

# **“Rationality and reality in the use of antiulcer drugs: A Comprehensive Review”**



**[In the partial fulfillment of the requirements for the degree of Bachelor of Pharmacy]**

## **Submitted To**

The Department of Pharmacy,  
Faculty of Allied Health Sciences,  
Daffodil International University

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**APPROVAL**

This project paper, Rationality and reality in the use of antiulcer drugs: A Comprehensive Review, submitted to the Department of Pharmacy, Faculty of Allied Health Sciences, Daffodil International University, has been accepted as satisfactory for the partial fulfillment of the requirements for the degree of Master of Pharmacy and approved as to its style and contents.

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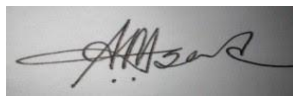
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## **Declaration**

I, Israt Jahan hereby declare that, this project is done by me under the guidance of Md.A.K. Azad, Assistant Professor, Department of Pharmacy, Daffodil International University, in partial fulfillment of the requirements for degree of bachelor of Pharmacy. The results embodied in this project have not been submitted to any other university or institute for the award of any degree or bachelor.

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# ***"Dedication"***

*To my father and my supervisor...*

## Abstract

A gastro-protective medication such as PPI,H2 Blockers,Antacids or others ulcer protective is found in one out of every four prescriptions written in out-patient departments.Only when there is a valid reason for prescribing these medications should they be used.In a tertiary care hospital setting,evaluate the appropriateness and rationality of gastro-protective agent prescriptions.The study is based on a systematic review of the rational use of antiulcer medications.We gathered data for this project using online platforms like google scholars, pubmed, scopus or others.After doing the research It has been observed that almost all NSAIDs drugs like Aspirin, Naproxen, Clopidogrel, Diclofenac etc are associated to ulcer-inducing effects and other than a very few number of drugs which are responsible for ulcer like Anticoagulants, Serotonin, Corticosteroids, Methotrexate etc.While others,such as Nitric-Oxide Donors (CINODs), Nebivolol etc are linked to ulcer healing effects and most common class of gastro-protective agents that are being used frequently is Proton Pump Inhibitors(PPIs).This present study also found that most of the drugs has no negative impact on GI tract.Patients may suffer the repercussion of irrational usage of gastro-protectants because clinicians prescribe them without examining the need for them.To reduce the overuse of gastro-protectants,a rational drug prescribing policy must be implemented in all settings.So,we should be more careful to prevent the irrational use of anti-ulcerant drugs.

**Key words:**Ulcer, antiulcer, rationality

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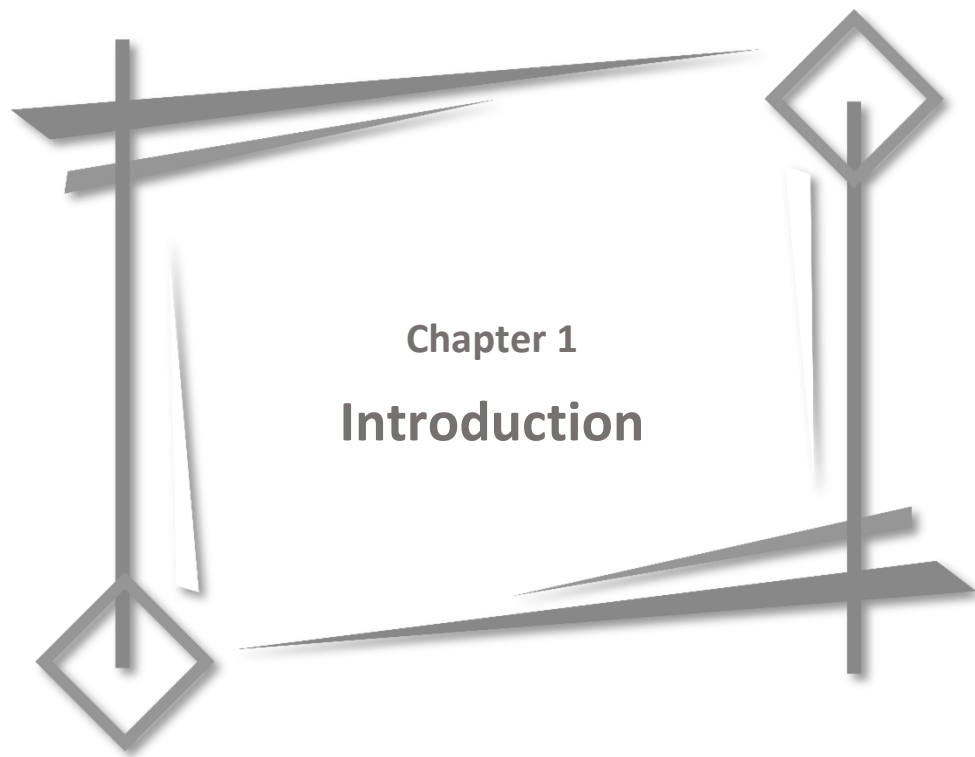


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## 1. Introduction

### 1.1. General Concept of Ulcer

Ulcer an open sore on an outer or interior surface of the body, brought about by a break in the skin or mucous film which neglects to mend. Ulcers range from little, difficult injuries in the mouth to bedsores and genuine sores of the stomach or digestive system. A gastro-protective medication (APUD)- PPIs, H2 Blockers, Antacids, and Ulcer Prevent security - is found in one out of every four arrangements written in out-patients division. Exactly when there is a real support underwriting these drugs should they be used. In a tertiary thought crisis facility setting, survey the appropriateness and thinking of gastroprotective expert prescriptions. Sloughing of searing dead tissue depicts ulcers, which are open wounds of the skin or natural liquid membrane[1]. Ulcers are wounds on the skin's or mucous layer's surface that cause a shallow loss of tissue. Ulcers are most routinely found on the skin of the lower extremities and in the gastrointestinal plot, anyway they can appear anywhere[2]. Ulcers have been portrayed as far back as 3000 BC, and possibly altogether earlier. Hippocrates (460-360 BC), known as the "Father of Medicine," described a ulcer while portraying danger, insinuating non-ulcer outlining and ulcer forming tumors as carcinosand carcinoma, independently.[3] In pre-sixteenth century Hippocrates himself depicted gastric ulcer and appearances related to it. In Corpus Hippocraticum, a variety of Hippocrates' work collected by his understudies, he even kept an eye on the treatment of ulcers[4]. Avicenna (980-1037), a recognizable Arabic specialist, examined the connection between gastrointestinal torture and mealtimes[5]. Marcello Donati (1538-1602), an Italian specialist, recognized the primary occasion of stomach ulcer in 1586. During that time, obviously gastrointestinal distress and ulcer had a tight alliance and were a significant part of the time subject to the person's lifestyle and dietary examples. Matthew Baillie, an English specialist, is credited with the fundamental clear portrayal of the appearances and unpleasant life frameworks of stomach ulcers in the year 1793, followed by his first dissemination on ulcer in the year 1799. G Bottcher and M Letulle proposed in 1875 that ulcers were achieved by microorganisms.

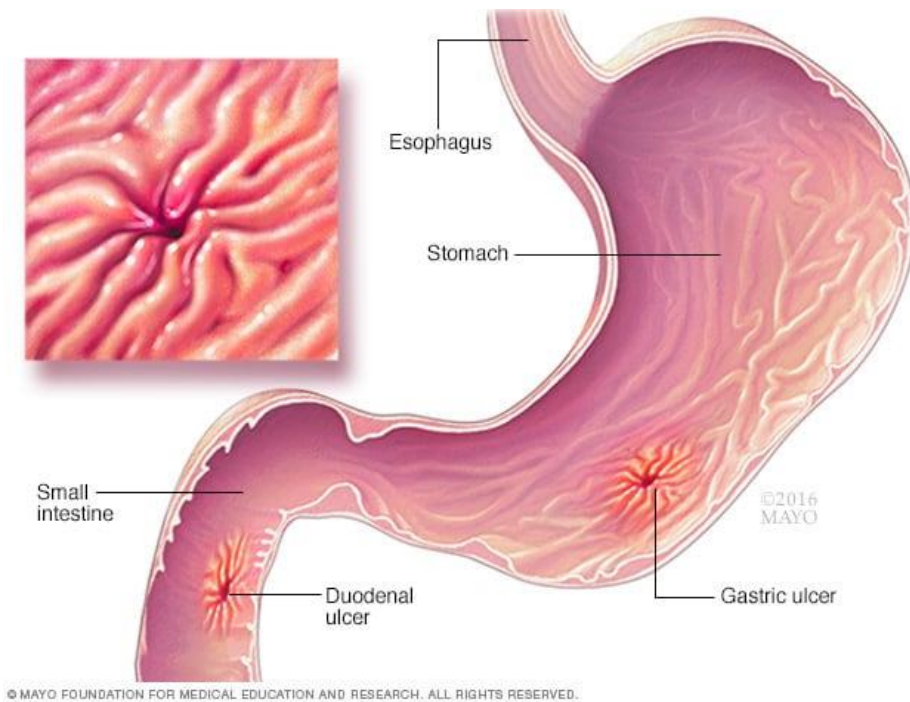


Figure 1:Ulcer

## 1.2.Types of ulcer

Mouth ulcers, esophageal ulcers, peptic ulcers, and genital ulcers are among the various combinations of ulcers. Various people experience the evil impacts of peptic ulcers as a result of them[2].

### 1.2.1.Peptic ulcer

Peptic ulcers are achieved by crumbling of the stomach or duodenal covering [2]. "Gastric ulcer" and "duodenal ulcer" are the two most normal kinds of peptic ulcer. The term hints the ulceration spot. Both stomach and duodenal ulcers can happen all the while. Gastric ulcers are troublesome ulcers that occur in the stomach. They are more ordinary in those past 50 years of age. Eating may upset rather than ease up torture. Disorder, hurling, and weight decrease are possible outcomes. Notwithstanding the way that patients with stomach ulcers have conventional or lessened destructive creation, ulcers can fill regardless, when there is no destructive present[6]. Duodenal ulcers are accessible close to the start of the little stomach related plot and cause genuine anxiety and a burning-through sensation in the upper midriff, arousing patients. Torture is most typical when the stomach is unfilled and subsides resulting to eating. Duodenal ulcers are

more ordinary in more young people and primarily impact men. Ulcers can occur on both the front and back dividers of the duodenum [7]. Peptic ulcers can be unsafe in specific conditions, with signs like draining stool, genuine stomach burden, and pressing, similarly as spewing blood [8]. A clumsiness between threatening (destructive, pepsin, and *Helicobacter pylori*) and defensive (mucin, prostaglandin, bicarbonate, nitric oxide, and advancement synthetic substances) sections causes peptic ulcer disease.[9]. Hot food and stress were prior plan to be the explanations behind peptic ulcers; in any case, research has tracked down that the certified causes are bacterial infection (*Helicobacter pylori*) or a reaction to explicit prescriptions, generally NSAIDS (nonsteroidal quieting drugs)[10]. The rule etiological elements related with peptic ulcer are *Helicobacter pylori*, NSAIDS meds, energetic pressing factor, alcohol usage, and smoking[11]. *Helicobacter pylori*, a Gram-negative bacterium, lives between the mucous layer and the gastric epithelium and is expressly intended to prosper in the stomach's adversarial environment. *Helicobacter pylori* is found in the antrum from the start, anyway it moves to the stomach's more proximal regions with time [12]. Peptic ulcer ailment is conceivably the most notable gastrointestinal illnesses, affecting 10% of the overall population.[13]. Duodenal ulcers address 19 of every 20 peptic ulcers.

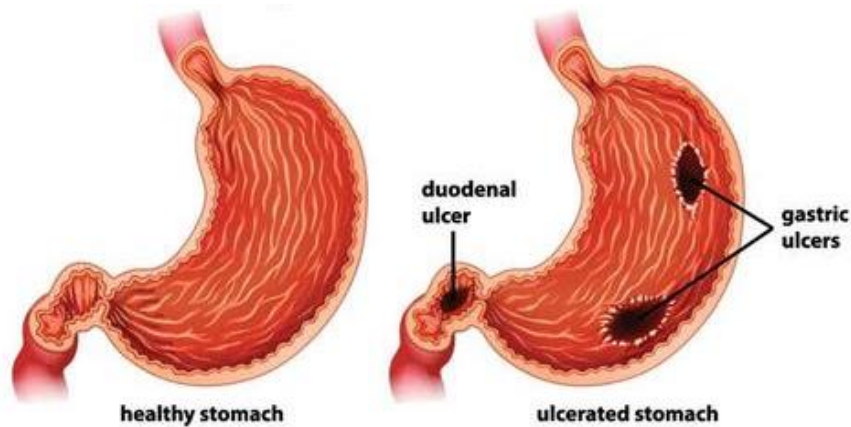


Figure 2:Peptic Ulcer

Consistently, a normal 15000 people pass on in light of a peptic ulcer. Peptic ulcer depleting and opening had yearly recurrence appraisals of 19.4–57 and 3.8–14 for each 100,000 people, independently. The ordinary 7-day depleting rehash rate was 13.9 percent, and the typical long stretch opening recurrent rate was 12.2 percent[14]. Stomach settling specialists and antiulcer

remedies address 6.2 billion rupees in the Indian medication business, or 4.3 percent of the market [9].

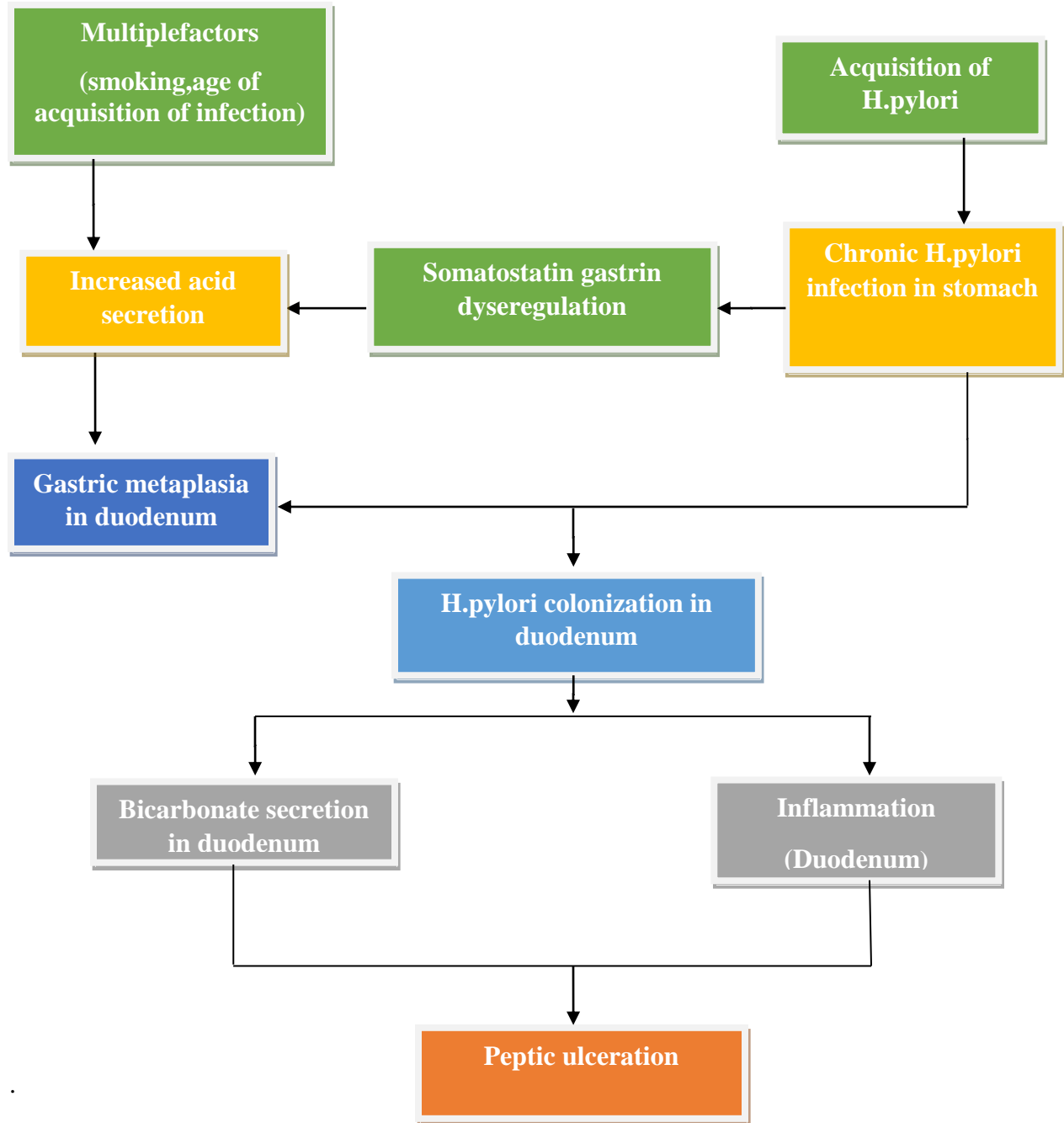


Figure 3: Pathophysiology of peptic ulcer

### 1.2.2. Arterial ulcer

Arterial (ischemic) ulcers are open bruises outwardly of lower leg, feet, toes, and impact points. Arterial ulcers are brought about by course harm brought about by an absence of blood supply to the tissue. These ulcers can require a very long time to mend and should be dealt with appropriately to keep away from contamination and different results. Arterial ulcers have a "finished off" appearance and an assortment of side effects, which include-

- Bruises that are red, yellow, or dark
- A absence of hair on the body
- Leg torment
- There is no dying
- Because of the absence of blood course, the influenced region is crisp to the touch.

The basic etiology of blood vessel ulcers decides the treatment. The initial phase in treatment is to get the harmed region's blood streaming once more. While anti-toxins may assist with lightening side effects, your primary care physician may propose a medical procedure to improve blood stream to your tissues and organs. Your PCP may propose removal in more genuine cases [15].

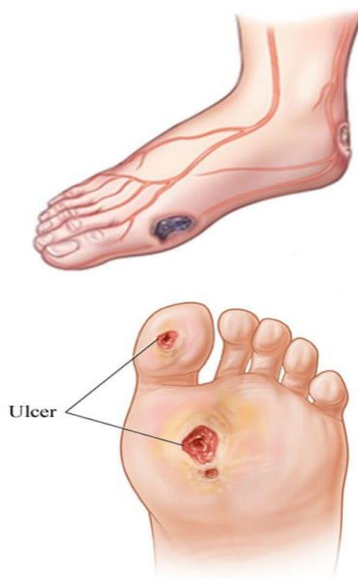


Figure 4: Arterial ulcers

### 1.2.3. Genital ulcer

The vulva, penis, perianal region, or rear-end would all be able to be influenced by genital ulcers. The worldwide pervasiveness of genital ulcers is assessed to be more than 20 million cases each year[16]. The most well-known reason for a genital ulcer differs relying upon a populace's qualities and locale. Herpes simplex diseases are the most common reason for vaginal ulcers in the United States, with syphilis coming in second and chancroid coming in third[17]. HSV-1, HSV-2, and treponemapallidum, which are generally predominant reasons for genital ulcer sickness, would all be able to be spread adequately through oral sex[18]. Irresistible specialists, the most common of which are physically communicated sicknesses, however which can likewise incorporate parasitic diseases and optional bacterial contaminations, are the most pervasive reasons for genital ulcers. While irresistible specialists are the most predominant reason, non-irresistible reasons like Behcet's ailment, lupus, or psoriasis can likewise deliver a genital ulcer.[19].

### 1.2.4. Mouth ulcer

Most of mouth ulcers are agonizing and can antagonistically influence eating and drinking. Thusly, patients with mouth ulcers frequently present in local area drug stores. Aphthous stomatitis (oral ulceration), which addresses a full-thickness penetrate in the epithelium covering the delicate tissues of the mouth, influences a high extent of the populace and can be the aftereffect of a wide scope of conditions[20],[21]. A few group may have ulcers for quite a while. Excruciating round or oval ulcers repeat at various regions in the mouth in repetitive aphthous stomatitis (RAS). It's been isolated into three classifications:

#### ❖ Minor RAS

- Occurs in groups of at least five minuscule ulcers.
- Ulcers on non-keratinized spaces of the mouth, like the buccal mucosa, labial mucosa, or the mouth floor, are each under 1cm in distance across.
- Ulcers recuperate in 10–14 days overall.

#### ❖ Major RAS

- Occurs as one to three ulcers at any one time;



- Ulcers are more prominent than 1cm in breadth;
- Involve any oral locales;
- May require half a month to recuperate.

#### ❖ **Herpetiform RAS**

Causes ten to fifty little ulcers in non-keratinized regions, which recuperate in 10–14 days[22]. The kind of RAS present will be controlled by the quantity of ulcers present out of nowhere, the spaces of the mouth influenced, and the period of time it takes for the ulcers to recuperate.

A mouth ulcer's indications differ contingent upon the reason, yet they may include-

- One or more agonizing ulcers on the skin lining the mouth.
- Swollen skin around the wounds
- Difficulty biting or brushing teeth because of agony
- Salty, hot, or sharp food sources aggravate the injuries
- Loss of appetite[23].

Ulcers in the mouth can be brought about by an assortment of conditions, including:

- A toothbrush-related injury, (for example, slipping while at the same time brushing).
- Constant scouring of teeth that are abnormal or have sharp/broken edges.
- Constant scouring against supports or false teeth
- Burns because of burning-through hot food sources.
- Strong germicides, like mouthwash, can disturb the mouth.
- Infections brought about by infections, for example, the herpes simplex infection (mouth blister).
- Hypersensitivity to specific medications.
- Rashes on the skin.
- Infection with the herpes simplex infection (mouth blister)
- Autoimmune ailments are a kind of immune system infection.

- A nutrient or iron deficiency is available.
- A gastrointestinal condition, like Crohn's infection or celiac illness, might be available.
- Cancer of the mouth.
- Ulcers can deteriorate on occasion of pressure, ailment, or outrageous fatigue.
- Autoimmune diseases iron lack Crohn's disease celiac sickness Mouth cancer stress[24].



Figure 5: Mouth ulcer

### 1.2.5. Venous ulcer

Venous ulcers are wounds that are believed to be brought about by flawed venous valves, most normally in the legs (in this manner leg ulcers)[25]. They are the most well-known sort of persistent injury, representing 70% to 90% of leg ulcer cases[26]. Venous ulcers are awkward and seriously affect one's personal satisfaction. They ordinarily structure along the average distal leg[27].

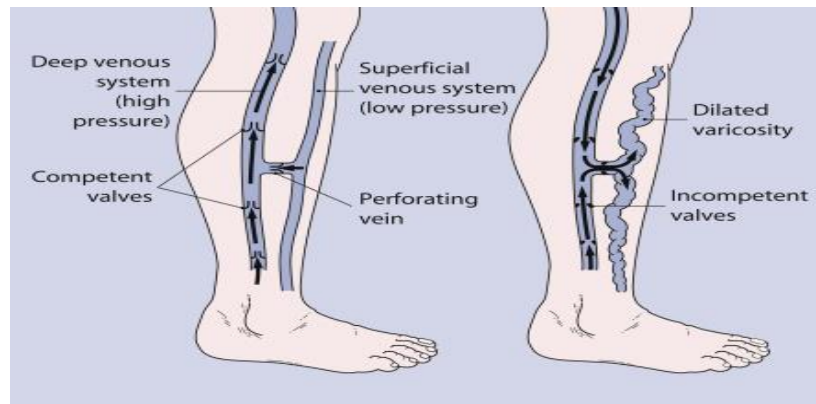


Figure 6: Venous ulcer

Coming up next are a portion of the signs and side effects of venous ulcers-

- Moderate distress that improves with height (instead of blood vessel ulcers that weaken with rise).
- Slanted, sporadic edges.
- Increased hydrostatic pressing factor causes oedema, which adds to 'atrophieblanche.
- 'Atrophieblanche,' which is described by a deficiency of skin pigmentation and scarring brought about by the demise of erythrocytes.
- Lipodermatosclerosis, a skin hardening that can give the leg a "modified champagne bottle" appearance.
- Associated shallow varicose veins, regularly known as "lower leg flare," which are a gathering of little, dim, engorged shallow veins.[28].

### 1.3. Mechanism of Drug Induce Ulcer

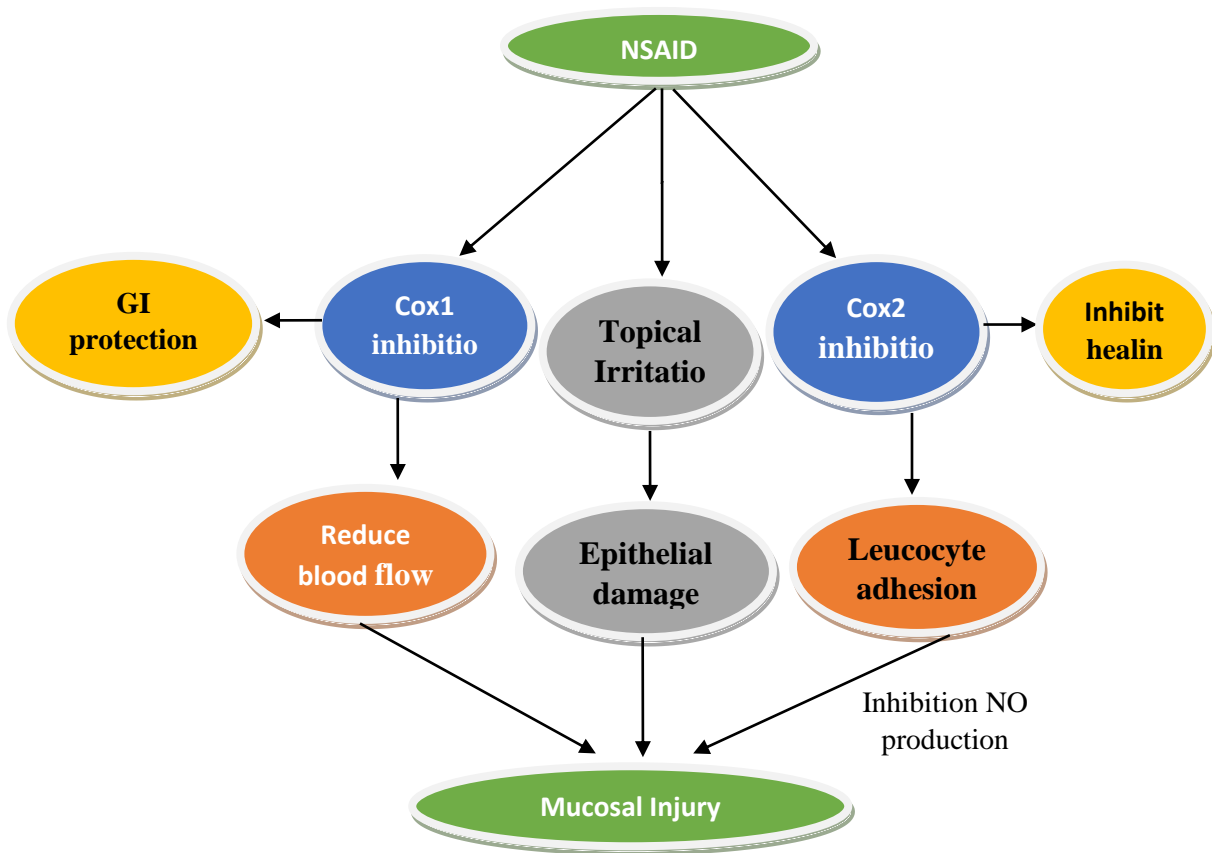


Figure 7: Mechanism of Drug Induce Ulcer<sup>[29]</sup>.

## **1.4. Conversion therapy**

Conversion therapy is the pseudoscientific demonstration of endeavoring to adjust an individual's sexual course from gay or physically open to hetero using mental, physical, or supernatural interventions. There is no strong evidence that sexual heading can be changed, and clinical establishments alert that change therapy practices are inadequate and possibly harmful[30-36]. Medical, consistent, and government relationship in the United States and the United Kingdom have imparted stress over the authenticity, reasonability and ethics of change therapy[37-38]. Various areas all through the planet have passed laws against Conversion therapy.

### **1.4.1. Conventional treatments of peptic ulcers**

Conventional treatments of peptic ulcers, for example, proton pump inhibitors (PPIs) and histamine-2 (H<sub>2</sub>) receptor opponents, have shown antagonistic impacts, backslides, and different medication associations[39].

### **1.4.2. Conventional therapy of Genital ulcer**

Extensive genital ulcers might be treated with cool water or saline, effective antimicrobials, effective or oral analgesics, perineal showers, effective or oral calming specialists, or cool packs with Burow answer for decline encompassing edema, aggravation, and torment.[40,41].

### **1.4.3. Conventional therapy of Mouth ulcer**

- Utilizing a wash of saltwater and preparing pop.
- Setting milk of magnesia on the mouth ulcer.
- Covering mouth ulcers with heating soft drink glue.
- Utilizing over-the-counter benzocaine (effective sedative) items like Orajel or Anbesol.
- Applying ice to ulcer[42].

### **1.4.4. Conventional therapy of Venous ulcer**

Pressure treatment is considered the "old standard" of care for delayed treatment of venous ulcers. Pressure treatment objectives incorporate edema the board, venous reflux improvement, and upgraded recuperating.

## 1.5. Anti-Ulcer Agents

### 1.5.1. General Concept of Anti-Ulcer:

Antiulcer medicines and treatments for acid peptic disease are widely prescribed treatments that seldom cause liver damage. The majority of agents work by reducing stomach acid production, neutralizing acid, or protecting the gastrointestinal mucosa from acid damage. . These medications are used to treat and prevent duodenal and gastric ulcers, as well as acid reflux, esophagitis, and other minor upper intestine discomforts[43]. Although there are several factors that contribute to the development of gastric ulcers, one of the most important is stomach acid secretion, which has been the focus of therapy for many years. H<sub>2</sub>-receptor blockers (such as ranitidine) and proton pump inhibitors (such as omeprazole) have been used to achieve this. Overall, PPIs are known to reduce stomach acid output more effectively than H<sub>2</sub>-receptor blockers[44]. These medicines currently have a significant drawback in that they induce several side effects[45]. Different specialists with various activity components used to treat or improve peptic ulcer or disturbance of the gastrointestinal plot. This has included antibiotics to treat helicobacter infections; histamine H<sub>2</sub> antagonists to lessen gastric acid emission; and antacids for indicative alleviation.

### 1.5.2. Classification of antiulcer drug[46]:

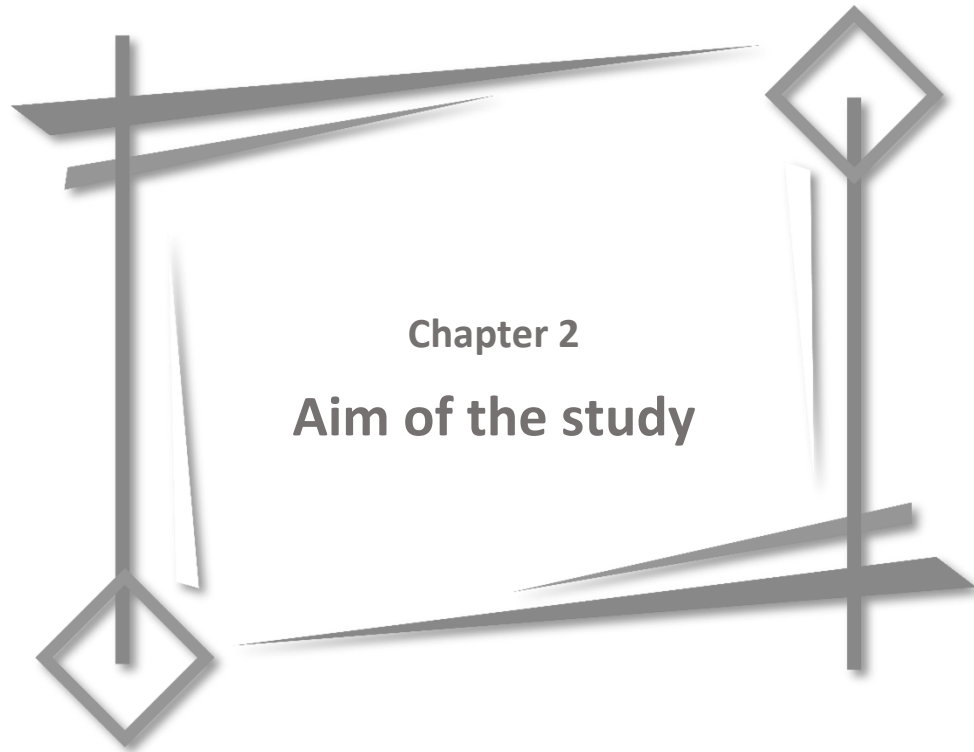
S.I	Classification	Drugs name
<b>1</b>	<b>Gastric acid secretion reducing agents</b>	
1.1	H <sub>2</sub> - receptor blocker	Cimetidine, Famotidine.
1.2	Proton pump inhibitors	Omeprazole, Lansoprazole, and Pantoprazole.
1.3	Anticholinergics	Pirenzepine, Propantheline.
1.4	Prostaglandin analogues	Misoprostol.
<b>2</b>	<b>Acid neutralizing agents</b>	
2.1	Systemic	Sodium bicarbonate, Sodium citrate
2.2	Non-systemic	Magnesium hydroxide, Aluminium hydroxide gel and Magnesium trisilicate.
<b>3</b>	<b>Ulcer protective</b>	Sucralfate, Colloidal Bismuth subcitrate (CBS)

4	<b>Anti-Helicobacter pylori Drugs</b>	Amoxicillin, Clarithromycin, Metronidazole, Tinidazole and Tetracycline.
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Table 1: Classification of antiulcer drug

❖ **Drugs**

- **Pantoprazole:** A proton pump inhibitor used to treat erosive esophagitis, gastric corrosive hypersecretion, and to advance mending of tissue harm brought about by gastric corrosive.
- **Lansoprazole:** A proton pump inhibitor used to assist gastrointestinal ulcers with recuperating, to treat manifestations of gastroesophageal reflux infection (GERD), to kill *Helicobacter pylori*, and to treat hypersecretory conditions like Zollinger-Ellison Syndrome.
- **Cimetidine:** A histamine H<sub>2</sub> receptor adversary used to oversee GERD, peptic ulcer illness, and acid reflux.
- **Nizatidine:** An H<sub>2</sub> receptor foe used to treat GERD and an assortment of ulcers.
- **Cisapride:** A drug used to treat indigestion related with GERD.
- **Pirenzepine:** An antimuscarinic specialist used to treat peptic ulcers, gastric ulcers, and duodenal ulcers.
- **Esomeprazole:** A proton siphon inhibitor used to treat GERD, decrease the danger of NSAID related gastric ulcers, kill *H. pylori*, and to treat conditions causing gastric corrosive hypersecretion.
- **Proprantheline:** An antimuscarinic specialist used to treat urinary incontinence, hyperhidrosis, just as issues and fits of the stomach, digestive organs, and bladder.

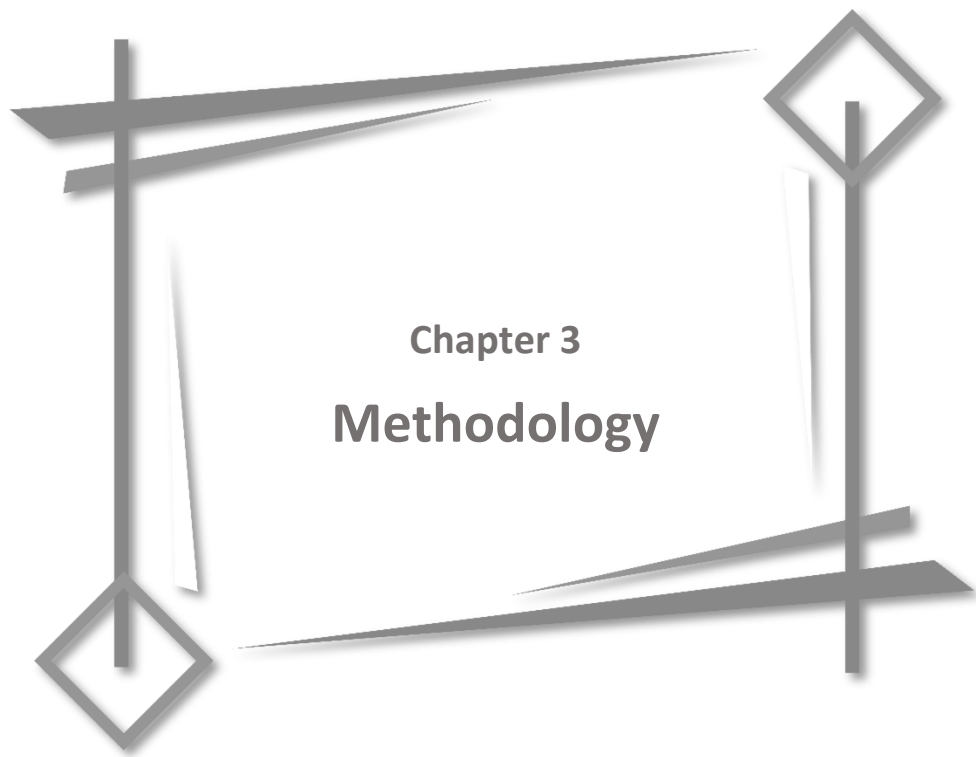


## **2. Aim of the study**

Now a day ulcer is an alarming condition, many people suffering from ulcer. So the appropriate management is must be necessary for ulcer because the misuse or abuse of anti-ulcer drugs Create many other major diseases. So the my main objectives of the study is

- To see which type of drug use in Anti-Ulcer therapy.
- To find out which type of Anti-Ulcer drug use for combination Drug therapy.
- To see how rationally use antiulcer drug.
- To open a new area of research and higher study.
- To increase public awareness about anti-ulcer therapy.





### **3. Methodology**

The study is conducted with a systematic review on rational use of antiulcer drugs. For this work, I utilized google researcher to discover article survey around 71 article for this study. I collet this article from different web site such as Google scholar, Research gate and another source. To finding this paper I applied a criteria to get update papers, about 20 articles were published from 1990-2001 and another 51 articles were published from 2001 to 2020. After gaining knowledge from this article I want to describe the problem and how we can rationally use antiulcer drugs.



**Chapter 4**  
**Results and Discussion**

## 4. Result

### 1.1.Ulcer inducing drug

Serial no	Drugs Name(Generic)	Used for those Diseases	Reference
01	Aspirin	Anti-inflamantory, Cardiovascular diseases	[47,48,49]
02	Nicotine	CNS Stimulate drug	[50]
03	Potassium Supplement	Hypokalemia	[51]
04	Corticosteroid	Crohn's disease, Addison's diseases	[52]
05	Anticoagulants	Prevent strokes and heart attacks	[53]
06	Crack	Illicit Drug	[54]
07	Serotonin	Antidepressant Drug	[55]

Table 2: Ulcer inducing drug.

### 1.2.UlcerInducing by combination Drug therapy

Serial No	Drugs Name	Therapeutic Class	Reference
01	Aspirin + Clopidogrel	Blood thinner and Antiplatelet drug	[56]
02	Etidronate + Risedronate	Treatment of osteoporosis	[57,58]
03	Alendronate + Naproxen	NSAID and Bisphosphonate group drug	[59,60]
04	Methotrexate+Chemotherapy	Cancer drug and Anti-cancer chemo	[61,62]

Table 3: Ulcer inducing by combination Drug therapy

**1.3.Non-Antiulcerantdrugs having ulcer healing effect:**

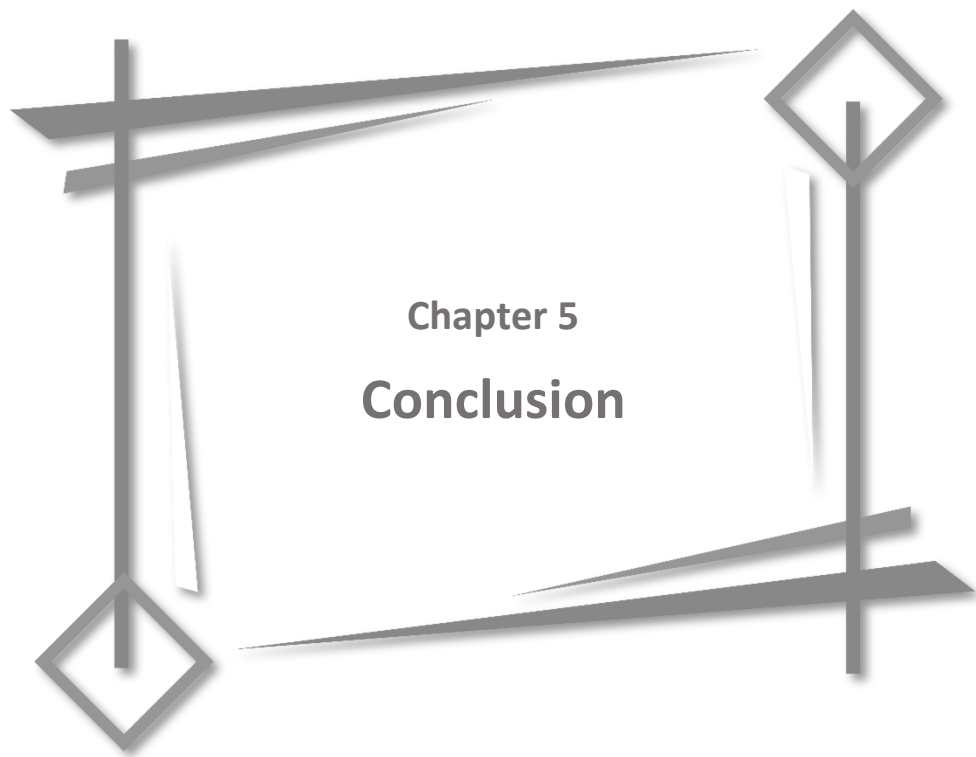
Serial No	Drugs Name(Generic)	Diseases	Reference
01	Nebivolol	Hypertension	[63]
02	Metformine	Diabetes	[64]
03	COX-inhibiting nitric oxide donators	Analgesic	[65,66]
04	NO-releasing Aspirin	NSAID	[67]

Table 4:Non-Antiulcerant drugs having ulcer healing effect

**Discussion:**

Anti-ulcerant like Proton pump inhibitors (PPIs) have been shown to effectively decrease stomach acid in a variety of upper gastrointestinal illnesses[68]. Many medicines, whether anti-ulcerant or not, can modulate stomach acid secretion in the body. After reviewing several journals, it was discovered that some medicines are linked to ulcer-inducing effects, while others are linked to ulcer-healing effects. The drugs named neproxane, aspirin, clopidogrel etc. induces ulcer after intake. Corticosteroids also induces ulcer while intaking more than 15 days or 1 month as well as serotonin causes ulceration at low dose[69]. In some special cases, to get better outcome combination drug therapy is required. But these combination therapies sometimes are responsible for ulceration. The combination of aspirin and clopidogrel, for example, causes serious ulcers in individuals with heart problems and stroke[70]. On the other hand, nitric-oxide donors (CINODs), although being conventional NSAIDs, have been shown to hasten ulcer healing[71]. Furthermore, while not being anti-ulcerants, nebivolol and metformin have a healing effect on ulcers. As a result, the majority of medicines are not linked to ulcer induction. Anti-ulcerants, but from the other side, are commonly prescribed without a clear indication and for longer periods of time than are recommended[72]. Because PPIs are commonly prescribed in general practice, practitioners may believe that they are safe to prescribe for lengthy periods of time when they are not[73]. Many practitioners continue to over-prescribe these medications at alarmingly high rates, disregarding the drugs approved indications[74,75]. This revealed the people's irrationality in their use of anti-ulcerants. The hazards of long-term PPI usage must be evaluated against the advantages of these medications in the general population, as with any treatments. Furthermore, in the primary care context, it is critical that doctors and general practitioners enhance their documentation practices[76]. A clear indication is required. Hence, by

continuously refining medication adherence and enhancing professional awareness of existing anti-ulcerant treatment recommendations, these irrationalities can be eliminated.



## **5. Conclusion**

From this current review, it can be concluded that there are 7 drugs which are responsible for ulcer inducing, further there are also 4 combination drug therapy which provide better outcome but induce ulcer as side effect. Moreover there are some drugs which have ulcer healing effect though they are not antiulcerant drugs. According to our country where maximum number of antiulcerant drugs are prescribed, need to consider that they are going through misuse or over use as maximum number of drugs don't induce ulcer. If this so we should decrease using antiulcerant drugs and go through further study. Finally, the use of anti-ulcer drug should be rational in our country in order to reduce the percentage of use of anti-ulcer drugs.





**Chapter 6**  
**References**

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