

Session 1. Theory: Introduction to Pharmacology: History, Importance, Terms and Definitions

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Introduction

- A drug is a chemical agent which can affect living processes. For purposes of this course we will mainly be talking about small molecules which affect cellular processes. Most of these are Xenobiotics (Gr. xenos - stranger) chemicals that are not synthesized by the body, but introduced into it from outside.
- There is inevitably a certain amount of ambiguity in this definition: Is oxygen or water a drug? How about Vitamin C in a glass of orange juice? How about an injection of Vitamin C to treat scurvy?

- Pharmacology (Gr. pharmakon - a drug or poison, logos - word or discourse) is the science dealing with actions of drugs on the body (pharmacodynamics) and the fate of drugs in the body (pharmacokinetics). It overlaps with pharmacy, the science of preparation of drugs; much of it deals with therapeutics, the treatment of disease (by whatever means).
- Toxicology is the branch of pharmacology dealing with the "undesirable" effects of drugs on biological processes (in the case of a nerve gas the bad effect may be a desired one).

Definitions

- **Agonist** is a drug which binds to its "receptor" and produces its characteristic effect. A drug may be a **full agonist** or **partial agonist**, depending on the maximal effect it produces. An antagonist binds to the receptor without causing an effect, thereby preventing an active substance from gaining access. Antagonists, like enzyme inhibitors, may be competitive, non-competitive or irreversible.
- **Dose-Response.** The sine qua non of drug effect. Simply put, as the dose of drug increases, the response should increase. [What if the response increases, then decreases as the dose is raised?] The curve generated is usually sigmoidal when effect is plotted against log dose (Dr. Strichartz will discuss the theoretical basis for this). Effect may be measured as a graded variable (change in blood pressure, force of contraction) or as a quantal variable (number dead/alive). The slope of the curve is characteristic of the particular drug-receptor interaction. When two drugs act by the same receptor mechanism, we expect to see two parallel log-dose response curves.

- **ED₅₀**. The median effective dose, or the dose which produces a response in 50% of subjects. If the response is death (lethality) we call it the **LD₅₀**. The EC50 refers to concentration rather than dose. Similar abbreviations are used for other response levels: ED₉₉, LD₁, etc.
- **Potency**. A terribly misused word – the lay public uses it to mean “effectiveness.” The potency of a drug refers to the dose (actually the molar concentration) required to produce a specific intensity of effect. [We usually specify the ED50, why?] If the ED50 of drug A and B are 5 and 10 mg, respectively, the Relative Potency of A is twice that of B. Relative potency specifically applies to the comparison of drugs which act by the same mechanism, and therefore have parallel dose-response curves.

- **Efficacy.** Also called **Maximal Efficacy** or **Intrinsic Activity**. This is the maximum effect of which the drug is capable. A potent drug may have a low efficacy, and a highly efficacious drug may have a low potency. For the clinician, efficacy is much more important than potency (within limits). Who cares if the pill contains 5 or 10 mg of drug?
- **Affinity.** This refers to the strength of binding between drug and receptor. It is quantified by the dissociation constant K_D (covered in the next lecture).
- **Selectivity.** This refers to the separation between desired and undesired effects of a drug. In the ideal case, a drug is completely

- **Therapeutic Window.** For every drug, there exists some concentration which is just barely effective (the **Effective Concentration**) and some dose which is just barely toxic (the **Toxic Concentration**). Between them is the therapeutic window where most safe and effective treatment will occur.
- **Therapeutic Index.** This is the ratio of toxic to effective doses at the level of 50% response: TD_{50}/ED_{50} . In animal toxicology studies, it is usually the LD_{50}/ED_{50} . Another measure sometimes utilized is the **Certain Safety Factor**, which is TD_1/ED_{99} .