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# Comparitive Evaluation of Different Anti-Ulcer Drugs using Standard Procedures

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**Abstract:- Ulcer is a common gastro intestinal disorder. It is fundamentally a kindled break in skin on the mucous film coating the wholesome lot. Ulceration happens when there is an unsettling influence in the typical balance brought about by either improved hostility (or) lessened mucosal obstruction. Ulcers are most common on the skin of the lower extremities and in the gastro intestinal tract, although they may be encountered at almost any site. Peptic ulcers are erosion lining of the stomach. Generally, pain occurs when the stomach is empty and relives after eating. A duodenal ulcer is most common in younger individuals and predominantly affects males. In some cases, ulcers are very dangerous and show lethal effect.Aims of the study evaluate the best anti ulcer activity of certain drugs. By using different standard procedures. In this review observed the significant number of lesions in the lumen and the antrum of stomach. Observed in these evaluation studies the number of lesions is inhibited by omeprazole more than ranitidine. In this studies observe the anti ulcer activity of respective drugs shows various anti ulcer activity and used to decrease lesions and redness of stomach, subside the gastric pain. Lastly omeprazole shows good anti ulcer activity than that of ranitidine and cimetidine, mesoprostol.**

***Keywords:-*** *Omeprazole, Cimetidine, ranitidine, Antrum, Evalution, Gastro intestinal.*

## I. INTRODUCTION

Ulcer is a typical gastrointestinal problem which is seen among many individuals. It is fundamentally a kindled break in the skin on the bodily fluid film covering the wholesome plot.

Ulceration happens when there is an unsettling influence in the typical harmony brought about by either improved hostility or lessened mucosal obstruction.

Anti ulcer activity is defined as tending to prevent or treat ulcers and especially ulcers of the walls of the stomach or duodenum. (or) The antiulcer activity can be attributed to different mechanisms, including inhibition of gastric acid secretion, reinforcement of gastric barrier.

- Ulcers are the open wounds of the skin or bodily fluid layer described by the sloughing of kindled dead tissue. Ulcers are sores on the outer layer of the skin or bodily fluid film portrayed by a shallow loss of tissue.
- Ulcers are most normal on the skin of the lower limits and in the gastrointestinal parcel, +in spite of the fact that they might be experienced at practically any site. There are many kinds of ulcers like mouth ulcers, throat ulcers, peptic ulcers, and genital ulcers of this peptic ulcer are such among individuals.
- The peptic ulcers are disintegration of coating of stomach or duodenum. The two most normal sort of peptic ulcer are called gastric ulcer and duodenal ulcer. The name alludes to site of ulceration. An individual might have both gastric and duodenal ulcers at same time.
- For the most part, torment happens when the stomach is vacant and family members subsequent to eating. A duodenal ulcer is more normal in more youthful people and dominatingly influences guys.
- In duodenum, ulcer might show up on both front and back walls.
- Now and again, peptic ulcers can be perilous with side effects like horrendous stools, serious stomach torment, and spasms alongside spewing blood.
- This can result in an effective physical issue and quick epithelial cell demise, shallow discharge,errosions [1]
- Peptic ulcers are acid-induced lesions found in the stomach and duodenum characterized by denuded mucosa with the defect extending into the submucosa or muscularis propria [2]

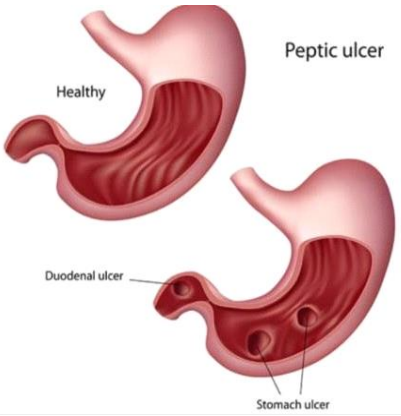


Fig. 1: Representation of peptic ulcers

### *A. INCIDENCE*

The rate of peptic ulcer sicknesses (PUD) changes overall and PUD difficulties.

- Among 4188 edited compositions screened, 178 full — text articles were distinguished and 29 occurrence concentrates on revealing frequency of PUD, its subtypes, or its complexities were incorporated.
- The rate of PUD and its complexities in the 21st century worldwide.

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- The most noteworthy yearly rate of all PUD (muddled and straightforward) was 141.9 per 100,000 man a long time in Spain, and the least was 57.75 in Sweden.
- The most noteworthy yearly rate of draining PUD was 79.70 per 100,000 man years.
- In Spain, and the most minimal was 1.80 in Malaysia. The most noteworthy yearly rate of punctured PUD was 12.17 Per 100,000 man a very long time in the UK, and the least was 3.88 in Spain.

| Country | Data Source | Peptic Ulcer | | | Gastric Ulcer | | | Duodenal Ulcer | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | General Incidence (person years) | Bleeding Incidence (person years) | Perforated Incidence (person years) | General Incidence (person years) | Bleeding Incidence (person years) | Perforated Incidence (person years) | General Incidence (person years) | Bleeding Incidence (person years) | Perforated Incidence (person years) |
| **N. America** Canada | Quan 2014 | | 37.85 | | | | | | | |
| USA | Feinstein 2010 | 62.03 | | | 33.70 | | | 24.40 | | |
| | Laine 2012 | | 40.16 | | | 21.85 | | | 16.15 | |
| **Asia** Israel | Hershcovici 2010 | | | | | 2.40 | | | 6.70 | |
| Malaysia | Lee 2014 | | 1.80 | | | | | | | |
| South Korea | Bae 2012 a,b | | 22.10 | 4.40 | | | | | | |
| Taiwan | Wu 2009 | | | | | | | | 56.39 | 6.14 |
| **Europe** Belgium | Bartholomeeusen 2007 | | | | 101.00 | | | 85.00 | | |
| Denmark | Lassen 2006 | | 57.78 | 8.30 | | | | | | |
| Finland | Malmi 2014 | 93.33 | 46.33 | | 61.33 | 22.17 | 6.67 | 31.67 | 12.00 | 3.50 |
| Germany | Ohmann 2004 | | 48.70 | | | 23.00 | | | 25.70 | |
| Greece | Theocharis 2008 | | 72.50 | | | 31.30 | | | 35.50 | |
| Italy | Loperfido 2009 | | 47.60 | | | 15.20 | | | 29.80 | |
| Netherland | Ramsoekh 2005 | | 21.50 | | | | | | | |
| | Post 2006 | | | | 16.03 | 7.34 | 4.37 | 11.33 | 6.79 | 1.30 |
| | Van Leerdam 2003 | | | | | 9.70 | | | 12.00 | |
| Norway | Bakkevold 2013 | | 45.00 | | | | | | | |
| | Thorsen 2013 | | | 6.50 | | | | | | |
| Slovakia | Ciernik 2009 | | | | | 56.86 | | | 52.86 | |
| Spain | Lanas 2011 | | 31.32 | 3.88 | | | | | | |
| | Perez-Aisa 2005 | 141.90 | 79.70 | 8.00 | 52.30 | | | 86.10 | | |
| Sweden | Lu 2012 | | 15.71 | | | | | | | |
| | Ahsberg 2011 | 57.75 | 38.15 | 10.66 | | 18.93 | | | 16.77 | |
| | Hermansson 2009 | | | | | 13.02 | 3.35 | | 11.28 | 2.24 |
| | Sadic 2009 | | | | | 15.54 | | | 13.07 | |
| UK | Taha 2008 | | | 12.17 | | | | | | |
| | Kang 2006 | | | | | | | 36.25 | 13.95 | 11.15 |
| | Bardhan 2004 | | | | | 9.38 | 1.90 | | 11.14 | 6.26 |

Table 1: Incidence of peptic ulcers in world wide

*B. In India*

Peptic ulcer sickness in everybody of Kashmir, not entirely set in stone by endoscopy in a haphazardly chosen test populace of 2763 grown-ups matured 15 years or more who were consulted utilizing a survey.

- Of 239 people with ulcer side effects, 193 (80.7%) had an oesophagogastroduodenoscopy. A haphazardly chosen 177 people from among the leftover populace without ulcer side effects, were likewise endoscoped.
- The point predominance of peptic ulcer was 4.72% and the lifetime commonness was 11.22%.
- The duodenal to gastric ulcer proportion was 17.1:1. Duodenal and gastric ulcer were normal in men.
- The predominance of peptic ulcer expanded with age, with a pinnacle commonness of 28.8% in the fifth 10 years of life. Peptic ulcer was not connected with financial status.
- The pervasiveness of entanglements, like dying, stenosis, or hole were like those detailed in the West.

## II. CAUSES

Stomach ulcer is a disease caused with bacterium Helicobacter pylori

- Long haul utilization of non steroidal mitigating medications like ibuprofen
- A condition known as zollinger elision disorder can cause stomach and gastrointestinal ulcers by expanding the body's development of corrosive
- This disorder is thought t cause under 1% of every peptic ulcer
- Peptic ulcers happens when corrosive in the gastrointestinal system destroys the internal surface of the stomach.
- Several pills,such as potassium , may cause esophageal irritation and ulcer especially if taken without sufficient or lying down immediately after taking .
- In individuals who have compromised resistant frameworks esophageal ulcers might be brought about by other bacterial ,contagious, viral diseases including : HIV, candida over development, herpes simplex infection , cytomegalovirus.

## III. TYPES OF ULCER

There are few types ulcers including

- arterial ulcers
- venous ulcers
- mouth ulcers
- genital ulcers

*A. ARTERIAL ULCERS:*

- Arterial ulcers are open sores that primarily develop on the smaller side of arterioles and capillaries, most often around the outer side of our ankle , feet ,heels
- Arterial ulcers develop from damage to the arteries due to lack of blood flow to thetissues
- These forms of ulcers can take months to heal

- **Symptoms**

  The main symptoms of arterial ulcers include the following:
  - Red, yellow sores
  - Hair less skin
  - Leg pain
  - No bleeding
  - Affected area cool to the touch from minimal blood circulation

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- Alarm symptoms include GI bleeding, weight loss, early satiety, dysphagia or odynophagia, family history of upper GI malignancy, iron deficiency anemia or new upper GI symptoms in patients older than [3]

- **Treatment**
  Treatment of arterial ulcers depends on underline cause. Primary treatment includes restoring blood circulation to the affected area

*B. VENOUS ULCERS:*

Venous ulcers are the most well-known sort of leg ulcers - are serious injuries that frequently structure on your leg , underneath your knee and on the inward region of your lower leg they commonly create from harm to your veins brought about by lacking blood stream back to your heart.

- **Symptoms:**
  Symptoms you may experience include:
  - Inflammation
  - Swelling
  - Itchy skin
  - Scabbing
  - Discharge

- **Treatment**
  Anti biotics can help prevent infection and reduce symptoms but they aren't enough toheal venous ulcers.

*C. GENITAL ULCERS:*

- Genital ulcers are wounds that foster on genital region , incorporate the penis, vagina, rear-end or encompassing regions .
- They normally cause by physically communicated contaminations( STIs), genital ulcers can likewise set off by injury , fiery sicknesses or even ,at times ,an Epstein-barr viral( EBV) disease

- **Symptoms:**
  - Rash or bumps in the affected area
  - Pain or itching
  - Swollen glands in the groin area
  - Fever
- Treatment:
  - Treatment depends upon the underline cause of your condition.
  - If you feel you have been exposed to an STI ,seek immediate medical attention

*D. MOUTH ULCERS:*

Mouth ulcers are little bruises or injury that foster on your mouth or the foundation of your gum , they're regularly known blister Types:

Kinds of mouth ulcers incorporate the accompanying

- Esophageal ulcers: an esophageal ulcer is a disintegration that structures in the covering of your throat - the long cylinder that associates the throat to the stomach. esophageal ulcers are substantially less, that different kinds of ulcers
- Gastric ulcers: the bruises that creates on the coating of the stomach or small digestive tract
- Duodenal ulcers: a peptic ulcer that creates in the initial segment of the little intestine(duodenum)

*E. PATHOPHYSIOLOGY:*

Pathophysiology of peptic ulcer infection includes an unevenness between hostile (corrosive, pepsin and helicobactor pylori) and guarded factors (mucin, prostaglandin, nitric oxide).

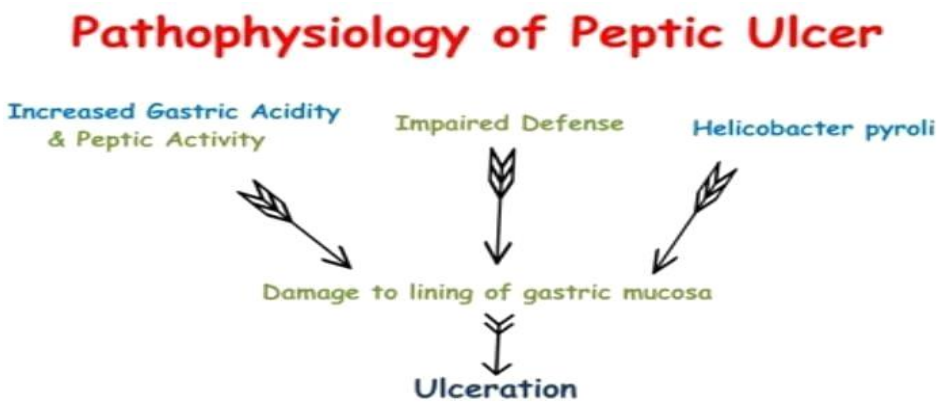


Fig. 2: Pathophysiology of peptic ulcers

Risk factors inclining toward advancement of PUD (peptic ulcer infection):

- H.pylori contamination
- NSAID use
- Headache medicine ulcers are additionally two times as liable to foster peptic ulcer as the general corporation[4-5]
- First degree relative with PUD
- Traveler from a created country

## IV. CLASSIFICATION

- Reduction of Gastric acid secretion:
  - H2 Anti Histaminics:
  - Cimetidine
  - Ranitidine
  - Famotidine
  - Roxatidine

- Protonpump Inhibitors:
  - Oxeprazole

- Lansoprazole
- Pantoprazole
- Rabeprazole

- Anti cholingergies:
  - Pirenprazole
  - Propantheline
  - Oxyphenonium

- Prostaglandin Analogue:
  - Misoprostol

- Neutralization of Gastric Acid(Antacids):
  - Systemic
  - Sodium bicorbanate
  - Sodium citrate

- Non systemic
  - Magnesium Hydroxide
  - Magnesium Tri silicate
  - Aluminium Hydroxide
  - Calcium Carbonate

- Ulcer protective
  - Sucralfate
  - Colloidal bismuth subsalicylate

- Ulcer healing drugs
  - NeoSporin
  - Polysporin
  - Bacitracin
  - Carbenoxolone Sodium

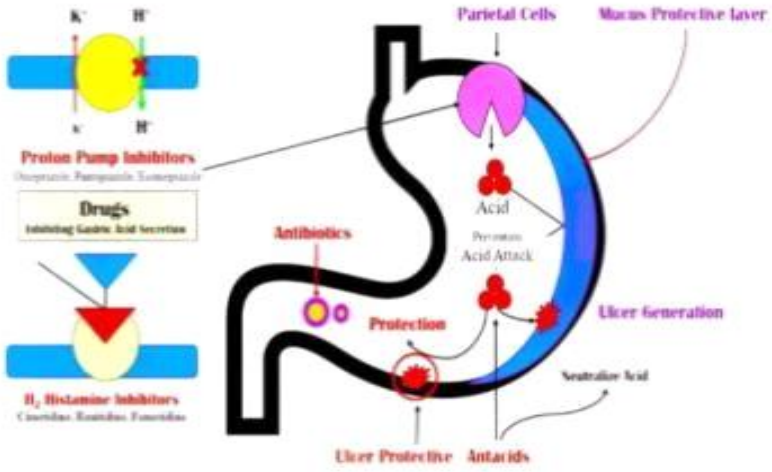


Fig. 3: Mechanism of various classes of ulcer medications

*A. TREATMENT*

- *Objectives:*
  - Quick alleviation of side effects.
  - Mending of ulcer.
  - Forestalling ulcer repeats.
  - Diminishing ulcer-related confusions.
  - Diminish the horribleness.
  - Diminish the mortality.
  - PPIs work synergistically with anti-toxins to destroy H. pylori[6]

*B. MANAGEMENT OF NSAID'S ULCERS:*

This should be possible as:

- The mending of a ulcer that has created during NSAID'S or COX-2 inhibitors treatment.
- Systems for forestalling NSAID'S ulcer in patients who are right now ulcer free.

Recuperating the laid out NSAID's related ulcer:

- On the off chance that conceivable NSAID'S ought to be halted as mending with a receptor 12-receptor bad guy will be quicker than if the NSAID whenever proceeded.
- PPI have been demonstrated in 3 randomized controlled trails to be more compelling than ranitidine or misoprostol for mending NSAID'S ulcers when the NSAID is proceeded.

- **Strategies for preventing NSAID'S ulcer:**
  - Use an Ointment as an Alternative to Oral NSAIDs
  - Adjust Your Dosage to Reduce Risk of Side Effects
  - Don't Mix NSAIDs
  - Take an NSAID That Has a Lower Risk of Ulcers
  - Proton Pump Inhibitors Reduce Ulcer Risk
  - Don't Ignore Medical Symptoms
  - Avoid Steroid Drugs or Blood Thinners With NSAID
  - Take NSAIDs on a Full Stomach

More established age and a more prominent number of comorbidities likewise influence the clinical course of patients with H. pylori and NSAIDs [7-8]

- **Management of stress induced ulcers:**
  - Stress ulcers are different shallow deteriorations which sopha for the most part in the resources and body of the stomach . they cultivate post-shake quake , sepsis and injury and are ofter found in patients with peritonitis and other continuous clinical sickness
  - The use of stomach settling specialist solution ex: pepto bismol ,or drug that lessens stomach destructive creation ex: omeprazole or pantoprazole is habitually proposed for treatment of stress-

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incited gastritis .this should be taken as facilitated by the trained professional.

- **Management of esophageal ulcers:**
  - An esophageal ulcer id a deterioration that designs in the covering of your throat the long chamber that relates the throat to the stomach
  - Treatment for by far most of the ulcers uses proton siphon inhibitors (PPIs), a destructive - hindering medication. If still up in the air to have an esophageal ulcer on endoscopy, you could require long stretch treatment with PPI remedy
  - If the ulcer is depleting , a provider can treat the depleting during an endoscopy

Another four-drug routine is used to get out the infinitesimal organic entities related with peptic ulcers and stomach irritation removed the bugs better contrasted with the standard three-drug treatment which is every now and again used .The new four-drug treatment is "tolerable and there is excellent compliance "says researcher p.Patric basu . Basu and his collegues compared a new four-drug regimen a seven-days-course and a 10 day course with standard 10 day, three-drug treatment .

The three-drug regimen , standard approach is called as LAC because it include :

1.lansopraozle(prevacid)- a proton pump inhibitor

2.Amoxicillin(amooxi)- an antibiotic

3. clarithromycin(biaxin) – another antibiotic The four-drug regimen , called LOAD incude:

- levofloxacin( levaquin)- an antibiotic
- omeprazole(Prilosec) an PPI
- nitazoxanide( alinia)-an another antibiotic

4.doxycycline(vibramycin)-another antibiotic

## V. AIM AND OBJECTIVES

### A. *AIM:*

The main aim of the present study is to evaluate the anti – ulcer activity of certain drugs by using some standard procedures**.**

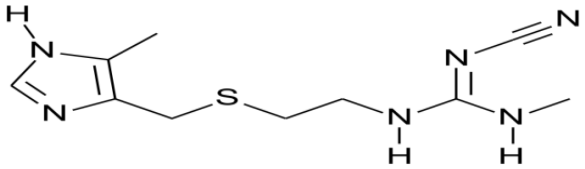
### B. *Objectives:*

- To select the suitable standard drug
- To select suitable animals for experimentation
- Evaluation of anti ulcer activity of drugs using pylorus ligated method
- Evaluation of anti ulcer activity of drugs using indomethacin induced duodenal ulcersmethod
- Evaluation of anti ulcer activity of drugs using ethanol induced duodenal ulcers method

## VI. DRUG PROFILE

### A. *CIMETIDINE*

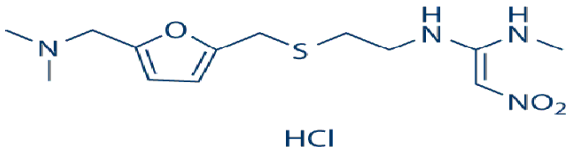
- **Structure:**



- **IUPAC nomenclature**: 1-cyano-2-methyl-3-[2-[(5-methyl-1H-imidazol-4-yl)methylsulfanyl]ethyl]guanidine
- **Classification** : H2-antihistamine ,Antiulcer drug
- **Molecular Formula**: C10H16N6S
- **Molecular Weight**: 252.34
- **Physiochemical Properties:**
  - Physical appearance-White crystalline solid Melting point-142ºC
  - Solubility-Soluble in alcohol
- **Mechanism of Action:** Cimetidine binds with H2 receptors present on the basolateral membrane of the gastric parietal cells. This results in blockage of histaminic effects. Due to this, there is reduction in gastric acid secretion and thus, reduction in acidity and gastric volume.
- **Pharmacokinetics:** Cimetidine is rapidly absorbed regardless of route of administration.The oral bioavailability of cimetidine is 60 to 70%. The onset of action of cimetidine when taken orally is 30 minutes,[and peak levels occur within 1 to 3 hours. Cimetidine is widely distributed throughout all tissues. It is able to cross the blood–brain barrier and can produce effects in the central nervous system (e.g., headaches, dizziness, somnolence). The volume of distribution of cimetidine is 0.8 L/kg in adults and 1.2 to 2.1 L/kg in children.Its plasma protein binding is 13 to 25% and is said to be without pharmacological significance.Cimetidine undergoes relatively little metabolism, with 56 to 85% excreted unchanged. It is metabolized in the liver into cimetidine sulfoxide, hydroxycimetidine, and guanyl urea cimetidine.The major metabolite of cimetidine is the sulfoxide, which accounts for about 30% of excreted material.Cimetidine is rapidly eliminated, with an elimination half-life of 123 minutes, or about 2 hours.It has been said to have a duration of action of 4 to 8 hours. The medication is mainly eliminated in urine[9-13]
- **Storage:** Store at room temperature away from light and moisture. Do not store in the bathroom. Keep all medications away from children and pets.

*B. RANITIDINE:*

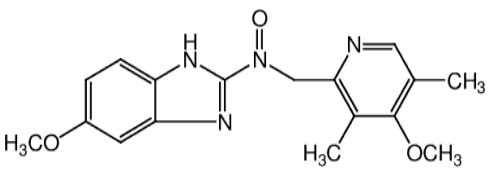
- **Structure:**



- **Classification:** Histamine H2 Antagonists
- **Molecular Formula:** C13H22N4O3S
- **Molecular Weight:**314.41
- **IUPAC Name**: I-1-N'-[2-[[5-[(dimethylamino)methyl]furan-2-yl]methylsulfanyl]ethyl]-1-N- methyl-2-nitroethene-1,1-diamine
- **Physico chemical properties**: Taste-Bitter taste Melting point- 69.5 °C Solubility- Water soluble Logp-0.27 (LogP)
- **Pharmacokinetics:** Ranitidine is rapidly absorbed from the GI tract following oral admin and from parenteral sites following IM injection; however, following oral admin, the drug undergoes extensive first-pass metabolism The absolute bioavailability of orally admin ranitidine has been reported to be about 50%; Ranitidine is widely distributed throughout the body and is 10-19% protein bound. The apparent volume of distribution of ranitidine is reported to be 1.2-1.9 l/kg.
- **Mechanism of Action:** Ranitidine is a competitive inhibitor of histamine H2-receptors. The reversible inhibition of H2-receptors in gastric parietal cells results in a reduction in both gastric acid volume and concentration. Ranitidine's acid-lowering effect is more pronounced for basal and nocturnal acid secretion than it is for food-stimulated acid secretion. Additional indirect effects of ranitidine are decreased pepsin secretion and increased nitrate-reducing bacterial flora.
- **Uses:** A non-imidazole blocker of those histamine receptors that mediate gastric secretion (H2 receptors). It is used to treat gastrointestinal ulcers.

*C. OMEPRAZOLE:*

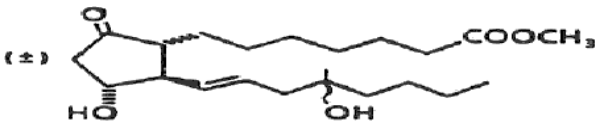
- **Structure:**



- **Molecular formula:** C17H19N3O3S
- **Molecular weight:** 345.4g/mol
- **IUPAC Name:** 6-methoxy-2-[(4-methoxy-3,5-dimethylpyridin-2-yl)methylsulfinyl]-1H-benzimidazole
- **Physico chemical properties:** Boiling Point-599.991 °C at 760 mmHg Melting Point -155 °C Solubility-35.4 [ug/mL]
- **Mechanism of action:** It suppresses stomach acid secretion by specific inhibition of the H+/K+-ATPase system found at the secretory surface of gastric parietal cells. Because this enzyme system is regarded as the acid (proton, or H+) pump within the gastric mucosa, omeprazole inhibits the final step of acid production.
- **Pharmacokinetics:** The absorption of omeprazole takes place in the small intestine and is usually completed within 3 to 6 hours. The systemic bioavailability of omeprazole after repeated doses is about 60%.Omeprazole has a volume of distribution of 0.4 L/kg. It has high plasma protein binding of 95%. OmeprazoleOmeprazole is completely metabolized by the cytochrome P450 system, mainly in the liver, by CYP2C19 and CYP3A4 isoenzymes.Identified metabolites are the sulfone, the 13sophage, and 13sophage-omeprazole, which exert no significant effect on acid secretion. About 77% of an orally given dose is excreted as metabolites in the urine, and the remainder is found in the feces, primarily originating from bile secretion.Omeprazole has a half life of 0.5 to 1 hour.
- **Medical uses:** Proton-pump inhibitor ,Omeprazole can be used in the treatment of gastroesophageal reflux disease (GERD), peptic ulcers, erosive esophagitis, Zollinger–Ellison syndrome, and eosinophilic esophagitis.

*D. MISOPROSTOL:*

- **Structure:**



- **Molecular formula:** C21H36O5
- **Molecular weight:** 368.5g/mol
- **IUPACName:** 7-[(1R,2R,3R)-3-hydroxy-2-[I-4-hydroxy-4-methyloct-1-enyl]-5-oxocyclopentyl]heptanoic acid
- **Physico chemical properties:**
  - Physical Description: Liquid Color/Form: Light yellow oil
  - Melting Point: 261-263
  - Solubility: 1.6mg/m –Water-soluble
- **Mechanism of Action**: Misoprostol is a synthetic prostaglandin E1 analog that inhibits basal and nocturnal gastric acid secretion through direct

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stimulation of prostaglandin E1 receptors on parietal cells in the stomach.

- **Pharmacokinetics**: Early studies concentrated on the pharmacokinetic properties after oral administration. After oral administration, misoprostol is rapidly and almost completely absorbed from the gastrointestinal tract. However, the drug undergoes extensive and rapid first-pass metabolism (de- esterification) to form misoprostol acid.
- **Uses:** Misoprostol is used to decrease the chance of having stomach ulcers in patients taking nonsteroidal anti-inflammatory drugs (NSAIDs) including aspirin. This medicine works by helping the stomach protect itself against acid damage, and decreases the amount of acid produced by the stomach.

## VII. METHODOLOGY

*A. PYLORUS LIGATED (SHAY) RATS:*

This is perhaps the oldest animal model of gastric ulcers developed by SHAY et al in 1945 . It is a very simple and maximally reproducible method for the production of gastric ulcers in rats which is caused by the accumulation of acid gastric juice in the stomach . Hence, it has been used for the preliminary screening of anti secretory activity of novel compounds .

- **METHODOLOGY:**
  Wister albino rats of either sex weighing 150-200g are housed in individual cages and fasted for 48hours prior to pylorus. 10 animals are used in each group. Under light ether anaesthesia the abdomen is opened by a small midline incision below the process pyloric portion of the stomach is slightly lifted out and ligated avoiding traction to the pylorus are damage to it's blood supply the stomach is replaced carefully and the abdominal wall is closed by interrupted sutures. The drugs are administered subcutaneously immediately after pylorus. The animals are deprived of both food and water during the post operative period are sacrificed at the end of 19 hr after pyloric. The abdomen is opened and a ligature id placed around the esophagus close to the diaphragm. The stomach is removed and the contents are drained in a centrifuge tube. The stomach is then opened along with a stereomicroscope for ulceration. In the rat, the upper two filths of stomach from the rumen with squamous epithelium and possess little protective mechanisms against the corrective action of gastric juice . below a limiting ridge, in the glandular portion of the stomach , the protective mechanisms are better developed in the mucosal region of the two medium filths of the stomach than in the lowest portion forming the antrum . therefore, the lesion occur mainly in the lumen and the antrum . The number of ulcers is noted and the severity is noted and the severity is recorded according to the scores given below.

  0= no visible ulcers
  1= 10 or less small ulcers, 1-3 mm in one diameter
  2=11 or more ulcers, 4-6mm in one diameter
  3= 1 or more ulcers, 4-6 mm in one diameter 4=1 or more ulcer, 7 mm or in one diameter 5= perforation of the gastric wall

The volume of gastric content is measured. After centrifugation free and total values determined for ANTphenolphthalein as indicators, respectively. Ulcer index, volume of gastric contents and the free and total acidity of the gastric content of treated animals are compared with the controls using various doses, dose response curves are established for ulcer formation and gastric acid secretion . the" SHAY RAT" has been used as a valuable tool for evaluating the anti0 gastric ulcer and anti-secretory activity of the novel compounds. Apart from these, estimation of dissolved mucosubastance is done by determining the total carbohydrates ( sum of total hexose , hexosamine, fructose and sialic acid )and the protein in 95% ethanol precipitate of gastric juice . The total carbohydrate **:** protein (C:P) ratio has been used as a reliable ibex of mucus secretion and mucosal resistance.

*B. INDOMETHACIN ACTUATED DUODENAL ULCERS IN RODENTS:-*

- **METHODOLOGY:**
  Wistar or Sprague dawley rats weighing 150-200 g are fasted for 24 hours with water ad libitum and randomly distributed in groups comprising of 6-8 rats. Indomethacin 5mg/kg s.c is first administered to these animals and subsequently histamine dihydrochloride (40mg/kg) is given three times at 2.5 hours intervals, beginning 30 min after the injection of indomethacin. The combined treatment induces one or two round lesions (9.8±1.44 $mm^2$) in the proximal duodenum at an incidence of 100%and few lesions in the corpus and antrum of the stomach. Indomethacin or histamine alone , in the doses mentioned above, have no effect on either the duodenum or the stomach .The lesions in the duodenum and antrum are inhibited by oral misoprostol and 16 16 – dimethylprostaglanin E2in a dose dependent manner, where as those in the corpus were inhibited only by misoprostol. The development of duodenal lesions induced by indomethacin plus histamine in rats is due to both an increase in gastric secretion and an impairment of acid induced duodenal HCO3- secretion. This model is expected to be useful for studying the pathogenesis of duodenal ulcers and for the screening of anti ulcer agents.

Prostaglandins increase secretion of bicarbonate and mucous ,increase mucosal blood flow and inhibit the cell proliferation to maintain the mucosal barrier .[14]

*C. ETHANOL INDUCED DUODENAL ULCERS IN RATS:*

- **METHODOLOGY**
  Male wistar rodents (170-250g) were kept up with in confines with raised floors and wide cross section, in a different creature room under standard circumstances like keep up with temperature (22±10c)and a12 h light/dim cycle. Furnish a standard eating regimen with water gave not obligatory all through the investigation. The creatures

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are taken in to 6 gatherings. All medicines were direct by intragastric gavage for eight sequential days, with the gastric ulcer instigated on the last day with 80%ethanol solution (1ml/animal).Group I(vehicle control )received the vehicle only (10ml/kg body weight (b w) of1% Tween -80 aqueous solution ).For all other groups, an ulcer was induced on the last day of treatment ,one hour after administering the corresponding compound. Group II (ulcer control)was given in the vehicle, group III 40 mg/kg bw omeprazole, group IV,V and VI the different concentrations of Ex Phy (100,200 and 400mg/kg bw, respectively).

One hour after inducing an ulcer, animals were scarified. The stomachs were excised, filled by injecting 2.5 ml of a 4% formaldehyde solution, and put in a beaker with formaldehyde. After 10 min, the stomachs were opened over the grater shape and washed with saline arrangement (0.9%) to eliminate the blood coagulations. From there on each gastric example was put on a slide. The gastric region still up in the air with "picture J" picture handling programming. The ulcer record (UI) for each rodent was determined with the accompanying recipe:

**UI= (TAML (mm2)×100) / (TMA (mm2))**

Where TMA is the total area and TMAL the absolute area of mucosal injury of each rodent The insurance rate (PP) was determined utilizing the accompanying equation:

**UI= (TMAL (mm2) × 100) / (TMA (mm2))**

**PP=control-UI treated)/ (UI control) ×100**

Where UI control is the ulcer index of the ulcer control (group II) and UI treated is the ulcer index of the treated group (group III-VI) (37).From the three concentrations tested for Ex Phy, the one with the least UI was adopted for all other tests.

## VIII. RESULTS

*A. PYLORUS LIGATION METHOD:*

| S.NO | DRUG | VOLUME OF GASTRIC JUICE | PH | FREE ACIDITY | TOTAL ACIDITY | ULCERINDEX |
|---|---|---|---|---|---|---|
| 1. | Ranitidine | 1.21±0.05426 | 2.9± 0.10 | 9.5± 0.42 | 38.33±1.430 | 2.0±0.3162 |
| 2. | Omeprazole | 0.82±0.37 | 6.19±0.13 | 9.0±0.5 | 16.65±0.304 | 2.80±0.25 |

Table 2: Effects of ranitidine omeprazole on ulcer parameters using pylorus ligated method

**(Figure no.4)Graphical representation of pylorus ligation method**

*B. INDOMETHACIN INDUCED DUODENAL ULCERS IN RATS:*

| S.NO | DRUG | PH | VOLUME OF GASTRIC JUICE | ULCER INDEX |
|---|---|---|---|---|
| 1. | Misoprostol | 4.51±0.12 | 2.17±0.19 | 1.06±0.11 |
| 2. | Control ( distilled water) | 2.25±0.09 | 3.28±0.33 | 3.60±0.10 |

Table 3: Effects of misoprostol and control on ulcer parameters using indomethacin induced ulcer method

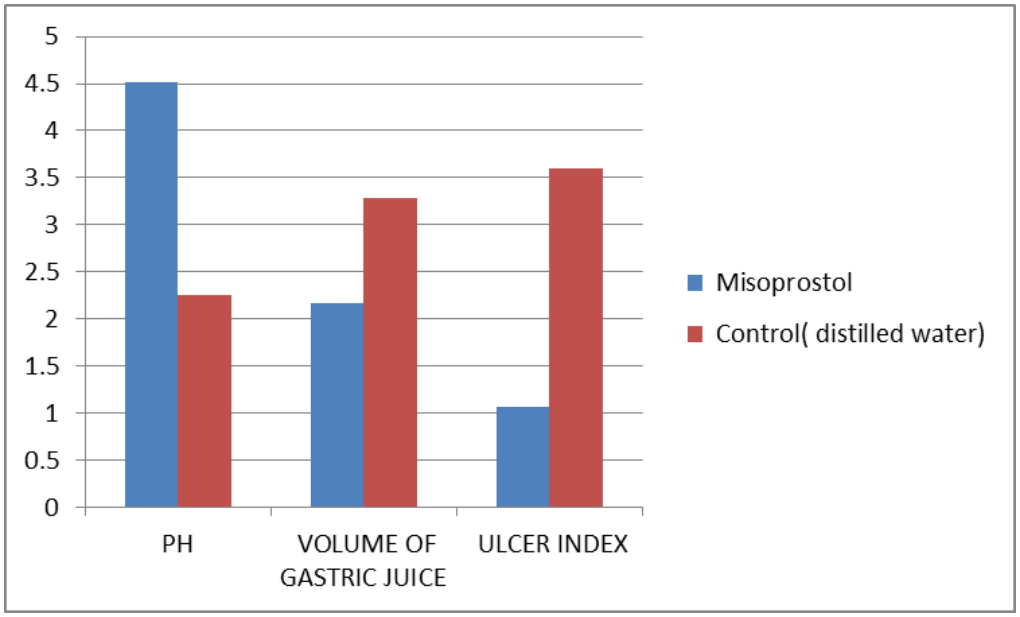


Fig. 4: Graphical representation of indomethacin induced method

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*C. ETHANOL INDUCED DUODENAL ULCERS IN RATS:*

| S.NO | DRUG | VOLUME OF GASTRIC JUICE | % PROTECTION | ULCER INDEX |
|---|---|---|---|---|
| 1. | Misoprostrol | 5.34±0.21(56.26) | 86% | 0.82±0.09 |
| 2. | Omeprozole | 4.65±0.12 | 90.36 | 1.32±0.96 |

Table 4: Effect of misoprostol and omeprazole on ulcer parameters using ethanol induced method

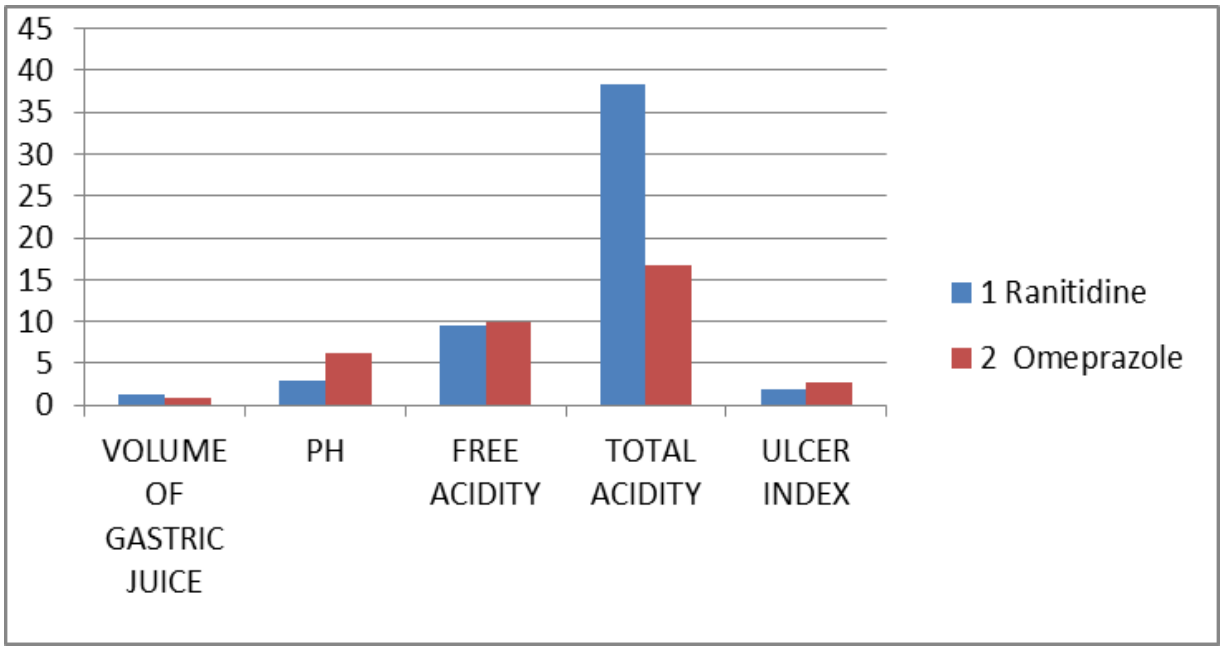


Fig. 5: Graphical representation of ethanol induced method

## IX. DISCUSSION OF RESULTS

*A. Evaluation of anti ulcer activity by pylorus ligated SHAY rat model:*

From the got results it was seen that there is a huge lessening in the quantity of sores in the lumen and the antrum of the stomach.

The ranitidine drug is administered by sub cutaneous immediately after pylorus ligation. The minimal number of lesions observed is compared with ranitidine, the omeprazole shows good results. The number of lesions are inhibited by omeprazole more than that of ranitidine. So the pylorus ligated method proved that enhanced pharmacological activity of omeprazole when compared to the ranitidine.

*B. Evaluation of anti ulcer activity by indomethacin induced duodenal ulcers in rats method:*

Indomethacin induced method is widely used for the assessment of anti ulcer activity in animal models . The administration of indomethacin leads to form lesions. The combined treatment of histamine dihydro chloride and indomethacin induces one or two round lesions in the proximal duodenum at an incidence of 100% and few lesions in the corpus and antrum of the stomach.

The lesions in the duodenum and antrum are inhibited by oral misoprostol and1616 dimethyl prostaglandin E in a dose dependent manner, the corpus region lesions are only inhibited by misoprostol.

The development of duodenal lesions induced by indomethacin plus histamine in rats is due to both an increase in gastric secretion and an impair of acid induced HCO-secretion.

*C. Evaluation of anti ulcer activity by ethanol induced duodenal ulcer method:*

This test is widely used for the assessment of ulcer index, % of protection of drugs.

There is a difference in volume of gastric juice content in stomach when administration of Omeprazole is more when compared to that of Misprostol. By this method ulcer formation is reduced by injecting standard drugs i.e., Omeprazol and Misprostol.

## X. SUMMARY AND CONCLUSIONS

The above studies and literature survey of screening procedures of anti-ulcer activity of respective drugs shows various anti-ulcer activities and used to decrease lesions, redness of stomach, subsides the gastric pain.

Omeprazole shows good anti ulcer activity than that of Ranitidine and cimetidine misoprostol.

The current work portrays the assessment of conceivable enemy of ulcer action of omeprazole in creature models.

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