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A REVIEW ON ANIMAL STUDIES IN DRUG DEVELOPMENT-ASTHMA

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ABSTRACT

Experimental Pharmacology deals with the effect of various pharmacological agents studied on different animal species. The domain "Experimental Pharmacology" comprises with 3 modules with different matters. Module one deals with etiology and pathophysiology of Asthma. The second Module illustrated with diagnosis and treatment of Asthma. The third module includes preclinical studies and regulations. The fourth Module describes the various screening methods for the study of Anti-asthmatics.

INTRODUCTION :

Asthma is a chronic respiratory condition characterized by inflammation and narrowing of the airways, which leads to difficulty breathing. This condition can cause symptoms such as wheezing, shortness of breath, chest tightness, and coughing. Asthma can be triggered by various factors, including allergens, respiratory infections, environmental pollutants, and physical activity. It affects people of all ages but often begins in childhood. Effective management of asthma typically involves avoiding triggers, using medications to control inflammation and symptoms, and monitoring lung function to maintain quality of life.

TYPES

1.On the basis of source of stimulus

i. Extrinsic Asthma
ii. Intrinsic Asthma
iii Mixed Asthma

2. On the basis of duration of action

i. Acute Asthma
ii. Chronic Asthma

3. On the basis of severity

i. Mild intermittent Asthma
ii. Mild persistent Asthma
iii. Moderate persistent Asthma
iv. Severe persistent Asthma

1.Extrinsic Asthma

It is also called allergic asthma. It is common in childhood and caused by exposure to definite allergens. It occurs in children and young adults who have atopic (Type-1) hypersensitivity to foreign proteins. Symptoms are induced by a hyperimmune response to the inhalation of specific allergen.

2.Intrinsic Asthma

It is also called non-allergic asthma. It usually develops beyond age of 40 and have many causes other than exposure to allergens. This type of asthma is triggered by the presence of irritants in the air that are not related to allergies. These irritants stimulate parasympathetic nerve fibres in the airways causing bronchoconstriction and inflammation.

In this case there is no history of childhood allergic reactions.

3. Mixed Asthma

combination of both allergic and non-allergic asthma. Many patients do not clearly fit in to either of the above two categories and have mixed features of both. This is the most common form of asthma.

4. Acute Asthma

Acute asthma is sudden in onset. Acute asthma exacerbation happens when there is a sudden episode of progressive worsening of symptoms of asthma, like wheezing, chest tightness, cough.

5. Chronic asthma

Chronic asthma exacerbation happens when the asthma symptoms are intense and there is chronic inflammation and narrowing of the airways in the lungs. In chronic asthma, an asthma attack, is called a flareup or exacerbation.

6.Mild intermittent Asthma

A person with intermittent asthma has mild symptoms. He will have symptoms up to two days per week or two nights per month and requires treatment with short-acting inhalers on 2 days per week or fewer. This type of asthma doesn't hinder any activities and can include exercise-induced asthma.

7. Moderate Persistent Asthma

A person with moderate persistent asthma has asthmatic symptoms every day. They use their asthma medicine every day. Symptoms interfere with daily activities. Nighttime symptoms occur more than 1 time a week, but do not happen every day.

8. Severe Persistent Asthma

A person with severe persistent asthma has symptoms multiple times during the day. These symptoms will occur almost every day. They have a decrease in their physical activity. Nighttime symptoms occur often, sometimes every night. Severe persistent asthma doesn't respond well to medications even when taken regularly.

ETIOLOGY

The exact cause of asthma is unknown. An asthma trigger is anything that irritates the airways and sets off asthma symptoms. There are some non-specific factors that may precipitate asthma attack include:

1. Genetic Factors:

Family History: Asthma often runs in families, suggesting a genetic predisposition. Specific genes have been associated with asthma susceptibility, particularly those related to immune system function and inflammation.

Genetic Variants: Variations in genes related to immune responses (e.g., IL4, IL13) and airway remodelling.

2. Environmental Factors:

Allergens: Exposure to allergens like pollen, Mold, pet dander, and dust mites can trigger asthma symptoms, particularly in those with atopic (allergic) tendencies.

Air Pollution: Exposure to pollutants such as tobacco smoke, ozone, and particulate matter can exacerbate asthma or contribute to its development.

Infections: Viral respiratory infections, especially during early childhood, can influence asthma development. For example, respiratory syncytial virus (RSV) infection is associated with an increased risk of asthma later in life.

Exposure to Irritants: Exposure to irritants such as smoke, strong Odors, and chemical fumes can trigger or worsen asthma symptoms.

3. Lifestyle Factors:

Obesity: Excess body weight is associated with an increased risk of asthma and can also worsen asthma symptoms.

Diet: Diets low in antioxidants and omega-3 fatty acids may be linked to an increased risk of asthma, although the evidence is still being explored.

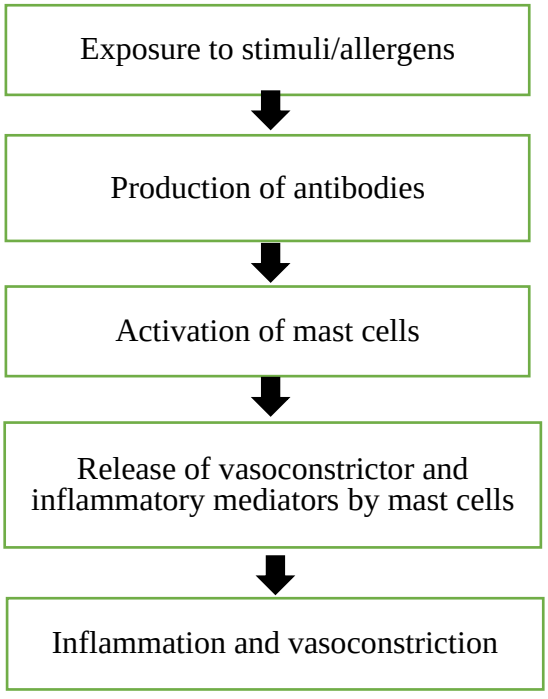
4. Developmental Factors:

Prenatal Exposure: Maternal smoking during pregnancy and exposure to certain environmental factors during foetal development can influence the likelihood of asthma in children.

Early Childhood Factors: Factors such as a lack of early exposure to diverse microbes (hygiene hypothesis) and the mode of delivery (caesarean section vs. vaginal delivery) may also play a role in asthma development.

Asthma is a complex condition with varied triggers and contributing factors, and its management often involves addressing multiple aspects of its etiology.

PATHOPHYSIOLOGY



The pathophysiology of asthma involves a complex interplay of genetic, environmental, and immunological factors that lead to inflammation and constriction of the airways. Here's a breakdown of the key components:

1. Airway Inflammation

Immune Response: In asthma, the immune system overreacts to various triggers (such as allergens, pollutants, or respiratory infections). This reaction primarily involves Type 2 helper T cells (Th2 cells), which release cytokines like interleukin-4 (IL-4), interleukin-5 (IL-5), and interleukin-13 (IL-13).

Inflammatory Cells: These cytokines attract and activate inflammatory cells, including eosinophils, mast cells, and neutrophils, to the airways. Eosinophils release toxic granules and cytokines that contribute to inflammation and tissue damage.

Airway Remodeling: Chronic inflammation can lead to structural changes in the airways, known as airway remodeling. This includes thickening of the airway wall, increased mucus production, and hyperplasia of smooth muscle cells.

2. Bronchoconstriction

Smooth Muscle Contraction: In response to triggers, the smooth muscle around the airway's contracts, leading to narrowing of the airways. This is mediated by the release of mediators like histamine and leukotrienes from mast cells.

Mucus Production: Inflammation and activation of goblet cells lead to increased mucus production, which can further obstruct the airways and contribute to breathing difficulties.

3. Airway Hyperreactivity

Increased Sensitivity: Asthmatic airways are more sensitive to various stimuli. This heightened reactivity means that even minor triggers can lead to significant bronchoconstriction and inflammation.

Hyperresponsiveness: The airways may react excessively to allergens, irritants, exercise, or changes in weather, leading to exacerbations of asthma symptoms.

4. Symptom Manifestation

Wheezing: The narrowed airways produce a characteristic wheezing sound during exhalation due to turbulent airflow.

Shortness of Breath: The reduced airflow and bronchoconstriction make it difficult for air to pass through the narrowed airways, leading to breathlessness.

Coughing: Increased mucus production and airway inflammation often result in a persistent cough.

Chest Tightness: The contraction of airway smooth muscles and inflammation can cause a sensation of tightness in the chest.

5. Triggers and Exacerbations

Allergens: Pollen, dust mites, mold, and pet dander can trigger asthma symptoms.

Irritants: Smoke, pollution, strong odors, and fumes can exacerbate asthma.

Infections: Respiratory infections, particularly viral ones, can worsen asthma symptoms.

Exercise: Physical exertion, especially in cold or dry air, can induce asthma symptoms.

Understanding the pathophysiology of asthma helps in developing effective treatments and management strategies, including anti-inflammatory medications, bronchodilators, and avoiding known triggers.

DIAGNOSIS :

Diagnosis is the process of identifying a disease or condition based on a person's symptoms, medical history, and test results. It involves several key steps:

Assessment: Gathering information through discussions with the patient about their symptoms, medical history, lifestyle, and any relevant family history

Examination: Performing a physical examination to observe signs and symptoms that might indicate a particular condition.

Testing: Conducting various tests (such as blood tests, imaging studies, or specialized diagnostic procedures) to gather more detailed information about the patient's condition.

Analysis: Evaluating all collected information to determine the presence or absence of a specific disease or condition.

Diagnosis: Formally identifying the condition based on the analysis of symptoms, test results, and clinical findings.

Treatment Planning: Developing a plan to manage or treat the diagnosed condition, which might include medications, lifestyle changes, therapies, or further monitoring.

In essence, diagnosis is about understanding what is causing a person's health issues so that appropriate treatment and management strategies can be applied.

DIAGNOSIS OF ASTHMA

Diagnosing asthma typically involves several steps to evaluate symptoms, medical history, and perform specific tests. Here's an overview of the common steps in diagnosing asthma:

Medical History: The healthcare provider will ask about your symptoms, such as wheezing, shortness of breath, coughing, and chest tightness. They will also inquire about triggers, family history of asthma or allergies, and any previous respiratory issues.

Physical Examination: The provider will perform a physical exam, often listening to your lungs with a stethoscope to detect wheezing or other abnormal sounds.

Pulmonary Function Tests (PFTs):

Spirometry: This test measures how much air you can exhale after taking a deep breath and how quickly you can do it. It helps assess the narrowing of the airways.
Peak Flow Measurement: This measures the maximum speed at which you can blow air out of your lungs, helping to monitor asthma control and detect worsening symptoms.
Bronchoprovocation Tests: If spirometry results are normal but asthma is still suspected, tests like methacholine challenge can be done. Methacholine is inhaled to see if it triggers asthma symptoms.
Exhaled Nitric Oxide Test: This test measures the level of nitric oxide in your breath, which can be elevated in asthma and inflammation of the airways.
Allergy Testing: Since allergies can trigger asthma symptoms, skin tests or blood tests might be performed to identify any allergic reactions.
Imaging: Chest X-rays or other imaging studies might be done to rule out other conditions that could be causing similar symptoms.
Response to Asthma Medication: Sometimes, a trial of asthma medication can be used to see if symptoms improve, which can help confirm the diagnosis.
A combination of these approaches helps in accurately diagnosing asthma and distinguishing it from other respiratory conditions. If you suspect you have asthma, it's essential to consult with a healthcare provider for a thorough evaluation and personalized treatment plan.

TREATMENT

1. Non-Pharmacological Treatment:
Avoid smoking.
Avoidance of allergens (e.g., Dust, mist, pollens etc.)
Avoid exposure to extreme cold condition.
In emergency oxygen therapy should be given.
Patient should be hospitalized with acute severe asthma.

2.PHARMACOLOGICAL TREATMENT

1. BRONCHODILATORS
Bronchodilators are a type of medicines that relieve asthma symptoms by relaxing the muscle bands that tighten around the airways. This action rapidly opens the airways, letting more air come in and out of the lungs. As a result, breathing improves. Bronchodilators also help to clear mucus from the lungs.
Examples: Salbutamol, Terbutaline, Theophylline
2. LEUKOTRIENE ANTAGONIST
Leukotrienes are the chemicals which play a key role in allergies, allergic rhinitis, and asthma. It causes tightening of airway muscular the production of excess mucus and fluid, making breathing difficult. Leukotriene is effective in improving asthma symptoms.
Examples: Montelukast, Zafirlukast
3.MAST CELL STABILIZERS
Mast cells are found all across the body, particularly in the lung's airways. They can release substances that cause inflammation, which cause asthma symptoms. Mast cell stabilizers inhibit inflammation-causing chemicals from being released by mast cells.
Examples: Sodium cromoglycate, Ketotifen
4.CORTICOSTEROIDS
Corticosteroids reduce the mucus secretion by inhibiting the release of secretagogue from macrophages
5.ANTI-IGE ANTIBODY
Anti-IgE antibody inhibits the binding of IgE to the high-affinity IgE receptor on the surface of mast cells and basophils and inhibit its production to attenuate type I hypersensitivity reactions.
Examples: Omalizumab

PRECLINICAL STUDIES :

Preclinical studies are an essential phase in the drug development process, conducted before a new drug or treatment is tested in humans. They provide crucial information about the safety, efficacy, and potential mechanisms of a new intervention. Here's an overview of the key aspects of preclinical studies:

1. OBJECTIVES

Safety Assessment: Determine the potential toxicity and side effects of a new drug or treatment.
Efficacy Evaluation: Assess whether the drug or treatment works as intended in animal models.
Mechanism of Action: Investigate how the drug interacts with biological systems and targets.

2. TYPES OF STUDIES

In-vitro Studies: Conducted in a controlled environment outside a living organism, such as in cell cultures. These studies help to understand the drug's effects on cellular processes and its potential toxicity.
In-vivo Studies: Performed in live animal models to evaluate the drug's overall safety, effectiveness, and pharmacokinetics (how the drug is absorbed, distributed, metabolized, and excreted).

3. KEY COMPOUNDS

Toxicology Studies: Assess acute, subacute, and chronic toxicity, including effects on different organs and systems.
Pharmacokinetics (PK): Study how the drug behaves in the body, including its absorption, distribution, metabolism, and excretion.
Pharmacodynamics (PD): Examine the drug's biological effects and its mechanism of action.

4. REGULATORY CONSIDERATIONS

Good Laboratory Practice (GLP): Preclinical studies must adhere to GLP guidelines to ensure the reliability and reproducibility of results.
Regulatory Submissions: Data from preclinical studies are used to support Investigational New Drug (IND) applications or similar regulatory submissions, allowing the drug to enter clinical trials.

5. CHALLENGES AND LIMITATIONS

Species Differences: Responses in animal models may not always predict human responses accurately.
Ethical Considerations: The use of animals in research raises ethical concerns, and researchers must adhere to strict ethical guidelines and obtain appropriate approvals.

6. IMPORTANCE

Preclinical studies are crucial for identifying potential risks and understanding the fundamental properties of a new drug, which helps to ensure that subsequent clinical trials are conducted safely and effectively.
These studies lay the groundwork for advancing a drug from the laboratory to human testing, ultimately aiming to improve therapeutic outcomes and patient safety.

GUIDELINES FOR CONDUCTING ANIMAL EXPIREMENTS

INSTITUTIONAL ANIMAL ETHICS COMMITTEE (IAEC)

INTRODUCTION:

Institutional animal ethics committee means a body comprising of a group of persons recognized and registered by the committee for the purpose of control and supervision on animals perform establishment which is constituted and operated in accordance with procedures specified for the purpose by the committee.

FUNCTION OF IAEC:

- IAEC should provide independent, competent and timely review of the ethics of a proposed study before the commencement of the same and regularly monitor the ongoing studies.
- IAEC will review and approve all research proposals involving animal experiments with a view to assure quality maintenance and welfare of animals used in laboratory studies while conducting research.

COMPOSITION OF IAEC:

Institutional Animal Ethics Committee shall include members as follows:

- A scientist from different biological discipline cum chairperson
- A scientist from different biological discipline
- A Biological Scientist
- One veterinarian involved in the care of animals.
- A scientist in charge of animal House facility cum member secretary
- A scientist from outside the institute
- One non- scientific socially aware person
- One main nominee of CPCSE
- One link nominee of CPCSEA

CPSCEA GUIDELINES

INTRODUCTION

- Committee for the purpose of the purpose of control and supervision of experiments on animals.
- Statutory body formed by the act of the Indian parliament under the prevention of cruelty to Animals act 1960.Formed in 1964, Received IN 1998, Under the committed chairpersonship of Menaka Gandhi. It includes various guidelines and subcommittees.
- Role of CPSCEA is to monitor animal experiments through ethics committees set up institutions (IAEC)

GOALS:

- To promote the human care of animals used in research.
- To provide specifications that will enhance Animals wellbeing and quality of research.

CARE AND MAINTAINENCE OF LABORATORY

VETERINARY CARE:

- It is provided by veterinarian, and daily observation of animals adopted.

QUARANTINE, STABILIZATION AND SEPERATION:

- Quarantine, period for small lab Animals: one week to one month. Large lab Animals: up to 6 weeks.
- Physiologic, psychological and nutritional stabilization required, and physical separation of animals by species to prevent anxiety and behavioural changes.

ANIMAL PROCUREMENT AND TRANSPORTATION:

- Procurement of animals done from established commercial vendors.
- During transport, stress avoided

1. Use of transport containers (cages or crates) of appropriate size.
2. Permissible number of animals accommodated in each container.

EXPERIMENTAL AREA:

Experiment should be carried out in a separate area away from the place where they are housed.
Separated functional areas for

1. Surgical support
2. Treatment of animals
3. Post operative and intensive care

PHYSICAL FACILITIES:

Building materials: durable, moisture -proof fire resistant and pest resistance.
Corridor: Wide enough to facilitate the movement of personnel and equipment.
Animal room doors: Should fit properly, should not be rust.
Floors: Smooth, moisture proof, non-absorbent, skid proof floors.
Drains: proper drainage, floor should be slopped.
Storage areas: Designed for feed, bedding and cages.

ANIMAL HUSBANDARY:

CAGING OR HOUSING SYSTEM:

The caging or housing system is one of the most important elements in the physical and social environment of research animals. It should be designed carefully to facilitate animal wellbeing, meet research requirements, and minimize experimental variables.

BEDDING:

It should be absorbent, free from toxic chemicals, Bedding should be absorbent, free from toxic chemicals or other substances that cause irritation, injure animals or personnel, and of aa type not readily eaten by animals. Bedding should be used in amounts sufficient to keep animals dry between cage changes without coming into contact with watering tubes. Bedding should be removed and replaced periodically with fresh materials as often as necessary to keep the animals clean and dry. The frequency is a matter of professional judgement of animal care personnel in consultation with the investigation depending on the number of animals and size of cages. In General, it is ideal to change the bedding twice a week or whenever requires

WATER:

Animals should have continuous access to fresh, potable, uncontaminated drinking water, according to their requirements. Periodic monitoring of microbial contamination in water necessary. Watering devices, such as drinking nozzles and automatic sprinklers should be examined routinely to ensure their proper operation. Sometimes it is necessary to train animals to drink water from automatic watering devices. It is better to replace fresh water bottles every day than to refill them, however, if bottles are to be refilled, care should be taken that each bottle is replaced on the cage properly from where it was removed.

FOOD:

Animals should be fed with palatable, non-contaminated, and nutritionally adequate food daily unless the experimental protocol requires otherwise. Feeders should allow easy access, while avoiding contamination by urine and faces. Food should be provided in sufficient amounts to ensure normal growth in immature animals and to maintain normal body weight, reproduction, and lactation in adults.

The animal feed should contain moisture, crude fibre, crude fat and carbohydrate for providing appropriate nutrition

PEST CONTROL:

Adaptation of Programs designed to prevent, control, or eliminate the presence of or infestations by pests are essential in an animal home environment.

SANITATION AND CLEANLINESS:

Sanitation is an essential activity in an animal facility. Animal rooms, corridors, storage spaces, and other areas should be properly cleaned with appropriate detergents and disinfectants as often as necessary to keep them free of dirt, debris, and harmful agents of contamination. Cleaning utensils, such as mops, pails, and brooms, should not be transport between animal rooms. Where animal waste is removed by hosing or flushing, this should be done at least twice a day. Animals should be kept dry during such procedures. For larger animals, such as dogs, cats, and non - human primates, soiled litter material should be removed twice daily. Cages should be sanitized before animals are placed in them

WASTE DISPOSAL:

Wastes should be removed regularly and frequently. All waste should be collected and disposed of in a safe and sanitary manner. The most preferred method of waste disposal is incineration. Incinerators should be in compliance with all central, state, and local Public Health and Pollution Control Board regulations.

EMERGENCY, WEEKEND AND HOLIDAY CARE:

There should be an institutional policy to care animals by qualified personnel every day, including weekends

and holidays, to safeguards their well - being including emergency veterinary care. In the event of an emergency, institutional security personnel and fire or police officials should be able to reach responsible persons for the animals. That can be enhanced by prominently posting emergency procedures, names, or telephone

numbers in animals; facilities or by placing them in the security department or telephone centre.

RECORD KEEPING:

It is essential that animal house should maintain following records:

Animal house plans, which includes typical floor plan, all fixtures etc.

Animal House staff record - both technical and non - technical.

Health record of staff and animals.

All SOPs relevant to experiments, care, breeding and management of animals.

Breeding, stock, purchase and sales records.

Minutes of institutional Animals Ethics Committee Meetings.

Records of experiments conducted with the number of animals used (copy of Form D).

Mortality, Postmortem Record.

Clinical record of sick animals.

Training record of staff involved in animal activities.

It is essential that animal House should maintain following records;

Animal House plans,Water, feed and bedding materials analysis report.

SCREENING METHODS :

Screening methods in drug development are techniques used to evaluate a large number of compounds or potential treatments to identify those that show promise for further investigation. These methods help researchers narrow down their options by assessing various factors such as efficacy, safety, and pharmacokinetics.

In-vitro Screening

Definition: This involves testing drugs on cultured cells or biological molecules outside of a living organism.

How it Works: Cells or proteins are exposed to potential drug compounds to observe effects on cell viability, enzyme activity, or receptor binding.

Purpose: To assess the preliminary efficacy and toxicity of compounds in a controlled environment.

In- vivo Screening

Definition: Testing of compounds in living organisms, such as animals, to evaluate their effects and safety.

How it Works: Compounds are administered to animal models to study their pharmacokinetics, pharmacodynamics, and overall impact on the organism.

Purpose: To understand how the drug behaves in a complex biological system and to identify any potential side effects.

SCREENING METHODS FOR ANTI ASTHMATICS

In vitro methods

(i) Binding assays

(a) Histamine receptor assay

(ii) Cell culture method

(a) Culture technique
(b) WST assay
(iii) Test in isolated organs
(a) Spasmolytic activity in guinea pig
(b) Vascular and airway responses lungs to the isolated lung
(c) Relativity of isolated perfused guinea pig trachea
In vivo methods
Air way inflammation in mice
(ii) Bronchial hyper activity in guinea pigs
(iii) Broncho spasmolytic activity in anesthetized guinea pigs
(iv) Arachidonic acid or PAF-induced respiratory and vascular
dysfunction in guinea pigs
(v) Anaphylactic micro shock in guinea pigs
(vi) Sedation aerosol induced asphyxia in guinea pig
(vii) Histamine induced bronchoconstriction in anesthetized guinea pigs
(viii) Pneumotachograph in guinea pigs (ix)
(ix) Micro shock in rabbits
(x) Airway micro vascular leakage in guinea pigs

HISTAMINE RECEPTOR ASSAY

Aim:

This method evaluates affinity of test compare to histamine - H, receptor to measure their inhibitory activity on binding of pyrilamine (E, antagonist) to guinea pig brain plasma membrane preparation.
Animals required: Male guinea pig (300 - 600 gm)
Chemicals required: Ice - cold Tri's buffer, aliquots 1 ml,
3H pyrilamine mepyramine (10' m)
Equipment required: Centrifuge, liquid scintillation counter
PROCEDURE:
i. Male guinea pigs (300g-600g) are sacrificed by CO, Necrosis
ii. Brain is homogenized in ice-cold tris buffer and homogenate is centrifuged for 10 mins at 4°C at 50000g
iii. Supernatant is discarded and pellet is resuspended in buffer, centrifuged again
iv. Pellet obtained is re-suspended in Tris-buffer and aliquots of 1ml are frozen at -70 °C.
V.50 ul of 3H pyrilamine and 50 ul of test compound is added in 100 ul of membrane suspension is incubated for 30min
vi. Make 11 conc. Of 3H pyrilamine and perform saturation studies vii. Add 3ml of scintillation cocktail to measure the radioactivity in scintillation counter
viii. Radioactivity denotes the binding of pyrilamine binding
ix. % inhibition of 3H pyrilamine binding is measured using scintillation counter

2.SPASMOLYTIC ACTIVITY IN GUINEA PIG

AIM: to check the spasmolytic activity induced by histamine and calcium ionophores.
Animal: albino guinea pigs
Sex: m/f
Weight: 300-450g
PROCEDURE:
i. Albino guinea pigs(300-450g) are sacrificed with an overdose of ether
ii. Chest is opened and the lungs are removed and cut into strips of 5 cm each and placed in physiological saline solution
iii. Lung strips are mounted in organ bath containing nutritive solution
iv. Prior to testing carbachol is added to the bath to test the lungs strip's ability to contract
v. After 30 min spasmogens (histamine, ca ionophore, leukotriene) are added to induce constriction
vi. After 5 min test drug is added and percentage inhibition of spasmogen induced constriction is measured.

3. BRONCHOSPASMOLYTIC ACTIVITY IN ANASTHETISED GUINEA PIG

AIM: Bronchospasm causes decrease in volume of inspired air & increase in volume of excess air
Rationale: To measure volume of air not taken up by lungs after bronchospasm
Animal used: Guinea pig
Anaesthetic used: urethane ip

Procedure:

i. Trachea is cannulated
ii. ARM 1 - connected to respiratory pump
ARM 2- connected to statham pressure transducer.
iii. Artificial ventilation at frequency 60 strokes/min is maintained
iv. Excess air not taken up by lungs is measured
v. Test drug administered (through jugular vein)
vi. BP is recorded
vii. Each animal placed in plastic container (histamine chamber)
viii. 0.25% histamine solution aerosol sprayed at 180 mmHg
ix. 5 min exposure time (test drug given orally 1 hr before exposure)
x. Spasmogen challenge is repeated
xi. Unprotected animals fall on their sides

4. ARACHIDONIC ACID/PAF INDUCED RESPIRATORY & VASCULAR DYSFUNCTION

Animal used - Guinea pigs (Male, 300-600g)
Aesthetics used - Pentobarbitone sodium 60mg/kg ip
Aim -To study & compare ...

% inhibition or increase of bronchospasm
BP reduction (measure magnitude & duration)
Thrombocytopenia & haematocrit

PROCEDURE:

i. Trachea – artificial respiration (70-75 strokes/min)
ii. Jugular vein-test drug
iii. Carotid artery-blood withdrawal and transducer attached for BP measurement
iv. Record BP and changes in airflow
v. Animal given multiple iv injection of arachidonic acid till 2 bronchospasms of equal intensity are obtained
vi. Test drug administered intravenously
vii. Repeat spasmogen injections

REFERENCE :

1. KD Tripathi. Drugs for cough and bronchial asthma. Essential of medical pharmacology.2006:217.
2. SOLIS-COHEN, S. (1900). The use of adrenal substances in the treatment of asthma. JAMA, 34, 1164–1169.
3. DiPiro J, Yee G, Posey M, Haines S, Nolin T, Ellingrod V. PHARMACOTHERAPY: a pathophysiologic approach, eleventh edition. S.L.: Mcgraw-Hill Education; 2020.
4. CPCSEA Guidelines for laboratory animal facility. Indian journal of pharmacology and clinical research.2003 Jul 1;35(4):257