

AIM: To study the Anti-inflammatory activity of drugs using carrageenan induced paw-edema model.

REQUIREMENTS:

Animal : Rats (200-250gm)

Instrument : Plethysmograph

Drugs :

- Carrageenan: Prepare 1 % W/V solution and inject 0.1 mL underneath the planter region.
- Indomethacin: Dose 20 mg/Kg S. C. (Stock solution 4 mg/ml, inject 0.5ml/100g of body weight of the animals)

PRINCIPLE:

Inflammation is a pathophysiological response of living tissue to injury that leads to local accumulation of plasmatic fluid and blood cells. Although it is a defense mechanism that helps body to protect itself against infection, burns, toxic chemicals, allergens or other noxious stimuli. The carrageenan-induced paw edema model in rats is known to be sensitive to cyclooxygenase inhibitors and has been used to evaluate the effect of non-steroidal anti-inflammatory agents, which primarily inhibit the cyclooxygenase involved in prostaglandin synthesis. Amongst the different methods applied for measuring inflammation, there have been estimates of the volume of edema by measuring the dorso-ventral diameter of rat hind paw pads or comparing the weights of excised limbs. Inserting the inflamed paw in a tube of fluid elevates the fluid level, and test and control levels can be compared. It is a rapid as well as reproducible method. It is used to estimate duration of action and potency of corticosteroid after systemic as well as local application. However, it is nonspecific methods and non-valid for assessment of currently used anti-inflammatory agents.



PLETHYSMOGRAPH

PROCEDURE:

1. Weigh the animal and number them.
2. Make a mark on both the hind paws (right and left) just beyond tibio-tarsal junction, so that every time the paws is dipped in the mercury (Hg) column up to fixed mark to ensure constant paw volume. Note the initial paw volume for both right and left legs of each rat by Hg displacement methods.
3. Divide the animals in to two groups each comprising at least four rats.
4. **Control group:** Inject saline
5. **Test group (Indomethacin treated group):** Inject indomethacin subcutaneously.
6. After 30 minutes inject 0.1 mL of 1% (w/v) carrageenan in to the plantar region of the left paw of control as well as indomethacin treated groups. The right paw will serve as reference non inflamed paw for comparisons.
7. Note the paw volume of both legs of control and indomethacin treated rats at 15, 30, 60 and 120 minutes after carrageenan challenges.
8. Calculate the % difference in the right and left paw volume of each rat of control and indomethacin treated group.
9. Compare the mean % change in paw volume in control and indomethacin treated rat and express as % oedema inhibition by the indomethacin.

OBSERVATION TABLE:

Sr. No	Groups of animal		Weight of animal	Drug treatment	Dose of Drug in mL	Paw volume as measured by Hg displacement at (Min)														
						0		15		30		60		120						
						R	L	R	L	R	L	R	L	R	L					
1.	Control	1.	295	Saline + Carrageenan																
2.		2.	290																	
3.		3.	300																	
4.		4.	270																	
5.	Test	1.	285	Indomethacin + Carrageenan																
6.		2.	280																	
7.		3.	300																	
8.		4.	270																	

DISCUSSION:

Inflammation is clinically characterized as rubor (redness), calor (heat), tumor (swelling) and dolor (pain). It has three phases. The first phase is due to increase in vascular permeability resulting in exudation of fluid from the blood into the interstitial space. The second phase involves infiltration of leukocytes from the blood the tissue and third phase is granuloma formation.

Phenylbutazone and indomethacin are powerful anti-inflammation agents with analgesic and antipyretic properties. They inhibit production of eicosanoids like prostacyclin, thromboxanes and prostaglandins by inhibition of cyclo-oxygenase (cox) and thereby reduced edema in this model.

Paw edema is the method used for testing acute inflammation.

QUESTIONS:

1. What is inflammation?
2. Explain the sign and symptoms of inflammation.
3. Classify NSAIDs.
4. Enlist the methods used for screening of anti-inflammatory.
5. Name the instrument used for screen of anti-inflammatory
6. Discuss the mechanism of action of indomethacin.
7. What is carrageenan-induced rat rat paw edema? Which pathological changes occur?
8. Explain cotton pellet granuloma and air-pouch inflammation method.

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