevent the hydrolysis of the dibenzylidene sorbitol (5). Other nonamine or amide stabilizers have been reported, such as C4-6 alkyl dicarboxylate, monocarboxylate, or benzoate (6). Other carboxylates, such as propoxylated C6-20 alc. carboxylate, also improve stability (7). The carboxylate serves as both an emolient and a clarifier to obtain a clear gel stick. Inorganic bases have been reported to improve the stability of these dibenzylidine alditol clear sticks (8) as will the addition of a borate salt, especially borax (9). The use of C2-12 polyhydric alcohols in gelled sticks is reported by P&G (10).

Other additives proposed for clear sticks based on dibenzylidene sorbitol include 3-alkyl-2-oxazolidinone, which reduces the gelling temperature of the initial solution (11). A method for preparing diol-soluble antiperspirant salts for use in clear sticks is described (12). It involves reacting an antiperspirant compound with a water-soluble diol in a water solution, adding zinc glycinate

to the reaction mixture, and removing the water to recover a powder antiperspirant active.

Other methods of formulating clear sticks that do not involve dibenzylidine alditols have been reported. A number of patents describing borate crosslinking agents for the preparation of clear sticks or gels have been issued (13–15). A typical composition includes an antiperspirant active, a borate crosslinker, a polymer binder (such as polyethylene glycol or a hydrophilic polyurethane), and a carrier of water and water-soluble solvent mixtures.

A Mennen patent describes a polyamide gelling agent for preparing clear sticks and gels (16). They use an antiperspirant active and a solvent system for the antiperspirant active, which can be gelled by a polyamide. Other methods for preparing clear sticks involve complexing and hardening agents such as mono- or dicarboxylic acids and lower alcohol amines, amides, or diamides (17).

A novel water-in-oil clear emulsion antiperspirant stick is described in a Unilever patent (18). It utilizes an antiperspirant salt, a nonionic surfactant such as a C11-18 ethoxylated fatty alcohol, a water-immiscible liquid oil, and water. Dow discloses a translucent stick antiperspirant in which a clear stick base is formed from a metal stearate and glycol into which an encapsulated antiperspirant salt is dispersed (19). Another clear stick formula using polar nonmonohydroxy alcohols, aprotic solvents, gelling agents and antiperspirant salts is reported (20). A water-based antiperspirant stick involving a reaction between aluminum chlorohydrol solution and sodium lactate and then adding a solution of sodium palmitate in alcohol is described in a patent from Poland (21).

2. *Reduced Whitening Sticks*

Claims for antiperspirant products that do not leave a white residue on the skin began in the late 1980s and carried over into the 1990s. What is most interesting about this phenomenon is that for almost 10 years before that, suspension roll-ons and sticks antiperspirants (solids) all produced a pronounced white residue when applied to the skin. While the formulations to solve the whitening problem were relatively straightforward, almost all the manufacturers overlooked the existence of the problem. Only after Carter (Arrid) began making claims for a low-residue solid did other manufacturers turn their attention to this problem.

A Dow patent describes the use of nonvolatile alkylmethylsiloxanes and/or arylmethylsiloxanes for reducing skin whitening in stick formulations (22). Dimethicone copolyol serves the same purpose (23). Similarly, dimethi-

cone and mineral oils or branched C16-18 hydrocarbons help mask the whitening produced by conventional stick products (24). Other patents describe combinations of high- and low-melting-point waxes combined with nonvolatile silicones and dimethicone copolyol (25). Residue-masking agents defined in terms of their refractive index (> 1.4) combined with a trihydroxystrearin suspending agent are also reported (26), as are combinations of high- and low-melting-point waxes with colloidal silica and a nonvolatile emolient (27).

Other nonwhitening formulas are defined in terms of the ratio of volatile silicone to water-insoluble emolient being > 2.5:1.0 (28) or masking agents that are nonvolatile aliphatic hydrocarbons or aliphatic compounds with single-bonded O functional groups such as alcohols or ethers (29).

3. *Special Additives*

A number of conventional stick formulas are reported with special additives for delivery of enhanced deodorancy and fragrance. These include sticks with zeolites, mordenites, and/or beta-zeolites as odor suppressants (30); microcapsules composed of starch and polysaccharide-encapsulated fragrance oils and esters (31); and malodor-counteractant mixtures encapsulated in a semipermeable wall material (32).

An enhanced water absorbancy stick using gelatin with a means of raising its sol-gel transition temperature is disclosed (33). A P&G patent reports on stick formulations containing polyoxyethylene ethers, esters, and glyceryl (di)esters for improved ease of wash-off (34).

The strength of sticks can be improved without undue brittleness with the addition of longer-chain fatty alcohols (35,36). Polysiloxane surface-active agents can be used to produce sticks with improved stability (37).

A highly crosslinked macroporous polymer, such as ethylene glycol dimethacrylate-lauryl methacrylate copolymer, which serves as a bulking agent, can be used to reduce the amount of settling during the processing of sticks (38). Other additives, such as porous silica beads filled with antiperspirant ingredients (39); inert particular materials such as miralite, which enhance the application aesthetics of sticks (40); and sticks with added ZnO and/or TiO_2 (41), are also described. Improved aesthetics in stick formulas containing hydrofluorocarbon radical–containing compounds is described in a L'Oreal patent (42).

4. *Gel and Miscellaneous Stick Patents*

The use of 12-hydroxy stearic acid and its derivatives is the subject of several patents issued to P&G. Gel sticks can be prepared using 12-hydroxy stearic

acid, a secondary gellant consisting of N-acyl amino acid amide derivatives, volatile silicone, and a nonvolatile cosolvent (43,44). The addition of chelating agents to help stabilize the gel is also disclosed (45). Improved gelling can be obtained by using optically enriched forms of 12-hydroxy acid or its derivatives (46). The optically enriched gellant in the presence of the secondary gellant favors the formation of twisted fibrils which align to provide a more ordered structure to the gel. Also disclosed is the use of dihyroxy acids that are optically enriched (47). A variety of dihydroxy stearic and docosanoic acids can be used.

Dow reports that alkylmethylsiloxane polymers can be used to strengthen volatile silicone gels made with 12-hydroxy stearic acid or its metal salts (48). Antiperspirant salts with specified refractive indices can be used in preparing gels starting with the tray-dried salt, an encapsulated salt, or a solvent solution of the salt. 12-Hydroxy stearic acid or its metal salt combined with volatile silicone, and an aromatic group containing silicone fluid are used (49).

Gel sticks can be prepared from n-acyl amino acid amides, a liquid base material and antiperspirant salt (50). A gel stick made from N-lauroyl-L-glutamic acid dibutylamide, mineral oil, C12-15 alcohol benzoates, and antiperspirant salt is described.

Sticks with film-forming polymers containing quaternized N atoms are reported in a Gillette patent (51). Powder or powderlike sticks can be prepared using compressed organophilic clays (52). These sticks show good payout and retain at least 90% of their original payout even after being contacted by water. Stick formulas using sericite, talc, zinc oxide, and volatile silicones are also described (53).

An aluminum salt–free antiperspirant stick is described based on liquid crystal-forming amphiphilic substances which form water-insoluble materials upon contact with perspiration (54).

5. *Processing and Packaging*

A two-phase stick in which the phases are mixed separately and then cast coaxially into the form of a two-component stick is covered in a patent issued to Reckitt and Colman (55).

Antiperspirant sticks can be attached to the base of the applicator package platform using an open cell foam pad anchored to the applicator platform. The molten stick formulation infuses the foam pad and is thereby attached to it (56).

A Bristol-Myers patent describes a method for shaping sticks with an oval cross section using a series of cutting members (57).

Agglomeration of antiperspirant salts during the manufacture of sticks can be minimized by taking the base through a heating and cooling cycle during the addition of the antiperspirant salt (58).

B. Roll-ons

As in the case of sticks, a significant number of roll-on patents were directed to the area of clear products and products that do not leave a visible residue. Both suspension roll-ons and emulsion roll-ons (water-in-oil and oil-in-water) were fields of active development (Table 2).

1. Clear Roll-ons

Suspension roll-ons, which are clear, can be made by suspending an antiperspirant salt in an anhydrous vehicle wherein the refractive index of the salt and the vehicle are matched between 1.46 and 1.56 to within 0.02 units (59).

Transparent roll-on formulations are described based on dissolving an antiperspirant salt in water and/or a water-soluble solvent and thickening the solution with a hydrophilic polymer (60,61).

Clear microemulsion roll-on formulations that do not leave a visible residue can be prepared using PEG-7-glyceryl cocoate, cyclomethicone, and isopropyl myristate (62). Modifications of this type of microemulsion system are also covered (63).

Transparent water-in-oil emulsions containing antiperspirants suitable for use in roll-ons are formulated with an aqueous phase of antiperspirant salt,

Table 2 Roll-on Patents

Category	No. of patents	Patents by company (more than one)	
Clear	7	General Electric	6
		Bristol-Myers	5
O/W emulsions	6	Dow Corning	3
		Helene Curtis	3
W/O emulsions	7	Unilever	3
		Gillette	2
Suspension	10	Other	10
Miscellaneous	2	(Companies and private inventors with one patent)	

an oil phase, and a stabilizing agent that has substantial solubility in both phases (64).

Clear roll-ons can also be prepared from solutions of antiperspirant salts in a polyhydric alcohol plus cosolvents such as dibutylene glycol and hydroxydimethylsiloxanes (65).

Transparent emulsions that leave no visible residue can be formulated by using oil and water phases with similar refractive indices (66).

2. *O/W Emulsions*

A non-whitening roll-on emulsion is prepared from an antiperspirant salt solution, steareth-2, steareth-21, and dimethicone (67). A Henkel patent describes preparation of O/W emulsions by the phase inversion method using antiperspirant salt solutions with nonionic emulsifiers and coemulsifiers (68). Other emulsions can be prepared with silicone-free surfactant blends and a volatile silicone or volatile hydrocarbon (69). The reaction between an aqueous solution of antiperspirant salt with a solution of an organophilic acid dissolved in linear or cyclic silicone results in the formation of a novel metal salt which helps stabilize the emulsion (70). Emulsions of antiperspirant salts can also be stabilized and thickened by the addition of water-soluble polymers, silicates or clays (71), or dimethyl diallyl ammonium chloride/acrylic acid-type polymers (72).

3. *W/O Emulsions*

A series of General Electric patents describes a variety of siloxane-polyoxyalkylene graft polymers, polyether-siloxane surfactants, and polyoxyalkylene-siloxanes grafted with long-chain alkyl groups for the preparation of W/O emulsions of antiperspirant salt solutions in an oil phase containing volatile silicones (73–77). Other methods for emulsifying antiperspirant salt solutions in a volatile silicone oil phase using an organopolysiloxane polyoxyalkylene copolymer are described in a Dow patent (78).

4. *Suspension Roll-ons*

Suspension formulations are reported in which antiperspirant salts are suspended in anhydrous alcoholic solvents using hydrophobically treated clay suspending agents with or without agents to retard the dissolution of the salt in the alcoholic vehicle. Antiperspirant salts are reported to possess higher efficacy from these formulations than from water solutions or when dissolved in alcohol (79–81).

Antiperspirant salt suspensions in volatile silicone can be prepared using a modified pyrogenic silica (made by reacting silica with organosilanes). These suspensions show little separation despite low viscosity (82). Similar suspensions are also reported using bentonite clay dispersing agents (83).

Hydrophilic macroporous highly crosslinked polymers such as ethylene glycol dimethacrylate-lauryl methacrylate copolymer can be used as a suspending agent for antiperspirant salts in volatile silicone vehicles (84). Volatile silicone suspensions of antiperspirant salts containing a particulate carbohydrate and glyceride ester are reported to form a translucent film upon drying (85). A rheological additive prepared from the reaction of sodium stearate with aluminum chlorohydrate solutions can be used to stabilize suspension roll-ons (86).

Aqueous solutions of antiperspirant salts can be suspended in organic liquid vehicles by encapsulating droplets of the aqueous phase in a pyrogenic hydrophobic silica or other hydrophobic metalloid oxides (87,88). The formulations are reported to have a dry feel despite the presence of substantial amounts of water.

5. *Miscellaneous*

Antiperspirant salts microencapsulated in waxes, lipids, oils, polymers, etc. can be used in roll-on formulations which are reported to offer controlled release and to minimize irritation (89). Phthalamate emulsifiers can be used to stabilize suspension type roll-ons (90).

C. Aerosols

A particularly interesting feature of the patents issued in this area is the large number (more than half) assigned to Japanese companies, Lion Corporation leading the list. Many of these concern the addition of particulate materials into aerosol formulations. Recent interest in reducing VOC emissions from aerosols has generated activity in low spray rate or low propellant systems (Table 3).

1. *Suspending Agents and Emulsifiers*

Amino functionalized siloxanes can improve antiperspirant salt suspension and redispersibility, and result in better adherence of the product to the skin (91). Water in volatile silicone oil emulsions made with silicone surfactants suitable for use in antiperspirant aerosols are described in a Unilever patent (92). Phosphate-type anionic surfactants are reported for antiperspirant aerosol

Table 3 Aerosol Patents

Category	No. of patents	Patents by company (more than one)	
Suspending agents and emulsifiers	7	Lion	7
		Unilever	5
Enhanced efficacy	5	Procter & Gamble	4
		Shiseido	3
Low spray/low propellant	5	Kosei	2
		Nonogawa	2
Nonwhitening and low dusting	4	Other (Companies and private inventors with one patent)	15
Particulate fillers	8		
Miscellaneous	9		

formulations (93), as are anionic surfactants such as polyoxyethyleneglyceryl tri-isostearate (94) and glucose fatty acid esters (95).

Inorganic powders such as talcs and magnesium aluminum silicates and/or organic powders can be used for improved suspension in aerosols (96). A Giulini patent describes a fatty acid–modified aluminum magnesium hydroxide salt which can be used to prepare lipogels that inhibit sedimentation and compaction of antiperspirant salts in aerosol formulations (97).

2. *Enhanced Efficacy*

The use of activated aluminum chlorohydrate antiperspirant salts in aerosol formulations is discussed in a P&G patent (98). Gillette reports on formulations containing ingredients that do not detract from the efficacy of the activated salts (99). Lion uses a combination of activated and nonactivated salts (100).

Suspensions of aluminum chlorohydrate in anhydrous alcohols containing a hydrophobically treated clay suspending agent are reported to show superior antiperspirant efficacy in aerosol formulations (101). The incorporation of additives (such as urea or amino acids) to such formulations inhibits the dissolution of the antiperspirant salt in the alcohol, and the additives serve as perfume stabilizing agents (102).

3. *Low Spray/Low Propellant*

Antiperspirant aerosol formulations containing $< 50\%$ propellant are described in a P&G patent (103). Formulations containing $< 60\%$ propellant

and a particulate filler material such as modified corn starch, polyacrylates, talc, or bicarbonate are also disclosed (104). Other particulate fillers, such as polyethylene and aluminum starch octenylsuccinate, also prevent clogging in low-propellant aerosols (105).

Low spray rate (0.5 g/sec or less) aerosol antiperspirants can be prepared using a silicone polymer and a volatile low-viscosity fluid which dissolves the polymer (106). Despite the slow spray rate, the formulation does not clog and has reduced dustiness and bounce-back. Unilever describes similar low–spray rate aerosols using a nonvolatile liquid containing a nonvolatile silicone or an oil-soluble emulsifier to reduce clogging (107).

4. *Nonwhitening and Low Dusting*

Low-visible-residue antiperspirant aerosols can be formulated with alkyl- and polyether-modified silicone surfactants (108). Polydimethylsiloxanes have been reported to reduce irritation and staining in aerosols (109).

Low-dusting aerosols have been prepared with combinations of propane-butane mixtures containing isopentane and/or pentane (110). Dustiness can also be reduced by the addition of silicone gum and an untreated reinforcing silica filler (111).

5. *Particulate Fillers*

A series of patents by Lion Corporation describes a wide variety of particulate fillers that are useful in antiperspirant aerosol formulations. Included in these are porous silica beads (112), hollow anhydrous silica beads (113), and porous spherical particles (114).

The use of powder fillers is also described for making powdery antiperspirant sprays. In some cases these are also intended for use on the feet (115–119).

6. *Miscellaneous*

Aerosol antiperspirants can be prepared using a combination of dimethyl ether and hydrocarbon propellants (120). Dimethyl ether with ethylmethyl ether and CO_2 are also reported (121). Single-phase antiperspirant aerosol formulations are described using aluminum chlorohydrate–propylene glycol solutions with added glycols and dimethyl ether propellant (122). The mixture forms a single-phase solution.

ABA-type triblock thermoplastic elastomers (e.g., styrene-isoprene-styrene block polymer) can be used to formulate film-forming aerosol antiperspi-

rants (123). The preparations are reported to form adherent films on the skin that are free from tackiness.

Additives mentioned for use in aerosol formulations include water-insoluble ground coloring materials for masking their appearance on skin (124) and cyclodextrins for odor entrapment (125).

Spherical aluminum chlorohydrate is used for antiperspirant formulations to inhibit clogging (126). Liquid antiperspirant formulations useful for roll-ons and aerosols with reduced incidence of skin irritation are discussed in a P&G patent (127). Dispensing systems for antiperspirant powders are disclosed in a Precision Valve patent (128).

D. Gels

Gels represent one of the newer categories of antiperspirant product forms. They were first introduced in the late 1980s by Carter-Wallace. They are usually soft, clear gels that are dispensed from sticklike packages with a slotted top. The gel is dispensed through the slots and rubbed into the underarm by the dome of the container. Patents in this field have tended to focus on the preparation of gels using thickeners, gelling agents, and clear emulsions

1. Emulsions

Dimethicone copolyols have been used for the preparation of antiperspirant gels for many years. Formulation patents using this material were issued to Gillette (129) and Mennen (130). The Mennen disclosure mentions the use of polypropylene glycols to reduce both tackiness and skin whitening. A processing patent relating to preparing these dimethicone copolyol gels is covered by Carter-Wallace (131).

Silicone-based surfactants can be used to prepare clear emulsion gels according to a Dow patent (132). An example of a silicone polyether surfactant is given. The reaction product of cholesteryl anthraquinone-2-carboxylate with organosilicone compounds can also be used for the preparation of antiperspirant gels (133).

An unusual antiperspirant gel emulsion (patented by Kelco) uses an aqueous gelled outer phase, a nonaqueous intermediate phase, and an aqueous inner phase containing the active antiperspirant salt. The active salt is incompatible with the gelled outer phase but is kept separated from it by the intermediate phase (134).

2. Miscellaneous Gelling Agents

Polyurethanes can be used to prepare phase-stable, nonwhitening antiperspirant gels (135). Transparent gels can also be made using polyamides as the gelling agent (136). These types of gels can also be formulated for stick and roll-on application. A Mennen patent discloses using poly(ethynlformamide) as a thickening agent for antiperspirant formulations with the addition of ammonium acetate to increase gel rigidity (137). Other gelling agents that have been mentioned as useful in antiperspirant-type gels include vinyl-silicone graft or block copolymers (138), sterol and/or starch hydrolyzed esters of C8-22 carboxylic acids (139), and polyhydroxy nonionic surfactants (140).

Additional gel formulations are discussed in the referenced patents (141–144).

E. Creams

Other than simple aqueous or aqueous-alcoholic solutions, creams represent the oldest product form of antiperspirant in the market. However, in recent years creams have been "reinvented" using nonaqueous formulations. The creams are applied from sticklike applicators. Unlike the old aqueous cream formulations, these products feel dry on application and dry very quickly without any stickiness (Table 4).

1. Particulate Thickening Agents

A series of patents describe anhydrous antiperspirant cream formulations that are essentially composed of a volatile silicone, a nonvolatile emolient, a colloidal inorganic thickening agent such as silica, and a particulate antiperspirant salt (145–147). A number of variations to these types of formulas include the

Table 4 Cream Patents

Category	No. of patents	Patents by company (more than one)	
Particulate thickening agents	10	Procter & Gamble	8
		Unilever	3
		Helene Curtis	2
Nonparticulate thickening agents	7	Other (Companies and private inventors with one patent)	4

incorporation of polyethylene (148); particulate hydrophilic cellulose ether polymers, polyamides, and/or polypeptides (149); suspending and thickening waxes (150–152); and bentonite suspending agents with structuring waxes (153).

A semisolid antiperspirant formulation has also been disclosed prepared from volatile silicone, a particulate antiperspirant salt, and a polyolefin microspherical particle (154).

2. *Nonparticulate Thickening Agents*

Anhydrous antiperspirant volatile silicone cream formulations can also be formulated without inorganic particulate thickening agents. Unilever patents disclose the use of alkyl ester and alkylmethyl siloxane waxes such as behenic acid silicone wax for preparing such creams (155,156). Procter and Gamble describes creams made with fatty acid alcohols C20–40 (157,158). Other gellants that can be used for the volatile silicone phase are glyceryltribehenate and other triglycerides made from long-chain fatty acids (159) and stearyl alcohol–hydrogenated castor oil combinations (160).

Aqueous creams useful for antiperspirants have also been described based on polyvinyl pyrrolidone-silicone encapsulated products (161). The high-molecular-weight silicones provide low tackiness.

F. Sprays

While pumps and spray antiperspirants make up only a small percentage of the U.S. antiperspirant market, these products are considerably more popular (often being the dominant product form) in many other countries. In spite of this popularity, there have been relatively few patents directed toward this product form.

Procter and Gamble describes clear spray formulations composed of alcohol-soluble antiperspirant salts, nonvolatile emollients esters, volatile silicones, nonvolatile silicones, branched-chain alcohols, and water (162). The formulations do not leave a residue and are quick-drying. Other nonstaining formulations are also reported (163).

Alcoholic antiperspirant formulations described by Shiseido are prepared with polyoxyethylene silicones to give good skin adherence and leave a smooth texture after drying (164). Formulations made with alcohols and polyols are covered in a Kao patent (165).

A method to inhibit the dissolution of antiperspirant salts in alcohols by

the addition of compounds having a basic nitrogen or basic oxygen function can be used to prepare alcoholic antiperspirants with enhanced activity (166).

Translucent antiperspirant microemulsions suitable for spraying can be prepared using nonionic surfactants such as alkyl polyglycosides and a lipophilic coemulsifier (167). They are claimed to have very low irritancy. The use of glycyrrhetic acid is covered in a Kao patent for use in liquid low-viscosity liquid antiperspirants (168).

G. Foot Products

Antiperspirants and deodorants for the feet represent a small product category compared to underarm products. However, a large number of deodorant patents (see next chapter) and a smaller number of antiperspirant patents have been issued directed toward treating the feet. An interesting point of these patents is that most are from private inventors or small companies. That suggests that major companies have not invested in R&D in this field because of the small market size. However, the private inventor seeing a problem for which there is a product need, has been trying to solve it. The author, as the father of five sons who grew up wearing athletic shoes all the time, also thinks (smells) that foot odor and perspiration are a consumer problem waiting for a better solution.

An aqueous alcoholic solution with a hydroxyalkylcellulose thickener absorbent, silica and aluminum chlorohydrol, is reported to reduce foot sweating and odor (169).

Foot odor and wetness can be treated with compositions containing benzoic acid, salicylic acid, and the antihistamine diphenhydramine-HCl (170).

Soaking the feet in 0.60% formaldehyde is claimed to reduce foot odor and sweating (171). Powders containing aluminum ammonium sulfate and boric acid (172), salicylic acid and tannins (173), and multicomponent formulations including aluminum chlorohydrol, carbonates, silicates, etc. (174) have been claimed to reduce foot sweating.

Hand and foot antiperspirant and grip-improving formulations containing magnesium carbonate have been described (175). Antiperspirant formulations for the feet are also claimed for preventing frostbite (176).

III. ACTIVE INGREDIENTS

Over 60 patents describing new forms of active ingredients for use in antiperspirants were issued in the time period studied. The majority of these relate

to processes for preparing what are now called ''activated'' aluminum salts, or zirconium/aluminum glycinates. These are conventional antiperspirant salts that are converted to more active forms by various treatments that modify their polymeric structure without changing their molecular formula. Many patents also discuss modified antiperspirant salts prepared by reacting or combining conventional salts with other ingredients. Finally, a number of patents continue to disclose new antiperspirant ingredients that are not based on aluminum or zirconium/aluminum salts (Table 5).

A. Modified Al or Zr/Al Salts

Encapsulated aluminum salts can be prepared by combining aqueous solutions of antiperspirant salts with a hydrophobic liquid and a carboxylic acid or other hydrophobes (177–179). As an example, an aqueous solution of antiperspirant salt is added to a solution of stearic acid in a mixture of silicones. The solution is heated to remove the water, and the encapsulated aluminum salt precipitates out as a controlled particle-size material for use in aerosols and sticks.

Antiperspirants comprising thick-walled, hollow, spherical particles es-

Table 5 Active-Ingredients Patents

Category	No. of patents	Patents by company (more than one)	
		Dow	4
Modified aluminum salts	15	Gillette	3
		Other[a]	8
Activated salts		Gillette	6
		Westwood	5
Alumunim	12	Mennen	3
		Reheis	3
Zr/Al	13	Unilever	3
		Bristol-Myers	2
Other Zr/Al	4	Dow Corning	2
		Somerville	2
		Other[a]	3
		Univ. Florida	5
Nonaluminum or Zr/Al	19	Unilever	4
		Other[a]	10

[a] Companies and private inventors with one patent.

sentially composed of a water-soluble antiperspirant salt are described in a Reheis patent (180). The hollow spheres can also be filled with a water-immiscible deodorant or fragrance material.

Anti-inflammatory antiperspirant salts can be made by reacting acylated alpha amino acids with aluminum sulfate or aluminum chloride in neutral solutions (181). Antiperspirants can be made using aluminum salt–silicone carboxylate inclusion compounds as the active ingredient (182). These are prepared by mixing the antiperspirant salt with a silicone fluid containing the silicone carboxylic acid and heating the system to evaporate the water. Monosaccharides, such as alpha-fructose, are claimed to be useful in decreasing hypersensitivity to antiperspirants (183). Low-skin-irritation antiperspirant salts can be prepared by combining the salts with organic acids (184).

Novel antiperspirant adduct compositions can be made by precipitating out an antiperspirant salt into a steric stabilizer from a solvent system (185). The steric stabilizers can be nonionic surfactants such as ethoxylated C12–18 fatty alcohols or polyethoxylated alcohols. The antiperspirant adducts do not leave white residues on the skin. Polyanionic aluminum salts have been reported as useful in antiperspirants (186). Antiperspirants can be prepared from aqueous alcoholic solutions of aluminum salts with inorganic powders (187).

A method of preparing aerogel antiperspirant salts is presented in a patent (188). Antiperspirant particles that are highly porous with a very low density are described. They are prepared by contacting the antiperspirant with fluids that are taken above their supercritical temperature.

Very high clarity and colorless antiperspirant salt solutions can be obtained by exposing the salt solutions to UV light in the wavelength range of 180 to 400 nm (189).

The efficacy of antiperspirant salts can be increased by mixing them with silicic acid in aqueous solution (190,191). The salt can be dried to powder which maintains its enhanced efficacy when dissolved in water.

B. Activated Al and Zr/Al Salts

Most patents issued in the 1990s relating to activated forms of antiperspirant salts cover a variety of specific processing procedures for converting the many different polymeric species found in conventional salts into polymeric species richer in the more active forms. It is beyond the scope of this chapter to discuss the often subtle differences among the processing procedures covered in the many issued patents. The interested reader is referred to Chapters 4 and 5 in

this book, which specifically review the chemistry of activated basic aluminum chlorides and activated zirconium/aluminum/glycine complexes.

1. Activated Al Salts

Westwood patents generally cover the production of activated aluminum salts starting with the reaction of aluminum metal with an acid or aluminum chloride (192–195). Unilever also describes the production of activated salts starting with the metal (196–198). A Reheis patent applies ultrasound as part of their processing procedure (199).

Other patents focus more on processing procedures carried out on solutions of conventional aluminum salts to convert them to activated forms (200,201).

Patents have also been issued describing general methods for preparing basic aluminum chlorides (202,203).

2. Activated Zr/Al Salts

Dow and Reheis patents describe the preparation of activated zirconium/aluminum salts starting with aluminum metal (204,205).

A number of Gillette patents cover the preparation of these activated salts which start with the activated aluminum salt and involve addition of the zirconium salt under a variety of conditions and processes (206–210).

Yet other methods for the preparation of activated zirconium/aluminum salts are described in Bristol-Myers, Westwood, and Beecham patents (211–214).

Glycol solutions of activated salts can be prepared by adding glycols to an aqueous solution of the activated salt and rapidly removing the water by evaporation (215). The activated salt is stable in the glycol solvent.

Other methods of preparing glycol solutions of activated salts can also be used (216).

C. Other Zr/Al Salts

Aluminum and zirconium/aluminum salts can be reacted with anionic organophilic salts to prepare useful antiperspirant compounds that can also function as rheological additives (217). Examples of organophilic compounds are mono- or polyvalent alkyl carboxylates, acyl lactates, alkyl ether carboxylates, etc.

Mennen describes several active antiperspirant salts using complex oxoanions of nitrogen or halogen which do not form strong coordination com-

pounds with the aluminum 31 polymer (218–220). Examples such as nitrates, chlorates, and iodates are presented.

D. Non-Al or Zr/Al Antiperspirants

A number of compounds that are neither aluminum salts nor zirconium/aluminum salts have been described as having antiperspirant activity. To the knowledge of the author, only one (a water-absorbing material) has been used in a test-marketed product. Some may actually be deodorant ingredients that have been incorrectly described as antiperspirants.

Titanium salts of carboxylic and hydroxycarboxylic acids are highly effective, low-irritant antiperspirants (221,222). Salts such as ammonium titanium lactate and titanium octanoate are presented as examples.

L'Oreal discloses the use of strontium salts in antiperspirant formulations (223). An example of an aerosol formulation is presented containing strontium nitrate.

Unilever describes formulations that can serve as antiperspirants by blocking sweat pores by physically swelling and forming a water-insoluble liquid crystal phase when contacted by sweat (224). An example of a stick formula is presented containing glyceryl monolaurate, isostearyl alcohol, sodium stearate, ethanol, and water.

A series of patents assigned to the University of Florida discloses anticholinergic compounds that are useful as antisecretory agents, mydriatics, and antiperspirants (225–229). Among the classes of compounds included are scopolamine metabolite ester derivatives, pyridine carboxylic acid esters, substituted quaternary ammonium compounds, and acetate and carboxylic acid derivatives.

Antiurease compounds combined with carob tannins are mentioned as useful antiperspirants (230). Long-lasting antiperspirancy can be achieved with silver nitrate aqueous ethanol solutions (231). 5-Alpha-reductase inhibitors are claimed as antiperspirants in a Merck patent (232).

A method of isolating tetraphenyl-borate salts by spray-drying can be used to prepare antiperspirants (233). The following compounds have also been described as antiperspirants; imidazole derivatives to inhibit sweating in rat foot pads (234); substituted benzoic acids (235); and burnt alum (236).

Combinations of natural ingredients have been patented as useful deodorant/antiperspirants (237,238).

Antiperspirant formulations that work by absorbing rather than inhibiting sweat can be prepared using highly crosslinked, porous absorbent particulate polymers (239).

IV. SPECIAL ADDITIVES

A wide variety of materials have been claimed as useful additives for antiperspirant formulations. Included are polymers which provide improved tactile properties, bicarbonate salts, encapsulated or specially modified fragrance materials, and moisture absorbers. While not serving a specific antiperspirant benefit, these additives are claimed to provide additional benefits to antiperspirant formulations to which they are added (Table 6).

A. Fragrance Materials

Firmenich discloses a nonaqueous perfuming compound for use in antiperspirant formulations, comprising two perfumes with different olfactive characters (240). One of the perfumes is a liquid and the other is encapsulated in a water-soluble polymer. Olfactory adaptation to the liquid perfume is overcome by release of the second perfume on contact with perspiration.

Long-lasting fragrances for use in sticks can be prepared by using cryogenically ground thermoplastic polymers containing fragrance compounds (241). The longevity of fragrances for use in antiperspirants can also be extended through the use of fragrances containing quaternized aminoalkyl lactams (242). A complexed vanillin fragrance in an antiperspirant persisted for 18 hours, versus 4 hours for the noncomplexed vanillin.

Fragrances combined with a emulsifying agent and a film former such as polyvinylpyrrolidone or other polymers are reported useful in antiperspirant formulations (243,244). Other encapsulating film-forming agents can also be

Table 6 Special-Additives Patents

Category	No. of patents	Patents by company (more than one)	
Fragrance	13	Church & Dwight	9
		Firmenich	3
		Kenebo	2
Bicarbonate	9	Kao	2
		Procter & Gamble	2
Miscellaneous	7	Shiseido	2
		Other (Companies and private inventor with one patent)	9

used (245). All of the above claim to give a strong fragrance boost when contacted by moisture or sweat, and have good reencapsulating properties when the formulation dries out again on the skin.

Zeolites or silica gel with pores containing fragrance can be used to extend fragrance life in antiperspirants (246). The particles allow control of the perfume intensity, and suppress unwanted fragrance loss.

Perfume compounds that have a long-lasting olfactory sensation and thereby minimize the need to use large amounts are described by Procter and Gamble (247,248). Other long-lasting fragrances are disclosed by Lion (249).

Kanebo reports the use of fragrance derivatives in antiperspirants which are broken down by skin microorganisms to release the fragrance material (250,251). Derivatives such as glycosides, phosphate esters, and amino acid derivatives can be used. Skin microorganisms, such as *Corynebacterium* and *Staphylococcus*, degrade these derivatives.

Encapsulated sodium bicarbonate in the form of crystallites that have liquid fragrance adsorbed on the crystallite can be used in stick and roll-on formulations (252). Polymers such as maltodextrin starch can be used for the encapsulating agent. Moisture triggers the release of the fragrance material.

B. Bicarbonate

A series of patents issued to Church and Dwight discuss the use of bicarbonate in antiperspirant and deodorant formulations. While in many cases the bicarbonate is more related to deodorant formulations, the technology is reported here since their use in antiperspirants is also mentioned.

Comicronized crystalline blends of sodium bicarbonate and zinc oxide coated with a polymer such as maltodextrin starch offer improved deodorancy to antiperspirant sticks and roll-ons (253). Methods to make the comicronized blend are also covered (254).

Antiperspirant stick products containing multiple fine crystallite bicarbonate encapsulated with a hydrophilic polymer show improved dimensional stability (255). Also useful are bicarbonate and an anticaking agent, such as talc, coated with a hydrophilic polymer (256).

Methods of making antiperspirant sticks containing bicarbonate using a phased order of addition and temperature control are disclosed (257,258). Microporous sodium bicarbonate which may also contain absorbed gases, liquids, or solid phase can be prepared to have densities that closely match those of the matrix phase of antiperspirant stick formulations (259,260). The particles do not settle during manufacturing, and they give added dimensional stability to the stick.

Antiperspirant sticks containing metallic carbonates which show very low visible residue are reported (261).

C. Miscellaneous

Water-absorbing polymers used in conjunction with antiperspirants are disclosed by Shiseido (262,263). Formulations using aluminum chlorohydrate and a sodium acrylate polymer or spherical calcium alginate as water absorbers are presented.

A method to manufacture water-absorbing polymers useful in antiperspirants is covered in a Kao patent (264). The method utilizes oil-in-water reverse-phase suspension polymerization. The same company also discloses using water-absorbent polymers in conjunction with hydrophobic substance–treated powders to prepare cosmetic formulations that do not become wet in perspiration (265).

Antiperspirant formulations showing good spreadability and having a smooth, light touch can be prepared using spherical silicone rubbers or polyorganosilsesquioxane powders (266,267).

Occlusive, water-insoluble, film-forming polymers can also be used in antiperspirants (268). The polymer is dissolved or dispersed in a volatile solvent containing other formulation ingredients. Upon evaporation of the solvent, a clear, water-impermeable film is left on the skin.

V. NEW APPLICATION CONCEPTS

New packaging concepts leading to improved methods for applying antiperspirants to the skin have often been the springboard for growth of the category. A number of new packages or other novel ways to apply the product or to achieve antiperspirant effects have been described in patents.

Gillette describes an applicator involving a water-insoluble, porous polymeric matrix containing an antiperspirant (269). The antiperspirant can be leached from the polymer matrix by water stored in a reservoir. The matrix can be shaped for application to the skin. A Unilever patent also involves a porous applicator (270). In this case the porous applicator shaped for application to the skin is connected to a reservoir containing an antiperspirant formulation. In both cases the antiperspirant formulation is applied to the skin through the polymer matrix by a wicking action.

A device for electrostatic spraying of antiperspirant formulations is described in a patent assigned to Imperial Chem. Ind. (271). A high electric

potential is supplied to the head so that a liquid is projected preponderantly under the influence of electrostatic forces.

Transdermal patches can be used for the sustained release of antiperspirant preparations (272).

A number of patents assigned to Kao describe application of antiperspirantlike materials from a bath. In some cases it is not clear whether antiperspirancy or other effects are being sought. Formulations containing antiperspirants, a polymer adsorbable to skin, and alcohol are applied to wet skin (273). Long-lasting antiperspirant effects are claimed. Also reported is a bath additive consisting of aluminum sulfate and a polymer containing quaternary nitrogen groups (274). Cationically modified cellulose, dextrin, chitosan, and vinyl pyrrolidones are cited as examples. The products are claimed to control perspiration after bathing. Menthol and other agents provide a cooling sensation when added to these antiperspirant baths (275). The use of bicarbonates to leave a refreshing feeling can also be used in antiperspirant bath preparations (276).

A cooling spray based on propellent mixtures can be used to cool the body and thereby inhibit sweating (277).

Clothing treated with antiperspirant salts can be used to inhibit sweating. Aluminum salts and antibacterials applied to the inside of medical gloves can be used to inhibit perspiration and bacterial growth (278). In a similar way, protective clothing such as helmets, boots, and gloves can be treated with antiperspirant salts to permit more comfortable wear (279). Aluminum antiperspirant salts are also reported for treating fabric materials (280).

A dehydrated or concentrated antiperspirant can be formulated as a tablet or as a liquid-filled capsule (281). The inventor claims the formulation has low transportation and packaging costs and minimizes loss of quality during storage or as a result of irregular use. The product is reconstituted with water prior to use.

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