Pharmaceutics

The science of dosage form design

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Contents

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The design of dosage forms

PRINCIPLES OF DOSAGE FORM DESIGN

Drugs are rarely administered solely as pure chemical substances but are almost always given in formulated preparations. These can vary from relatively simple solutions to complex drug delivery systems, through the use of appropriate additives or excipients in the formulations to provide varied and specialized pharmaceutical functions. It is the formulation additives that, amongst other things, solubilize, suspend, thicken, preserve, emulsify, improve the compressibility and flavour drug substances to form various preparations or dosage forms.

The principal objective of dosage form design is to achieve a predictable therapeutic response to a drug included in a formulation which is capable of large scale manufacture with reproducible product quality. To ensure product quality, numerous features are required — chemical and physical stability, with suitable preservation against microbial contamination if appropriate, uniformity of dose of drug, acceptability to users including both prescriber and patient, as well as suitable packaging and labelling. Ideally, dosage forms should also be independent of patient to patient variation although in practice this feature remains difficult to achieve. Future developments in dosage form design may well attempt to accommodate to some extent this requirement.

Reference is made in Part 2 of this book to differences in bioavailability between apparently similar formulations and possible causative reasons. In recent years increasing attention has therefore been directed towards eliminating variation in bioavailability characteristics, particularly for chemically equivalent products since it is

recognized that formulation factors can influence their therapeutic performance. To optimize the bioavailability of drug substances it is often necessary to carefully select the most appropriate chemical derivative of the drug, for example to obtain a specific solubility requirement, as well as its particle size and physical form, to combine it with appropriate additives and manufacturing aids that will not significantly alter the properties of the drug, to select the most appropriate administration route(s) and dosage form(s) and to consider aspects of manufacturing processes and suitable packaging.

There are numerous dosage forms into which a drug substance can be incorporated for the convenient and efficacious treatment of a disease. Dosage forms can be designed for administration by all possible delivery routes to maximize therapeutic response. Preparations can be taken orally or injected, as well as being applied to the skin or inhaled, and Table 1.1 lists the range of dosage forms which can be used to deliver drugs by the various administration routes. However, it is necessary to relate the drug substance and the disease state before the correct combination of drug and dosage form can be made since each disease or illness will require a specific type of drug therapy. In addition factors governing choice of administration route and the specific requirements of that route which affect drug absorption need to be taken into account when designing dosage forms.

Table 1.1 Range of dosage forms available for different administration routes

Administration route	*Dosage forms*
Oral	Solutions, syrups, elixirs, suspensions, emulsions, gels, powders, granules, capsules, tablets
Rectal	Suppositories, ointments, creams, powders, solutions
Topical	Ointments, creams, pastes, lotions, gels, solutions, topical aerosols
Parenteral	Injections (solution, suspension, emulsion forms), implants, irrigation and dialysis solutions
Lungs	Aerosols (solution, suspension, emulsion, powder forms), inhalations, sprays, gases
Nasal	Solutions, inhalations
Eye	Solutions, ointments
Ear	Solutions, suspensions, ointments

Versatile drugs are often formulated into several dosage forms of varying strengths, each having particular pharmaceutical characteristics which are suitable for a specific application. One such drug is the glucocorticoid prednisolone. Through the use of different chemical forms and formulation additives a range of effective anti-inflammatory preparations are available including tablet, enteric coated tablet, injections, eye drops and enema. The extremely low aqueous solubility of the base prednisolone and acetate salt makes these forms useful in tablet and slowly absorbed intramuscular suspension injection forms, whilst the soluble sodium phosphate salt enables a soluble tablet form, and solutions for eye drops, enema and intravenous injection to be prepared. The antibacterial drug combination co-trimoxazole, consisting of a mixture of five parts of sulphamethoxazole and one part trimethoprim, is also available in a range of dosage forms and strengths to meet specific needs of the user, including tablets, dispersible tablets, double strength tablets, double strength dispersible tablets, paediatric mixture, intramuscular injection, and a strong sterile solution for the preparation of an intravenous infusion. Because of the low aqueous solubility of both drug substances, specialized solvents are used for the intramuscular injection: 52% glycofurol, and strong sterile solution, 40% propylene glycol.

It is therefore apparent that before a drug substance can be successfully formulated into a dosage form many factors must be considered. These can be broadly grouped into three categories:

1 biopharmaceutical considerations, including factors affecting the absorption of the drug substance from different administration routes,
2 drug factors, such as the physical and chemical properties of the drug substance, and
3 therapeutic considerations including consideration of the disease to be treated and patient factors.

Appropriate and efficacious dosage forms will be prepared only when all these factors are

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