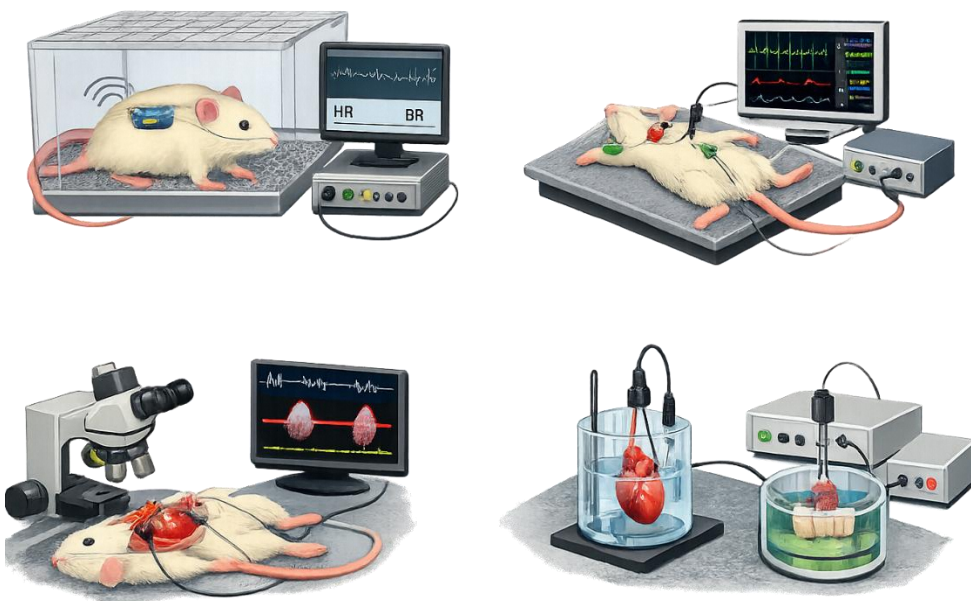


Preclinical Screening Models for ANS Activity

Preclinical Screening Models for ANS Activity



What is the Autonomic Nervous System (ANS)?

- The Autonomic Nervous System (ANS) is the part of the nervous system that controls involuntary functions in the body.
- **These include:**
 - Heart rate
 - Blood pressure
 - Breathing
 - Digestion
 - Pupil size
 - Sweating
 - Urine output
- The ANS is divided into two major branches:
 - **Sympathetic Nervous System (SNS):**
 - "Fight or flight" responses (increases heart rate, opens airways, etc.)
 - **Parasympathetic Nervous System (PNS):**
 - "Rest and digest" functions (slows heart rate, stimulates digestion, etc.)
- Drugs acting on the ANS are used for many medical conditions, such as hypertension, asthma, heart problems, digestive issues, and more.

Why is screening needed?

- Before using any new drug that acts on the ANS, it must be tested in animal models to determine:
 - **What part of the ANS it affects**
 - **How strong its action is**
 - **Whether it has side effects on vital organs**

General Screening Approaches for ANS Drugs



A. In Vivo Models (Whole Animals)

- These models involve giving the drug to live animals (**usually rats, mice, cats, dogs**) and **observing changes in**:
 - Heart rate (tachycardia or bradycardia)
 - Blood pressure (hypertension or hypotension)
 - Pupil size (mydriasis or miosis)
 - Intestinal movement (increased or decreased)
 - Urine output or salivation
- **Common procedures:**
 - Blood pressure and heart rate are measured using cannulated animals connected to pressure transducers.
 - Pupil size is observed in animals after drug administration.
 - Gastrointestinal motility is tested by giving charcoal meal and measuring how far it moves through the intestine.

B. Isolated Organ Preparations (Ex Vivo Models)

- **These models use isolated organs such as:**
 - Ileum (intestine) – for parasympathetic activity
 - Vas deferens – for sympathetic activity
 - Trachea – for bronchodilation/constriction
 - Heart (Langendorff preparation) – for cardiac effect
- **Additional points:**
 - The organs are placed in an organ bath, supplied with oxygenated fluid, and connected to a recording system.

- Drugs are added to see how the tissue contracts or relaxes.
- Helps to determine the receptor type involved (e.g., alpha, beta, muscarinic, nicotinic).

C. Use of Antagonists for Confirmation

- To confirm whether the drug acts on the sympathetic or parasympathetic system, blocking agents are used:
 - **Atropine** – blocks parasympathetic (muscarinic) receptors
 - **Propranolol** – blocks sympathetic beta receptors
 - **Phentolamine** – blocks alpha receptors
 - If the effect of the test drug is stopped by one of these blockers, it suggests what type of receptor it acts on.

Screening Models for Sympathomimetics

What are sympathomimetics?

- Sympathomimetic drugs are drugs that stimulate the sympathetic nervous system.
- They mimic the action of adrenaline (epinephrine) and noradrenaline (norepinephrine).
- They act on adrenergic receptors, which are of **two main types**:
 - Alpha receptors (**α_1 , α_2**)
 - Beta receptors (**β_1 , β_2 , β_3**)
- **Different sympathomimetic drugs** may act on one or more of these **receptors to produce effects such as**:
 - Increased heart rate and blood pressure
 - Bronchodilation (airway opening)
 - Pupil dilation
 - Decreased digestion
 - Increased blood glucose

Why is screening important?

- **To check:**
 - Which adrenergic receptors are involved
 - Potency and duration of action
 - Specific effects (e.g., heart vs lungs)
 - Side effects like excessive stimulation

Common screening models:



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