

# A comprehensive analysis of Peptic ulcer and *Nerium Oleander* as an anti-inflammatory agent and Medicinal plants have been traditionally used for their anti-ulcer properties.

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**Abstract:** Peptic ulcers are a type of ulcer that occurs in the stomach or upper intestines, characterized by tissue loss and epigastric pain. Important elements in the pathophysiology of PUD include defensive elements like mucus, prostaglandins, bicarbonate, and nitric oxide, as well as inflammatory elements like pastic acid and pepsin. Traditional risk factors for PUD include spicy foods, *Helicobacter pylori*, NSAIDs, stress, alcohol, and smoking. However, research has also identified endogenous chemicals that play a role in the development of intestinal diseases.

*Oleander* has various medicinal properties and has been used in folk medicine to treat various diseases. The study aims to investigate the effect of methanolic leaf extract of *oleander* on pyloric ligation and indomethacin-induced ulcer in rats.

*Helicobacter pylori* is a gram-negative, motile, flagellated bacillus that causes inflammation of the mucosa, neutralization of the acidic environment, injection of bacterial proteins and cytotoxins, stimulation of inflammatory response, and production of reactive oxygen species (ROS) and reactive nitrogen species (RNS). NSAIDs are widely used to treat various conditions, but long-term use can cause stomach pain and increase the risk of peptic ulcers. A number of processes contribute to the pathophysiology of NSAID-induced peptic ulcers, including increased lipid peroxidation, suppression of prostaglandin synthesis, disruption of gastric acid secretion and mucosal blood flow, suppression of mast cell and leukocyte activation, suppression of platelet aggregation and thromboxane production, and inhibition of mast cell and leukocyte activation. Ethanol-induced gastric ulcers have several mechanisms of action, including reduced mucus production, reduced blood flow to the mucosa, and increased inflammation.

**Keywords:** Peptic ulcer, *H.pylori*, Methanolic extract of leaves, NSAID, Ethanol induced gastric ulcer, Pyloric ligation induced gastric ulcer, Indomethacin induced gastric ulcer

## INTRODUCTION

Ulcers are wounds characterized by tissue loss on the skin or mucosal surface. Although ulcers can be found almost anywhere, the diseases usually occur on the skin of the lower extremities and in the digestive system. There are many types of ulcers, such as mouth ulcers, esophageal ulcers, peptic ulcers, genital ulcers, etc. One of the more dangerous types of ulcers is peptic ulcer.....(1)

A rupture in the lining of the stomach or upper intestines (similar to a gastric ulcer). It is a usually nonfatal disease caused by symptoms of epigastric pain that are usually relieved by food or alkali and often occur cyclically. In an epidemic, the annual incidence of physician-diagnosed PUD ranges from 0.10% to 0.19%, while the annual incidence of hospital-diagnosed PUD ranges from 0.03% to 0.17%.....(2)

The struggle between protective (mucins, prostaglandins, bicarbonate, nitric oxide, and adult) and inflammatory (pastic acid, pepsin, and *Helicobacter pylori*) components is linked to the etiology of peptic ulcer disease. ....(3)

Peptic ulcer

Peptic ulcers were previously believed to be mostly caused by *Helicobacter pylori*, spicy foods, NSAIDs (non-steroidal anti-inflammatory medicines), stress, alcohol, and smoking. Numerous endogenous substances have also been identified and demonstrated to contribute to the development of intestinal disorders in animals. Some bacteria, different medications and chemicals, stomach secretions, lipid metabolites, neuropeptides, inflammatory mediators, and reactive

free radicals are the most significant of these. One of the primary causes of inflammation is oxidative stress, which also directly malfunctions the body and encourages the destruction of organs such as the nucleus, mitochondria, and lysosomes.

....(4)

Oleander has many medicinal properties such as bitter, pungent, astringent, anthelmintic, aphrodisiac, stomachic, antipyretic, diuretic, vomiting inducer, expectorant, cardiogenic and anticancer. Kidney disease, cysts etc

It Treat many diseases. However, there is no scientific evidence to show the immunity of this plant. Therefore, the use of oleander is investigated in this study

*Oleander Mill.* (Family: Apocynaceae) It is a green plant with a long history of medicinal use in many countries of the world, especially in tropical and subtropical countries. The plants are used in the treatment of many diseases. Heart tonics, diaphoretics, diuretics (to enhance excretion), emetics, and expectorants are among the plants used in traditional medicine. To treat infections, the leaves' decoction is applied externally. Leprosy and scaly skin conditions are treated with the oil extracted from its roots. The bark and crushed leaves are used as an antibiotic, rat poison, and pesticide.

.This study looked at how methanolic oleander leaf extract affected rats' pyloric ligation and ulcers caused by indomethacin. ....(1)

#### DEFINATION

ULCER: Ulcers are diseases of the skin or mucous membranes characterized by tissue loss. The disease usually occurs in the lower abdominal skin and intestines, but the disease can be found almost anywhere. There are many types of ulcers, such as mouth ulcers, esophageal ulcers, peptic ulcers, genital ulcers, etc

It is Defined as destruction of protectional Mucosal layer and LOSS OF TISSUE Due To Aggressive factors

#### TYPES

1. Gastric Ucer
2. mouth ulcer
3. Stomach ulcer

4. Esophagal Ulcer
5. Intestinal Ulcer

Etc

Causative Agents And Pathogenesis:

#### 1)Helicobacter pylori

Helicobacter pylori is a gram-negative, motile, flagellated bacillus first discovered in the stomach and duodenum by Australian researchers Barry J. Marshall and J. Robin in 1982. The main cause of pain.

Pathogenesis:

A Helicobacter pylori infection initially results in mucosal inflammation, which is followed by persistent pain. Helicobacter pylori must first penetrate the stomach's fixed mucus/HCO<sub>3</sub>-layer before moving on to the epithelial surface and colonizing there in order to be harmful. Thus, by using urease to produce ammonia, the bacteria initially counteract the stomach's acidic environment. Bacterial proteins and cytotoxins, especially those generated by the A gene (cagA)-related cytotoxins, are directly injected by H. pylori once it has adhered to the epithelial surface.

Tyrosine transphosphorylation results from the injection of the cagA protein, other Helicobacter pylori cytotoxins, and other cytosolic proteins into mucosal cells. Strong cytokines were released For instance, nuclear factor kappa B (NF- $\kappa$ B) uses interleukin-8. Furthermore, H. Helicobacter pylori in the stomach triggers the release of chemicals [C5a, N-formaldehyde peptide (fMLP), platelet activating factor (PAF), leukotrienes B<sub>4</sub> (LTB<sub>4</sub>)] that are absorbed by white blood cells, chemokines, and tumor necrosis factor (TNF)- $\alpha$ , which causes neutrophils and macrophages to produce more ROS and contributes to a strong inflammatory response in the host's body.

The ability of H. pylori's reactive nitrogen species (RNS), which include neutrophils, vascular endothelial cells, gastric mucosal cells, and Helicobacter pylori, can cause gastric inflammation. The actual H. pylori. The primary source of ROS and RNS is thought to be neutrophils. Nicotinamide adenine dinucleotide phosphate oxidase (NADPH oxidase) on the cell membrane is one of them; it catalyzes the formation of ROS. When the body is invaded by harmful microorganisms, neutrophils. Gastric inflammation can be brought on by Helicobacter pylori's reactive nitrogen species (RNS),

which comprise neutrophils, vascular endothelial cells, gastric mucosal cells, and *Helicobacter pylori*. genuine *H. pylori*. Neutrophils are believed to be the main generator of ROS and RNS. One of these is the cell membrane's nicotinamide adenine dinucleotide phosphate oxidase (NADPH oxidase), which catalyzes the production of ROS. When pathogenic microbes infiltrate the body, neutrophils. The activity of the stomach enzyme urease, which breaks down urea into ammonia (NH<sub>3</sub>), is one of the primary signs of *Helicobacter pylori*.

You are shielded from its consequences.

In the stomach, this NH<sub>3</sub> combines with the hypochlorous acid (OCl<sup>-</sup>) anion generated by active neutrophils to form poisonous monochloramine (NH<sub>2</sub>Cl).

NH<sub>2</sub>Cl can enter tissues on its own and oxidize intracellular components since it is lipophilic.

.....(5,6,7)

## 2)nonsteroidal anti-inflammatory drugs (NSAIDs)

Because of their anti-inflammatory and anti-inflammatory qualities, nonsteroidal anti-inflammatory medicines (NSAIDs) are frequently used to treat fever, joint pain, osteoarthritis in the knee, and heart disease. Long-term usage of these medications, which include ibuprofen, aspirin, and indomethacin, might result in stomach pain.

Pathogenesis:

NSAIDs prevent cyclooxygenase (COX-1 and COX-2) from converting arachidonic acid to prostaglandins. mechanism of defense capacity. Through prostaglandin receptors (EP) 1–4, they control the release of stomach acid, mucus/bicarbonate, and mucosal blood flow, all of which contribute to gastroprotection. In addition to the aforementioned processes, prostaglandins also prevent mast cell activation, leukocyte activation, and platelet adhesion to the vascular endothelium. Thromboxane production inhibition results in platelet aggregation, bicarbonate secretion from epithelial cells, mucus and blood flow secretion, and elevated lipid peroxidation, all of which may exacerbate intestinal inflammation. Pastyric acid, on the other hand, can result in deep skin wounds, prevent platelet aggregation, and delay wound healing, all of which can hinder the effectiveness of nonsteroidal anti-inflammatory medications for mucosal damage.

.....(8,9,10,11)

## 3)Ethanol-induced gastric ulcer mechanism

The stomach ulcers caused by ethanol possess a sophisticated and varied mode of action. By decreasing the synthesis of mucus, decreasing blood flow to the mucosa, and secreting acid (a process akin to histamine), ethanol harms the body. ....(12)

Due to the solubility of mucus in ethanol and its exposure to the hydrolytic and proteolytic actions of pepsin and hydrochloric acid, ethanol readily permeates damaged membranes and the stomach mucosa, dissolving their phospholipids. By boosting xanthine oxidase activity, ethanol can throw off the cellular antioxidant mechanism. It causes the mucosa to suffer significant harm.

Additionally, by decreasing HCO<sub>3</sub> release, ethanol lowers mucus, which makes room for necrotic lesions in the stomach mucosa. Strong lipid peroxidation has been documented as a result of ethanol metabolism, which releases superoxide and hydroxide as free radicals. Cell turnover brought on by increased lipid and free radical peroxidation results in membrane damage, cell death, shedding, and epithelial erosion. Mice given pure ethanol acutely also exhibit lysosomal labeling and the release of many enzymes, such as acid phosphatase, which exacerbates mucosal injury.

.....(5,8,13)

Ethanol has an impact on bacteria in that a high concentration of it can burn the stomach mucosa directly, induce inflammation, and result in bleeding, erosion, ulcers, congestion, and edema. Ethanol can really harm the stomach by reducing the mucosa's protective qualities, increasing the calcium level of the cells, and further harming the mucosa. When ethanol is taken into the stomach by the enzymes xanthine oxidase and alcohol dehydrogenase, acetaldehyde is produced by alcohol dehydrogenase and transformed into free radicals when xanthine oxidase is present to catalyze metabolism. Alcohol-induced tissue damage is significantly influenced by free radicals. By decreasing mucus (degrading its qualities) and raising oxygen levels even further, they harm blood vessels and endothelial cells and cause lipid peroxidation of mucosal cells. They promote the production and permeability of vasoactive mediators such histamine, leukotriene C<sub>4</sub>, and endothelin 1. By preventing blood flow to the mucosa, these vasoactive substances result in tissue necrosis, bleeding, and eventually the breakdown of the mucosal barrier, which causes intestinal inflammation. Since there is proof that

oxidative stress is linked to ethanol-induced gastric mucosal lesions, ethanol inhibits the action of antioxidant enzymes and regulates the generation of free radicals that produce oxygen. Since the infiltration and activation of neutrophils are directly linked to an excess of free radicals generated by ethanol gavage, one of the free radicals may be the infiltration and buildup of neutrophils in the gastric mucosa, which leads to the creation of in the stomach. Damage is caused by mucosal cells, including lipids and proteins. ....(14,15,16)

#### LITERATURE AND REVIEW

1)HISTORY: The 19th century saw a rise in peptic ulcer disease, gastric, and duodenal ulcers in Western countries, possibly due to a change in *Helicobacter pylori* (*H. pylori*) infections. This review examines the history of *H. pylori*-related diseases, including gastric cancer, gastric ulcer, and duodenal ulcers over the last two millennia. It reveals that while *H. pylori* has been prevalent throughout human history, clinical manifestations changed recently in some Western countries. The sudden appearance of duodenal ulcer disease in the late 19th century is also explained. Since ancient Greece, traditional medical education has been grounded on classical thought and literature. However, by the middle of the 20th century, this tradition was beginning to fade as a result of an abundance of new knowledge. Increased specialization and the disregard or amnesia of pre-20th century medical observations resulted from this. Although electronic databases made it easier to retrieve recent literature, they were unable to index works published prior to the middle of the 1960s. Significant changes in the clinical symptoms of *H. pylori* infection occurred in the United States and Europe in the later half of the 19th and early part of the 20th centuries. These changes included a decline in gastric cancer and alterations in the kind and incidence of peptic ulcer disease. These developments were mostly restricted to industrialized Western nations and were not global in scope. Many Asian nations are also going through similar transitions as they move from developing to developing status. Every element of life underwent tremendous change between 1800 and 1950, thus any shifts in the clinical signs of *H. pylori* and its associated illnesses must be viewed in light of other changes that occurred during that time. According to a 1979–1984 study of 351 patients with peptic ulcers confirmed by endoscopy, 20% of ulcer episodes involve bleeding. In patients with duodenal ulcers, the male to female ratio was 2.4:1, whereas in patients with gastric and

prepyloric/pyloric ulcers, it was 1:1. In comparison to patients with prepyloric/pyloric or duodenal ulcers, patients with bleeding ulcers were substantially older than those without bleeding ulcers and gastric ulcers. In the unselected group, the annual chance of dying from peptic ulcer disease was 0.6%, and the 10-year cumulative mortality was 43%. Patients who had bleeding ulcers at inclusion and those who did not had the same 10-year recurrence rate, although their yearly risk of bleeding was 5.3% and 0.8%, respectively. 51% of the patients who responded to the questionnaire said they had experienced upper abdomen pain in the previous year of follow-up. In summary, over half of patients with peptic ulcer disease had ulcer symptoms after ten years, and over half of patients had a recurrence during that time. H2-receptor antagonist maintenance therapy probably ought to have been more widely available in the 1980s. Numerous factors can cause ulcers. The symptoms that a person's body would exhibit under such circumstances were used to identify the ulcer. Numerous factors, including the ones listed below, can lead to peptic ulcers..

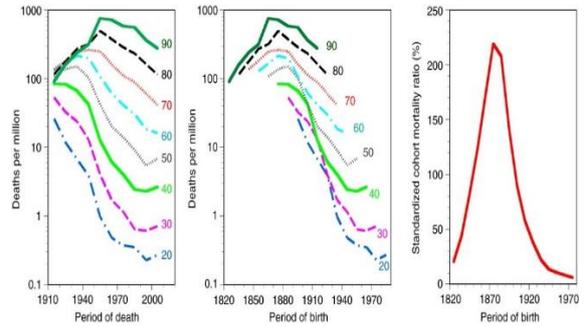
1. :Consistent use of nonsteroidal anti-inflammatory medications (NSAIDs), such as aspirin, ibuprofen, or naproxen
2. Drinking too much alcohol
3. Smoking cigarettes or chewing tobacco
4. Being very ill, such as being on a breathing machine
5. Radiation treatments
6. Stress
7. *Helicobacter pylori* (*H. pylori*)

#### 2)Helicobacter pylori (*H. pylori*)

In Europe, reports of punctured stomach ulcers date back to the Renaissance. Necropsy and severe peritonitis were common adverse effects. Until the early nineteenth century, when it suddenly started to gain popularity, the disease was still rare. Jennings published a noteworthy paper in the *Lancet* in 1940 that summarized early trends in duodenal and stomach ulcers and provided evidence for the abrupt increase in holes at the beginning of the nineteenth century. Initially affecting primarily young women, gastric ulcers became more prevalent in middle-aged women and men as the century went on. At the turn of

the century, physicians noticed a sharp rise in the incidence of duodenal ulcers, which primarily affected young males and comparatively fewer women. These global shifts were not limited to Britain; Scandinavia and Central Europe also witnessed them. More than 10% of adults suffered from peptic ulcer disease throughout the first half of the 20th century. Because the virus crippled young men who would fight in the armed services of World Wars I and II, its containment became a matter of national interest and military protection. Well-maintained, quantifiable records of various European and American therapeutic facilities that began at the beginning of the nineteenth century may in fact acknowledge the first increase and subsequent decline in gastric ulcers today. The findings support the pattern of events where a stomach ulcer first appears in women and then men, followed by a duodenal ulcer wave that typically affects men and women to a lesser extent 20–30 years later. Several agents noted a decline in the incidence of peptic ulcer infection in the last quarter of the 20th century, which had a significant impact on the number of peptic ulcer-related doctor visits, hospital stays, surgeries, and deaths. Plotting the period of passage at period-age forms against the age-specific passing rates of stomach ulcers in Britain and Ridges. Age-specific passing rates during a 10-year period and a 10-year age group are discussed in each information point. For example, comparing the total number of deaths among individuals aged 45–54 from 1971 to 1980 with the total number of people living in Britain at the same time period as the deaths was done separates the total number of deaths. The passing rates per million residing people were shared. Each age group in the plot was given a name based on its center year; for example, 20 denoted the age group of 15–24 and 30 denoted the age group of 25–34. For example, the 1955 instep of 1951–1960 and the 1965 instep of 1961–1970 were named after the midyear of passing. In general, older age groups had a significantly greater mortality rate than younger ones. The passing rates in the youngest and most experienced age groups varied by a factor of 1000. A logarithmic y-axis was selected in order to show the temporal patterns of every age group in a single graphic. The more experienced age groups' period-age forms showed an initial increase followed by a subsequent decline. The most seasoned age group experienced the longest and most articulate ascent. This initial increase became more shorter in the younger age groups and was typically absent in the younger age groups of 35–44. The overall look of a fan-like design is caused by these disparate patterns

among the passing rates of successive age groups. Such different age-specific patterns make it difficult to absorb changes in healthcare. Generally speaking, one would expect that improvements in infection control or anticipation would benefit different age groups equally. For the most part, a simple birth-cohort pattern is demonstrated by the fan-like behavior of period-age forms.



In Figure 1, age-specific passing rates were plotted against the passing period and cohort-age forms, which were then re-plotted against the birth period. With an initial increase and subsequent decline associated with successive long times of birth, the person cohort-age forms were modified in a manner modeled after a hyperbola. While younger age groups essentially contributed to the later collapse, the most experienced age groups were interested in the first surge and some of the ensuing decay. Around 1880, the cohort-age variants of stomach ulcers had the highest fatality rate. Within a single chart, the relative changes of successive period-age or cohort-age forms might be compared thanks to the logarithmic scale of the y-axis.

The SCMR, which is the ratio of observed (O) to expected (E) deaths associated with each continuous birth cohort, showed that gastric ulcer mortality increased among cohorts born during the nineteenth century until 1880, at which point it decreased in all subsequent generations. Additionally, a birth cohort analysis of stomach cancer mortality showed the similar pattern. According to all three analyses, the risk of dying increased for those born in the eighteenth century. Sometime around the turn of the century, the chance peaked among those born between the ages of 10 and 30, and then it started to drop in all subsequent eras.

### 3)The Trend of H. pylori

Similar patterns of Helicobacter pylori disease in the general population are thought to be responsible for

the later deterioration in gastric cancer and peptic ulcers. The origins of *H. pylori* can be traced back to Africa, and it is widely acknowledged that it first appeared in the stomachs of non-Africans. *H. pylori* was the only intestinal disease to decline during the nineteenth century due to changes in hygiene standards. As rivals disappeared, *H. pylori*'s biological niche grew, leading to an increase in stomach malignancies and ulcers.

Encouragement of cleaning improvements, however, ultimately led to the elimination of *H. pylori* and its associated analysis. Acidophilic lactobacilli were used as potential gastric commensals in drain sanitization, although this practice was widely used as of the turn of the century and might not have explained the first increase. Various intragastric life forms may have been impacted by open wellbeing measurements, but no specific tiny species that meet this design have been identified. The birth cohorts with the highest risk of stomach cancer in Britain were born 10–20 years before those with gastric ulcers and 20–30 years before those with duodenal ulcers. Why do the three infections have different time patterns among successive periods born in the nineteenth century if they are all related to *H. pylori*? Those who contract *H. pylori* disease soon after birth are at an increased risk of developing chronic gastritis and stomach cancer later in life. It has been hypothesized that acquiring *H. pylori* from an early age and continuing into later childhood predisposes individuals to stomach ulcers, whereas acquiring it during or after childhood was more likely to cause duodenal ulcers. In the past, the age of first security may have shifted towards older age groups with a higher risk of developing stomach cancer or duodenal ulcers as *H. pylori* contamination decreased among the populations of western countries. A declining disease rate and an increasing division of age-delayed disease could have caused the rising and falling patterns of duodenal and stomach ulcers. Compared to individuals with duodenal ulcers, those with stomach ulcers have a more stable previous crest of gastric ulcers at a younger age, when the disease first manifests. In contrast to gastric cancer, this explanation explains the cohort shift of duodenal and stomach ulcers, but it leaves the initial increase in gastric cancer unexplained. In order to check for *H. pylori* predominance in historical human populations, methods are required. Banatvala et al. conducted a birth-cohort study to examine the time patterns of *H. pylori* predominance and evaluated antibodies against *H. pylori* in serum tests taken over three consecutive

time periods. According to their data, contamination rates appear to have clearly decreased among generations born during the 20th century, with a beginning increase among generations born without further ado around the turn of the century. ....(In literature and review, The History, *H. pylori* and The Trend of *H. pylori* is taken as the Reference NO.17,18,19)

#### 4)Recent Studies

##### a)*Nerium Oleander*:



Fig: *Nerium oleander* Linn.

Oleander is a member of the family Apocynaceae. It is a tiny tree or evergreen that grows in North America, Anatolia, and the Eastern Mediterranean region. To combat oxidative damage, they create antioxidants. It has a protective impact on the heart. Patients with malignant tumors are treated with this herb. Ringworm, ulcers, hemorrhoids, leprosy, herpes, and abscesses are all treated with oleander. Additionally, it is used to treat cancer, leprosy, malaria, asthma, and heart disease.

1. Phytochemical Present in Plant *Nerium Oleander*
  2. Carbohydrate test
  3. Tannin test
  4. Saponin test
  5. Steroid test
- .....(42)

##### General Information

1. Kingdom: Plantae
2. Division: Angiosperms
3. Class: Magnoliopsida
4. Subclass: Asteridae
5. Order: Gentianales

6. Family: Apocynaceae
7. Genus: *Nerium L.*
8. Species: *oleander*. .....(20)
9. ETHNOMEDICINAL VALUE

Oleander (*Nerium oleander L.*) has been mentioned in ancient texts and legends for many years. Scientific data show that most of its plants, such as flowers, leaves, bark and latex leaves, are used in the treatment of microbial and fungal diseases.. Legends claim that the plant can cure a wide range of ailments, and all portions of it are also utilized as medicine. Its bark and leaves have diuretic, expectorant, cardiotoxic, emetic, and diaphoretic properties. ....(21)

When heated in water, the roots aid in the treatment of ringworm, herpes, and skin infections. Small amounts of the juice can be used to deadly bites, including snakebite. Eye conditions are treated using the juice of the tiny leaves. Leprosy, ulcers, hemorrhoids, and certain types of cancer are all treated with the root paste. ....(22,23,24,25)

Leprosy and skin conditions are treated using oil extracted from the root (Saini 2010). The leaves' decoction has been administered externally to treat scabies and lessen swellings. The flowers and leaves have sternutatory, expectorant, diuretic, cardiotoxic, diaphoretic, and emetic properties. ....(20)

Oleander can result in miscarriage and is used to treat wounds (Hseini and Kahouadji 2007). The leaves are macerated and applied externally to treat toothaches, diabetes, lice, infections, and hair loss in Morocco and other regions of Africa. ....(26)

**BIOLOGICAL ACTIVITIES**

**Antimicrobial activity:**

The flower extract of *N. oleander* is tested for antibacterial activity against a variety of clinical pathogens, including *Salmonella*, *Pseudomonas aeruginosa*, *Escherichia coli*, *Bacillus subtilis*, and *Staphylococcus aureus*.

Bacterial isolates	Zone of inhibition in diameter (mm)			
	ETA	CHL	AQE	Control*
<i>Bacillus subtilis</i>	17 ± 0.5	9 ± 0.2	15 ± 0.5	25 ± 1.5
<i>Escherichia coli</i>	20 ± 1.5	10 ± 0.5	22 ± 1.5	30 ± 2.5
<i>Pseudomonas aeruginosa</i>	28 ± 2.6	18 ± 1.5	25 ± 1.7	36 ± 3.6
<i>Staphylococcus aureus</i>	21 ± 1.2	12 ± 1.5	10 ± 0.5	35 ± 2.5
<i>Salmonella typhi</i>	25 ± 3.0	15 ± 1.5	20 ± 1.5	30 ± 3.0

All values are expressed as Mean ± Standard deviation of four replicates  
ETA - Ethanol extract, CHL - Chloroform extract, AQE - Aqueous extract, \*Control - Chloramphenicol

**Table 1**

Table 1 lists the antibacterial activity of *Nerium oleander* water, ethanol, and chloroform extracts against various bacterial isolates.

The ethanol extract has the greatest and strongest inhibitory zone against *Pseudomonas aeruginosa* (28 mm), *Salmonella* (25 mm), *Staphylococcus aureus* (21 mm), *Escherichia coli* (20 mm), and *Bacillus subtilis* (17 mm), according to the above data. *Nerium oleander* flower extracts' antifungal properties

The flower extract from *N. oleander* exhibits antifungal action. is taken and tested for antifungal activity against *Rhizopus* species, *Aspergillus fumigatus*, *Aspergillus niger*, and *Aspergillus flavus*.

Fungal isolates	Zone of inhibition in diameter (mm)			
	ETA	CHL	AQE	Control*
<i>Aspergillus niger</i>	13 ± 0.5	15 ± 1.3	14 ± 1.2	15 ± 0.5
<i>Aspergillus flavus</i>	18 ± 1.5	17 ± 1.5	18 ± 1.5	13 ± 1.5
<i>Aspergillus fumigatus</i>	17 ± 0.5	16 ± 1.5	13 ± 0.5	15 ± 0.5
<i>Rhizopus</i>	18 ± 1.5	17 ± 0.5	10 ± 0.5	17 ± 0.5

All values are expressed as Mean ± Standard deviation of four replicates  
ETA - Ethanol extract, CHL - Chloroform extract, AQE - Aqueous extract, \*Control - Nystatin

**Table2**

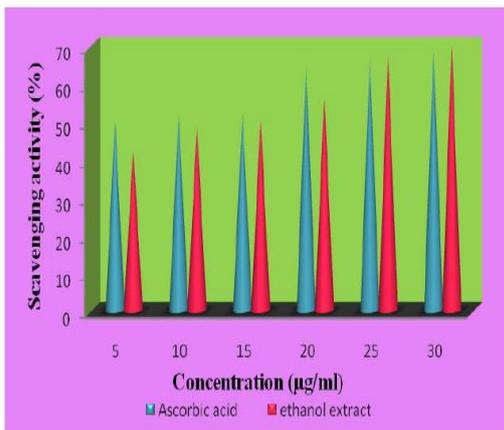
Table 2 displays the antifungal properties of *N. oleander*.

Ethanol extract also showed the best activity compared to other extracts. The maximum inhibition zone was against *Kojima flavus* (18 mm) *Rhizopus* (18 mm) and the least activity was against *Kojima fumigatus* (17 mm) and *Kojima niger* (13 mm).

**Antioxidant activity**

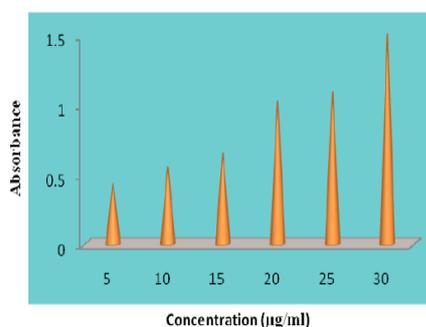
Activity of DPPH radical scavenging  
The percentage of DPPH free radical scavenging activity is the way the measured findings are presented. Calculating the DPPH of oleander ethanol extract with a solution of ascorbic acid

Fig.1 DPPH radical scavenging activity of *Nerium oleander* flower



The low potency of different oleanders is very important. As its concentration gradually increases, the absorbance of each concentration also increases gradually. They are energy donors and can reduce oxidative intermediates in free radical reactions, thus acting as primary and antioxidant agents. 2) It is evident that the existence of radioactive components in the extract is indicated by the rising reduction power in tandem with the extract's increased absorption. Its function has no intermediates. reactions scavenging radicals. Numerous illnesses can be treated with flower extracts, either by itself or in combination. Numerous investigations have demonstrated their ability to explain the chemical makeup of floral components. The phytochemical, antibacterial, and antifungal characteristics of floral extracts were identified in this investigation.

Fig.2 Reducing power ability of *Nerium oleander* flower extract



All floral extracts were discovered to include alkaloids, flavonoids, phenolics, and triterpenoids. ....(27)

ANTI DIABETIC

After 20 days of therapy, *Nerium oleander* lowers blood sugar by 73.79% due to its anti-hyperglycemic properties. The oral glucose tolerance test (OGTT),

which was conducted three hours after therapy, showed a rise in glucose and a 65.72% drop in blood glucose. Triglyceride and cholesterol levels, as well as the percentages of several liver enzyme indicators, are also decreased, suggesting a potent anti-inflammatory impact. Rats treated with NOLE with alloxan showed improved restoration of peroxidase and catalase activity in the liver, kidney, and skeletal muscle, as well as a reduction in lipid peroxidation and a return to normal hepatic glycogen. GC-MS and HPLC analysis were used to identify several bioactive plants with potent anti-diabetic effects. ....(29,30)

ANTI ULCER: The impact of oleander leaf extract on mucus and stomach acid production. Gastric acid stays in the stomach when the pyloric end of the stomach is Ligated. Pain in the stomach may be caused by too much acid.

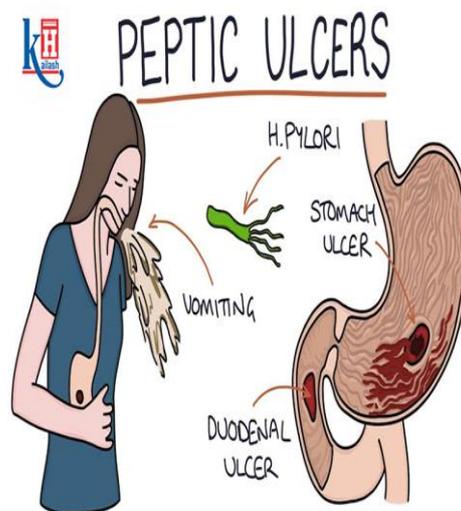


FIG : ULCER

Four hours following the pyloric ligation, the wound index was determined. Ranitidine and oleander extract lower overall acidity. ....(31,32)

ANTI CANCER

The phrase Cancer is characterized by unchecked cell proliferation brought on by abnormalities in the cell's growth-controlling machinery. The cancerous cells proliferate all over the body.

The contradictory findings in several research highlight the significance of using consistent methodology when gathering information and making macroscopic inferences on OLE's effects on tumor

malignancy, including growth. Although its dosage eliminates cardiotoxicity, oleandrin has been demonstrated to have anticancer effects in a variety of cancer types as a cytotoxic agent, supporting its development as a favorable factor in human clinical trials. These findings support more research into its potential as a treatment to enhance patient survival, stop metastases, and lessen tumor symptoms. The contradictory findings in several research highlight the significance of using consistent methodology when gathering information and making macroscopic inferences on OLE's effects on tumor malignancy, including growth.

.....(38,39,40,41)

How to treat ulcer

A) Traditional methods using plants

1. *Scientific name* :*Alstonia Scholaris* R. Br.
2. Local name: *Saptaparna*
3. Family: *Apocynaceae*
4. Classification:
5. Kingdom: plantae
6. Order: Gentianales
7. Genus: *Alstonia*

Description:

The Sanskrit name Satamuli refers to the many spindle-shaped tubers of this plant. They are considered to have cooling, soothing, diuretic, tonic and aphrodisiac properties and are taken and used in the preparation of various medicinal oils. The tuber is cold in nature and can be eaten as a candy. However, this preparation has little flavor or scent other than the candy

Active constituent:

1. Alkaloid
2. Coumarins
3. Flavonoids,
4. Phlobatannin,
5. Reducing sugars,
6. Simple phenolic,
7. Steroids,
8. Saponins
9. Tannins.

Use:

1. To treat ulcers,
2. To treat dysentery

3. wood paste is used in treatment of rheumatism
4. treat toothache

*Asparagus Racemosus*:

1. *Scientific name* :*Asparagus racemosus* Willd
2. Local name: Satawari, satavari.
3. Family: Asparagaceae
4. Classification:
5. Kingdom: plantae
6. Phylum: Magnoliophyta
7. Class: liliopsida
8. Order: Asparagales
9. Family: Asparagaceae
10. Subfamily: Rhododroideae
11. Tribe: rhododendreae
12. Genus: *Asparagus*
13. Specific epithet: *Racemosus* Willd.

Habitat: The plant grows best in tropical and subtropical dry and deciduous forests. Part used: Shoots and tuberous roots

Principal constituents:

- A) Shatavarin (steroidal saponin) (Shatavarin I-IV)
- B) quercetin-3-glucorinide
- C) rutin
- D) sitosterol
- E) stigma stero

Description:

The Sanskrit name Satamuli refers to the many spindle-shaped tubers of this plant. They are considered to have cooling, soothing, diuretic, tonic and aphrodisiac properties and are taken and used in the preparation of various medicinal oils. The tuber is cold in nature and can be eaten as a candy. However, this preparation has little Flavour and smell other than the candy.

Use

1. Treat leucorrhoea
2. Treat headache
3. Treat acidity
4. Reduce pain in pregnancies
5. antiinflammatory,
6. antiulcerogenic,
7. antitumor activity

*Azadirachta indica* Juss. Syn.

1. Botanical name: *Azadirachta indica*

2. Family: Meliaceae
3. Common names: Neem, nim, Indian lilac, nimmi, limbo, limda
4. Part used: leaves, flower, oil and seed.
5. Habitat: It is evergreen and grows throughout India.

#### Description:

Neem is a native tree of India and is a tropical tree, particularly adapted to semiarid conditions. It is now cultivated in many Asian countries and in the tropics of the Western Hemisphere. Neem is considered part of Indian genetics. It is a medium to large tree with a short, straight trunk, wrinkled dark brown to gray bark, densely pinnate leaves, and a rounded crown. The most active substance identified in neem so far is azadirachtin. It is used for neem based pesticide formulations which are safe, natural, biodegradable, easy to manage by farmers and environment friendly unlike chemical and synthetic pesticides that leave residues that pollute the air, water and soil.

#### Chemical constituents

1. Azadirachtin : repellent, anti-hormonal and anti-feedant properties
2. Nimbin: anti-inflammatory, antipyretic, antihistamine and antifungal properties
3. Nimbidin: antifungal, antibacterial, antiulcer, analgesic, and antiarrhythmic qualities
4. Nimbidol's antipyretic, antitubercular, and antiprotozoan qualities
5. Sodium nimbinatate: anti-arthritic, spermicidal, and diuretic effects
6. Quercetin: antiprotozoal, antioxidant, antiinflammatory and antibacterial properties

#### Use:

1. Used in the management of skin diseases
2. Used in the management of rheumatism
3. Used in in the management of malarial fever  
....(33)

#### Modern Methods to treat ulcer

A chronic condition linked to digestive issues, peptic ulcers are typified by mucosal damage brought on by acid and pepsin. Rarely, it affects the distal duodenum, lower esophagus, jejunum, and ectopic gastric mucosa. It often affects the proximal duodenum and stomach. One of the main causes of stomach ulcers is the release of histamine from HCL. It causes parietal

cells' H2 receptors to paracrinely bind. The stomach antral G cells are the main source of gastrin. They regulate the release of gastrin and the activation of the central nervous system, chemical composition, and local expansion of the stomach contents. effects of phytostimulation and gastrin on mast cells' and paracrine ECL cells' histamine release.

Growing intracellular Ca<sup>2+</sup> levels of cyclic AMP and Ach/gastrin levels of histamine are the causes of acid secretion. The last stage of acidification is catalyzed by H<sup>+</sup>/K<sup>+</sup> ATPase. The stomach proton pump is another name for it. The pathophysiology of peptic ulcers is caused by activation of the parietal cell cAMP, Ca<sup>2+</sup> ion dependent pathway, or H<sup>+</sup>/K<sup>+</sup> ATPase. Acid-pepsin imbalance and intestinal mucosal inactivity are the hallmarks of gastric illness. There are three potential peptic ulcer etiological categories.

...(34,35,36)

#### FUTURE SCOPE OF STUDY

Anti ulcer: Ulcer is the most common illness condition in the world, characterized by increased production of aggressive elements and mucous layer breakdown. One plant that has long been utilized as an anti-ulcer agent is oleander. In Ayurveda, there are indications of oleander's anti-ulcer properties. However, the toxicity of the plant is the primary obstacle to creating an anti-ulcer drug from oleander; thus, a strategy to reduce the plant's toxicity must be developed.

To assess the oleander's anti-ulcer properties, more research is required.

#### Additional scopes

Anti cancer: Through cell proliferation, the oleander plant also has anti-cancer properties.

To assess the oleander's anti-cancer properties, more research is required.

Anti diabetic: Diabetes is a condition when the body's system for regulating blood sugar is not functioning properly. The hallmark of diabetics is a rise or fall in blood sugar levels, which can have fatal consequences. The further study is needed formulate anti diabetic product .

Anti Microbial: The plant produces antimicrobial compounds that are used to defend against microorganisms. The difficulty in developing a process to extract these compounds and create an

antimicrobial agent is that plants use them as a defensive mechanism.

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