Pharmaceutical Preformulation and Formulation

A Practical Guide from Candidate Drug Selection to Commercial Dosage Form

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Oral Solid Dosage Forms

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In the last 15 to 20 years, there has been a huge resource in both academia and industry devoted to the development of drug delivery systems that target drugs more effectively to their therapeutic site. Much of this work has been successful and is reported within this text. In spite of this, oral solid dosage forms such as tablets and hard gelatin capsules, which have been in existence since the nineteenth century, remain the most frequently used dosage forms. This is not simply a reflection of the continued use of established products on the market, tablets and capsules still account for about half of all new medicines licensed (Table 11.1).

There are several reasons for the continued popularity of the oral solid dosage form. The oral route of delivery is perhaps the least invasive method of delivering drugs, it is a route that the patient understands and accepts. Patients are able to administer the medicine to themselves. For the manufacturer, solid oral dosage forms offer many advantages: they utilise cheap technology, are generally the most stable forms of drugs, are compact and their appearance can be modified to create brand identification.

Tablets and capsules are also very versatile. There are many different types of tablets which can be designed to fulfil specific therapeutic needs (Table 11.2). It is beyond the scope of this chapter to cover all these dosage forms, instead it will review the common principles, with more specific detail being given for those most commonly used.

For drugs that demonstrate good oral bioavailability and do not have adverse effects on the gastro-intestinal (GI) tract, there may be very little justification for attempting to design a specific drug delivery system. It is likely, therefore, that tablets and capsules will continue to remain one of the most used methods of delivering drugs to the patient in the future.

This chapter reviews the science behind the development of solid dosage forms, particularly tablets and hard gelatin capsules. Solid dosage forms are one of the most widely

Table 11.1
Number of FDA drug approvals for tablet and capsules from 1995 to 1999.

	No. of Tablets Approved	No. of Capsules Approved	No. of Other Dosage Forms Approved	Proportion of Tablets and Capsules (%)
1995	14	0	14	50
1996	69	17	101	46
1997	70	15	96	47
1998	48	9	66	46
1999	20	10	30	50

Source: Centrewatch.com, Clinical trials listing.

Table 11.2
Types of solid dosage forms.

Formulation Type	Description
Immediate release	The dosage form is designed to release the drug substance immediately after ingestion.
Delayed release	The drug substance is not released until a physical event has occurred, e.g., time elapsed, change in pH of intestinal fluids, change in gut flora.
Chewable tablets	Strong, hard tablets to give good mouth feel.
Lozenges	Strong, slowly dissolving tablets for local delivery to mouth or throat. Often prepared by a candy moulding process.
Buccal tablets	Tablets designed to be placed in buccal cavity of mouth for rapid action.
Effervescent tablets	Taken in water, the tablet forms an effervescent, often pleasant-tasting drink.
Dispersible tablets	Tablets taken in water, the tablet forms a suspension for ease of swallowing.
Soluble tablets	Tablets taken in water, the tablet forms a solution for ease of swallowing.
Hard gelatin capsules	Two-piece capsule shells which can be filled with powders, pellets, semi-solids or liquids.
Soft gelatin capsules	One-piece capsules containing a liquid or semi-solid fill.
Pastilles	Intended to dissolve in mouth slowly for the treatment of local infections. Usually composed of a base containing gelatin and glycerin.

researched areas of pharmaceutics and, given the space allowed, this chapter can only cover the science at a very basic level. It is an area that is served by a number of excellent texts, and these will be referenced at the appropriate points.

POWDER TECHNOLOGY

Virtually all solid dosage forms are manufactured from powders, and an understanding of the unique properties of powder systems is necessary for their rational formulation and manufacture. Powders consist of solid particles surrounded by spaces filled with fluid (typically air) and uniquely possess some properties of solids, liquids and gases. Powders are not solids, even though they can resist some deformation, and they are not liquids, although they can be made to flow. Still further, they are not gases, even though they can be compressed. Powder technology is concerned with solid/fluid interactions, interparticle contact and cohesion between particles. These are strongly influenced by particle size and shape and by adsorption of the fluid or other contaminants onto the surface of the particles.

While tablets and capsules, the two most common solid dosage forms, have their own unique requirements, there are similarities between them. They both require the flow of the correct weight of material into a specific volume, the behaviour of the material under pressure is important; and the wetting of the powder is critical for both granulation and subsequent disintegration and dissolution of the dosage form.

While it is not possible to deal with all aspects of powder technology in a textbook covering such a diverse range of formulations, some basic principles of powder flow, mixing and compaction and compression properties will be described. For those interested in a more in-depth treatment of the topic, there are a number of excellent texts available (Rhodes 1990; Nystrom 1995).

Particle Size and Shape

A knowledge of the particle shape and size distribution is essential to the understanding of the behaviour of powders, as it will contribute to knowledge of the secondary properties of a powder, such as flow and deformation, which influence the processability. This topic is dealt with in detail in Chapter 6.

Density

When a powder is poured into a container, the volume that it occupies depends on a number of factors, such as particle size, particle shape and surface properties. In normal circumstances, it will consist of solid particles and interparticulate air spaces (voids or pores). The particles themselves may also contain enclosed or intraparticulate pores. If the powder bed is subjected to vibration or pressure, the particles will move relative to one another to improve their packing arrangement. Ultimately, a condition is reached where further densification is not possible without particle deformation.

The density of a powder is, therefore, dependent on the handling conditions to which it has been subjected, and there are several definitions that can be applied either to the powder as a whole or to individual particles.

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