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PEMULEN AS A VERSATILE EMULSIFIER

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ABSTRACT:

Many emulsifiers are currently employed in a wide area of pharmaceutical as well as cosmetologic applications to stabilize the oil-water system. These emulsifiers work on the principle of micelle formation and reduction of interfacial tension between two immiscible components. Thus the applicability of many surface active agents as primary emulsifier is dependent on its HLB range. In contrast to these agents, Pemulen polymeric emulsifier is having wider coverage of the stabilization ability due to its unique emulsification mechanism. Pemulen is a polymeric emulsifier composed of a block copolymer consisting of a poly acrylic acid similar to the Carbopol resins presently used to make aqueous and solvent gels in art conservation. These are novel oil-in-water (o/w) emulsifiers which provide numerous benefits to emulsions prepared with them. Thus the oil droplets are protected by the very high yield polymeric gel environment formed around the oil droplet by Pemulen and held in place. As a result Pemulen provides a highly stable emulsion. Due to efficient stabilization, it can be used in number of preparations which are discussed in this review.

KEYWORDS: Carbopol, o/w emulsion, Pemulen, Polyacrylic acid, Polymeric Emulsifier.

INTRODUCTION:

In the recent times of research and development, there has been considerable concern in using Pemulen as an excipient in a diverse range of pharmaceutical as well as non pharmaceutical applications.

The first polyacrylate polymers, developed in 1958, used benzene as the polymerization solvent. In 1980s, new products and processes using ethyl acetate and ethyl acetate/cyclohexane co-solvents were introduced to enhance product safety.

Pemulen polymeric emulsifiers are novel oil-in-water (o/w) emulsifiers which provide numerous benefits to emulsions prepared with them. They are predominantly high molecular weight poly acrylic acid polymers. These novel primary emulsifiers have a small lipophilic portion in

addition to a large hydrophilic portion. This chemical structure allows these copolymers to function as primary emulsifiers in oil-in-water emulsions. The lipophilic portion adsorbs at the oil-water interface and the hydrophilic portion swells in the water forming a gel network around oil droplets. This mechanism provides surpassing emulsion stability to a panoptic range of oils. Hence, Pemulen polymers are versatile polymeric emulsifier having ability to emulsify up to 30% oil by weight, within a pH range of 4-5.5, and up to 20% oil over the pH range of 3-11.

CHEMICAL NATURE:

Pemulen is a polymeric emulsifier composed of a block copolymer consisting of a poly acrylic acid similar to the Carbopol resins presently used to make aqueous and solvent gels in art conservation (Carbopol 934, Carbopol 940, and Carbopol 941). This block copolymer is cross-linked with a long-chained methacrylate having a lipophilic regions (the methacrylate) as well as hydrophilic regions (the acrylic acid).

In the cosmetic industry literature, Pemulen is part of a class of copolymers, referred to as acrylate/C10-30 alkyl acrylate cross polymers, having the following structure ^[1]. The molecular weight of a monomer in the Pemulen polyacrylate copolymer is 72.06266 g/mol with molecular formula $C_3H_4O_2$. The general structure of the structural unit is depicted in Fig.1. According to IUPAC nomenclature system, general structure of Pemulen is considered as prop-2-enoic acid. Pemulen is also known by different synonymous terms *viz.* Acrylic Acid, 2-Propenoic acid, Propenoic acid, Acroleic acid, Vinyl formic acid, Propene acid, enoates, Carbomerum, Polyacrylate.

Pemulens are produced from primary polymer particles of about 0.2 μm diameter. Each primary particle can be viewed as a network structure of polymer chains interconnected by cross-links (Fig. 2). Without the cross-links, the primary particle would be a collection of linear polymer chains intertwined but not chemically bonded. Linear polymers are usually soluble in polar solvents such as water; while cross-linked polymers are water swellable.

Cross-linked polymers can swell in water up to 1,000 times their original volume to form a gel. Cross-linked polymers do not dissolve in water but can be dispersed, and at times, appear to be soluble to the naked eye.

PHYSICAL PROPERTIES:

Pemulen remains as a versatile polymer and emulsifier amongst the present pharmaceutical excipients due to the distinguished physicochemical properties ^[2]. Different physical characteristics of Pemulen are depicted in Table. 1.

DIFFERENT GRADES AVAILABLE:

Depending on different structural features and physicochemical characteristics, Pemulens are available in different commercial grades. The available grades and their characteristics are as follows:

i) Pemulen 1621 Polymer:

Pemulen 1621 polymer is a high molecular weight, cross-linked copolymer of acrylic acid and C₁₀-C₃₀ alkyl acrylate that is designed to form stable oil-in-water emulsions. It has relatively medium viscosity compared to other Pemulen polymers.

ii) Pemulen 1622 Polymer:

Pemulen 1622 polymer is similar to Pemulen 1621. It has relatively low viscosity compared to other polymers.

iii) Pemulen TR-1 Polymer:

Pemulen TR-1 polymer is a versatile polymeric emulsifier, which can emulsify up to 30% oil by weight, within a pH range of 4-5.5, and up to 20% oil over the pH range of 3-11. While Pemulen TR-1 thickens the water, Carbopol polymers should be used with Pemulen TR-1 to provide greater thickening properties where higher viscosity emulsions are required.

iv) Pemulen TR-2 Polymer:

Pemulen TR-2 is a polymeric emulsifier. A block copolymer consisting of a poly acrylic acid cross-linked with a long-chained methacrylate, this carbomer has a lipophilic regions (the methacrylate) as well as hydrophilic regions (the acrylic acid).

EMULSIFICATION MECHANISM:

Principal emulsification action of stabilization of oil-in-water emulsions by traditional ionic or non-ionic surfactants is adsorption and formation of lamellar liquid crystalline layers at the emulsion interface. This mechanism requires use of surfactant at levels of 3–7%. The

concentration of surface active agent is a very crucial parameter in emulsified formulation as the concentration of these agents affects the micellar structure. Hence, the hydrophilic-lipophilic balance (HLB) of the oil phase and surfactant must be carefully matched to insure good stability of emulsion. Along with HLB, viscosity is the factor affecting the emulsion stability. Higher the viscosity, more stable will be the emulsion. Due to this reason, polymeric hydrocolloids, such as Carbopol resins, are often incorporated to enhance the stability of the oil-in-water emulsions by thickening and adding yield value or structure to the water phase.

Emulsions created with very low concentration of Pemulens are highly stable. Pemulen is having good ability of forming very high yield polymeric gel environment around the oil droplet. Thus the oil droplets are protected and held in place as a result of the aqueous gel around each oil droplet. On forming o/w emulsions, Pemulen molecules form an adsorbed gel layer around each oil droplet, with the hydrophobic portions of the polymer anchored in the oil phase. Thus, when two oil droplets approach each other, a physical repulsive force is generated by the presence of these adsorbed gel layers ^[3] (Fig.3).

One of the interesting features possessed by Pemulen is that it is designed to break when the gel is in contact with a salt concentration similar to what one would find on human skin. This is desirable in the cosmetics industry where moisturizers need to be quickly delivered and absorbed into the user's skin, but this may be a less desirable characteristic of an emulsion designed to clean works of art. In practice, this breakage of the emulsion has been observed when attempting to clean very grimy areas and allowing the gel to dwell for an extended period.

Viscosity & Effect of pH:

While Pemulen TR-1 thickens the water, Carbopol polymers should be used with Pemulen TR-1 to provide greater thickening properties where higher viscosity emulsions are required.

THICKENING MECHANISM:

Polyacrylate polymers as supplied are dry, tightly coiled acidic molecules. Once dispersed in water, the molecules begin to hydrate and partially uncoil. The most common way to achieve maximum thickening from Carbopol polymers is by converting the acidic Carbopol

polymer to a salt ^[4]. This is easily achieved by neutralizing the Carbopol polymer with a common base such as sodium hydroxide (NaOH) or triethanolamine (TEA). Carbopol polymers must be neutralized in order to achieve maximum viscosity. Unneutralized dispersions have an approximate pH range of 2.5-3.5 depending on the polymer concentration. Optimum neutralization is achieved at a pH of 6.5-7.0; viscosity begins to decrease after a pH of 9.0, and will continue to decrease if the pH is increased.

ADVANTAGES OF PEMULEN:

Pemulen polymers form stable oil-in-water emulsions with no or low levels of co-surfactant. Pemulen polymers provide efficient suspension and stabilization of insoluble materials and particles. These polymers provide shear thinning rheology which enables easy pumping and spraying of finished products. Thus Pemulens are highly beneficial in many pharmaceutical as well as non-pharmaceutical applications. The advantages of Pemulen polymers can be given as follows:

i) Universal Emulsification ability

Pemulen emulsifiers are water soluble polymers that readily anchor at the oil-water interface independent of oil type. Pemulen emulsifiers do not depend on building liquid crystalline structures to provide emulsion stability. So they can be used with almost any oil phase, irrespective of the oil phase HLB or temperature of emulsification. ^[5]

Oil-in-water emulsions have been made with many non-reactive, non-ionic oil types, e.g. mineral oil, volatile silicone oils, aromatic oils, fatty ethers or esters, and hydrocarbons/waxes. Oils can be emulsified at room temperature and fats or waxes are emulsified at their molten temperature.

ii) Emulsion Stability

A broad range of emulsions have remained stable in the bottle for years, even at elevated temperatures of 40°C. (See Fig. 2) These emulsions are also stable to repeated freeze-thaw conditions ^[6, 7].

iii) Low Concentration

Due to their hydrogel nature and highly efficient properties, typical usage levels of

only 0.1-0.3% of a Pemulen emulsifier are required to replace 3-7% of conventional emulsifiers [8].

iv) Low Irritancy

Due to less required concentration compared to the traditional surfactants, Pemulens do not cause any irritation to the applied part. Thus, it can be considered as patient compliant product [9].

v) Rapid Release

Emulsions created with Pemulen emulsifiers have a triggered release mechanism. The acrylic hydrophilic portion of the Pemulen emulsifier hydrogel instantly swells upon contact with the surface characteristics and salt content common on skin. The oil phase is released and provides immediate coverage of the substrate, eliminating the lengthy lag time seen in traditional o/w emulsions.

In traditional emulsions, lamellar liquid crystals, comprised of oil, water and surfactant, retard the rate of deposition of the oil phase to the substrate. These liquid crystal structures persist for up to ninety minutes after application. The liquid crystal structures may be observed by polarized light microscopy. The time lag from application to the formation of the continuous oil phase is caused by the slow evaporation of the water phase from the liquid crystal structures.

These products are used as thickeners, suspending agents, stabilizers and to control dissolving rates of other ingredients when used to manufacture pharmaceuticals, cosmetics, home and industrial products. They have important properties that make them particularly well-suited for a variety of pharmaceutical applications including use in oral solid and liquid dosage forms, topical gel and cream formulations, bioadhesive formulations and bulk laxatives. Pemulen polymers provide consistent functionality in pharmaceutical applications for: controlled release properties in tablets and capsules, bioadhesion, rheology modification, suspension of insoluble ingredients and emulsification of oil-in-water systems. Their use can range from 1% to 30% of the finished product weight in pharmaceutical tablets and capsules.

vi) Enables Unusual New Product Forms

Provides yield value to allow for the suspension of a wide variety of insoluble materials or particles. Yield value enables finished products to have vertical cling which is an important characteristic for products that are dispensed via a trigger spray or nozzle ^[10].

APPLICATIONS OF PEMULEN:

Pemulen polymer has an extensive applicability in different drug and cosmetic preparation due to its wide range of emulsification ability. Different patents have been reported in which the use of Pemulen is done ^[8, 11, 12]. The different applications of Pemulen include use in drug delivery systems and personal care cosmetic preparation.

Drug Delivery System:

- i. Matrix ^[13, 14]
- ii. Transdermal DDS ^[15]
- iii. Sprayable Formulations
- iv. Solid lipid Nanoparticles ^[5]
- v. Oral-based controlled release formulations using poly(acrylic acid) micro gels ^[16, 17]
- vi. Herbal contraceptive formulation

Personal care preparations:

- i. Household, Institutional and Industrial applications
- ii. Hand cleaners and sanitizers
- iii. Air fresheners and deodorizers
- iv. Automotive care products
- v. Polishes and waxes
- vi. Paint strippers
- vii. Surface protectant
- viii. Solvent degreasers

Cosmetic preparations:

- i. Stress-Relief Calming Body Cream
- i. Stimulating Eye Serum
- ii. Sunscreen Lipstick

- iii. Intensive Rinse-Off Hair Conditioning Balm
- iv. After Shave Fluid Emulsion
- v. PEG-Free Emulsion for Baby Wipe
- vi. Gentle PEG-Free Emulsion for Baby Wipe
- vii. Anti-Acne Cream Gel for Sensitive Skin
- viii. Anti wrinkle day cream

TOXICOLOGY:

The safety of Pemulen is supported by a history of safe use in drugs, cosmetics and household applications. The Cosmetic Ingredient Review Expert Panel and subsequent toxicology testing have demonstrated a low toxicity and irritation potential. As a result of this, and the properties offered by the polymers, they have gained wide acceptance in a variety of pharmaceutical, cosmetic and detergent applications. These products have a long history of safe use in pharmaceutical, personal care, and home and industrial products.

STABILITY:

Generally, Pemulen is considered as a chemically stable excipient in the formulation. Heat may be generated if polymer comes in contact with strong basic materials such as ammonia, sodium hydroxide, potassium hydroxide or strongly basic amines causing incompatibility resulting in lack of stability.

REGULATORY STATUS OF CARBOPOL POLYMERS:

Pemulen polymeric emulsifiers as a class have received extensive review and toxicological evaluation. These are classified as Category 1 GRAS (Generally Recognized as Safe) materials. The toxicity of Carbopol polymers have been summarized by the Cosmetic Ingredient Review Expert Panel in their assessment of the safety of the Carbopol polymers for cosmetic ingredients. This assessment and subsequent toxicology testing have demonstrated a low toxicity and irritation potential.

As a result of the intensive testing and the properties offered by the polymers, they have gained wide acceptance in a variety of pharmaceutical, cosmetic, and detergent applications

FUTURE TRENDS:

The large variety of applications as well as the steadily increasing number of research workers engaged in studies of Pemulen polymers due to their unique properties, have made significant contributions to many types of pharmaceutical as well as non-pharmaceutical applications indicating the potential of Pemulen as novel and versatile emulsifier in future.

REFERENCES

1. Goddard, Desmond, E., James, Gruber, V., Informa Healthcare, 1999, 22, 607.
2. Pemulen TR-1 Polymeric Emulsifier, Product Specifications, Lubrizol, 1997.
3. Simovic, Tamburic, S., Jela, M., Dusan, R., Int. J. Pharm. 1999, 184 (2), 207-217
4. Szucs, M., Sandri, G., Bonferoni, M.C., Caramella, C.M., Vaghi, P., Szabo-Revesz, P., Eros, I., Eur. J. Pharm. Sci. 2008; 34(4-5):226-35.
5. Pople, P.V., Singh, K.K., AAPS Pharm. Sci. Tech. 2006, 7(4), 91.
6. Szucs, M., Vaghi, P., Sandri, G., Bonferoni, M.C., Caramella, C.M., Revesz, P.S., Eros, I., J. Thermal Analysis and Calorimetry. 94(1), 271-274.
7. Esposito, E., Bortolotti, F., Nastruzzi, C., Menegatti, E., Cortesi, R., J. Cosmetic Sci. 2003, 54, 239-250.
8. Johnson, S.C., & Son, Inc. Patent 1983; 4,389,418.
9. Cutler, R.A., Drobeck, H.P., Jungerman, E., Cationic Surfactants. 1970, 4, 527-613.
10. Ghirardi, D., Cosmetic symposium. 2001, 105-108.
11. Riesgraf, Su, Dean, T., Topical tale containing compositions Patent. 1999, 5959019.
12. Chandar, P., Lam, T., Lips, Y., Pham A., Richardson Q.T., Norman Kramer Non-sticky cosmetic moisturizer for skin and hair, Patent 2006, 6991799.
13. Aboofazeli, R., Mortazavi, S.A., Iranian J. Pharma. Res. 2003, 33-38.
14. Aboofazeli, R., Mortazavi, S.A., Iranian J. Pharma. Res. 2003, 23-27.
15. Shahin, M., Hady, S.A., Hammad, M., Mortada, N., Drug Dev Ind Pharm. 2010.
16. Wahlgren, M., Christensen, K.L., Jorgensen, E.V., Svensson, A., Ulvenlund, S., Drug Dev Ind Pharm. 2009, 35(8), 922-29.
17. Savic, S., Milic, J., Vuleta, G., Primorac M., STP Pharma. Sci. 2002, 12(5), 321-327.

ILLUSTRATIONS:

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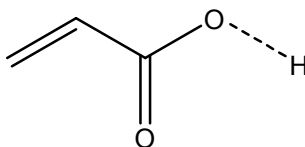


Figure 1: General Structure of Pemulen Polymers

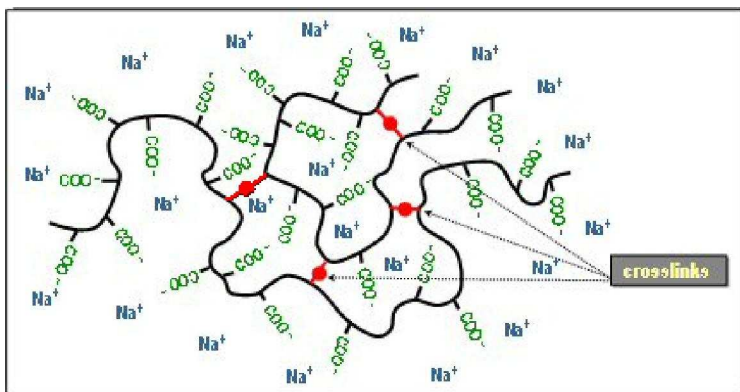


Figure 2: Cross-linked structure of Pemulen

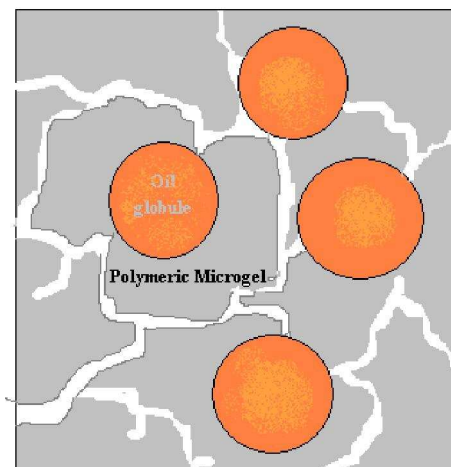


Figure 3: Emulsification mechanism

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Table 1: Physicochemical properties of Pemulen

Bulk Density	0.19-0.24 g/ml
% Volatile Weight (moisture)	< 2%
Specific Gravity	~ 1.40
Solubility in Water	Appreciable
pH Value	2.5-3.0 @ 1% in water
Appearance & Odor	White powder, slight acetic odor

Table 2: Comparison of Different grades of Pemulen

Properties	Pemulen-1621	Pemulen-1622	Pemulen-TR-1	Pemulen-TR-2
Primary Emulsification	Yes	Yes	Yes	Yes
Oil Loading	Up to 30%	Up to 70%	Up to 30%	Up to 70%
Relative Viscosity	Medium	Low	High	Low
Yield Value	High	High	High	High
Effective pH Range	4 – 9	4 – 9	4 – 9	4 – 9
Typical Use Conc.	0.2 – 0.5%	0.15 – 0.3%	0.2 – 0.5%*	0.15 – 0.3%*

* Higher levels may be needed in high electrolyte