Introduction to pharmacodynamics

Abstract

In this second article in the series of ‘bite sized’ pharmacology we will start to look at the principles of pharmacodynamics. It is important that prescribers are aware of the actions their drugs have in the body after administration. They should know the SITE of action (where the drug works), the MODE of action (how the drug works) and the time to ONSET and DURATION of action (when the drug starts to work and how long for). This helps prescribers decide on drug choice, drug dose and the dose schedule as well as the length of time the drug needs to be prescribed for. This knowledge can also assist the prescriber in prediction and prevention (or minimising) of adverse drug reactions and to help educate their patients on possible side effects. In this article we will look at SITEs of action; receptors, ion channels, enzymes, and transport systems. We will also introduce the concepts of agonism and antagonism and their relationship to MODE of action.

Pharmacology is the study of drugs (chemicals) and their interactions with the body.

The word pharmacology is derived from the Greek word *pharmakon* which can meanboth remedy and poison. There are two ways we can study the interactions of drugs with the body, those being pharmacokinetics and pharmacodynamics.

Pharmacodynamics can be defined in its simplest terms as the effect(s) that the drug has on the body. These can be categorised into 3 areas

* Desired effects- the reason we take the drug in the first place
* Side effects- effects that can be cause by the drug and are often known about and may be desired or unwanted
* Adverse effects- effects that can be cause by the drug but are usually unknown and always unwanted

Drugs can act at a variety of different sites in the body that we call molecular (chemical) targets. The main *sites of action* that can be identified as chemical drug targets are outline as follows.

Receptors

Many commonly used drugs act at receptors and most of you reading this will be familiar with the name. Receptors are found in virtually all cells within the body. Examples include;

1. Ionotropic receptors (also known as ligand gated ion channels) such as the GABAA receptor, which respond to the class of drugs known as benzodiazepines.
2. G-protein coupled receptors such as adrenoceptors.
3. Kinase linked receptors such as the insulin receptor.
4. Nuclear receptors such as the thyroid receptor.

Cell Membrane

Receptor

Figure 1. Drug A Binding at a cellular receptor

Ion Channels

### Drug action at ion channels can take two forms (see Figure 2)

### Channel blockers

### The drug blocks permeation of the channel by sitting in it and prevention passage of other ions and chemicals.

### Channel modulators

### The drug binds to a receptor site within the ion channel and modulates permeation. This can happen by the drug altering the channels response to its normal mediator or by changing the shape of the channel.

a.

b.

Figure 2. Drug Binding at Ion Channels

In a. A drug molecule blocking the actual ion channel itself

In b. A drug molecule binding to the channel but not sitting within the channel itself.

Enzymes

Enzymes are biological catalysts that increase the rate of chemical reactions in the body. They are part of many normal physiological functions and reactions without which the body could not function as efficiently. Many drugs target enzymes to prevent them from carrying out their normal function. For example, the drug ramipril acts on angiotensin converting enzyme (ACE), to prevent its conversion from angiotensin I to angiotensin II (Figure 3). This action (inhibition) of ACE leads to a reduction in blood pressure.

Figure 3- ACE action on angiotensin 1

Transport Systems

These are distinct from plasma transport and are located on cells in many areas of the body. These are also known as carrier molecule interactions. In some neurotransmitter systems, there is normal physiological reuptake of the transmitters after release from a neurone into the synapse. The transmitter serotonin is an example of this reuptake. After serotonin is released from a neurone into the synaptic space, it is taken back up by that same neurone using a serotonin selective reuptake (SSR) system. A drug belonging to the class of SSRI (selective serotonin reuptake inhibitors) such as citalopram has its action at this transport system. It acts to block the uptake transporter. This means that serotonin molecules are in the synapse longer and results in an increased level of serotonergic activity. This mechanism has an onward effect which increases mood and makes these good antidepressant drugs (see Figure 4).

Neurones

Figure 4 Transport System Interaction

 Selective serotonin reuptake system

 Serotonin molecule

Exercise

Using available pharmacological resources such as a pharmacology textbook, the BNF or the online electronic medicines compendium, find out the SITE of action of a drug from your area of practice.

The Concept of Affinity

Drugs have what we call affinity for their receptors, or chemical targets. This tells us how well a drug can bind to its target. Some chemicals and drug molecules have a higher affinity for their targets than others. Drugs possessing high affinity will bind in preference to other drug molecules available. Sometimes a drug molecule has a higher affinity for the targets than the normal endogenous mediator for that target. This can be therapeutically useful, especially where the endogenous agonist is abundant and may be causing the problem or symptom the patient is experiencing. Higher affinity means that even small amounts of the drug will bind preferentially. A good example is that antihistamines such as chlorphenamine have a good affinity for the histamine receptor over its endogenous agonist histamine and are useful in treating allergic responses.

Agonistic and Antagonistic Drug Action

Drugs can either be described as agonists or antagonists at their target sites. This is best explained using receptors as an example of a target site (see Figure 5).

* Agonists: these are drugs that bind to their targets and form a drug-receptor complex. The agonists activate the receptors to produce a response.
* Antagonists: these 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.

## AGONISTS

 DRUG RECEPTOR

DRUG/RECEPTOR COMPLEX

**RESPONSE**

## ANTAGONISTS

 DRUG RECEPTOR

**NO RESPONSE**

DRUG /RECEPTOR COMPLEX

# Figure 5. Basic Receptor Theory

Exercise

Using available pharmacological resources such as a pharmacology textbook, the BNF or the online electronic medicines compendium, find out the MODE of action of a drug from your area of practice, HOW does it exert its effect?

This has been a brief introduction to the concepts of pharmacodynamic actions. In future articles in this series we will explore aspects of pharmacodynamic actions in more detail, looking at drug onset and duration of action

Further Reading

<https://www.medicines.org.uk/emc/>

Barber and Robertson (2015) *Essentials of Pharmacology for Nurses* 3rd Edition McGraw Hill London