Unit 1

What is 'pharmaceutics'?

Pre-reading tasks

A. Think of the following questions before reading the text:

1. How do you understand the term 'pharmaceutics'?

. . . . . .

. . . . . .

2. What subject areas would you associate with it?

. . . . . .

. . . . . .

B.

We read texts for various reasons. Sometimes it is necessary for the reader to understand all the information included, whereas some others the reader simply needs to get a general idea of the kind of information included (skimming) or is looking for a particular piece of information (scanning).

Can you scan the text to answer the following question?

Which part of the book should a student refer to if s/he is looking for:

a) information concerning asepsis and sterilization of medicines?

. . . . . .

b) information concerning the effect of drugs on individual cells?

. . . . . .

Can you skim the text to find....

What kind of text this is? Where could you find it?

. . . . . .

. . . . . .

One of the earliest impressions that many new pharmacy and pharmaceutical science students have of their chosen subject is the large number of long and sometimes unusual-sounding names that are used to describe the various subject areas within pharmacy and the pharmaceutical sciences. The aim of this section is to explain to the reader what is meant by just one of them – '*pharmaceutics*'. I will describe how the term has been interpreted for the purpose of this book and how pharmaceutics fits into the overall scheme of pharmaceutical science and the process of designing a new medicine. I will also lead the reader through the organization of this book and explain the reasons why an understanding of the material contained in its chapters is important in the design of modern drug delivery systems.

The word 'pharmaceutics' is used in pharmacy and pharmaceutical science to encompass many subject areas that are all associated with the steps to which a drug is subjected towards the end of its development, i.e. it is the stages that follow the discovery or synthesis of the drug, its isolation and purification, and testing for advantageous pharmacological effects and absence of serious toxicological problems. Put at its simplest – *pharmaceutics converts a drug into a medicine*.

Just a comment here about the word 'drug'. This is the pharmacologically active ingredient in a medicine. 'Drug' is the correct word but because it is often confused by the general public with the common term for a substance of misuse, alternatives are used increasingly, such as 'medical agent', 'active ingredient' or 'active pharmaceutical ingredient (API)'. I still use the simpler and still correct word 'drug' here. To me, phrases like 'active ingredient' suggest that the other ingredients of a dosage form have no activity or function. This book will teach you loud and clear that this is not the case.

Pharmaceutics, and therefore this book, is concerned with the scientific and technological aspects of the design and manufacture of dosage forms. Arguably, it is the most diverse of all the subject areas in pharmaceutical science and encompasses:

- *an understanding of the basic physical chemistry necessary for the efficient design of dosage forms (physical pharmaceutics)*
- *an understanding of relevant body systems and how drugs arrive there following administration (biopharmaceutics)*
- *the design and formulation of medicines (dosage from design)*
- *the manufacture of these medicines on both a small (compounding) and large (pharmaceutical technology) scale and*

– *the avoidance and elimination of microorganisms in medicines (pharmaceutical microbiology).*

Medicines are drug delivery systems. That is, they are means of administering drugs to the body in a safe, efficient, reproducible and convenient manner. The introductory chapter to the book discusses the overall considerations that must be made so that the conversion of drug to medicine can take place. It emphasizes the fact that medicines are very rarely drugs alone but require additives to make them into dosage forms and this in turn introduces the concept of formulation. The chapter explains that there are three major considerations in the design of dosage forms:

1. *the physicochemical properties of the drug itself*
2. *biopharmaceutical considerations, such as how the administration route of a dosage form affects the rate and extent of drug absorption into the body, and*
3. *therapeutic considerations of the disease state to be treated, which in turn decide the most suitable type of dosage form, possible routes of administration and the most suitable duration of action and dose frequency for the drug in question.*

The first chapter provides an excellent introduction to the subject matter of this book and clearly justifies the need for the formulation scientist and pharmacist to understand the science contained in this text. New readers are encouraged to read this chapter first, thoroughly and carefully, so that they can grasp the basics of the subject before delving into the more detailed information that follows.

The book is then divided into various Parts that group the chapters into related subject areas. Part 1 collets some of the most important physiochemical knowledge required to design and prepare dosage forms. The chapters have been designed to

give the reader an insight into those scientific and physiochemical principles that are important to the formulation scientist. They are not intended as a substitute for a thorough of physical chemistry and many specific, more detailed, texts are available with this information.

For many reasons, that are discussed in the book, the vast majority of dosage forms are administered orally in the form of solid products such as tablets and capsules. This means that one of the most important stages in drug administration is the dissolution of solid particles to form a solution in the gastrointestinal tract. The formulation scientist thus needs knowledge of both liquid and solid materials, in particular the properties of drugs in solution and the factors influencing their dissolution from solid particles. Once solutions are formed, the formulation scientist must understand the properties of these solutions. The reader will see later in the book how drug release from the dosage form and absorption of the drug by the body are strongly dependent on the properties of the drug in solution, such as degree of dissociation and speed of diffusion of the drug molecules. Knowledge of the flow properties of liquids is useful in solving certain problems relating to the manufacture and performance of solutions and semi-solids as dosage forms in their own right.

The properties of interfaces are described next. These are important to an understanding of adsorption onto solid surfaces as involved in the dissolution of solid particles and the study of disperse systems such as colloids, suspensions and emulsions. The scientific background to the systems mentioned is also discussed.

Part 2 collects together those aspects of pharmaceutics associated with powdered materials. By far the majority of drugs are solid (mainly crystalline) powders and, unfortunately, most of these have numerous adverse characteristics that must be overcome during the design of medicines to enable their satisfactory manufacture and subsequent performance in dosage forms.

The book therefore explains the concept of the solid state and how the internal and surface properties of solids are important and need to be characterized. This is followed by an explanation of the more macroscopic properties of powders that influence their performance of dosage forms – particle size and its measurement, size reduction and size separation of powders from those of other sizes. There follows an explanation of the many problems associated with the mixing and flow of powders. In high-speed tablet and capsule production, for example, powders must contain a satisfactory mix of all the ingredients in order to achieve uniformity of dosage in each dosage form, and fast and uniform powder flow in high-speed tableting and encapsulation machines. For convenience, the mixing of liquids and semi-solids is also discussed here as the basic theory is the same.

Another extremely important area that must be understood before a satisfactory dosage form can be designed and manufactured is the microbiological aspects of medicines development and production. It is necessary to eliminate microorganisms from the product both before and during manufacture. Microbiology is a very wide-ranging subject. This book concentrates only on those aspects of microbiology that are directly relevant to te design, production and distribution of dosage forms. This mainly involves avoiding (asepsis) and eliminating (sterilization) their presence (contamination) in medicines, and preventing the growth of any microorganism which might enter the product during storage and use of the medicine (preservation). Techniques for testing that these intentions have been achieved are also described. The principles and practice of sterilization are discussed also. The relevant parts of pharmaceutical microbiology and sterilization are considered in Part 3.

It is not possible to begin to design a satisfactory dosage form without an understanding of how drugs are absorbed into the body, the various routes that can be use for this purpose and the

fate of the drugs once they enter the body and reach their site(s) of action.

The terms 'bioavailability' and 'biopharmaceutics' are defined and explained in Part 4. The factors influencing the bioavailability of a drug and methods of its assessment are described. This is followed by a consideration of the manner in which the frequency of drug administration and the rate at which it is released affect its concentration in the blood plasma at any given time. This book concentrates on the preparation, administration, release and absorption of drugs but stops short at the cellular level and leaves to other texts the detail of how drugs enter individual cells, how they act, how they are metabolized and eliminated.

Having gathered this understanding of the basics of pharmaceutics, the formulation scientist should now be equipped to begin a consideration of the design and manufacture of the most suitable dosage forms for the drug in question.

The first stage of this process is known as preformulation. This, as the name implies, is a consideration of the steps that need to be performed before formulation proper can begin. Preformulation involves a full understanding of the physicochemical properties of drug molecules and excipients and how they interact in dosage forms. An early grasp of this knowledge is of great use to the formulation scientist as the data gathered will strongly influence the design of the future dosage form. Results of tests carried out at this stage of development can give a much clearer indication of the possible (and indeed impossible) dosage forms for a new drug candidate.

The chapters collected together in Part 5 cover the formulation of, the rate and extent of drug release from, advantages and disadvantages of, and large-scale manufacture of the many dosage forms. Dosage forms suitable for the administration of drugs through almost every possible body orifice and external

surface are discussed, as well as a consideration of novel and future drug delivery systems that will be necessary for tomorrow's biotechnology products.

The pack and any possible interactions between it and the drug or medicine it contains are so vitally linked that the pack must not be considered as an afterthought. Packaging considerations should be uppermost in the minds of the formulators as soon as they receive the drug powder on which to work. The technology of packaging and filling of products is also discussed.

At this point we consider further the possible routes of microbiological contamination of medicines and the ways in which this can be prevented or minimized and how the presence of preservatives in the medicine can minimize its consequences.

Before finalizing on the formulation and the packaging of the dosage form there must be a clear understanding of the stability of drug(s) and other additives in the formulation with respect to the reasons why and the rates at which they degrade. There must be an awareness of the means of inhibiting decomposition and increasing the shelf life of a product. These points are discussed.

The book ends at the 'hard end' of manufacturing, and includes a discussion of the design of manufacturing facilities, manufacturing construction materials and the use of steam (it is still used!).

At this point the pharmaceutical technologist passes the product on to another aspect of pharmacy – the interface with the patient, i.e. dispensing and pharmacy practice. These disciplines are dealt with in the companion volume *Pharmaceutical Practice*, 3rd edition (2003), eds A. J. Winfield and R. M. E. Richards (Elsevier/Churchill Livingstone).

Aulton, M. E., 2007: 1-3

C.

When reading texts in a foreign language, the reader is bound to have unknown words. The use of a dictionary is not the only way s/he can cope with them. There are times when s/he can guess the meaning of a word with the help of its context and the knowledge s/he already posseses concerning the subject the text is about.

With this in mind, could you try to guess the meaning of the following words? (the number of the paragraph they appear in is given in the brackets). This could also help you to express yourself more fluently, either in writing or orally, since it can give you practice in finding synonymous expressions or increase the skill of circumlocution (paraphrase).

encompass (2): . . . . . .

alternatives (3): . . . . . .

administer (5): . . . . . .

substitute (7): . . . . . .

particles (8): . . . . . .

adverse (10): . . . . . .

contamination (12): . . . . . .

assessment (14): . . . . . .

orifice (17): . . . . . .

discipline (22): . . . . . .

Reversing the above, could you try to find words from the text that mean the following?

(2) change into another form, substance or state: . . . . . .

(3) measured amount of medicine to be taken at a time: . . . . . .

(5) action of taking or sucking in liquids: . . . . . .

(8) liquid containing a solid or gas mixed into it, usu. without chemical change: . . . . . .

(8) qualities, power or effects that belong to something: . . . . . .

(9) place or area where different things meet and have an effect on each other: . . . . . .
(20) change from a compound chemical to a simpler one: . . . . . .
(20) act of decaying or breaking up and separating into simple parts:. . . . . .

D.

If you are interested in the information of this text, read it more carefully and try to answer the following questions by referring to it but not copying it. This rephrasing could help you practice expressing your ideas in written form, which differs significantly from the oral form of the language, especially when academic writing is concerned.

1. What is a 'drug' and how does it differ from a medicine?

. . . . . .
. . . . . .

2. What is 'pharmaceutics'?

. . . . . .
. . . . . .

3. What factors should be considered when designing a medicine?

. . . . . .
. . . . . .

4. What knowledge should a scientist formulating a medicine have?

. . . . . .
. . . . . .

E. The text contains words which are pertinent to your field of studies. If you would like to check some of them, you can try to find to do the following crossword puzzle.

Across

5. belonging to the stomach and the intestine
6. a pharmacologically inert, adhesive substance, used to bind the contents of a pill or tablet
7. act of gathering (a gas, liquid or dissolved substance) on a surface or in a condensed layer
9. chemical substance used to hinder decomposition or fermentation

Down

1. creamy mixture of liquids which do not really unite, such as oil and water
2. the separation of a thing into its parts
3. liquid mixture with very small pieces of solid material contained but not combined in the liquid
4. make up and distribute medicine, esp. on prescription
8. the yellowish liquid in which the blood cells are held