Preclinical screening models

Preclinical Screening Models

What is it?

- Preclinical screening models are scientific methods used to test the effects, safety, and actions of a drug on animals or tissue samples before it is tested on humans.
- These models help researchers predict how the drug might behave in the human body.



Purpose:

- To evaluate **efficacy** (whether the drug works)
- To check **toxicity** (whether the drug is harmful)
- To understand the **mechanism of action** (how the drug works)
- To identify **side effects**

Types of Preclinical Screening Models

These models are divided into two major types:

A. In-vitro Models

- ("In-vitro" means outside a living body, like in a test tube or petri dish)
- These involve using isolated tissues, cells, or organs.

Examples

- Testing a drug on isolated heart tissue to see how it affects heart rate.
- Using cell cultures to see if a cancer drug kills tumor cells.

Advantages

- Controlled environment
- Less costly and faster
- No ethical concerns like in live animals

Limitations

- May not show the full-body effect
- Cannot simulate complex body interactions (e.g., metabolism)

B. In-vivo Models

- ("In-vivo" means inside a living body, like live animals)
- These involve testing the drug in live animals (mice, rats, rabbits, etc.)
- Helps assess absorption, distribution, metabolism, excretion (ADME) and toxicity

Examples

- Giving a drug to rats to observe anti-inflammatory effect
- Testing a drug on mice to observe behavioral changes (like anti-anxiety effects)

Advantages

- Gives more realistic results
- Shows whole-body response
- Helps to observe long-term effects

Limitations

- Ethical concerns
- More expensive
- Animal data may not always match human results

Types of Pharmacological Screening (based on purpose)

- **Screening for activity** (e.g., anti-diabetic, anti-depressant, anti-cancer)
- **Screening for toxicity** (e.g., acute, subacute, chronic)
- **Screening for mechanism of action** (how drug works in the body)

Dose Selection, Calculation, and Conversions

What is Dose Selection?

- In pharmacological screening, before testing a drug on animals, we must choose a suitable **dose** — the amount of drug to be given.
- This is called **dose selection**.

Why is Dose Selection Important?

- Giving **too little** drug may not show any effect.
- Giving **too much** may cause **toxic effects or death** of animals.
- The goal is to find a dose that shows the **expected pharmacological effect** without harming the animal.

How is the Dose Chosen?

1. **Based on literature** – Previous studies or published research.

2. **From human dose** – If the drug is already used in humans, the dose is converted for animals (called human-to-animal dose conversion).
3. **Using pre-experiments** – Small studies to test different doses on a few animals.

What is Dose Calculation?

- Once the correct dose is selected, we need to calculate the **exact amount of drug** to be given, based on:
  - The **weight of the animal** (usually in kg or g).
  - The **required dose per kg** (e.g., 10 mg/kg).
- **Example:**
  - If a rat weighs 200g (0.2 kg) and the dose is 10 mg/kg:

$$\text{Required drug} = 10 \text{ mg/kg} \times 0.2 \text{ kg} = 2 \text{ mg}$$

- So, **2 mg** of the drug will be given to this rat.

What are Dose Conversions?

- Different animals have **different metabolisms**, so we can't give them the same dose as humans.
- We use **conversion factors** based on **body surface area (BSA)**.
- **Human to Animal Dose Conversion Formula:**

$$\text{Animal dose (mg/kg)} = \text{Human dose (mg/kg)} \times \left(\frac{\text{Human Km}}{\text{Animal Km}}\right)$$

- **Km** is a constant for each species based on body surface area.
- **Common Km values:**
  - Human = 37
  - Rat = 6
  - Mouse = 3
- **Example:**
  - If the human dose is 10 mg/kg, then for a rat:

$$\text{Rat dose} = 10 \times \frac{37}{6} \approx 61.6 \text{ mg/kg}$$

- So, rats require a higher dose compared to humans for the same effect.

Preparation of Drug Solutions/Suspensions

Why Prepare Drug Solutions or Suspensions?

- Most drugs come in powder or tablet form.

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