

Preclinical screening of CNS Pharmacology

General Principles of Preclinical Screening

- **Preclinical screening** refers to the testing of new chemical substances (drugs) before they are given to humans.



- It is a very important step in pharmacological and toxicological screening methods, because it helps determine whether a drug is effective and safe.

Basic Concept

- Conducted on laboratory animals, isolated tissues, cells, or alternative models
- Done before clinical trials (human studies)
- Helps to predict human response

Main Objectives

- To identify pharmacological activity (what the drug does)
- To evaluate toxicity and safety
- To determine dose range
- To study mechanism of action

Types of Experimental Models Used

**In Vivo
Models
(Animal
Studies)**

**In Vitro
Models
(Laboratory-
Based)**

**Alternative
Models
(Non-animal
methods)**

1. In Vivo Models (Animal Studies)

- Experiments performed on whole living animals (rats, mice, rabbits, guinea pigs)
- Provide realistic biological responses
- **Used to study:**
 - Behavior
 - Organ function
 - Drug metabolism
- **Example:**
 - Testing sedative drugs by observing sleep in mice

2. In Vitro Models (Laboratory-Based)

- Conducted on **isolated tissues, cells, or organs**
- More controlled and less variable
- **Used to study:**
 - Receptor binding
 - Enzyme activity
- **Example:**
 - Isolated heart tissue to study cardiac drug effects

3. Alternative Models (Non-animal methods)

- Developed to reduce animal use
- **Include:**
 - Cell cultures
 - Computer simulations (in silico models)
 - Organ-on-chip systems
- **Useful for:**
 - Early screening
 - Toxicity prediction

Key Principles

A. Selection of Suitable Model

- **Choose appropriate:**
 - Animal species (rats, mice, rabbits)
 - Tissue or cell system

- Model should resemble human disease condition

B. Dose Selection

- Start with low dose and gradually increase
- **Determine:**
 - Minimum effective dose
 - Maximum tolerated dose

C. Route of Administration

- **Same as intended in humans:**
 - Oral
 - Intravenous
 - Intraperitoneal

D. Control and Standard Groups

- Control group receives no drug
- **Standard group:** receives known drug
- Test group receives new drug

E. Reproducibility

- Results should be consistent and repeatable
- Same conditions must be maintained

F. Ethical Considerations

- Follow CPCSEA and GLP guidelines
- Use minimum number of animals
- Reduce pain and distress

G. Observation and Data Recording

- **Monitor:**
 - Behavior
 - Physiological changes
 - Toxic effects
- Record data accurately

Importance in Pharmacological Screening

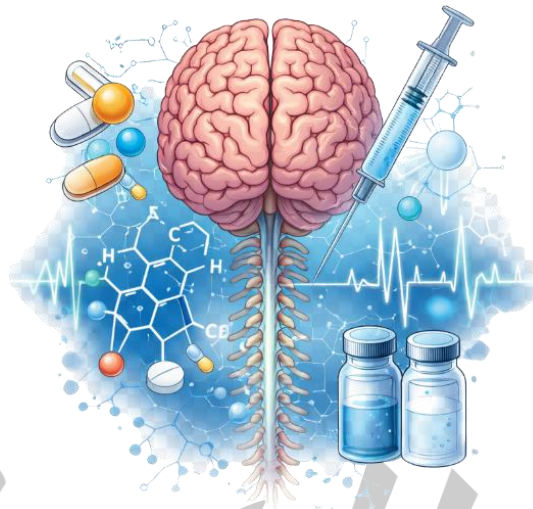
- Identifies therapeutic effects
- Helps in drug selection for further study

Importance in Toxicological Screening

- Detecting **harmful effects early**
- Prevents unsafe drugs from reaching humans

CNS Pharmacology: Behavioral Studies

- Behavioral studies in CNS pharmacology involve observing changes in animal behavior after administration of a drug.



- These studies help to understand how drugs affect the brain, emotions, learning, memory, and movement.

Why Behavioral Studies are Important

- To evaluate effects of drugs on the central nervous system
- To identify whether a drug is stimulant or depressant
- To assess anxiety, depression, and psychotic conditions
- To study learning and memory

Types of Behavioral Observations

1. Locomotor Activity (Movement)

- Increased activity → CNS stimulant
- Decreased activity → CNS depressant

2. Exploratory Behavior

- Animals naturally explore new environments
- **Reduced exploration indicates:**
 - Sedation
 - Anxiety
 - CNS depression

3. Emotional Behavior

- Fear, aggression, or calmness
- **Help in evaluating:**
 - Anxiolytics
 - Antipsychotics

4. Learning and Memory

- Tested using maze experiments
- Important for evaluating **nootropic drugs**

Common Behavioral Tests

A. Open Field Test

- Animals are placed in an open box
- Movement is recorded
- Increased movement → CNS stimulant
- Decreased movement → CNS depressant

B. Actophotometer Test

- Measures locomotor activity using light beams
- Animal movement breaks light beams
- More counts indicate stimulation
- Fewer counts indicate depression

C. Elevated Plus Maze (EPM)

- Used to study anxiety
- Plus-shaped apparatus with open and closed arms
- Anxiolytic drugs increase time spent in open arms

D. Forced Swim Test

- Used to evaluate antidepressant activity
- Animal placed in water
- Less immobility indicates antidepressant effect

E. Tail Suspension Test

- Animal suspended by tail
- Measures immobility
- Reduced immobility indicates antidepressant action



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