**Lecture 1**

**In medicinal chemistry, the chemist attempts to design and synthesize a medicine or a**

**pharmaceutical agent which will benefit humanity. Such a compound could also be**

**called a 'drug', but this is a word which many scientists dislike since society views the**

**term with suspicion.**

With media headlines such as 'Drugs Menace', or 'Drug Addiction Sweeps City

Streets', this is hardly surprising. However, it suggests that a distinction can be drawn

between drugs which are used in medicine and drugs which are abused. Is this really true.

Can we draw a neat line between 'good drugs' like penicillin and 'bad drugs' like

heroin? If so, how do we define what is meant by a good or a bad drug in the first

place? Where would we place a so-called social drug like cannabis in this divide? What

about nicotine, or alcohol?

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The answers we would get would almost certainly depend on who we were to ask.

As far as the law is concerned, the dividing line is defined in black and white. As far as

the party-going teenager is concerned, the law is an ass.

As far as we are concerned, the questions are irrelevant. To try and divide drugs

into two categories—safe or unsafe, good or bad, is futile and could even be dangerous.

First of all, let us consider the so-called 'good' drugs—the medicines. How 'good'

are they? If a medicine is to be truly 'good' it would have to satisfy the following

criteria. It would have to do what it is meant to do, have no side-effects, be totally

safe, and be easy to take.

How many medicines fit these criteria?

The short answer is 'none'. There is no pharmaceutical compound on the market

today which can completely satisfy all these conditions. Admittedly, some come quite

close to the ideal. Penicillin, for example, has been one of the most effective antibacterial

agents ever discovered and has also been one of the safest. Yet it too has drawbacks. It has never been able to kill *all* known bacteria and as the years have gone by, more and more bacterial strains have become resistant.

Nor is penicillin totally safe. There are many examples of patients who show

an allergic reaction to penicillin and are required to take alternative antibacterial agents.

Whilst penicillin is a relatively safe drug, there are some medicines which are

distinctly dangerous. Morphine is one such example. It is an excellent analgesic, yet it

suffers from the serious side-effects of tolerance, respiratory depression, and addiction.

It can even kill if taken in excess.

Barbiturates are also known to be dangerous. At Pearl Harbor, American

casualties undergoing surgery were given barbiturates as general anaesthetics. However,

because of a poor understanding about how barbiturates are stored in the body, many patients received sudden and fatal overdoses. In fact, it is reputed that more casualties died at the hands of the anaesthetists at Pearl Harbor than died of their wounds. To conclude, the 'good' drugs are not as perfect as one might think.

What about the 'bad' drugs then? Is there anything good that can be said about

them? Surely there is nothing we can say in defence of the highly addictive drug heroin?

Well, let us look at the facts about heroin. Heroin is one of the best painkillers known to man. In fact, it was named heroin at the end of the nineteenth century because it was thought to be the 'heroic' drug which would banish pain for good. The drug went on the market in 1898, but five years later the true nature of heroin's addictive properties became evident and the drug was speedily withdrawn from general distribution. However, heroin is still used in medicine today—under strict control of course.

The drug is called diamorphine and it is the drug of choice when treating patients

dying of cancer. Not only does diamorphine reduce pain to acceptable levels, it also produces a euphoric effect which helps to counter the depression faced by patients close to death. Can we really condemn a drug which can do that as being all 'bad'?

By n3w it should be evident that the division between good drugs and bad drugs is a

woolly one and is not really relevant to our discussion of medicinal chemistry. All drugs have their good points and their bad points. Some have more good points than bad and vice versa, but like people, they all have their own individual characteristics.So how are we to define a drug in general.

One definition could be to classify drugs as 'compounds which interact with a

biological system to produce a biological response'. This definition covers all the drugs we have discussed so far, but it goes further. There are chemicals which we take every day and which have a biological effect on us. What are these everyday drugs. One is contained in all the cups of tea, coffee, and cocoa which we consume. All of these beverages contain the stimulant caffeine. Whenever you take a cup of coffee, you are a drug user. We could go further. Whenever you crave a cup of coffee, you are a drug addict. Even kids are not immune. They get their caffeine 'shot' from coke or pepsi. Whether you like it or not, caffeine is a drug. When you take it, you experience a change of mood or feeling.



There can be little doubt that alcohol is a drug and as such causes society more

problems than all other drugs put together. One only has to study road accident statistics to appreciate that fact. It has been stated that if alcohol was discovered today, it would be restricted in exactly the same way as cocaine or cannabis. If oneconsiders alcohol in a purely scientific way, it is a most unsatisfactory drug. As many will testify, it is notoriously difficult to judge the correct dose of alcohol required to gain the beneficial effect of 'happiness' without drifting into the higher dose levels which produce unwanted side-effects. Alcohol is also unpredictable in its biological effects. Happiness *or* depression may result depending on the user's state of mind. On a more serious note, addiction and tolerance in certain individuals have ruined the lives of addicts and relatives alike. Even food can be a drug. Junk foods and fizzy drinks have been blamed for causing hyperactivity in children. It is believed that junk foods have high concentrations of certain amino acids which can be converted in the body to neurotransmitters. These are chemicals which pass messages between nerves. If an excess of these chemical messengers should accumulate, then too many messages are being transmitted in the brain, leading to the disruptive behaviour observed in susceptible individuals. Allergies due to food additives and preservatives are also well recorded. Our definition of a drug can also be used to include compounds which we might not at first sight consider to be drugs.

Consider how the following examples fit our definition.

• Morphine—reacts with the body to bring pain relief.

• Snake venom—reacts with the body and may cause death!

• Strychnine—reacts with the body and may cause death!

• LSD—reacts with the body to produce hallucinations.

• Coffee—reacts with the body to waken you up.

• Penicillin—reacts with bacterial cells and kills them.

• Sugar—reacts with the tongue to produce a sense of taste.

All of these compounds fit our definition of drugs. It may seem strange to include

poisons and snake venoms as drugs, but they too react with a biological system and produce a biological response—a bit extreme perhaps, but a response all the same. The idea of poisons and venoms acting as drugs may not appear so strange if we consider penicillin. We have no problem in thinking of penicillin as a drug, but if we were to look closely at how penicillin works, then it is really a poison. It interacts with bacteria (the biological system) and kills them (the biological response). Fortunately for us, penicillin has no effect on human cells. Even those medicinal drugs which do not act as poisons have the potential to

become poisons—usually if they are taken in excess. We have already seen this with morphine. At low doses it is a painkiller. At high doses, it is a poison which kills by suffocation. Therefore, it is important that we treat all medicines as potential poisons and keep them well protected from children searching the house for concealed sweets. There is a term used in medicinal chemistry known as the therapeutic index which indicates how safe a particular drug is. The therapeutic index is a measure of the drug's beneficial effects at a low dose versus its harmful effects at a high dose, A hightherapeutic index means that there is a large safety margin between beneficial and toxic doses. The values for cannabis and alcohol are 1000 and 10 respectively. If useful drugs can be poisons at high doses, does the opposite hold true. Can a poison be a medicine at low doses? In certain cases, this is found to be the case. Arsenic is well known as a poison, but arsenic-based compounds were used at the beginning of the century as antiprotozoal agents. Curare is a deadly poison which was used by the Incas to tip their arrows such that a minor arrow wound would be fatal, yet compounds based on the tubocurarine structure (the active principle of curare) have been used in surgical operations to relax muscles. Under proper control and in the correct dosage, a lethal poison may well have an important medical role. Since our definition covers any chemical which interacts with any biological system, we could include all pesticides and herbicides as drugs. They interact with bacteria, fungi, and insects, kill them and thus protect plants. Sugar (or any sweet item for that matter) can be classed as a drug. It reacts with a biological system (the taste buds on the tongue) to produce a biological response (sense of sweetness).Having discussed what drugs are, we shall now consider why, where, and how drugs act.

***Why should drugs work?***

Why indeed? We take it for granted that they do, but why should chemicals, some of

which have remarkably simple structures, have such an important effect on such a complicated and large structure as a human being? The answer lies in the way that the human body operates. If we could see inside our bodies to the molecular level, we would no doubt get a nasty shock, but we would also see a magnificent array of chemical reactions taking place, keeping the body healthy and functioning. Drugs may be mere chemicals but they are entering a world of chemical reactions with which they can interact. Therefore, there should be nothing odd in the fact that they can have an effect. The surprise might be that they can have such specific effects. This is more a result of *where* they react in the body.

***Where do drugs work?***

Since life is made up of cells, then quite clearly drugs must act on cells. The structure

of a typical cell is shown in Fig. 2.1. All cells in the human body contain a boundary wall called the cell membrane. This encloses the contents of the cell—the cytoplasm. The cell membrane seen under the electron microscope consists of two identifiable layers. Each layer is made up of an ordered row of phosphoglyceride molecules such as phosphatidylcholine (lecithin). Each phosphoglyceride molecule consists of a small polar head-group, and two long hydrophobic chains (Fig. 2.2). In the cell membrane, the two layers of phospholipids are arranged such that the hydrophobic tails point to each other and form a fatty, hydrophobic centre, while the ionic head-groups are placed at the inner and outer surfaces of the cell membrane (Fig. 2.3). This is a stable structure since the ionic, hydrophilic head-groups can interact with the aqueous media inside and outside the cell, while the hydrophobic tails maximize van der Waals bonding with each other and are kept away from the aqueous environments. The overall result of this structure is to construct a fatty barrier between the cell's interior and its surroundings.





The membrane is not just made up of phospholipids, however. There are a large variety of proteins situated in the cell membrane (Fig. 2.4). Some proteins lie on the surface of the membrane. Others are embedded in it with part of their structure exposed to one surface of the membrane or the other. Other proteins traverse the whole membrane and have areas exposed both to the outside and the inside of the cell. The extent to which these proteins are embedded within the cell membrane structure depends on the type of amino acid present. Portions of protein which are embedded in the cell membrane will have a large number of hydrophobic amino acids, whereas those portions which stick out on the surface will have a large number of hydrophilic amino acids. Many surface proteins also have short chains of carbohydrates attached

to them and are thus classed as glycoproteins. These carbohydrate segments are thought to be important towards cell recognition. Within the cytoplasm there are several structures, one of which is the nucleus. This acts as the 'control centre' for the cell. The nucleus contains the genetic code—the DNA—and contains the blueprints for the construction of all the cell's enzymes. There are many other structures within a cell, such as the mitochondria, the golgi

apparatus, and the endoplasmic reticulum, but it is not the purpose of this book to look at the structure and function of these organelles. Suffice it to say that different drugs act at different locations in the cell and there is no one target site which we could pinpoint as **the** spot where drugs act. Nor would we get any closer to understanding how drugs work by cataloguing which drug acts at which particular cell component. We need to magnify the picture, move down to the molecular level, and find out what types of molecules in the cell are affected by drugs. When we do that, we find that there are three main molecular targets:

(1) lipids

(2) proteins (glycoproteins)

(3) nucleic acids

The number of drugs which interact with lipids are relatively small and, in general,

they all act in the same way—by disrupting the lipid structure of cell membranes. Anaesthetics work by interacting with the lipids of cell membranes to alter the structure and conducting properties of the cell membrane.

The antifungal agent-amphotericin B (Fig. 2.5)-(used against athletes foot) interacts with the lipids of fungal cell membranes to build 'tunnels' through the membrane. Once in place, the contents of the cell are drained away and the cell is killed.





Amphotericin is a fascinating molecule in that one half of the structure is made up of double bonds and is hydrophobic, while the other half contains a series of hydroxyl groups and is hydrophilic. It is a molecule of extremes and as such is ideally suited to act on the cell membrane in the way that it does. Several amphotericin molecules cluster together such that the alkene chains are to the exterior and interact favourably with the hydrophobic centre of the cell membrane. The tunnel resulting from this cluster is lined with the hydroxyl groups and so is hydrophilic, allowing the polar contents of the cell to escape (Fig. 2.6). The antibiotics valinomycin and gramicidin A operate by acting within the cell membrane as ion carriers and ion channels respectively (see Chapter 10).

These drugs apart, the vast majority of drugs interact with proteins or nucleic acids,

and in particular with proteins. We shall therefore concentrate our attention in the next three chapters on proteins, then consider nucleic acids in Chapter 6.



The primary objective of medicinal chemistry is the design and discovery of new compounds that are suitable for use as drugs. The discovery of a new drug requires not only its design and synthesis but also the development of testing methods and procedures, which are needed to establish how a substance operates in the body and its suitability for use as a drug. Drug discovery may also require fundamental research into the biological and chemical nature of the diseased state. This and other aspects of drug design and discovery require input from specialists in other fields, such as biology, biochemistry, pharmacology, mathematics, computing and medicine amongst others, and the medicinal chemist to have an outline knowledge of these fields.

This chapter seeks to give a broad overview of medicinal chemistry. It attempts to provide a framework for the topics discussed in greater depth in the succeeding chapters. In addition, it includes some topics of general interest to medicinal chemists.

Drugs are strictly defined as chemical substances that are used to prevent or cure diseases in humans, animals and plants. The activity of a drug is its pharmaco- logical effect on the subject, for example, its analgesic or b-blocker action. Drugs act by interfering with biological processes, so no drug is completely safe. All drugs can act as poisons if taken in excess. For example, overdoses of paracetamol can cause coma and death. Furthermore, in addition to their beneficial effects, most drugs have non-beneficial biological effects. Aspirin, which is commonly used to alleviate headaches, may also cause gastric irritation and bleeding. The non-beneficial effects of some drugs, such as cocaine and heroin, are so undesirable that the use of these drugs has to be strictly controlled by legislation. These unwanted effects are commonly referred to as side effects.

COOH

OCOCH3

Aspirin

HO

Paracetamol

NHCOCH3

The over-usage of the same drugs, such as antibiotics, can result in the evelopment of resistance to that drug by both the patients, microorganisms and virus the drug is intended to control. Resistance occurs when a drug is no longer effective in controlling a medical condition. Drug resistance or tolerance, often referred to as tachyphylaxis, arises in people for a variety of reasons. For example, the effectiveness of barbiturates often decreases with repeated use because repeated dosing causes the body to increase its production in the liver of mixed function oxidases that metabolize the drug, thereby reducing the drug’s effectiveness. An increase in the rate of production of an enzyme that metabolizes the drug is a relatively common reason for drug resistance. An- other general reason for drug resistance is the down-regulation of receptors (Appendix 5). Down-regulation occurs when repeated stimulation of a receptor results in the receptor being broken down. This results in the drug being less effective because there are fewer receptors available for it to act on. Drug resistance may also be due to the appearance of a significantly high proportion of drug resistant strains of microorganisms. These strains arise naturally and can rapidly multiply and become the currently predominant strain of that microorganism. For example, antimalarial drugs are proving less effective because of an increase in the proportion of drug resistant strains of the malaria parasite.

New drugs are constantly required to combat drug resistance, even though it can be minimized by the correct use of medicines by patients. They are also required for the improvement in the treatment of existing diseases, the treatment of newly identified diseases and the production of safer drugs by the reduction or removal of adverse side effects.

Since ancient times the peoples of the world have used a wide range of natural products for medicinal purposes. These products, obtained from animal, vege- table and mineral sources, were sometimes very effective. However, many of the products were very toxic. Information about these ancient remedies was not readily available to users until the invention of the printing press in the 15th century. This invention led to the widespread publication and circulation of herbals and pharmacopoeias. This resulted in a rapid increase in the use, and misuse, of herbal and other remedies. However, improved communications between practitioners in the 18th and 19th centuries resulted in the progressive removal of preparations that were either ineffective or too toxic from herbals and pharmacopoeias. It also led to a more rational development of new drugs. Initially this development was centred around the natural products isolated from plant and animal material, but as knowledge increased a wider range of pharmaceutically active compounds were used as the starting point for the development of drugs. The compounds on which a development is based are now known as lead compounds, while the synthetic compounds developed from a lead are referred to as its analogues.

The work of the medicinal chemist is centred around the discovery of

new lead compounds with specific medical properties. It includes the devel- opment of more effective and safer analogues from both these new and existing lead compounds. This usually involves synthesizing and testing many hundreds of compounds before a suitable compound is produced. It is currently estimated that for every 10 000 compounds synthesized one is suitable for medical use.

The first rational development of synthetic drugs was carried out by Paul Ehrlich and Sacachiro Hata, who produced the antiprotozoal arsphemamine in 1910 by combining synthesis with reliable biological screening and evaluation procedures. Ehrlich, at the begining of the 20th century, had recognized that both the beneficial and toxic properties of a drug were important to its evaluation. He realized that the more effective drugs showed a greater selectiv- ity for the target microorganism than its host. Consequently, to compare the effectiveness of different compounds, he expressed a drug’s selectivity, and hence its effectiveness, in terms of its chemotherapeutic index, which he defined as

Determination and cataloging of the chemotherapeutic index of the 600 com- pounds Ehrlich and Hata synthesized enabled them in 1909 to discover arsphe- mamine (Salvarsan). This drug was very toxic but safer than the then currently used *Atoxyl*. It was used up to the mid-1940s, when it was replaced by penicillin.

Today, Ehrlich’s chemotherapeutic index has been updated to take into account the variability of individuals and is now defined as its reciprocal, the therapeutic index or ratio:

In theory, the larger a drug’s therapeutic index, the greater is its margin of safety. However, in practice index values can only be used as a limited guide to the relative usefulness of different compounds. The term structure–activity relationship (SAR) is now used to describe Ehrlich’s approach to drug discovery, which consisted of synthesizing and testing a series of structurally related compounds (see section 4.1).

Attempts to quantitatively relate chemical structure to biological action were first initiated in the 19th century, but it was not until the 1960s that Hansch and Fujita devised a method that successfully incorporated quantitative measure- ments into SAR determinations (see section 4.4). The technique is referred to as QSAR (quantitative structure–activity relationships). One of its most successful uses has been in the development in the 1970s of the antiulcer agents cimetidine and ranitidine. Both SARs and QSARs are important parts of the foundations of medicinal chemistry.

An alternative approach to drug design was initiated by the work of John Langley. In 1905 he proposed that so called receptive substances in the body could accept either a stimulating compound, which would cause a biological response, or a non-stimulating compound, which would prevent a bio- logical response. It is now universally accepted that the binding of a chemical agent, referred to as a ligand (see also section 7.4), to a so called receptor sets in motionaseries of biochemical events thatresult in abiological orpharmacological effect. Furthermore, a drug is most effective when its structure or a significant part of its structure, both as regards molecular shape and electron distribution (stereo- electronic structure), is complementary with the stereoelectronic structure of the receptor responsible for the desired biological action. The section of the structure of a ligand that binds to a receptor is known as its pharmacophore. Furthermore, it is now believed that side effects can arise when the drug binds to either the receptor responsible for the desired biological response or to different receptors. The mid- to late 20th century has seen an explosion of our understanding of the chemistry of disease states, biological structures and processes. This increase in knowledge has given medicinal chemists a clearer picture of how drugs are distributed through the body and transported across membranes and their mode of operation and metabolism. It has enabled medicinal chemists to place groups that influence absorption, stability in a bio-system, distribution, metabol- ism and excretion in the molecular structure of a drug. For example, the intro- duction of a sulphonic acid group into the structure of a drug will increase its water solubility. This may improve its absorption and/or its rate of excretion from the body. However, because of the complex nature of biological systems, there is always a degree of uncertainty in predicting the effect of structural changes on the activity of a drug. As a result, it is always necessary to carry out extensive testing to determine the consequences of modifying a structure. Furthermore, changing a group or introducing a group may change the nature of the activity of the compound. For example, the change of the ester group in procaine to an amide (procainamide) changes the activity from a local anaesthetic to anti-rhythmic. The introduction or removal of charged groups or groups that can form ions into or out of a structure may also have a marked affect on drug action. This is because drugs normally have to cross nonpolar lipid membrane barriers (Appendix 3) in order to reach their site of action. Consequently, as the polar nature of the drug increases, it usually becomes more difficult for that drug to cross these barriers. For example, quaternary ammonium salts, which are permanently charged, can be used as an alternative to an amine in a structure in order to restrict the passage of a drug across a membrane. The structure of the anticholinesterase neostigmine, developed from physostig- mine, contains a quaternary ammonium group, which stops the molecule from crossing the blood–brain barrier (Appendix 11). This prevents unwanted CNS activity. However, its analogue miotine can form the free base. As a result, it is able to cross lipid membranes, which may cause unwanted CNS side effects.

Both SAR and QSAR studies rely on the development team picking the correct starting point. Serendipity inevitably plays a significant part in select- ing that point. However, modern techniques such as computer modelling (Chapter 5) and combinatorial chemistry (Chapter 6) introduced in the 1970s and 1990s respectively are likely to reduce the number of intuitive discoveries.

Computer modelling has reduced the need to synthesize every analogue of a lead compound. It is also often used retrospectively to confirm the information derived from other sources. Combinatorial chemistry, which originated in the field of peptide chemistry, has now been expanded to cover other areas. The term covers a group of related techniques for the simultaneous production of large numbers of compounds for biological testing. Consequently, it is used for structure action studies and to discover new lead compounds. The procedures may be automated.

The discovery of a new drug is part luck and part structured investigation (see section 3.1). It originally started with drugs and lead compounds derived from natural sources, such as animals, plants, trees and microorganisms. Marine sources were not utilized to any extent until the mid-20th century. Today, natural sources are still important, but the majority of lead compounds are synthesized in the laboratory. The nature of these synthetic compounds is initially decided from a consideration of the biochemistry of the pathogenic condition.

Today, many discoveries start with biological testing (bioassays or screening programme) by pharmacologists of the potential sources in order to determine the nature of their pharmacological activity as well as their potencies. These screening programmes may be random or focused. In random screening pro- grams all the substances and compounds available are tested regardless of their structures. The random screening of soil samples, for example, led to the discovery of the streptomycin and tetracycline antibiotics as well as many other lead compounds. Random screening is still employed, but the use of more focused screening procedures where specific structural types are tested is now more common.

Once a screening programme has identified substances of pharmacological activity of interest, the compound responsible for this activity is isolated and used as a lead compound for the production of related analogues. These com- pounds are subjected to further screening tests. Analogues are made of the most promising of these compounds and they in turn are subjected to the screening procedure. This sequence of selective screening and synthesis of analogues may be repeated many times before a potentially useful drug is found. Often the sequence has to be abandoned as being either unproductive or too expensive.

**Natural sources**

Natural sources are still important sources of lead compounds and new drugs. However, the large diversity of potential natural sources in the world makes the technique of random screening a rather hit or miss process. The screening of local folk remedies (ethnopharmacology) offers the basis of a more systematic approach. In the past this has led to the discovery of many important thera- peutic agents, for example, the antimalarial quinine from cinchona bark, the cardiac stimulant digitalis from fox gloves (Figure 2.1) and the antidepressant reserpine isolated from *Rauwolfia serpentina*.

Once screening identifies a material containing an active compound, the problem becomes one of extraction, purification and assessment of the pharma- cological activity. However, the isolation of useful quantities of a drug from its land or sea sources can cause ecological problems. The promising anticancer agent Taxol (Figure 2.2), for example, was originally isolated from the bark of the Pacific yew tree. However, the production of large quantities of Taxol from this source would result in the wholesale distruction of the tree, a state of affairs that is ecologically unacceptable. It is vitally important that plant, shrub, tree and marine sources of the world are protected from further erosion,as there is no doubt that they will yield further useful therapeutic agents in the future.

 **Drug synthesis**

The most popular approach to drug design by synthesis is to start with the pathology of the diseased state and determine the point where intervention is most likely to be effective (see Chapter 7). This enables the medicinal chemist to suggest possible lead compounds. These compounds are synthesized so that their pharmacological action may be evaluated. Once a suitably active lead is found, structural analogues of that lead are produced and screened in the hope that this procedure will eventually produce a compound that is suitable for clinical use. Obviously this approach is labour intensive and a successful out- come depends a great deal on luck. Various modifications to this approach have been introduced to reduce this element of luck (see Chapters 4–6).

####  **Market forces and ‘me-too drugs**

The cost of introducing a new drug to the market is extremely high and continues to escalate. One has to be very sure that a new drug is going to be profitable before it is placed on the market. Consequently, the board of direct- ors’ decision to market a drug or not depends largely on information supplied by the accountancy department rather than ethical and medical considerations. One way of cutting costs is for companies to produce drugs with similar activities and molecular structures to their competitors. These drugs are known as the ‘me-too drugs’. They serve a useful purpose in that they give the practitioner a choice of medication with similar modes of action. This choice is useful in a number of situations, for example when a patient suffers an adverse reaction to a prescribed drug or on the rare occasion that a drug is withdrawn from the market. Drugs are classified in a number of different ways depending on where and how the drugs are being used. The methods of most interest to medicinal chemists are chemical structure and pharmacological action, which includes the site of action and target system. Unfortunately, classifying drugs according to their chemical structural type has the disadvantage that members of the same structural group often exhibit very different types of pharmacological activity. Steroids (see section 1.5.4), for example, may act as hormones (testosterone), diuretics (spironolactone) actibacterial agents (fusidic acid) amongst other forms of activity.

The term prodrug (see section 2.7.1 and 9.8) is often used for drugs whose active form is produced by enzyme or chemical action at or near to its site of action. However, it is emphasized that other classifications, such as the nature of the illness and the body system on which the drug acts (physiologicalclassification), are also used in medicinal chemistry as well as other fields depending on the purpose of the information.