

Essentials of Pharmacology for Nurses

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Open University Press

Open University Press
McGraw-Hill Education
McGraw-Hill House
Shoppenhangers Road
Maidenhead
Berkshire
England
SL6 2QL

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world wide web: www.openup.co.uk

and Two Penn Plaza, New York, NY 10121-2289, USA

First published 2009

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A catalogue record of this book is available from the British Library

ISBN-13: 978-0-33-523404-2 (pb) 978-0-33-523403-5 (hb)
ISBN-10: 0335234046 (pb) 0335234038 (hb)

Library of Congress Cataloging-in-Publication Data
CIP data applied for

Typeset by YHT
Printed in UK by Bell and Bain Ltd, Glasgow.

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Introduction

Administration of medicines, medicines management, nurse prescribing, clinical governance and risk management are all key areas of the role of the nurse. New medicines are being introduced daily and it is the nurse's responsibility to gain knowledge regarding the medicines they are dealing with. Recently there have been calls for nurses, particularly in their pre-registration period of education, to become more knowledgeable about aspects of pharmacology and the calculation of drug dosages.

Where then do we start with the process of education? It is our belief that the key to education is through a process of motivation. We both remember, as students, sitting and trying to come to terms with scientific language and almost falling asleep in an attempt to unravel the intricacies of mathematical formulae and biochemical presentations of molecular function.

Learning about medicines is a fundamental part of the nurse's role, whichever branch of nursing you decide to choose as a career pathway. This book is written in an attempt to bring to life and engage you in the subjects of pharmacology and calculation of drugs. First, you will notice that not all drugs are listed. Indeed, we have tried to focus on some of the major drug groups so as to give you a taste of how interesting the subject can be, without initially overwhelming you. Chapters that discuss major drug groups have been enhanced by the inclusion of relevant aspects of physiology.

When putting the initial idea for the book together, we decided that it should include both aspects of pharmacology and drug calculations. However, the book does not contain detailed types of formulae – rather it gives you a basic structure on which to build upon. We wanted the calculations to reflect each of the chapters' contents and give you a sense of what might be expected in

practice. You will not find many examples of the giving of intravenous fluids as we felt this is well covered in other texts, some of which you will find in the recommended reading section at the end of each chapter. These sections deliberately repeat the key texts in this field for your ease of reference, and in addition include works specific to the chapter's topic.

A further feature of the book that we thought might be helpful is the inclusion of case studies. Most chapters contain at least two scenarios and, unlike most other books, we have included examples of some of the points that you should have been considering in analysing these scenarios.

Where possible we have also tried to focus the pharmacology on nursing practice. You will notice that in each chapter there are at least five or six boxes entitled 'Clinical tips'. These have been created to increase your understanding of the importance of pharmacology within nursing. The 'Clinical tips' should also assist you to reflect upon your everyday practice in medicines' management.

Finally, we have included 10 multiple choice questions for each of the 10 chapters in the book. All the questions are based on information included in the chapter so there are no trick questions. We thought the idea of evaluating what you have gained in knowledge from reading each chapter was important and we hope you enjoy getting them all right!

Well dear student, it is now time to embark on what we hope will be a fascinating journey. We hope this journey will assist you with your initial learning needs, inspire you to ask more questions, and also motivate you to move on to more detailed texts. As we said earlier, motivation is the key to education. You are now our judge and jury. Enjoy!

About the Authors

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Paul Barber (MSc Practitioner Research, BSc (Hons) Nursing, Dip N (Lond), Cert Ed, RNT, SRN, RMN) commenced his nursing career in 1974 as a cadet nurse, where he completed both his Registered Mental Nurse and State Registered nurse training. Paul spent his early career in Surgery, high dependency and accident and emergency and then progressed to become manager of a small surgical unit. Paul commenced a teaching career in October 1988 and has held a variety of positions in education from senior lecturer to head of an educational centre. Paul's current role is that of senior lecturer and he teaches both Pre and post registration nurses.

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Pharmacodynamics and pharmacokinetics

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Learning objectives

Introduction

Absorption

Distribution

Biotransformation

Hepatic metabolism

Excretion

General and molecular aspects

Receptors

Ion channels

Enzymes

Transport systems

Drug action

First pass metabolism

The concept of affinity

Agonistic and antagonistic drug action

Basic introduction to units and conversions

Basic formula

Case studies

Key learning points

Calculations

Multiple choice questions

Recommended further reading

Learning objectives

After studying this chapter you should be able to:

- Understand what is meant by pharmacokinetics and pharmacodynamics.
- Describe aspects of absorption, distribution, metabolism and excretion of a drug.
- List the principal routes of drug administration.
- Name the phases in hepatic metabolism.
- Describe what is meant by the term 'cell receptor'.
- Outline how drugs affect the body.
- Give three examples of different cell receptors.
- Outline what is meant by 'ionic channel'.
- Describe the term 'first pass metabolism'.
- Understand at a basic level the term 'affinity'.
- Differentiate between a drug that is an agonist and a drug that is an antagonist.
- Use basic maths to calculate simple drug dosages.



Introduction

Part of the nurse's role, alongside the pharmacist, is the need to ensure that medicines are administered appropriately. That is why it is essential that the nurse has a good knowledge and understanding of pharmacology and the relevant calculations in terms of patient care. Pharmacology is the study of drugs (chemicals) and their interactions with the body. The term is derived from the Greek *pharmakon* which can mean both 'remedy' and 'poison'. In modern medical practice we use drugs more and more to treat and manage disease, so it is vital that as nurses we understand the basic mechanisms of drug action.

The aim of this chapter is to introduce the basic principles of pharmacology in relation to nursing practice. The chapter will give you an appreciation of *pharmacodynamics* and *pharmacokinetics*. It will identify the main targets for drug action and allow you to develop an understanding of drug absorption, metabolism and excretion.

Put simply:

- *pharmacodynamics* is the effect that drugs have on the body; while
- *pharmacokinetics* is the study of the way in which drugs move through the body during absorption, distribution, metabolism and excretion.

For drugs to produce their effects they must interact with the body. This can happen in many ways and depends on the properties of the drug, and will be discussed later in this chapter. Pharmacokinetics influence route choice and occur after administration can be broken down into four distinct areas:

- A** Absorption of the drug
- D** Distribution of the drug molecules
- M** Metabolism of the parent drug
- E** Excretion or elimination of the drug and its metabolites

Absorption

Before a drug can begin to exert any effect on the body it has to be absorbed into the body systems.

This absorption process can be affected by many things but the main factor relating to absorption is the route of administration (see Box 1.1).

It is important that nurses understand the implications attached to choosing routes of administration of drugs based on their absorption. Many patients may need to have their medication administration tailored to their particular medical condition or the medication which they are prescribed and this is an important factor to consider as it can impact on the patient's ability or desire to take their medication.

Other factors controlling the rate and reliability of drug absorption can be said to be *physiological* or *physico-chemical*.

Physiological factors relate to human physiological functions:

- **Blood flow to absorbing site.** The better the blood supply to the area the greater the rate of absorption. Therefore if a person has a good circulation they will have the ability to absorb the drug well.
- **Total surface area for absorption.** The greater the surface area the greater the rate of absorption. The intestine has a very large surface area, making it an ideal target for drug absorption. That is why you will find that most drugs where possible are given orally.
- **Time of arrival and contact time at absorption site.** The longer the drug is in contact with the absorbing surface the greater the rate of absorption. That is why if a person is suffering from diarrhoea the chances of a drug given orally being absorbed completely are lowered and other means of administration must be considered.

Physico-chemical factors relate to the chemical make-up of the drug in relation to human physiological function:

- *Solubility:* how soluble the drug is in body fluids. As the body is made up of a large amount of water, drugs can dissolve readily. However, certain drugs do not dissolve into small enough particles to ensure rapid absorption.
- *Chemical stability:* will it break down readily?



- Lipid to water partition coefficient:** is it more fat soluble than water soluble? This is an important area to consider. As your cells are made up of a phospho-lipid layer, any drug that can dissolve well in lipids will pass through your tissues far more rapidly. Examples of drugs that are highly lipid soluble are anaesthetic agents and benzodiazepines.
- Degree of ionization:** Some drugs are weak acids and weak bases (alkalis). These drugs tend to disassociate when given to a person. Basically, this means that some of the drug remains active and some is inactive. Often this depends on the pH of the solution (i.e. its acidity or alkalinity) in which the drug is being dissolved. For example, a weak acid does not

Box 1.1 Principal routes of drug administration



ROUTE	ADVANTAGES	DISADVANTAGES
ENTERAL ROUTES		
ORAL	convenient, non-sterile, good absorption for most drugs	GI irritation, potential for interactions, first pass destruction, inactivated by acids, variable absorption
SUBLINGUAL/BUCCAL	Avoids first pass (see p. 7), avoids gastric acid	Few preparations suitable
RECTAL	Avoids first pass, avoids gastric acid	Less dignified for the patient
PARENTERAL (refers to IV, IM and SC) ROUTES		
INTRAVENOUS (IV)	Rapid action, complete availability	Increased drug levels to heart, must be sterile, risk of sepsis and embolism
INTRAMUSCULAR (IM)	Rapid absorption	Painful, risk of tissue damage
SUBCUTANEOUS (SC)	Good for slower absorption	Absorption variable
INHALED (LUNGS)	Large absorption area, good for topical use	Few disadvantages
Other routes include intra-arterial, intrasternal, intrathecal, intra-articular, intraperitoneal, intraventricular, nasal, bronchial, vaginal, skin and conjunctiva		

disassociate as much if dissolved in an acid environment. This means that the drug can cross membranes in a more active form than if it had been dissolved in a neutral or base solution.

Clinical tip



It is very important that the patient takes the medicine as directed in order that they get the best therapeutic value from it. Therefore as a nurse it is important that you understand the mechanics of absorption so that you can explain to the patient the reason for the drug being taken at the correct time.

Clinical tip



As a nurse in practice it is important you are aware of drugs such as Warfarin so that you can be aware of the symptoms which the patient may display if they become toxic with the drug.

Distribution

Once drugs have been administered and absorbed, they have to be distributed to their site of action. For some drugs that site is known and such drugs are available to give locally or topically. All other drugs need to be distributed throughout the body.

There are four main elements to this:

- 1 *Distribution into body fluids.* These are mainly plasma, interstitial fluid and intracellular fluid. Molecular targets for drugs are found in these areas.
- 2 *Uptake into body tissues/organs.* Specific tissues take up some drugs – for example, iodine and thyroid gland.
- 3 *Extent of plasma protein binding.* Plasma proteins such as albumin can bind drug molecules. This varies widely amongst drugs. Drugs bound to plasma proteins are pharmacologically inert; only free drugs are active. Some drugs do not bind (e.g. caffeine) and some are highly bound (e.g. Warfarin which is 99 per cent bound to plasma proteins). Some drugs can displace others from their binding sites on the plasma proteins – for example, phenylbutazone can displace Warfarin from plasma proteins. This is an important consideration for drugs which have this effect.

- 4 *Passage through barriers.* The two main examples are the placenta and the blood-brain barrier (BBB). Drugs must be highly lipid soluble to pass across these barriers. If not, they may not be able to reach their site of action.

The factors which affect drug distribution are taken into consideration by drug companies when developing and formulating medications. While these factors are of interest, the nurse's role in monitoring drug distribution is mainly in monitoring the onset of the effect of, or the response to, the medication. If analgesia is given and the patient reports reduced or relieved pain, the drug has been distributed to its target site.

Biotransformation

Biotransformation of drugs is the process of metabolizing the parent drug compound and occurs mainly in the liver (hence the term *hepatic metabolism*) to different compounds called metabolites. The drug metabolite may have decreased, increased or undergone no change in pharmacological activity compared to the Parent drug. It may also have a different activity. Some drugs are what are termed *pro-drugs* – that is the drug itself is pharmacologically inactive until it is metabolized by the liver to its active form. A good example is codeine, which is metabolized to morphine by the body. The metabolite is more polar (i.e. chemically charged) than the parent drug and therefore is more readily excreted by the kidney. Drug metabolism can influence dose and frequency of dosing. Drugs which are metabolized quickly have a short duration of action and need to be administered more often (two, three or four times daily). Drugs which are metabolized slowly can have a



longer duration of action and may only need to be given on a once-daily basis.

Hepatic metabolism

Phase	Process
Phase I metabolism	Oxidation
	Reduction
	Hydrolysis
Phase II metabolism	Conjugation

Table 1.1 Metabolic phases and processes

The terms shown in Table 1.1 are different chemical reactions that change the properties of drugs to facilitate their removal from the body by excretion. Most drugs undergo phase I oxidation followed by phase II conjugation.

Clinical tip



It is important as a nurse to recognize that babies, particularly those less than 6 months old may not have a mature liver and therefore drugs are given with great caution.

Also, patients who have diseases which have an impact on liver function – for example, congestive heart failure, should be given drugs cautiously as their ability to metabolize a given drug will be greatly impaired.

Excretion

Once drugs have had their desired effect they need to be excreted by the body. Principles of excretion include renal elimination and clearance, secretion into bile for faecal elimination and enterohepatic recirculation. As previously outlined, some drug metabolites can also have pharmacological effects. If these compounds were not eliminated, they would accumulate in the bloodstream and could cause toxic and unwanted effects.

The main method of renal elimination is by active glomerular filtration. This is where ionized drugs are actively secreted into the proximal

tubule. These ionized compounds are actively excreted by the kidney and are 'pushed' out into urine. A more passive form of drug compound movement occurs in the distal tubule of the kidney. Here there is passive absorption and excretion of drug molecules and metabolites according to a concentration gradient. Molecules move from a high concentration to a lower concentration by diffusion. This applies to unionized compounds (drugs without charge), and prevents the entire dose of a drug being excreted at once. This helps to maintain circulating plasma levels to allow the drug effect to continue until the next dose is taken.

Clinical tip



People who have renal impairment may require dosage alterations to achieve a therapeutic level. Older patients also need special consideration, as the kidney does not perform as well as we get older, resulting in a lower glomerular filtration rate.

Excretion into bile is another method of eliminating drug molecules and metabolites. These are secreted from the liver into bile and into the gut for faecal elimination. As in renal excretion, not all of the drug and its metabolites are eliminated entirely at once. Some drugs undergo enterohepatic recirculation. This is where some of the drug is reabsorbed from the gut, back into the blood stream and represented to the liver for further metabolism. This can help to maintain circulating levels of active molecules to prolong drug effect until the next dose. An important example of a drug that undergoes this is the combined oral contraceptive pill.

General and molecular aspects

It is important that nurses involved in medicines management are aware of the sites of action for many commonly used drugs. Drugs exert their effects at molecular (chemical) targets, of which there are many. Below are some of the commonest.

**Receptors**

The plasma membrane of a human cell is selectively permeable in that it helps control what moves in and out of the cell. The cell membrane consists of a thin structured bilayer of phospholipids and protein molecules. The surfaces of plasma membranes are generally studded with proteins that perform different functions, like the reception of nutrients. In biochemistry these protein molecules are referred to as *receptors*. Molecules which bind to these receptors are called *ligands*. Examples of ligands are neurotransmitters, hormones or drugs.

A large number of drugs, which are clinically effective, exert their action by interaction with receptors. Examples include:

- ligand-gated ion channels (ionotropic receptors) such as the GABA_A receptor, which binds benzodiazepines;
- G-protein coupled receptors such as adrenoceptors;
- kinase-linked receptors such as the insulin receptor;
- nuclear receptors such as the thyroid receptor.

Ion channels

Ion channels provide receptors which drugs can interact with. Drug actions at ion channels can take two forms (see Figure 1.1). The first form is *channel blockers*, whereby the drug blocks permeation of the channel, and the second is *channel modulators* whereby the drug binds to a receptor

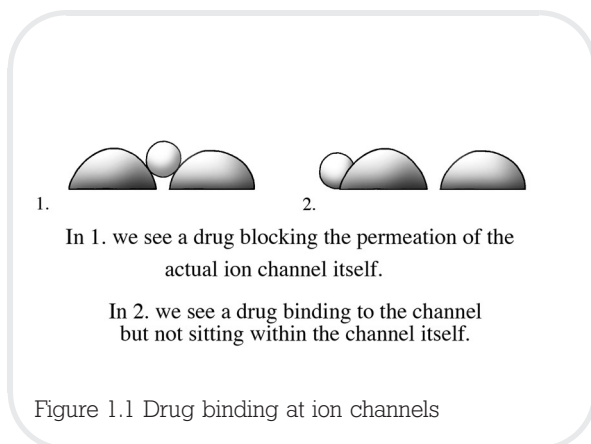


Figure 1.1 Drug binding at ion channels

site within the ion channel and modulates permeation. This can happen by the drug altering the channels response to its normal mediator.

Enzymes

Enzymes are biological catalysts that increase the rate of chemical reactions in the body. They are integral to many normal physiological functions. Many drugs target enzymes to prevent them from carrying out their normal function – for example, Captopril acts on angiotensin converting enzymes, thereby preventing an increase in blood pressure.

Transport systems

These are also known as carrier molecule interactions. In some transmitter systems, there is normal physiological recycling of the transmitters, such as serotonin. After the release of serotonin from a neurone, it is taken back up by that same neurone using a serotonin-selective re-uptake system. The drug fluoxetine blocks the uptake transporter for serotonin as its mode of action. This results in an increased level of serotonin in the neuronal synapse. This mechanism has an onward effect which facilitates an increase in mood and makes Fluoxetine and drugs similar to it good antidepressants.

Drug action

The time to the onset of drug action involves delivery of the drug to its site of action. This is largely controlled by:

- route of administration;
- rate of absorption;
- manner of distribution.

These are important considerations, as often we want the drug to have its effect within a certain time frame. We can speed up the time to the onset of drug action in many ways. If the drug is given orally, we can use liquid or dispersible formulations instead of regular tablets. If drug action is needed more quickly, we can use the intramuscular (IM) or intravenous (IV) route as necessary.



For example, if a patient requires pain relief following myocardial infarction they would be given intravenous morphine rather than an oral preparation.

It is also possible to delay drug onset or prolong the effect by using enteric-coated or slow release preparations orally, or by using transdermal or subcutaneous (SC) routes. For example, people suffering with chronic pain from conditions such as rheumatoid arthritis may be given analgesia in the form of a transdermal patch. This is much preferred by the patient as it decreases the amount of oral analgesia required.

The duration of drug effect relates to the time it takes for the drug to be removed from its site of action. This is largely controlled by:

- rate of hepatic metabolism;
- rate of renal excretion.

It is important to be aware of the duration a drug will have its effect for. Drug companies do extensive studies to determine this information. They use the data they obtain to decide upon dosing schedules. It is vital that nurses know the normal dosing schedules for the drugs they are administering (this can easily be found in the British National Formulary – BNF) so that the correct regimen is implemented. Drugs need to be given more than once to have continued effect. Some drugs need to be given daily, while others need to be given two, three or four times per day to maintain effective action.

First pass metabolism

Some drugs undergo destruction by *first pass metabolism*. When absorbed through the stomach after oral administration, the drugs enter blood vessels which go directly to the liver. We call this the *portal circulation*. This means that drugs which are largely destroyed by liver enzyme systems will not enter the general systemic circulation. An example of such a drug is glyceryl trinitrate (GTN) which is metabolized completely by the liver at this stage. This is why you will find GTN being given via routes other than orally.

The concept of affinity

Drugs have what is termed an *affinity* for their receptors, or chemical targets. This is a measure of how well a drug can bind to its chemical target. The tighter the bond, the better the drug action. Some drugs have a higher affinity for their chemical targets than others. Those with a higher affinity will bind first, in preference to any other drug molecule present. Some drugs have a higher affinity for their targets than even the normal physiological molecule. This can be very useful in drug action, especially where the normal molecule is abundant and causing the problem or symptom the patient is experiencing. Higher affinity means that even small amounts of the drug will bind preferentially.

Agonistic and antagonistic drug action

Drugs can either be *agonists* or *antagonists* at their target sites. This is best explained using receptors as an example (see Figure 1.2).

Agonists are drugs that bind to their targets and form a drug-receptor complex. Agonists activate the receptors to produce a response (known as *full agonists*) and have what is termed *positive efficacy*. Antagonists are drugs that bind to their targets and form a drug receptor complex, but without causing activation or response. They can block the receptor to its endogenous activator, thereby blocking normal function. They have what is termed *zero efficacy*.

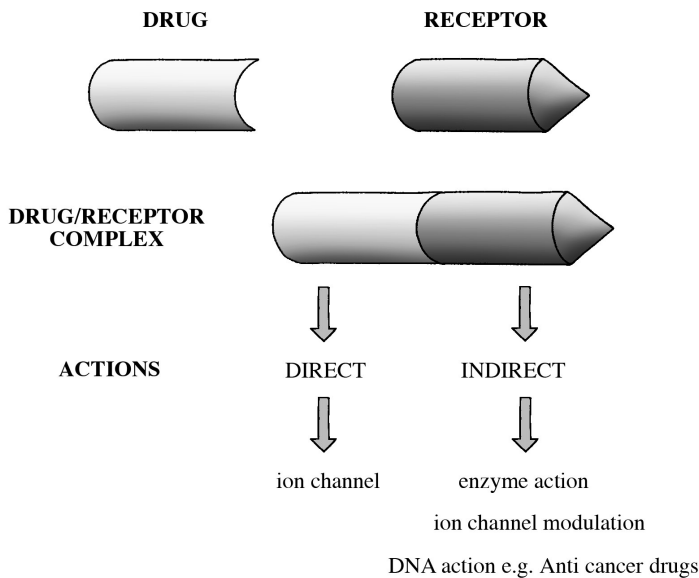
This is a simplistic view of the concepts of agonism and antagonism as the response of a drug at its chemical target is actually graded.

For agonists we have:

- *Partial agonists*: drugs that bind to their targets and activate them to produce a response which is less than that we would expect from a full agonist. They have what is termed *partial efficacy*.
- *Inverse agonists*: drugs that bind to their targets and can reduce the normal activity of that chemical target. They have what is termed *negative efficacy*.



AGONISTS



ANTAGONISTS

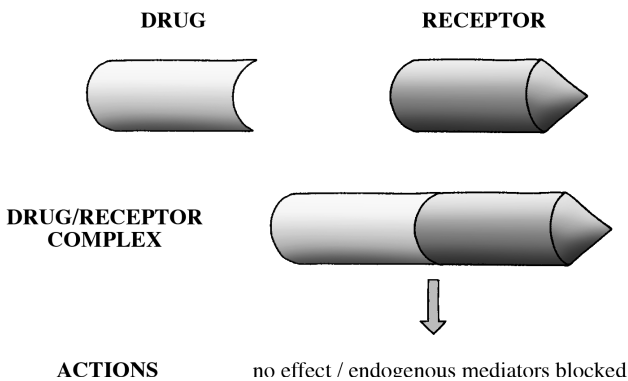


Figure 1.2 Basic receptor theory

For antagonists we have:

- *Competitive antagonists*: drugs that bind to the chemical targets and prevent activation by the normal target agent.
- *Non-competitive antagonists*: drugs that do not necessarily bind to the chemical target but at a point in the chain of events block target activation.

Basic introduction to units and conversions

Nurses need to be able to make accurate drug calculations in order to safely administer drugs to their patients. It is therefore important that student nurses begin to engage with mathematics early in their education. This brief introduction is aimed at motivating you to engage with other purpose-designed texts to help you develop your skills to the required level.

Before performing many drug calculations you will need to convert the numbers you use in the


Box 1.2 Equivalencies of weight


UNIT	SYMBOL	EQUIVALENT	SYMBOL
1 kilogram	kg	1000 grams	g
1 gram	g	1000 milligrams	mg
1 milligram	mg	1000 micrograms	m _{cg} or μg
1 microgram	m _{cg}	1000 nanograms	ng

- To convert from a smaller unit to the next higher unit divide by 1000
- To convert from a larger unit to a smaller unit multiply by 1000

calculation so that they all appear in the same units. You should be familiar with the units in Box 1.2 as they are the most common encountered in drug calculation.

To convert from a smaller unit (e.g. a gram) to a larger unit (e.g. a kilogram) you should divide by 1000, so:

$$5000\text{g} \div 1000 = 5\text{kg}$$

To convert from a larger unit (e.g. a gram) to a smaller unit (e.g. a milligram) you should multiply by 1000, so:

$$5\text{g} \times 1000 = 5000\text{mg}$$

It is important to be comfortable with unit conversions before progressing to using a drug calculation formula. Practise some conversions before you move on.

Basic formula

There is more than one way to do a drug calculation, but the simplest and most widely used method is the basic formula show here:

$$\frac{D \times Q}{H} = X$$

Where:

- D = desired dose
- H = strength available
- Q = quantity or unit of measure (for tablets Q = 1, for liquids Q can vary)
- X = dose to be determined/amount to be given

The steps for using the basic formula method are as follows:

- first, memorize the formula;
- remember to convert all the units to same system and size;
- place all of the unit information into the correct position within the basic formula;
- calculate your answer;
- label all answers (e.g. tablets, capsules, ml).

Here are some examples.

The doctor orders a dose of 0.05mg to be given orally

You have 25 microgram tablets

How many tablets should you give?

$$\frac{50}{25} \times 1 = X$$

$$\frac{2}{1} \times 1 = 2$$

$$X = 2 \text{ tablets}$$

The patient requires 400mg of liquid to be given orally

You have 250mg in 5ml of solution

What volume of drug should be given?

$$\frac{400}{250} \times 5 = X$$

$$\frac{8}{5} \times 5 = 8$$

$$X = 8\text{ml}$$

The patient needs 240mg of drug D by injection.

150mg in 5ml of liquid is available

How many ml will you administer?

The dose has to be given at a rate of 1ml every 30 seconds: how long with each dose last?

$$\frac{240}{150} \times 5 = X$$

$$\frac{24}{15} \times 5 = 8\text{ml to be given}$$

1 ml every 30 seconds =
2ml every minute

$$\frac{8}{2} = 4 \text{ minutes}$$

You should now be able to attempt the practice questions at the end of this and each relevant chapter.

Case studies



① Mrs Asamoah is a 72-year-old woman who has been admitted to the medical unit following a general deterioration in her mobility and ability to carry out most of the activities of living independently. She has suffered from rheumatoid arthritis for many years and takes co-codamol with moderate effect. On admission she looks pale, lethargic and is complaining of pain in her knees and hands. She informs you that she has also been taking Atenolol 50mg daily for the past five years.

Following a discussion with her daughter, you learn that she has recently commenced a course of trimethoprim to treat a urinary tract infection but has been reluctant to take it as she claims that she has too many tablets to take and they tend to get stuck when swallowing.

- What information from Mrs Asamoah's assessment could you now obtain which would help you identify factors influencing the absorption and distribution of the medication she is taking?

② Mr Mambety is a 42-year-old man who is recovering from emergency gastric surgery. He has a history of heavy drinking and cigarette smoking. His post-operative pain is being controlled by a patient-controlled analgesic device and he is beginning to mobilize with assistance.

- What factors may influence Mr Mambety's ability to metabolize and excrete any drugs he is prescribed during his post-operative recovery?



Key learning points

Introduction

- Pharmacology is the study of drugs.
- Pharmacodynamics is the effect that drugs have on the body.
- Pharmacokinetics is the effect the body has on the drugs.
- Pharmacokinetics includes absorption, distribution, metabolism and excretion of drugs.

Absorption

- The main factor which relates to absorption of drugs is the route of administration.
- Physiological considerations in absorption are blood flow, total surface area, time of arrival of the drug and time of drug at absorption site.
- Other considerations for absorption are solubility, chemical stability and how soluble the drug is in lipids.

Distribution

- Drugs are distributed into major body fluids (e.g. plasma).
- Specific tissues may take up certain drugs (e.g. iodine is taken up by the thyroid gland).
- Drug distribution is affected by the extent that the drug binds to plasma proteins.
- Drug distribution is affected by barriers (e.g. the placenta and the blood-brain barrier).

Biotransformation

- This is a process of metabolising drugs in the body.
- It occurs mainly in the liver and is therefore often called hepatic metabolism.
- Some drugs are given that are activated by this hepatic metabolism. These are called pro-drugs.
- Drug metabolism is split into two phases in the liver.
- An example of phase one metabolism would be oxidation.
- An example of phase two metabolism would be conjugation.

Excretion

- Excretion includes renal elimination and faecal elimination.
- The main method of renal elimination is by active glomerular filtration.
- Drugs can also be eliminated by passive methods in the distal tubules.
- Drugs can be eliminated from the body in bile and so removed in the faeces.

General and molecular aspects

- Drugs exert their effects at molecular (chemical) targets (e.g. adrenaline receptors).
- Drugs can also act by stopping or partially stopping important ions entering the cell (e.g. calcium channel blockers).





- Drugs can interfere with enzymes that are produced by the body.
- Drugs can work on the transport of chemicals into and out of cells.

Drug action

- Drug action relies on route of administration, rate of absorption and manner of distribution.
- The duration of drug effect involves how quickly it is removed from the body.
- Some drugs when absorbed from the stomach enter the portal circulation and pass through the liver. This is called the first pass effect.
- Drug action can also be affected by drug affinity.
- The greater the affinity the better the drug action.

Agonistic and antagonistic drug action

- Agonists activate receptors to produce a response.
- Antagonists bind with receptors but do not activate them or cause a response. They can actually block the activation of receptors.
- Partial agonists produce a response. However, this is less than would be expected by a full agonistic drug.
- Inverse agonists are drugs which can reduce the normal activity of the cell.
- Competitive antagonists are drugs that prevent activation of the cell by their normal agent.
- Non-competitive antagonists are drugs that may block the receptor but not in a permanent way.



Calculations

- 1 How many micrograms are in 2mg?
- 2 How many grams are in 600mg?
- 3 How many milligrams are in 1.2g?
- 4 Which strength is the weakest: 1 in 100, 1 in 1000 or 1 in 10,000?
- 5 If a patient has a fluid intake of 30ml each hour, how much fluid (in ml) have they had after 12 hours?
- 6 A doctor has prescribed 0.25mg of digoxin. You have 125 microgram tablets in stock. How many should you give?
- 7 How many 25mg tablets should be administered for a prescribed dose of 0.05g?

For further assistance with calculations, please see Meriel Hutton's book, *Essential Calculation Skills for Nurses, Midwives and Healthcare Practitioners* (Open University Press, 2009).



Multiple choice questions

Try answering these multiple choice questions to test what you have learned from reading this chapter. You can check your answers on page 175.

1 A drug that binds to a cell receptor and affects a response is called

- a) An agonist
- b) An antagonist
- c) A receptor blocker
- d) A channel blocker

2 Most drugs and metabolites are excreted by

- a) The kidneys
- b) The lungs
- c) Bile
- d) Saliva

3 The four processes in pharmacokinetics are

- a) Stomach, liver, kidney and lungs
- b) Receptors, ion channels, transport systems and enzymes
- c) Administration, absorption, metabolism and elimination
- d) Absorption, distribution, metabolism and excretion

4 Pharmacodynamics is defined as

- a) The effect our body has on drugs
- b) The action of the liver on drug molecules
- c) The effect a drug has on our bodies
- d) The movement of a drug around the body

5 The main method of renal elimination of a drug is by

- a) Passive distal excretion
- b) Active glomerular filtration
- c) selective reabsorption
- d) Active secretion into the collecting duct

6 How many phases of hepatic metabolism are there?

- a) 1
- b) 2
- c) 4
- d) 10





7 What route should drugs subject to first pass metabolism *not* be given by?

- a) IV
- b) IM
- c) Sublingual
- d) Oral

8 Which of the following is a plasma protein?

- a) Prostacyclin
- b) Albumin
- c) Protamine
- d) Meatamine

9 A pro-drug is

- a) A drug given to promote growth
- b) A drug given in its active form
- c) A drug given to prevent metabolism of another drug
- d) A drug given in its inactive form, requiring metabolism

10 An antagonist can be

- a) Competitive and non competitive
- b) Competitive and complimentary
- c) Competitive and comparative

Recommended further reading

Beckwith, S. and Franklin, P. (2007) *Oxford Handbook of Nurse Prescribing*. Oxford: Oxford University Press.

Brenner, G.M. and Stevens, C.W. (2006) *Pharmacology*, 2nd edn. Philadelphia, PA: Saunders Elsevier.

Clayton, B.D. (2006) *Basic Pharmacology for Nurses*, 14th edn. Edinburgh: Mosby Elsevier.

Coben, D. and Atere-Roberts, E. (2005) *Calculations for Nursing and Healthcare*, 2nd edn. Basingstoke: Palgrave Macmillan.

Downie, G., Mackenzie, J. and Williams, A. (2007) *Pharmacology and Medicines Management for Nurses*, 4th edn. Edinburgh: Churchill Livingstone.

Gatford, J.D. and Phillips, N. (2006) *Nursing Calculations*, 7th edn. Edinburgh: Churchill Livingstone Elsevier.

Karch, A.M. (2008) *Focus on Nursing Pharmacology*, 4th edn. Philadelphia, PA: Lippincott Williams & Wilkins.

Lapham, R. and Agar, H. (2003) *Drug Calculations for Nurses: A Step-by-step Approach*, 2nd edn. London: Arnold.

Simonson, T., Aarbakke, J., Kay, I., Coleman, I., Sinnott, P. and Lyssa, R. (2006) *Illustrated Pharmacology for Nurses*. London: Hodder Arnold.

Trounce, J. (2000) *Clinical Pharmacology for Nurses*, 16th edn. New York: Churchill Livingstone.

Adverse drug reactions and interactions

Chapter contents

Learning objectives

Introduction

Main mechanisms of drug interactions

Absorption

Distribution

Metabolism

Excretion

Adverse drug reactions

Type A: augmented

Type B: bizarre

Clinical significance of drug interactions to the patient

Type A ADR

Type B ADR

Major groups of drugs involved in adverse drug interactions

Steps in minimizing the effects of adverse drug interactions

Age-related adverse drug reactions

Absorption

Distribution

Metabolism

Excretion

Case studies

Key learning points

Multiple choice questions

Recommended further reading

Learning objectives

After studying this chapter you should be able to:

- Convey the importance of recognizing adverse drug reactions and interactions.
- Describe why drug interactions occur in absorption, distribution, metabolism and excretion of drugs.
- Explain what is meant by the terms enzyme inducer and inhibitor.
- Define the term adverse drug reaction.
- Give two examples of different drug reactions.
- List three common drugs which are frequently implicated in drug reactions.
- Discuss the steps taken in minimizing drug interactions in patient care.
- Describe why elderly people and children are at a higher risk of drug interaction than other age groups.