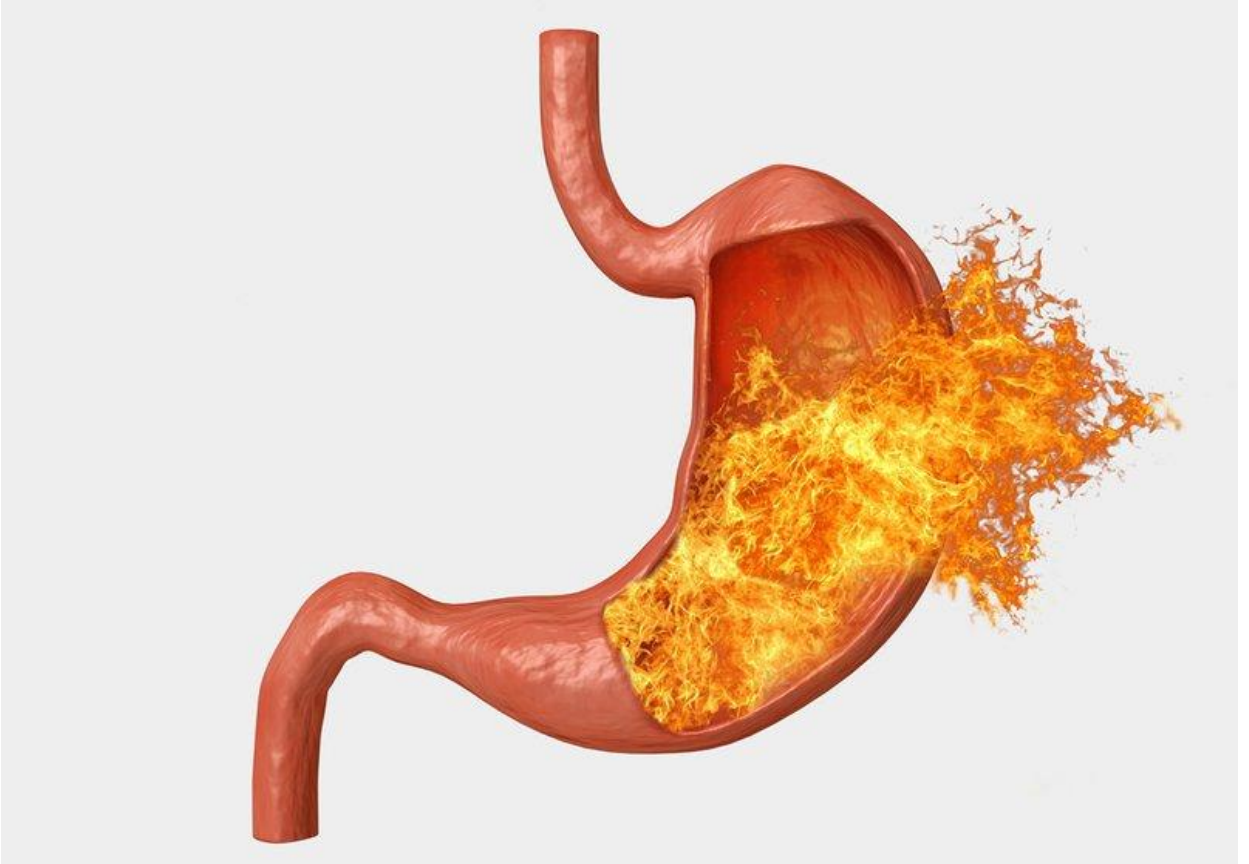
Content

- Introduction
- Cause of ulcer
- Symptoms of ulcer
- Type of ulcer
- Classification of anti-ulcer drug
- Preclinical evaluation
- In vivo
- In vitro

Introduction

- Peptic ulcer is one of the most prevalent chronic gastrointestinal disorder.
- Gastric ulcer may located at the stomach duodenum.
- Stomach ulcer are called peptic ulcer’s and intestine ulcer are called duodenal ulcers.



- Ulcers occurs due the imbalance between the offensive(gastic acid secretion) and defensive(gastric mucosal integrity) factors.
- A peptic ulcer is a sore on the lining of your stomach, small intestine or esophagus.
- A peptic ulcer in the stomach is called a gastric ulcer.

Causes Of Ulcer

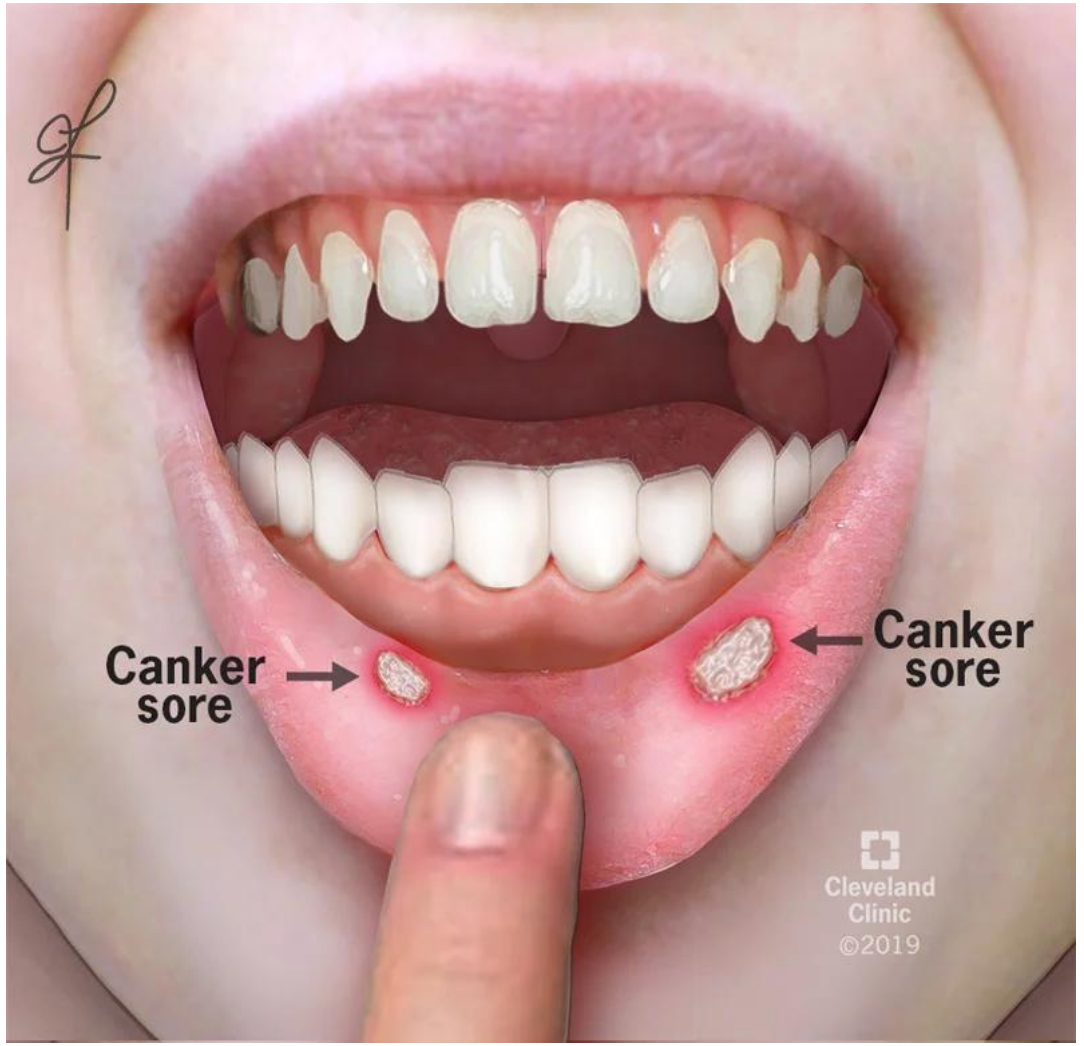
- Helobacter pylori infection
- Nonsteroidal anti-inflammatory drug(NSAIDs)
  eg. Aspirin,Ibuprofen,Naproxen.
- Excess stomach acid production
- Smoking
- Stress
- Alochol
- Spicy or acidic food

Symptom Of Ulcer

- Burning sensation
- Pain in the middle of the Abdomen
- Nausea or vomiting
- Bloating stomach
- Heart burn(burning sensation in the chest)

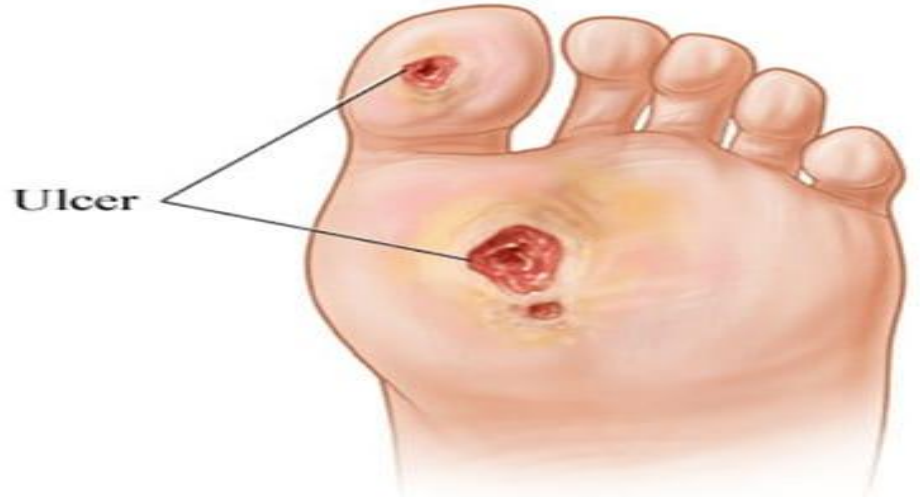
Type Of Ulcer

- **Mouth Ulcer** - Also known as canker sores, these are painful, shallow sores that appear on the inside of the mouth.



Arterial Ulcer

- Caused by poor circulation due to narrowed or blocked arteries, these ulcer often appear on the feet,toes,heels.

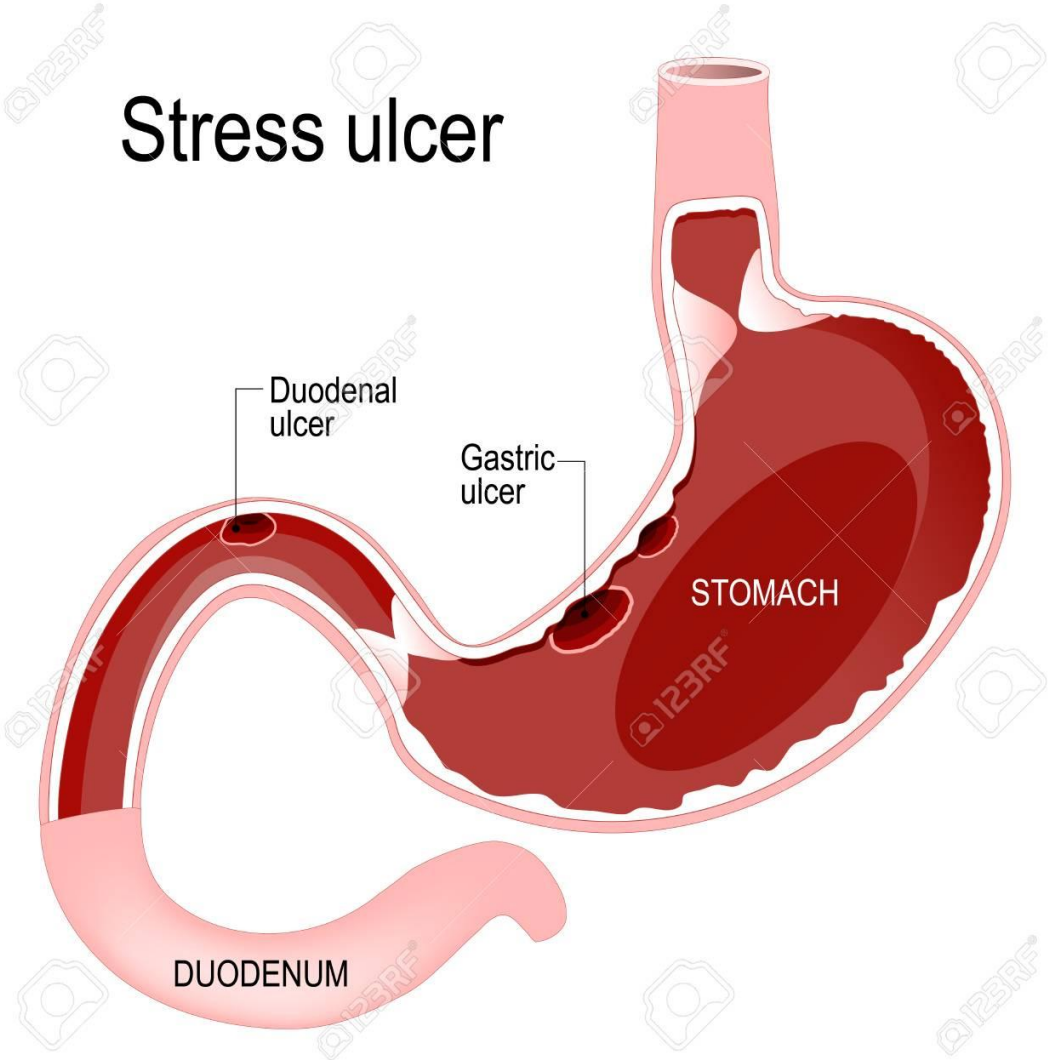


Diabetic Ulcer

- Common in people with diabetes, these ulcer often occur on the feet due to nerve damage and poor circulation.

Stress Ulcer -

- Severe physical stress such as from surgery injury or critical illness can lead to stress ulcer in the stomach or small intestine.



Corneal Ulcer

These occur on the surface of the eye's cornea and can result from infection injuries or underlying condition.

Gential Ulcer -

Sexually transmitted infection(STIs) like herpes and syphilis can cause ulcer in the gential area.

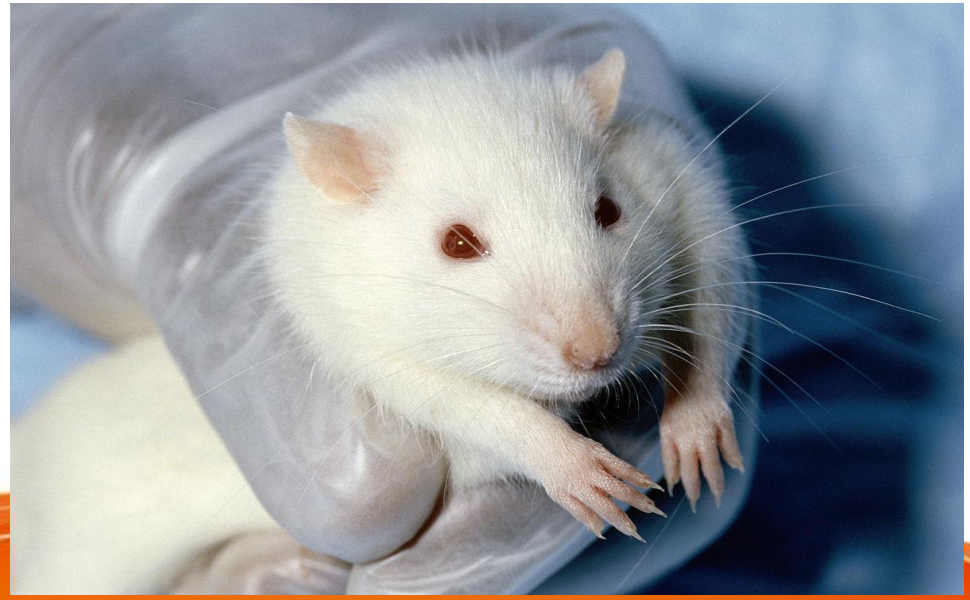
Ischemic Ulcer -

These ulcer develop due to inadequate blood supply to a particular area of the body often seen in people with peripheral artery diseases.

Classification Of Anti-ulcer Drug

- H2 receptor antagonist - Cimetidine,Famotidine,Ranitidine
- Proton pump inhibitors - Omeprazole,Pantoprazole, Rabeprazole.
- Anticholinergics - Pirenzepine,Telenzepine
- Prostaglandin analouge - Misoprostal
- Antacids - Sodium bicarbonate, Aluminum hydroxide gel Pepto-Bismol.
- Ulcer protective - Sucralfate,Colloidal bismuth subcitrate.
- Anti H-pylori - Amoxicillin,Metronidazole, Clarithromycin.

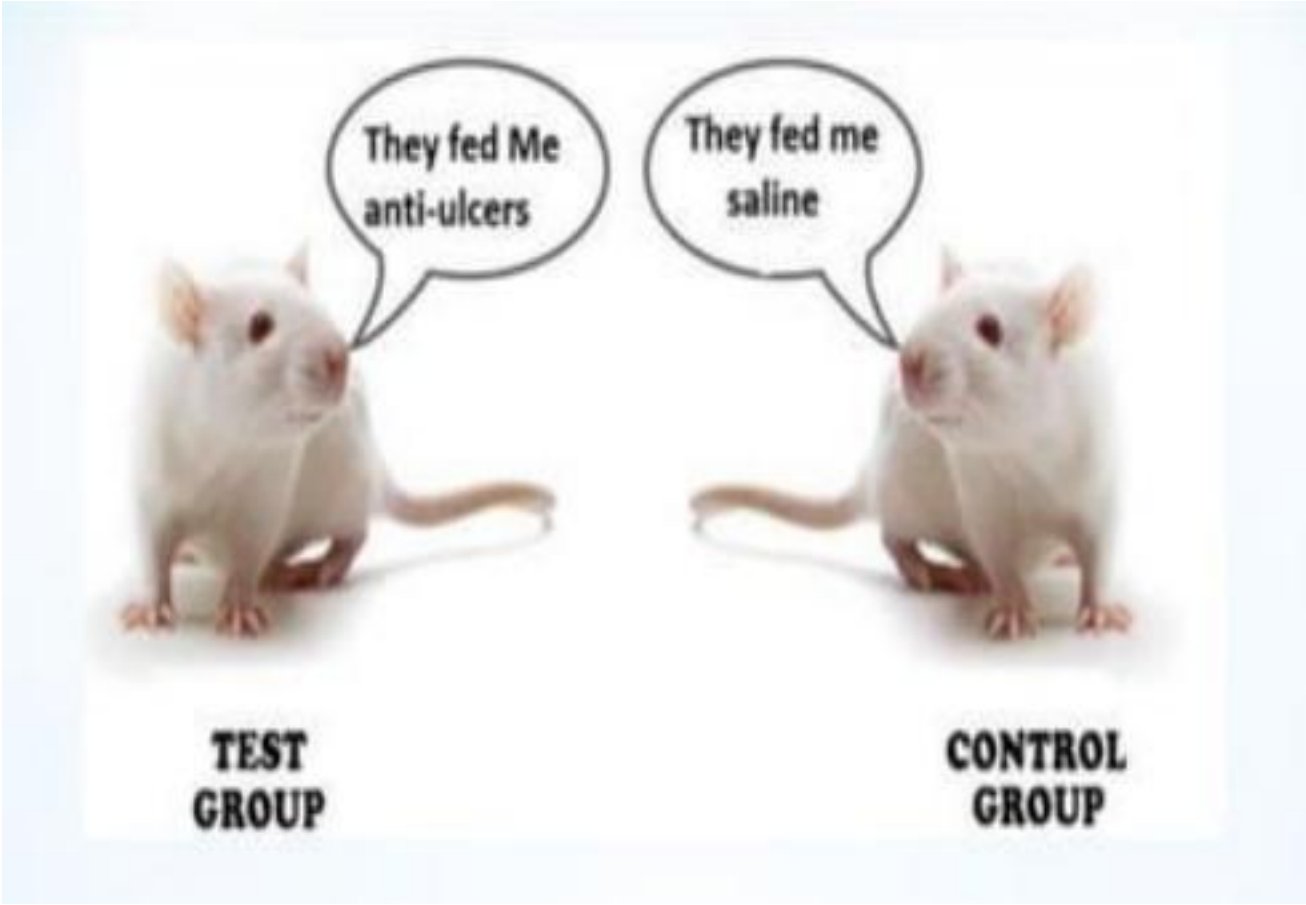
PRECLINICAL EVALUATION



Ideal Animal For Screening of anti-ulcer Drug

RATS because

- Of continuous secreation of acid.
- Glandular portion of Rat stomach analogous to body of stomach in man both anatomically and functionally.
- Guinea pigs are used when Histamine is used to induce ulcer.



In Vitro Method

- Gastrin Binding Assay
- Tiotidine Binding Assay
- H+/K+ - ATPase Inhibition Assay

In Vivo Method

- Pylorus ligation in rats
- Histamine-induce Gastric Ulcer
- Ethanol-induce mucosal damage
- NSAIDs-induce Gastric lesions
- Acetic acid-induce Gastric Ulcer
- Stress ulcer model

Pylorus Ligation In Rats

Aim- Study of Anti-ulcer Activity of Drug using Pyloric Ligation Rat Model.

Requirements- Animal: Wistar rats (150-170g)

Drug: Cimetidine,Ranitidine(15mg/kg)

Saline: 0.1NaOH

Equipment: Scissor,suturing needle,thread,cord bord,centrifugation tubes.

Procedure

- 150-200 g Wistar rats are fasted for 48hr but having acess to drinking water.
- During this time, they are to be housed single in cages with raised bottom of wide wire mesh in order to avoid coprophagy.
- 10 animals to be used per dose and as controls.under ether anesthesia an midline abdominal incision has to be made.

- Pylorus is ligated without damaging its blood supply. Stomach is replaced and abdominal wall closed with sutures.
- Test compounds are given either orally or injected S.C.
- The animal are placed in plastic cylinder with an inner diameter of 45mm being closed on both ends by wire mesh.
- After 17-19 hr the animals are sacrificed by CO2 anesthesia.
- The stomach is removed, contents of the stomach are drained into a graduated centrifuge tube and subjected to analysis for pH, free and total acidity carbohydrates:protein ratio etc.
- Along the greater curvature the stomach has to be opened and pinned on a cork plate.

- The mucosa to be examined with help of a stereomicroscope.

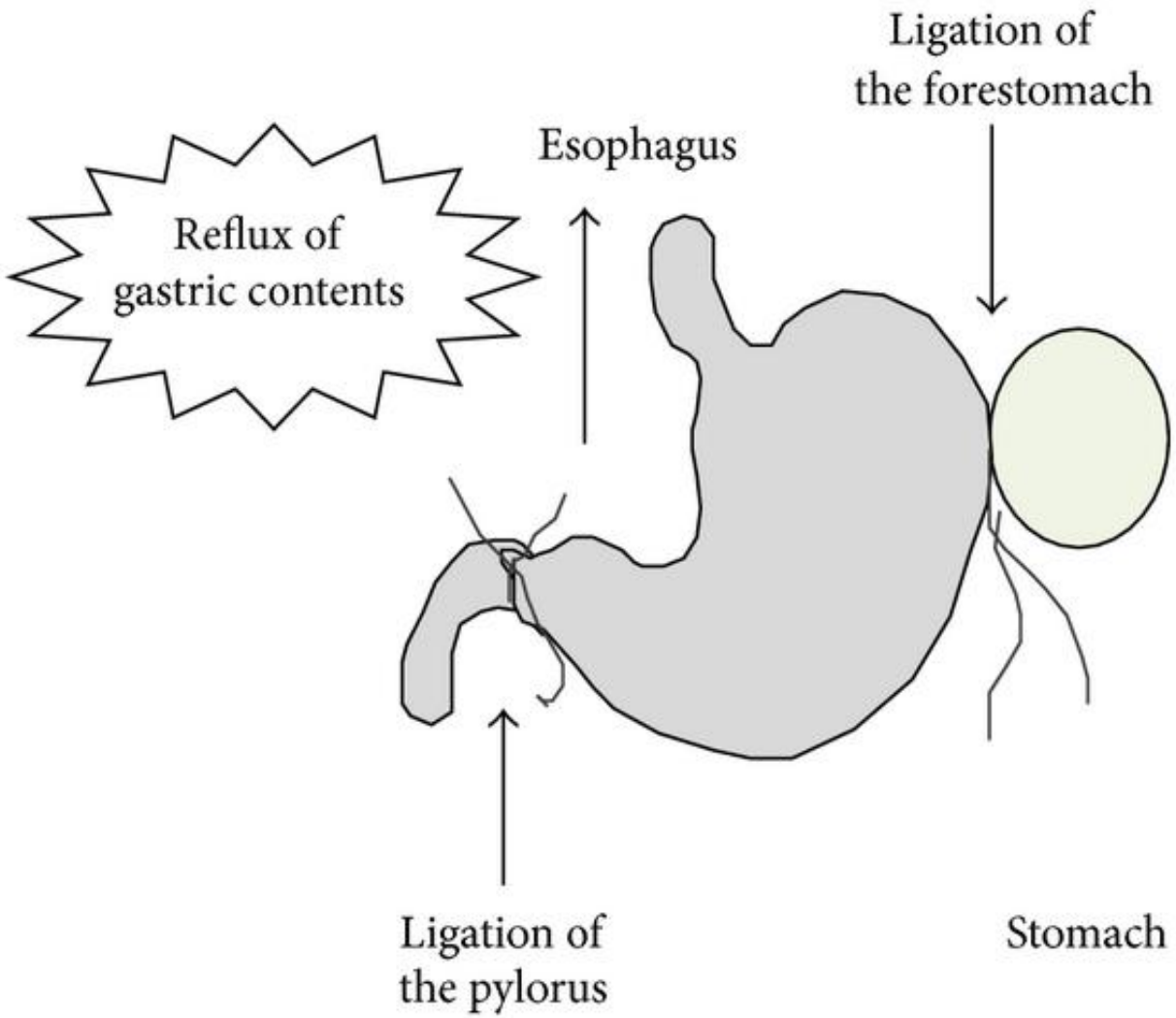


Figure 1

Figure 2

Figure 3

Figure 4

Figure 5

In control group **(Figure 1),** bleeding observed with red coloration. In ranitidine

Evaluation

- Ulcer severity- 0 = No ulcer
  1 = Superficial ulcer
  2 = Deep ulcer
  3 = Perforation
- Ulcer index- (UN+US+UP)/10
  UN is average number of ulcer per animal
  US is average severity score
  UP is percentage of animal with ulcer

- Ulcer index of test drug compared with control group to detect anti-ulcer effect of test drug.

Observation table:

Group	BW	Dose (mg/kg)	Vol (ml)	pH	Acidity (mEq/l/100g)		Gastric erosion				Ulcer Index	% Ulcer Protection
							Ulcer score					
					Free	Total	0	1	2	3		

Histamine-Induce gastric ulcer

Principal- Gastric acid secreation is increased when histamine is administered intraperitoneal.

Procedure- 300-400g guinea pig are taken,fasted for 36 hours before experiment only give water.

- 1ml of histamine acid phosphate was administered by i.p.
- Promethazine hydrochloride 5mg was injected i.p. 15 min before and after15min histamine to protect the animal against histamine toxicity.

- The standard/test drug were administered s.c. 45min before the histamine injection.
- After 4 hour, guinea pig were sacrificed and stomach dissected out.
- Stomch was open along the greater curvature ulcer were identified.

Evaluation - ulcer scoring

Type0 - No visible ulcer

Type1 - 10 or less small ulcer 1-3mm in diameter

Type2 - 11 more ulcer 1-3 mm in diameter

Type3 - 1 or more ulcer 4-6 mm in diameter

- Type4 - 1 or more ulcer 7mm or more in diameter
- Type5 - Perforation of the gastric wall

- Produces 100% gastic ulceration.
- Increased volume of gastric acid secreation.

Ethanol-induced Mucosal damage

Principal- Ethanol being a necrotizing agent damage the superficial epithelial layers and inhibits the release of mucosal prostaglandins.

Procedure-

- Wistar rats weighing 150-200 grams are taken
- Fasted for 18hours before experiments water ad libitum.
- Rats are given test drugs or standard drug orally.
- 30min later 1ml/200gm of 99.80% alcohol is administered orally.
- After 1hour rats are sacrificed and stomach dissected out.
- Severity score and ulcer index are calculated.