EXPERIMENT NO.: 1 **DATE:**

AIM: GENERAL INTRODUCTION OF PHARMACOLOGY AND EXPERIMENTAL PHARMACOLOGY

DEFINITIONS:

1. **PHARMACOLOGY:** The word pharmacology is made of two parts, pharmacon (drug) and logus (discourse or study). Pharmacology means study of drugs, their pharmacodynamics, pharmacokinetics and toxicities.
2. **CLINICAL PHARMACOLOGY:** The branch concerned with the scientific studies on the effects of drug treatment in human being.
3. **PHARMACOKINETICS:** It is study of absorption, distribution, metabolism and excretion of drugs. i.e study of what body does to the drug.
4. **PHARMACODYNEMICS:** It is study of mechanism action and site of action of the drugs i.e it is study of what drug does to the body.
5. **ABSORPTION:** Drug goes from site of administration to systemic circulation or blood.
6. **DISTRIBUTION:** Drug goes from systemic circulation to various compartments like fat, muscles, tissue, organ etc.
7. **METABOLISM:** Conversion of drug in to excretion form.
8. **ELIMINATION OR EXCRETION:** Removal of drug from the body.
9. **BIOAVAILABILITY:** Fraction of an administered dose of unchanged drug that reaches the systemic circulation
10. **DRUG:** It is the active ingredient which is useful for diagnosis, treatment, mitigation and prevention of any disease or disorder in human beings or animals.
11. **MEDICINE:** The substances used to deliver drug in stable and acceptable form and it consist lubricant, binder, sweetener like other additives constituents with active ingredients.
12. **PHARMACOEPIDEMIOLOGY:** Study of effects of drugs in large numbers of people.
13. **PHARMACOGENOMICS:** Application of genomic technologies to new drug discovery and further characterization of older drugs.
14. **NEUROPHARMACOLOGY:** Effects of medication on central and peripheral nervous system functioning.
15. **PSYCHOPHARMACOLOGY:** Effects of medication on the psyche; observing changed behaviors of the body and mind, and how molecular events are manifest in a measurable behavioral form.

16. **PHARMACOGENETICS:** Clinical testing of genetic variation that gives rise to differing response to drugs.
17. **THEORETICAL PHARMACOLOGY:** Study of metrics in pharmacology.
18. **POSOLOGY:** How medicines are dosed. It also depends upon various factors like age, climate, weight, sex, and so on.
19. **PHARMACOGNOSY:** A branch of pharmacology dealing especially with the composition, use, and development of medicinal substances of biological origin and especially medicinal substances obtained from plants.
20. **PHARMACOVIGILANCE (PV)**: It is defined as the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug-related problem.
21. **SIDE EFFECTS:** A secondary but predictable effects, typically undesirable effect of a drug or medical treatment.
22. **ADVERSE EFFECTS:** A secondary but unpredictable effects, typically undesirable effect of a drug or medical treatment.
23. **TOXIC EFFECTS:** Harmful effects of the drug which is related to dose (Excess).

OBJECTIVES OF EXPERIMENTAL PHARMACOLOGY

1. To screen drug substance for their biological activities.
2. To study the toxicity of drugs.
3. To study mechanism of action and site of action of the drug.

Experimental Pharmacology involves:

a) Preclinical Experiments:

- Which consist of animal studies for deciding the safety, efficacy, pharmacokinetics and pharmacodynamics of a new drug or a new drug formulation.
- The purpose of pre-clinical study is to develop adequate data to decide that it is reasonably safe to proceed with human trials of the drug.
- Experiments are generally performed on rodent like mouse, rat, guinea pig, hamster, rabbit.
- After successful result, experiments are performed on larger animals like cat, dog, monkey.
- As the evaluation progresses unfavorable compounds get rejected at each step.
- So, that only few out of thousands reach the stage when administration to man is considered.

b) Clinical Experiments:

These follow preclinical studies. In clinical pharmacology, efficacy, safety, and pharmacokinetics of a drug substance is determined through its use in healthy human volunteers and patient populations under controlled conditions. Only those drugs which are found safe and effective in preclinical (animal) studies are further investigated in such studies.

Phases of Clinical Trial

1. **Phase I** : First in man → safety
2. **Phase II** : First in patient →dose, dosage form
3. **Phase III** : Efficacy, ADRs
4. Post marketing surveillance or **Phase IV** : Evaluation in the real clinical setting

1. **Phase I:**

- **Objectives**
  1. To assess a safe & tolerated dose
  2. To see if pharmacokinetics differ much from animal to man
  3. To see if kinetics show proper absorption, bioavailability
  4. To detect effects unrelated to the expected action
  5. To detect any predictable toxicity

– **Inclusion criteria**
  - Healthy volunteers : Uniformity of subjects: age, sex, nutritional status [Informed consent a must]
  - Exception: Patients only for toxic drugs Eg AntiHIV, Anticancer

– **Exclusion criteria**
  - Women of child bearing age, children

– **Methods:**
  - First in Man : Small number of healthy volunteers
  - First in a small group of 20 to 25
  - Start with a dose of about 1/10 to 1/5 tolerated animal dose
  - Slowly increase the dose to find a safe tolerated dose
  - If safe → in a larger group of up to about 50 –75
  - No blinding
  - Performed by clinical pharmacologists
  - Centre has emergency care & facility for kinetics study
  - Performed in a single centre
  - Takes 3 – 6 months [70% success rate]

2. **Phase II**

- First in patient [different from healthy volunteer]
- Early phase [20 – 200 patients with relevant disease]
  - Therapeutic benefits & ADRs evaluated
  - Establish a dose range to be used in late phase
  - Single blind [Only patient knows] comparison with standard drug
- Late phase [50 – 500]
  - Double blind

- Compared with a placebo or standard drug

- Outcomes
  - Assesses efficacy against a defined therapeutic endpoint
  - Detailed P.kinetic & P.dynamic data
  - Establishes a dose & a dosage form for future trials
- Takes 6 months to 2 years [35% success rate]

3. Phase III:

- Large scale, Randomised, Controlled trials
- Target population: 250 – 1000 patients
- Performed by Clinicians in the hospital
- Minimises errors of phases I and II
- Methods
  - Multicentric → Ensures geographic & ethnic variations
  - Diff patient subgroups Eg. pediatric, geriatric, renal impaired
  - Randomised allocation of test drug /placebo / standard drug
  - Double blinded:
  - Cross over design
  - Vigilant recording of all adverse drug reactions
  - Rigorous statistical evaluation of all clinical data
- Takes a long time- up to 5 years [25% success]
- Cross Over Design

Group	Week 1	Week2	Week3
I	Standard	Placebo	Test
II	Placebo	Test	Standard
III	Test	Standard	Placebo

* A wash out period of a week between two weeks of therapy

4. Phase IV or Post marketing Surveillance

- No fixed duration / patient population
- Starts immediately after marketing
- Report all ADRs
- Helps to detect
  - Rare ADRs
  - Drug interactions

* Also new uses for drugs [Sometimes called Phase V]

TEACHER'S SIGNATURE