Pharmacodynamics - Part 1: How Drugs Act on the Body

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Pharmacodynamics How do drugs act on the body? In the Chalk Talk episodes on pharmacokinetics, we looked at what the body does to a drug, that is, how it's absorbed, distributed, metabolised, and excreted from the body. In these next two episodes on pharmacodynamics, we'll be taking a detailed look at the effect of a drug at its site of action. In general, drugs don't initiate new metabolic processes in the body but alter biochemical processes.

To do so, they interact with specific target structures in the body, for example, receptors and enzymes. These interactions can either enhance or inhibit downstream biochemical processes. Drugs that activate a receptor or an enzyme are termed agonists, whereas drugs that have an inhibiting effect are called antagonists.

(1:00 - 1:37)

So, the effect of an agonist is comparable to that of a natural enzyme effector or an endogenous signalling molecule for a receptor. In contrast, antagonists are analogous to natural inhibitors of enzymes or receptors. Besides these drugs, there are other types.

Some interact with DNA, whereas others interfere with osmotic cell balance. In this Chalk Talk episode, we won't be focussing on such drugs but on the various mechanisms of drug-receptor interactions. Imagine a receptor on the surface of a cell to which a drug is able to bind.

(1:37 - 3:26)

Under physiological conditions, the extracellular binding of a signalling molecule to this receptor activates an intracellular signalling cascade. For the drug, the presence of this receptor makes the cell a potential site of action to which it can bind to. Let's assume that the drug is an agonist that elicits signal transduction at a receptor.

Principally, it can act in one of two ways. The agonist could bind to the receptor and produce an effect similar to that of the endogenous signalling molecule. Such drugs are termed direct agonists.

Alternatively, instead of causing a signal itself, the drug could enhance the action of the endogenous signalling molecule, for example, by increasing the release of signalling molecules. Such drugs are termed indirect agonists. If the aim is to impair signal transduction at the receptor, then antagonists are used.

Antagonists can also act in different ways and are typically classified as competitive and noncompetitive. A competitive antagonist binds to the same site as the endogenous signalling molecule, blocking its binding site at the receptor. As a result, a lower amount of signalling

molecules bind to the receptor on the cell surface, reducing their overall effect.

A noncompetitive antagonist binds to a site other than the usual receptor binding site, but as this binding causes conformational changes in the structure of the receptor binding site, it decreases or even abolishes the physiological effect of the signalling molecule. To get a more complete picture, we'd also like to mention the presence of substances termed functional antagonists. Despite their name, their mechanism of action strongly differs from that of other antagonists.

(3:27 - 4:51)

In fact, functional antagonists act like agonists. They bind to a receptor and actively promote a reaction, which then physiologically counteracts a downstream process. The induced reaction therefore reduces the effects of the downstream process without any direct interaction between the functional antagonist and this process.

In short, the drug doesn't antagonise the endogenous signalling molecule but rather a physiological function. This may sound somewhat confusing initially, but you probably already know a drug with such a mechanism of action. It's adrenaline, which is a functional antagonist.

In allergic reactions, adrenaline antagonises vasodilation caused by histamine without both signalling molecules binding to the same receptor. Let's go back to drugs that directly affect signal transduction at the receptor. This process isn't only regulated by competitive and non-competitive antagonists but also by partial agonists.

These drugs bind directly to the receptor where they generate a signal that is similar yet weaker than the endogenous signal. As a result, drug binding to the receptor leads to an overall weaker signal. The physiologic effects of a drug don't only depend on its mechanism of action but especially on its dose.

We'll be taking a detailed look at the relationship between dose and response in our next episode on pharmacodynamics.