

SECOND EDITION

Pharmaceutics

THE SCIENCE OF DOSAGE FORM DESIGN

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Note

Medical knowledge is constantly changing. As new information becomes available, changes in treatment, procedures, equipment and the use of drugs become necessary. The editor, contributors and the publishers have taken care to ensure that the information given in this text is accurate and up to date. However, readers are strongly advised to confirm that the information, especially with regard to drug usage, complies with the latest legislation and standards of practice.

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are absorbed more effectively in the small intestine than in the stomach, effervescent tablets can thus show a fast drug bioavailability, which can be advantageous, for example, for analgesic drugs. Another aspect of the short residence time of the drug in the stomach is that drug-induced gastric irritation can be avoided, e.g. for aspirin tablets, as the absorption of aspirin in the stomach can cause irritation.

Effervescent tablets also often include a flavour and a colourant. A water-soluble lubricant is preferable in order to avoid a film of a hydrophobic lubricant on the surface of the water after tablet dissolution. A binder is normally not included in the composition.

Effervescent tablets are prepared by both direct compaction and by compaction via granulation. In the latter case, traditional wet granulation is seldom used; instead, granules are formed by the fusion of particles as a result of their partial dissolution during wet massing of a moistened powder.

Effervescent tablets should be packaged in such a way that they are protected against moisture. This is accomplished with waterproof containers, often including a desiccant, or with blister packs or aluminium foils.

Lozenges

Lozenges are tablets that dissolve slowly in the mouth and so release the drug dissolved in the saliva. Lozenges are used for local medication in the mouth or throat, e.g. with local anaesthesia, antiseptic and antibiotic drugs. They can thus be described as slow-release tablets for local drug treatment.

Disintegrants are not used in the formulation, but otherwise such tablets are similar in composition to conventional tablets. In addition, lozenges are often coloured and include a flavour. The choice of filler and binder is of particular importance in the formulation of lozenges, as these excipients should contribute to a pleasant taste or feeling during tablet dissolution. The filler and binder should therefore be water soluble and have a good taste. Common examples of fillers are glucose, sorbitol and mannitol. A common binder in lozenges is gelatin.

Lozenges are normally prepared by compaction at high applied pressures in order to obtain a tablet of high mechanical strength and low porosity which can dissolve slowly in the mouth.

Sublingual and buccal tablets

Sublingual and buccal tablets are used for drug release in the mouth followed by systemic uptake of

the drug. A rapid systemic drug effect can thus be obtained without first-pass liver metabolism. Sublingual tablets are placed under the tongue and buccal tablets are placed in the side of the cheek.

Sublingual and buccal tablets are often small and porous, the latter facilitating fast disintegration and drug release.

Extended-release tablets

Classification of extended-release tablets

In recent years there has been great interest in the development and use of tablets which should be swallowed and thereafter slowly release the drug in the gastrointestinal tract. Such tablets are denominated in various ways, such as slow release, prolonged release, sustained release and extended-release. In the European Pharmacopoeia the term extended-release has been chosen as denominator for these types of tablets and so is used here. Extended-release tablets are often referred to as controlled-release preparations. This latter term is somewhat misleading, as all tablets, irrespective of their formulation and use, should release the drug in a controlled and reproducible way. (The nomenclature for extended-release preparations is subject to some debate and no worldwide acceptable system exists. The reader is referred to Chapter 20 for further discussion on this subject.)

After the release of the drug from the tablet the drug should normally be absorbed into the systemic circulation. The aim is normally to increase the time period during which a therapeutic drug concentration level in the blood is maintained. However, the aim can also be to increase the release time for drugs that can cause local irritation in the stomach or intestine if they are released quickly. Examples of the latter are potassium chloride and iron salts. In addition, drugs for local treatment of diseases in the large intestine are sometimes formulated as extended-release tablets.

An extended-release tablet contains one dose of the drug which is released for a period of about 12–24 hours. The release pattern can vary, from being nearly continuous to two or more pulses. In the latter case the pulses can correspond to a rapid release of the drug, or can be a combination of a rapid release of one portion of drug followed by a slow release of a second portion.

An extended-release preparation can also be categorized as a single-unit or a multiple-unit dosage form. In the first case the drug dose is incorporated into a single-release unit, and in the latter is divided into a large number of small release units. A multi-