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Diploma in Pharmacy 2nd Year
Pharmacology
Experiment
To Study Experimental Pharmacology

Aim:

To Study Experimental Pharmacology

Reference :

‘ Dr. P.Mudagal Manjunatha , “Practical Manual of Pharmacology” Published by Nirali Prakashan, Page no 1 - 4

Theory :

Pharmacology is the study of various characteristics of drug molecules and related compounds. The term Pharmacology originated from Greek words Pharmacon (meaning drug,) Logos (studied in, i.e., studies in drugs) which means the study of drug and its action. Experimental pharmacology is the youngest branch of basic medical sciences. Advancement in the field of electrophysiology, biochemistry, molecular biology and electronic or digital recording systems and software have enriched and broadened the horizons of experimental pharmacology.

Related Terms

1) **Pharmacology:** Pharmacology (from Gk. Pharmacon = drug, Logos = studied in, i.e., studies in drugs) is the study of drug and its action. It involves the study of interactions taking place between a living organism and an exogenous chemical, which in turn alters normal biochemical functions.
2) **Pharmacokinetics:** Pharmacokinetics (Greek word 'kinesis' means movement) in simple terms means the action of body on the drug.

Pharmacokinetics includes the study of drug absorption, distribution, metabolism and excretion.

3) **Pharmacodynamics:** Pharmacodynamics (Greek word, 'dynamics' means power) implies the action of drugs on the body. The studies included under pharmacodynamics explain the mechanism of drug action and correlate with the effects of the drug.
4) **Pharmacoepidemiology:** Pharmacoepidemiology involves the study of utilisation of drugs and its effects on a large population. The study of pharmacoepidemiology emphasises on clinical patient outcomes from therapeutics by using methods of clinical epidemiology.
5) **Pharmacoeconomics:** It evaluates the ratio of cost (in monetary terms) and beneficial effects (in terms of efficacy or enhanced quality of life) of a drug with other drug therapies or with comparable drugs, including both, financial costs and quality of life.
6) **Pharmacogenomics:** It involves study of the effect of genetic structure of an individual on drug response. This is a new field which combines the subject of pharmacology (science of drugs) with genomics (study of genes and their functions) to facilitate the development of safe, efficient drugs, and doses that can differ according to the genetic constitution of an individual
7) **Therapeutics:** Therapeutics is the art and science of healing, dealing with the treatment of diseases and infectious conditions. It deals with drug usage- and the method in which it should be administered for treating a disease.
8) **Toxicology:** The study of adverse effects of chemicals on living organisms is termed as toxicology. It includes the study of symptoms, mode of action, treatments, and detection of poisoning, especially those affecting the humans.
9) **Pharmacovigilance:** It is the part of the pharmacoepidemiology that involves the study of pharmacokinetic and pharmacodynamic features

of a drug which is already present in the market. It includes continuous monitoring of the unwanted effects, and other safety concerns arising from drugs on a population.

10) **Clinical Pharmacology:** Clinical pharmacology includes the scientific study of drugs (pharmacology) on clinical resources (human beings).
11) **Affinity:** Affinity of a drug is the ability of it to bind to its receptors. It correlates inversely with the dissociation constant of the drug-receptors complex.
12) **Competition:** Competition is the condition in which two different drugs identify the same binding site. Reciprocal hindrance between two drugs decreases their apparent affinity for the binding site.
13) **Effectiveness:** Effectiveness is the measurement of the effects generated by therapeutic agents. Firstly, the term was coined to compare the agonists that upon binding to the same extent to a receptor population, produced effects of different entity.
14) **Potency:** Potency is the amount or concentration of dose needed to produce desired effects of a given entity (e.g., 50% of the maximal effect). Low potent drugs are taken in greater amount, and high potent drugs require low concentration.
15) **Selectivity:** At molecular level, selectivity of a drug is the ability of it to interact and bind with the limited number (preferable only one) of macromolecules. At organism level, it is the ability to generate responses that contributes to the modulation of a single functional system.
16) **Tolerance:** Tolerance is the decreased ability of an organism to respond to repeated administrations of drug. It may be result of down regulation or receptor desensitisation. Tachyphylaxis is the condition when tolerance develops very rapidly.

17) **Addiction:** Addiction is the habitual use of a psychoactive drug that results due to repeated and continuous use of these drugs; and an abrupt discontinuation of drug may result to withdrawal syndromes.
18) **Side Effects:** These are effects of drugs other than the therapeutic effects Harmful side effects of any therapeutic substance are known as adverse drug reaction.
19) **Therapeutic Index:** It is the ratio between the dose (or concentration) that can produce useful effects (ED-Effective Dose) and the dose (or concentration) responsible for side/toxic effects (e.g.. Toxic Dose (ID) or Lethal Dose (L.D))
20) **Agonist:** These are therapeutic substances which bind and activate a receptor and result to pharmacological responses that are mimic or similar to naturally-occurring substances Agonist may be full, partial or inverse.
21) **Full Agonist:** An agonist drug that produces a maximum response and show complete efficiency at that receptor site is known as a full agonist.
22) **Partial Agonist:** An agonist drug that binds with and activates a receptor but is able to bring about only partial efficiency at that receptor site is known as a partial agonist. They are not capable of giving maximum effects even when the concentration of drug is increased.
23) **Inverse Agonist:** They give an effect that is pharmacologically opposite to an agonist, yet bind at the same receptor. The receptor must elicit intrinsic or basal activity in the absence of a ligand and the addition of an inverse agonist will decrease the activity below the basal level.
24) **Antagonist:** A drug is said to be an antagonist if it does not produce any biological response even on binding with a receptor but, in its place, it either blocks or decreases the effect of an agonist.

Objectives of Experimental Pharmacology

1) Identify a therapeutic agent suitable for human use
2) Study a drug's toxicity
3) Study the mechanism of action of drugs.

Experimental pharmacology involves the discovery of new drugs or to study the action of existing drugs, thus, it is done in the following two stages

1) **Preclinical experimental pharmacology** involves identification and optimisation of novel chemical lead structures and testing them on animals and animal tissues or organs for their biological actions
2) **Clinical pharmacology** involves testing of drugs on human volunteers and patients for assessing the pharmacokinetics, safety and efficacy in humans

Drug Development

Three stages are mainly involved in drug development:

Stage I (Hit and Lead Compound Development Phase): In this stage, the lead compounds are selected among the million compounds for further study.

Stage II (Preclinical Studies): In this stage, the experiments are performed on animals in in vitro and in vivo both.

Stage III (Clinical Studies): In this stage, clinical trials phase 0, I, II, III, IV and V are conducted on humans.

There are usually a number of stages taken before discovering a new drug for a certain ailment. Drug discovery mostly entails in vitro and in vivo studies in various animals. Pharmaceutical companies played a significant role in research and development (R & D) in the late 18 century and expanded rapidly due to their focused and planned activity in the drug discovery

Target identification is the most significant step in the initial phase of drug development, which is followed by lead compound identification. The target protein is cloned to identify the lead compound. Due to the species to

species variation, the human sequence is preferred among several species sequences.

The main techniques used to identify hit compounds and then lead compounds for the next stage are cloning the target protein, determining the functional activity of the target protein, combinatorial chemistry research, and High Throughput Screening (HTS) or Ultra High Throughput Screening (UHTS). Lead compound identification is followed by lead compound optimisation that generally comprises increasing the potency of the compound in terms of selectivity, metabolic stability, pharmacokinetics, and toxicological effects on the selected target.

Identifying one or more drug candidates that is suitable for continued development is the objective of the lead optimisation phase Stage II of the drug's development, known as preclinical research, involves studies to identify and characterise receptors as well as pharmacodynamics, pharmacokinetic, and toxicity tests (acute toxicity, chronic toxicity, genotoxicity, etc.) in animals. The goal of the preclinical study is to establish the human Maximum Recommended Starting Dose (MRSD). Various in vitro (cell line, enzyme inhibition, etc.) and in vivo (animal model) experiments are used to accomplish this.

After acquiring the MRSD in stage III, the dosage can be extrapolated and calculated for the Safe Starting Dose (SSD) with the use of a safety factor. After the selection of SSD, the clinical trial of Phase I is started with healthy volunteers, however, exceptionally patients having cancer, HIV, cystic fibrosis, etc., are preferred.

Result :

Experimental pharmacology was studied.