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A REVIEW ON ANTI-ULCEROGENIC PROPERTIES OF *ORIGANUM VULGARE* L. AND *NELUMBO NUCIFERA*: PHARMACOLOGICAL EVIDENCE AND MECHANISMS

Nandini Rangi[*1] Dr. S. S. Sisodia[2]

[*]Research scholar, Faculty of pharmacy, B. N. University, Udaipur 313001 Rajasthan

[1] Department of Pharmacology, B. N. University, Udaipur 313001 Rajasthan

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Corresponding author: Nandini Rangi

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Abstract:

Traditional medicine has a long history in India. India's Materia medica has a wealth of knowledge about traditional characteristics of therapeutically significant natural items as well as folklore practices. Ayurveda, Siddha, and Unani are some of the systems that form the foundation of Indian traditional medicine. Chromatography, microscopy, and other instrumental procedures are among the phytochemical, pharmacological, and related approaches that are primarily used to evaluate these substances. There is no denying the distinctiveness of these traditional Indian medical systems, but there is a commonality among them in their core beliefs and methods, as seen by the growing global interest in adopting and study the traditional systems and to adopt and study the traditional system and to exploit their potentials based on different healthcare systems. According to estimates from the World Health Organization (WHO), around 80% of people in underdeveloped nations get their main medical treatment nearly entirely from traditional medicine. Medicinal plants are the foundation of traditional medicine and play a significant part in nearly all forms of traditional medicine. Nearly all of the approximately 2000 natural medications found in Indian Materia Medica are derived from various ancient systems and folklore practices. Four hundred of these traditional system-derived medications are generated from minerals and animals, while the remaining medications are sourced from vegetables. The government and commercial sectors have worked hard to develop the traditional system based on these three approaches.

Key words: Anti-Ulcerogenic, *Origanum Vulgare* L., *Nelumbo Nucifera* and Ulcer

1. INTRODUCTION

1.1 Natural Product for Modern Medicine

Herbal medications have a significant role in all traditional medical systems. A triumph of popular therapeutic diversity is herbal medicine. Above all other agents, plants have been employed for medicinal purposes since the beginning of time because they are readily available, affordable, and meet urgent personal needs. Ayurveda and other traditional medical systems use about 1250 Indian medicinal herbs to create therapeutic preparations (Mills et al, 2000). Numerous governmental and commercial organizations have started screening programs for natural resources. Among these was the Central Drugs Research Institute's (CDRI) screening program, which was started in 1964 and encompassed about 2500 plants with a range

of biological activity over a 25-year period [1]. In addition, various universities and institutions are conducting research on Indian medicinal plants used in various TSM; these studies are still ongoing, and the findings are published in scholarly journals. The world's abundant herbal resources are being used more efficiently. Additionally, plant products can be used as a starting point for the semi-synthetic synthesis of additional medications. For instance, the plant is utilized to make steroidal hormones and oral contraceptives [2]. The primary substances employed are hecogenin from sisal leaves (*Agave sisalana*) and diosgenin from various yam species (Dioscorea). There are other natural items that are utilized to make medications besides plants. Since Fleming discovered that *Penicillium notatum* has antibacterial properties, microorganisms have been thoroughly examined for amtonoptoc smoke. Cephalosporin-C and griseofulvin are antibiotics derived from fungi. Bacteria belonging to the Streptomyces species produce a variety of antibiotics, such as streptomycin, neomycin, chioramphenicol with tetracycline [3]. The majority of historical medical systems also made substantial use of animal products, albeit few of the traditional remedies have been proven to be effective. On the other hand, certain medications are made from animal sources. These include hormones like bovine and procine insulin, human growth hormone, and the anticoagulants ancrod (derived from the venom of the Malayan pit viper, *Calloselasma rhodestoma*) and batroxobin (derived from the venom of the South American snake, *Bothrops atrox*) [4].

1.2 Role of Traditional System of Medicine in Primary Health Care

Ayurveda, a reputable healthcare system developed in India, covers every aspect of human health and promotes personal well-being. However, there is now a need to codify and standardize the entire system because of some interference with it over time. Establishing the criteria for Ayurvedic medications is crucial in this regard [5]. This is especially true now that the business is producing more and more Ayurvedic medications instead of Ayurvedic doctors compounding them. Additionally, commercially available Ayurvedic medications can have an impact on global markets that are searching for alternative medicine to treat illnesses that even there is no solution in the current system [6]. Metabolic or degenerative diseases such as arthritis, heart disease, diabetes, cancer, dementia, age-related disorders, immunological disorders, and gynecological issues are among these conditions. These items, which use the aforementioned disorder, have a sizable market. First, we have an overview of the state of plant-based goods worldwide, highlight how other nations see these medications, and attempt to consider our own situation [7]. Globally, interest in traditional medication systems. Natural drugs derived from plants can be utilized directly, meaning they can be gathered, dried, and used as therapeutic agents (crude drugs), or their main ingredients or active principles can be isolated through a variety of chemical procedures and used as medications [8]. Carbohydrates, glycosides, tannins, lipids, alkaloids, etc. could be the active ingredients.

1.3 Prospects of Traditional Medicine

With more than 45,000 distinct plant species, India is one of the top 12 biodiversity hotspots in the world. With 16 distinct agroclimatic zones, 10 vegetation zones, 25 biotic provinces, and 426 biomes (habitats of certain species), India's diversity is unparalleled. There are between 15,000 and 20,000 plants with good therapeutic effect. However, traditional communities only use between 7,000 and 7,500 plants for

their medicinal properties. About 600 species are used in the Siddha medical system, 700 in Ayurveda, 600 in Amchi, and 700 in Unani. Worldwide, over 100 species of higher plants yield about 130 pure medicinal compounds that are used as medicines. As said in a According to a 1994 United Nations Development Project (UNPD) research, medicinal plants from underdeveloped nations are worth around $32 billion (Rs. 100,000 crore) annually [9]. Theoretically, 325,000 species discovered in tropical rain forests may include 328 novel contemporary medications. There are already 47 significant plant-based medications available on the global market, and the estimated value of the remaining 328 potential medications is $147 billion [10].

1.4 Phytomedicine

The World Health Organization (WHO) defines phytomedicine as herbal preparations made by extracting, fractionating, purifying, concentrating, or using other physical or biological processes on plant materials. These preparations can be made to be consumed right away or used as the foundation for other herbal products. In addition to the active compounds, these plant products may also comprise recipient or inactive substances [11]. Additionally, basic botanical resources were used in more or less primitive forms in the early generations of plant medicine. These medications, which include aloe, belladonna, opium, and cinchona, were chosen based on empirical data collected by traditional healers [12].

1.4.1 Phytomedicine Demand

Globally, interest in natural therapies primarily phytomedicine has grown during the past few years. Consumer inclination for natural medicines is one of the many factors driving the global phytotherapeutic market's rise [13]. Since phytomedicine has been used for thousands of years by millions of people worldwide, it is believed to have no negative side effects. It is also believed that phytomedicine can be used to treat certain diseases where conventional medicine is ineffective due to improvements in its quality, efficacy, and safety [14].

1.5 Therapeutic Benefit of Phytomedicine over Synthetic Drugs

Compared to comparable phytomedicines, synthetic or chemical medications may have stronger or faster effects, but they also carry a larger risk of adverse consequences. For example, phytomedicine acts on the body by regulating and balancing its vital processes rather than stopping or combating certain symptoms, whereas psycho-pharmacological products with sedative and axiolytic action are likely to have unfavorable side effects like drowsiness and uncoordinated motor skills [15]. Disorders and unbalanced mental conditions are prevented by its balancing action on the central nervous system. The respiratory system benefits greatly from phytomedicines. because they have a genuine cleansing effect on excessive mucus in the interior of the airway, rather than only neutralizing the symptoms of any disease [16].

1.6 Economic Benefits

The majority of pharmaceutical businesses interested in commercializing phytomedicines have been drawn to the growing interest in natural remedies, which has also expanded worldwide trade in phytomedicine. The manufacturing, processing, and marketing of phytomedicine products provide jobs in the nations that produce them. In 1997, the European market alone reached $7 billion; the German market accounts for roughly 50% of this total, at $3.5 billion, or roughly $42.90 per person; France's market is at $1.8 billion; Italy's is at $700 million; the UK's is at $400 million; and the sales in Spain and the Netherlands are at $300 million and $100 million, respectively [17]. In 1996 and 1999, the U.S. phytomedicine trade was around $3.2 billion and $5 billion,

respectively. The markets in Japan and Asia reached roughly $2.1 billion and $2.3 billion, respectively [18].

1.7 Challenges in the Use And Development of Phytomedicine

To advance the World Health Agenda, a number of issues that are impeding the global development of phytomedicine must be completely resolved. These issues consist of: The formulation of phytomedicine, especially in crude-drug form, necessitates a specific expert field that involves training and expertise, making the synthesis of drugs from their natural source more challenging than the production of synthetic drugs [19]. Inadequate quality control and standardization of herbal medications utilized in clinical trials and procedures. the possibility of adverse effects from toxicity, overdosing, interactions with conventional medications, and a number of manufacturing issues, including incorrect plant identification, a lack of standardization, a failure to follow good manufacturing practices, contamination from field microbial contamination, poor packaging, the use of chemicals, environmental conditions (temperature, light exposure), plant substitution and adulteration, improper preparation, and dosage [20].

1.8 Pharmacognosy Can Help Minimize Accidental Misuse of HerbalMedicine

According to a World Health Organization (WHO) estimate, between 85 and 90 percent of people worldwide use traditional herbal remedies. Recently, both industrialized and developing nations have seen an upsurge in the use of herbal therapies; in the West and the Near East, the use of traditional herbal medicines has grown dramatically [21]. In 2000, the US market for herbal medicines alone was valued at US$17 billion; currently, it is believed to be worth US$60 billion worldwide. India's herbal health care and personal care market is thought to be worth between Rs 2500 and three thousand crores [22]. As these numbers continue to climb, so does the number of fatalities and other adverse effects brought on by the usage of herbal remedies [23]. In essence, pharmacognosy is the research, standardization, and verification of natural medications. It works closely with related subjects, such as toxicological screening of natural materials and phytochemistry. The majority of research in pharmacognosy has focused on identifying contentious plant species and authenticating widely used traditional medicinal plants using morphological, histological, physico-chemical, and toxicological parameters, particularly heavy-metal estimation and radiobiological contamination in plants, as recommended by an authoritative source. In recent years, pharmacognosy has become increasingly important [24].

1.9 New Insights from Inter-Cultural Research to the World of Medicine

The intercultural approach can help pioneer new contributions to the medical field, even though it is crucial for interpreting and comprehending THS. Pharmacogenomics is one fascinating area that is emerging as a result of cross-cultural research. It is widely acknowledged that this area is crucial for medication research in the future [25]. It is now known that a drug's effects vary depending on a person's genetic composition. One of the main challenges in this new profession is the correlation between genes and phenotypes. Since popularly used ethnic designations are imprecise representations of genetic clusters and do not reflect the underlying genetic make-up, attempts to tie phenotypic characteristics associated with ethnicity, geographical divisions, or diseases to genotypes have had minimal success [26]. Bhushan Patwardhan's group at the Interdisciplinary School of Health Sciences, University of Pune, has proposed a "human

phenome" project based on the Ayurvedic concept of Prakriti. The project aims to find broad-based genomic representation by creating comprehensive phenotypic datasets from various populations. Nevertheless, there is disagreement over the definition of phenotypes and the characteristics that should be included in the database [27]. Therefore, classifying the human population continues to be a significant difficulty for the medical sciences. It's in this Given that the human phenome project can be guided by the Ayurvedic phenotypic categorization scheme known as Prakriti, which can classify all human bodies into seven phenotypes. Patwardhan's group's PCR-based gene polymorphism investigations on the HLA and DRBI genes provide evidence for the potential genetic foundation of Ayurvedic population classification [28].

1.10 Future of Plant Drugs

For a very long time, the kingdom of plants has provided us with many high-quality medications. However, sound scientific study in this area is currently lacking, and some have expressed concern about its future. In 1985, almost $190 million worth of herbs were sold in American health food stores, and an additional $33 million was made from books and pamphlets detailing the purported uses of these products. In Germany, the field of herbal research and development is still thriving [29]. A sizable number of businesses are constantly bringing new plant medication preparations (Phyto pharmaceuticals) and even new plant constituents to the market. According to a poll, about 76% of the women surveyed drank herbal teas for their positive effects, and over 52% of them used herbal treatments as a first line of treatment for mild illnesses [30].

The advancements in science and technology over the next 25 years will be so enormous that, when applied to the natural mysteries that have long baffled us, they will reveal their secrets with astounding speed. It will be an exciting and exciting time. For the majority of diseases, we will know both the cause and the remedy [31]. The As they have done since the beginning of time, the kingdoms of plants and animals will continue to save humanity in the twenty-first century. Important new natural medications and innovative production techniques will remain crucial components of such service [32].

2. ULCER

Barry Marshall and Robin Warren discovered in 1982 that Helicobacter pylori is a type of bacteria that lives and grows in the stomach. The stomach's and upper small intestine's protective layer is weakened by these bacteria. The delicate tissues lining the digestive system beneath are then exposed to acid. This lining is immediately irritated by acid and germs to the point that sores or ulcers develop [33]. Saliva also contains this bacteria. An ulcer is an open, painful wound in the body's mucous membranes or mucosal linings. The stomach and duodenum, which have the highest levels of acid and pepsin activity, are common sites for gastrointestinal ulcers. A human's digestive system is a complex system consisting of many hollow organs. The stomach is the most important organ for food digestion. Alcohol, reflux bile salt, and hydrochloric acid are just a few of the many harmful stimuli that the stomach may withstand [34]. The stomach's remarkable resistance to dangerous substances is caused by a number of defensive characteristics. However, when detrimental factors outweigh these protective aspects, peptic ulcers result. Peptic ulcer disease is characterized by a rupture in the lining of the gastrointestinal mucosa, which is rich in pepsin and acid. A stomach ulcer

is the most prevalent gastrointestinal condition, affecting 10% of individuals globally. illness [35]. Up to 10% of people have peptic ulcers or other symptoms severe enough to require medical attention. The more serious illnesses that are medically necessary are ulcers and gastroesophageal disorders. Over 4 million duodenal and stomach ulcers occur in the United States; 350 000 new cases are recorded annually; 180 000 individuals are admitted to hospitals and given medicine each year; and 5,000 of these patients die from their ulcer disease. The lifetime risk of getting a peptic ulcer is about 10% for American men and 4% for women [36]. Peptic ulcers are thought to be caused by an imbalance between mucosal protective factors and stomach aggressive forces. Peptic ulcers are Pepsinogen secretion, which is produced by parietal cells, can be classified as esophageal, duodenal, or stomach depending on the location. Examples of aggressive and defensive elements that affect the aetiology of gastroduodenal ulcers include mucosal barrier, mucosal production, blood supply, and endogenous shielding chemicals [37]. A risk factor for peptic ulcers is linked to hematemesis, a symptom of frequent UGI bleeding. The vomiting of blood, a substance that resembles coffee grounds, and digested food (melana) is known as hematemesis. The nasogastric tube lavage utilized for the clinical diagnosis of UG I contains blood or coffee-like substance. Most bleeding patients can be managed with a mix of medication, endoscopic surgery, and blood and fluid resuscitation [38].

2.1 Ulcers Perforation

In the small intestine, esophagus, and large intestine, ulcers account for 60, 40, and 20% of perforations, respectively. Penetration: When an ulcer penetrates a section of the colon without completely separating from the wall and filters all of its contents into the peritoneal cavity, it is referred to as ulcer penetration [39]. Although only a tiny percentage of these ulcers would be clinically important, the surgical treatment procedure recommended that 20% of ulcers have permeation. Common signs of these issues include diarrhea, weight loss, and acidic irritation. Water-induced vomiting is uncommon. yet suggestive indication [40]. There is insufficient clinical data to support the treatment approach and guidelines for penetrating ulcers. Obstruction: One of the most typical signs of an ulcer is occlusion of the stomach wall. The majority of cases are caused by duodenal or pyloric section ulcerations, which affect 5% of patient populations. Lifestyle and dietary changes: Treatment for peptic ulcers may be hampered by aspirin and related NSAIDs (non-steroidal anti-inflammatory drugs), alcohol, coffee, including decaf, tea, and other substances. Smoking prolongs the healing process of ulcers. Researchers have found that people who experience ulcer symptoms consume more carbs than those without them. Furthermore, it has been observed that sugar increases the pH of the stomach. The stomach and intestines may become irritated by salt. People who eat a lot of salt have been found to have a higher incidence of stomach ulcers due to a specific amino acid. Glutamine is an essential energy source in the cells lining the gut and stomach [41].

2.2 Types of Ulcer

The ulcer was classified as Peptic ulcer, Duodenal ulcer, Stress ulcer, Mouth ulcer, Antral or propyloric ulcer, Gastric ulcer and NSAID ulcer [42-44].

When acid and pepsin in the stomach juice cause a discontinuity in the entire thickness of the gastric or duodenal mucosa, it is referred to as a peptic ulcer. Clinicians see dyspepsia as a symptom of peptic ulcer disease. Peptic ulcer disease is not present in every patient with dyspepsia, though. Persistent or recurrent upper abdominal pain is known as dyspepsia. About 50% of dyspeptic patients have a known cause for their symptoms, such as pancreatic or biliary disease, gastric cancer, gastric ulcers, or gastroesophageal reflux disease; another 20% have anomalies of unclear significance, such as upper gastrointestinal dismotility or gastritis; and the remaining 30% have no obvious anomalies [45]. The final two groups are typically classified as non-ulcer dyspepsia. Thirty to forty percent of the population experiences dyspepsia at some point in their lives, according to primary care doctors. Up to 70% of patients referred to a gastrointestinal unit have dyspepsia, accounting for 5–10% of cases. An ulcer caused by physiological stress, such as burns, head trauma, or surgery, is known as a stress ulcer. Superficial mucosal erosion results from these types of injury. These could result in perforation or bleeding. The signs of Stress ulcers are characterized by reduced prostaglandin protection, reduced blood supply to the stomach mucosa, decreased cell renewal, and increased acid output. Mycobacterium ulceran was the etiology of Buruli ulcer [46]. This slow-growing environmental mycobacterium develops best at 32 degrees Celsius. The organism produces myco lactone, a powerful tissue necrotizing toxin, and infects skin, subcutaneous tissue, and frequently bone. a sore that appears on the stomach, oesophagus, or small intestinal lining. When the lining of the digestive tract is harmed by stomach acid, ulcers develop. Two common culprits are the H. Pylori bacteria and anti-inflammatory medications like aspirin [47]. Most stomach ulcers are single and have a diameter of less than 20 millimeters. Persistent gastritis is the main cause of ulcers in the smaller curvature, but adverse effects from non-steroidal anti-inflammatory drugs are typically linked to ulcers in the larger curvature [48].

2.3 List of Chemicals Known to Induce Gastric Ulcer

Among the substances that cause ulcers are aspirin, indomethacin, alcohol, caffeine, diclofenac, flufenamic acid, histamine, ibuprofen, nicotine, phenacetin, glucocorticoids, paracetamol, piroxicam, methylphenyl tetrahydro pyridine, and 5-hydroxytryptamine. Dealing with the causes of stomach wall ulcers is of interest. These can be traditionally explained by three categories of ulceration-related variables [49].

General Factors: Histamine and adrenaline, the vagal hormone impact, poor circulation, shock, general ischemia, etc. Environmental and constitutional elements include age, sex, temperature, family history, social status, geographic distance, and occupation.

Aggressive Factors: NSAIDs, alcohol, pancreatic proteolytic enzyme, HCL, pepsin, refluxed bile, ingested irritants, bacterial toxins, and physicochemical stress.

Digestive Factors: Mucus, bicarbonates, blood flow, resolution epithelium [50].

2.4 Physiological Factors Associated with Gastric Ulcer

Chemical or *H. pylori* gastritis, which damages the epithelium, nearly usually coexists with the development of gastric ulcers. The majority of gastric ulcer sufferers create less acid than both duodenal ulcer sufferers and healthy individuals. The following components are at play: Acid back-diffusion into the mucosa; a decrease in the bulk of parietal cells; and issues with the parietal cells themselves acid hypersecretion is rare in patients with gastric ulcers [51]. These people typically have duodenal ulcers near the pylorus. The

significant gastric hypersecretion associated with Zollinger-Ellison's syndrome is more often associated with severe duodenal and jejunal ulceration than stomach ulcers [52].

2.5 Treatment approaches for gastric ulcer

Medications that lessen the generation of acid. Acid blockers, also known as histamine (H-2) blockers, reduce the production of stomach acid in the digestive tract, which lessens ulcer agony and accelerates healing. An antacid is a fast-acting analgesic that also neutralizes any existing stomach acid [53]. Depending on the underlying substances, constipation or diarrhea may occur as a side effect.

2.6 Duodenal Ulcer

An ulcer or crater in the duodenum, the initial segment of the lining of the small intestine. Helicobacter infection is the cause of ulcer formation. Duodenal ulcers typically occur on the duodenum's wall near the pylorus [54].

Physiological factors associated with duodenal ulcer

The total mass of parietal cells is reflected in the stomach's greatest capacity to create acid. Patients with duodenal ulcers have up to twice as much parietal cell masses and maximum acid secretion. However, there is a considerable overlap with normal readings, and only one-third of these individuals exhale excessive amounts of acid. Accelerated gastric emptying has been noted in patients with duodenal ulcers, which may lead to the duodenum being more acidic. However, like with other factors, there is a considerable overlap with normal rates. Additional gastric emptying is prevented by normal acidity of the duodenal bulb. The equilibrium between the production of gastric juice and its neutralization by The pH of the duodenal bulb reflects biliary, pancreatic, and duodenal secretions [55]. An acidic pH in the bulb is necessary for the development of duodenal ulcers or an excess of acid over neutralizing secretions. The post-meal drop in duodenal pH is longer and slower in ulcer sufferers than in healthy individuals. There is a connection between weakened mucosal defenses and peptic ulcers. Prostaglandin function and other mucosal factors may or may not be similar to those protecting the stomach mucosa [56].

Treatment approaches for duodenal ulcer

A duodenal ulcer is usually caused by an infection with the Helicobacter pylori bacteria. After using acid-suppressive medicine for four to eight weeks, the ulcer will heal. Additionally, the H. pylori infection may usually be eliminated with a one-week course of treatment consisting of two antibiotics and an acid-suppressive medication [57].

2.7 Regulation of Acid Secretion

The parietal cells in the stomach release roughly two liters of hydrochloric acid each day. This acid facilitates digestion by increasing food solubility and eliminating microorganisms. Establishing the proper pH (between 1.8 and 3.5) is necessary for the digestive enzyme pepsin to work properly. An essential protein for the production of acids is the H+/K+-ATPase (also known as the proton pump). This protein uses the energy from ATP hydrolysis to pump hydrogen ions into the lumen in exchange for potassium ions [58]. Acid secretion is triggered by H+/K+-ATPases moving to the parietal cell's apical membrane. Vesicles include H+/K+-ATPases. inside a cell while it is not active, or at rest. When the cell is active, these vesicles attach to the plasma membrane, boosting the membrane's surface area and proton pump count. Three regulator y molecules acetylcholine, histamine, and gastrin promote the production of acid, while somatostatin, a fourth regulator y molecule, inhibits the secretion of acid. Acetylcholine is a neurotransmitter released by enteric neurons [59]. Entrochromaffin-like (ECL) cells emit

histamine, a paracrine chemical. The hormone gastrin is released by G cells, which are endocrine cells found in the stomach epithelium. The endocrine cells of the stomach epithelium also release somatostatinan aparacrine or hormone. The diagram demonstrates how acid secretion is stimulated by the interaction of the positive and negative regulators. Histamine and acetylcholine directly enhance the quantity of acid released by parietal cells. Gastrin promotes the release of histamine from ECL cells, which raises the generation of acid. Furthermore, gastrin directly affects parietal cells, promoting their growth. Somatostatin synthesis is increased when the stomach's pH is too low. By directly controlling acid secretion, somatostatin parietal cells and preventing the production of gastrin and histamine, which are positive regulators. As food is consumed and moves through the different parts of the upper gastrointestinal tract, the balance of activity between the various regulators shifts [60].

Many pharmaceutical treatments, such as anticholinergics, histamine antacids, H2 antagonists, and more recently, PPIs (proton pump inhibitors), are used to treat both acid reflux and peptic ulcers. Even though they can have a number of negative consequences, They are generally harmless, though they may cause headaches, rash, diarrhea, flatulence, nausea, and stomach pain [61]. Alternative medicines, especially those derived from plants, have garnered more attention in recent years due to their relatively lower side effects and accessibility. Plants with a long history of ethnomedical usage in the treatment of peptic ulcers should have their antiulcer properties examined [62]. This study examined the prevention of aspirin-induced stomach ulcers in albino Wistar rats using a methanolic extract of Celosia cristata leaves because the plant has long been utilized as an anti-ulcer drug for stomach ulcers [63].

3. DRUG THERAPY OF PEPTIC ULCER

3.1 H_2-Receptor Antagonists

The treatment of peptic ulcers has been transformed by H2-receptor antagonists, the most popular and successful new medication in recent decades. Conventional therapy for the prevention of peptic ulcers includes cimitidine and famotidine [64]. More than 90% of the basal-food stimulated and natural secretion of stomach acid induced by histamine, gastrin, cholinomimetic medicines, and vagal stimulation can be reduced by these medications because they competitively inhibit H2-receptor antagonists [65].

3.2 Proton Pump Inhibitors (PPI)

The first PPI, omeprazole, was released in 1989, making them relatively new medications. Acid is suppressed by them. They are the most effective medications for treating duodenal and gastric secretions because they specifically inhibit the H+, K+, and ATPase enzyme system at the secretary surface of parietal cells, which is more effective than H2 blocking pharmaceuticals in lowering basal and stimulated acid production [66]. Stomach ulcers as well as conditions like reflux esophagitis and Zollinger-Ellision syndrome that call for the control of gastric acid output. By interacting with the sulphohydryl group of bacteria, PPI also affects Helicobacter pylori metabolism.

3.3 Prostaglanding (PGS)

Robert discovered in 1979 that PGs prevent experimental ulcers brought on by NSAIDs, nutrition, and lifestyle factors (such as stress and alcohol consumption). The commercially available synthetic prostaglandins misoprostol, enprostil, arbaprostol, and trimoprostol are recommended for the prevention of NSAID-induced stomach ulcers[67].

3.4 Muscarinic Receptor Antagonists

Muscarinic cholinergic antagonists have a 40–50% reduction in basal stomach acid

production. There is less inhibition of stimulated secretions. The specific muscarinic antagonist pirenzepine is just as effective as cimitidine at preventing duodenal ulcer recurrence. Because they are hydrophilic, telezepine and pirenzepine both cross the blood barrier [68]. Pirenzepine works best when taken orally two to three times a day, whereas Telezepine, which is more powerful, works best when taken orally at a dose of three milligrams per day.

3.5 Mucosal Coating Agents

Sucralfate is a combination of sulfated sucrose and aluminum hydroxide that, when exposed to acid-released aluminum, takes on a significant negative charge and binds to positive charge groups in proteins, glycoproteins, etc [69]. It can create a complex gel with mucus, reducing the amount of mucus that pepsin breaks down and, to some extent, the transport of hydrogen ions.

3.6 Bismuth Compounds

Helicobacter pylori involvement in peptic ulcers is treated with a combined regimen that includes bismuth chelate (colloidal bismuth subcitrate tri potassium dicitrate dicitrato bismuthate). In addition to preventing ulcers by adhering to the mucosa or inhibiting its proteolytic enzymes, it has toxic effects on the *bacillus* [70]. By covering the ulcer base, adsorbing pepsin, boosting local prostaglandin synthesis, and stimulating bicarbonate, it is thought to have additional mucosal protective effects.

3.7 Carbenoxolone

A synthetic derivative of liquorice's glycyrrhizinic acid, which has been demonstrated to be beneficial in accelerating the healing of peptic ulcers. Although the exact mechanism of action is unknown, it is thought to have an impact on mucus, increasing its secretion and viscosity and shielding the mucosa from acid and pepsin attacks. Its main side effect is sodium retention, which can cause oedema, hypertension, and heart failure [71]. This restricts its use, particularly in elderly individuals.

4. HERBAL DRUG STANDARDIZATION

Good Manufacturing Practices (GMP) must be used in order to standardize herbal formulations. Furthermore, it is thought to be crucial to investigate a number of factors, including pharmacodynamics, pharmacokinetics, dose, stability, self-life, toxicity assessment, and chemical profiling of the herbal formulations. Equally significant are other elements including aflatoxine level, heavy metal contamination, pesticide residue, and Good Agricultural Practices (GAP) in the standardization of herbal drugs. Standardization is the process of ensuring that each packet of medication being supplied contains the right ingredients in the right amounts and will have the desired therapeutic effect [72]. It is crucial that a system of Because there is a great deal of room for variance in different batches of medication, standardization is established for all plant medicines available on the market. Plant material may differ in its phytochemical content and, consequently, in its therapeutic effect depending on where it is collected, when it is collected throughout the year [73], when it is collected at the same time and location but in different years, and depending on the environmental conditions surrounding the cultivation of a specific medicinal plant. The fact that multiple plants may be combined in a single preparation in herbal therapy adds to this variety. This implies that in order to guarantee the product's quality, a quality control test should be conducted during the entire preparation process. The World Health Organization (WHO) supports, advocates, and encourages the use of traditional and herbal remedies in national health care programs since these medications are widely accessible,

reasonably priced, safe, and trusted [74]. The WHO assembly has stressed in several resolutions the necessity of employing appropriate standards and contemporary methods to guarantee the quality control of medicinal plant products.

4.1 Pharmacopoeial Standards

The pharmacopoeia provides references that prove the validity, quality, and purity of herbal medicines. The pharmacopoeia specifies (numerical value) standards for the medications, such as structural, analytical, and physical [75]. The production of herbal formulations necessitates a rigorous analysis and identification of crude medications due to the wide range and variety of their chemical characteristics. All pharmacopoeias have established specific guidelines to address this issue. The following lists specific testing for specific plant materials. Foaming index, hemolytic activity, and volatile oil content Iodine value, acid value, saponification value, fat content, tannin content, and bitter value [76]. Aluminum, arsenic, borate, calcium, camphor, chloride, copper, gold, iron, lead, magnesium, mercury, and phosphate assays Potassium, Silica, Silver, Sodium, Sulpher, Sulphat, Tin [77].

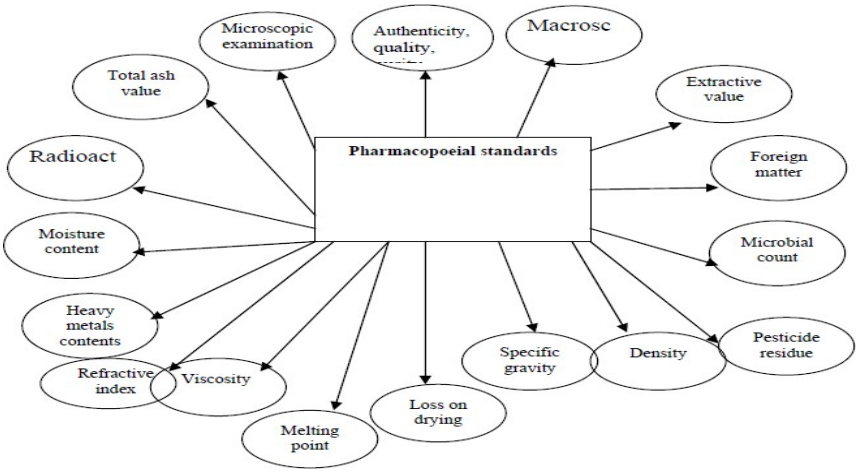

Figure No. 1: Pharmacopeial standards of herbal drugs

5. NATURAL REMEDIES

5.1 Bari ilayachi (*Elettaria cardamomum* and *Amomum subulatum*)

The gastroprotective effects of these medications may result from a reduction in stomach motility. They relax the circular muscles, which may flatten the wrinkles and preserve the stomach mucosa. This will release the amount of gastric agents on the rugal crest and increase the mucosal region exposed to narcotizing agents. It has been suggested that this activity contributes to prostaglandins' cytoprotective effects [78].

5.2 Black berry

Capsaicin is one of the most intriguing compounds extracted from cold peppers and found in spicy plants like ginger or black pepper. This material stimulates the membrane receptors of sensory neurons, primarily vaniloid (VR)-1 receptors, and releases a variety of kinins, including substance P. Large doses of capsaicin cause the selective destruction of C-fiber neuronal terminals, which results in the inactivation of sensory nerves and the loss of all reflexes involving these nerves. Capsaicin is a powerful gastroprotective and stomach microcirculation stimulator when taken in smaller doses [79]

5.3 Chamomile (Matricaria recutita)

Traditionally, chamomile has been used to

treat digestive issues, such as gastric ulcers, and as a light sedative to reduce anxiety. Additionally, chamomile may help promote digestion and relieve irritated or inflamed mucous membranes in the digestive tract. The digestive system is calmed by chamomile. Peptic ulcers, acid reflux, and indigestion might all benefit from its mildly calming effects. Additionally, it contains a lot of apigenin, another flavonoid that has stopped H. pylori from growing in test tubes [80].

5.4 Dong quai (*Angelica sinensis*)

Dong quai may relieve ulcers, according to research on animals, but human trials are required before a firm conclusion can be made. Glycyrrhiza glabra, or licorice: Licorice root has a strong history of calming irritated and injured digestive tract mucous membranes. By increasing the synthesis of mucin, which shields the lining of the HCl and other chemicals, licorice also protects the stomach and intestinal sections. Preclinical study suggests that licorice flavonoids may also inhibit H. pylori growth [81]. 5.6 Marshmallow root (*Althaea officinalis*)

In traditional medicine, marshmallows have been used for decades to treat stomach ulcers. Mucilage, a gelatinous material found in plants, is present in the marshmallow's roots. This mucilage swells and forms a soft, protecting gel when it comes into touch with water. This is thought to offer a barrier of defense against irritants that could exacerbate ulcers [82].

5.7 Tea root extract (*Camellia sinensis*)

Tea root extract might primarly decrease the leakage of plasma proteins into the gastric juice with strengthening of the mucosal barrier and increase in its resistance to the damaging effect of ethanol induced ulcer [83].

5.8 Turmeric (*Curcuma longa*)

Curcuma longa's constituents protect the gastrointestinal system in a number of ways. It was shown that p-tolymethylcarbinol, a component of turmeric, could increase the secretion of gastrin, secretin, bicarbonate, and pancreatic enzymes, while sodium curcuminate, a salt of curcumin, inhibited intestinal spasm. In rats, turmeric has also been demonstrated to prevent the development of ulcers brought on by stress, alcohol, indomethacin, pyloric ligation, and reserpine. In rats exposed to severe gastrointestinal injuries, our study showed that turmeric extract dramatically increased the amount of mucus on the stomach wall [84].

6. MEDICINAL PLANT FOR ULCER

Due to its greater cultural acceptability, better human body enforcement, and fewer adverse effects, 75–80% of people worldwide still utilize herbal treatments today, primarily in developing nations. These medicinal plants did not exhibit any acute toxicity, according to histological testing. Essential secondary metabolites like flavanoids and tannins were found in this medicinal plant during preliminary photochemical screening [85]. For each of the peptic ulcer medicinal plants, the Indian Ayurvedic book Meteria Medica and online databases like Science Direct, Pubmed, Scopus, and Google Scholar were investigated. All of the articles gathered were examined to find any in vitro, in vivo, or clinical evidence of their effectiveness and possible mechanisms [86]. The research findings either clearly shows the usefulness of these herbs or inadvertently shows how they affect the underlying mechanisms in the treatment of stomach sores. Meteria Medica provides a wealth of information about ethnomedical herbs that have been clinically studied and proven to have antiulcerative properties [87, 88].

6.1 *Acasia Arabica*

In the traditional Indian medical system, fresh plant parts are regarded as antimicrobials with high nutritional value.

To heal ulcers, the wet leaves are poulticated [89]. It works well as a gargle for cleaning wounds and hemorrhagic ulcers. Acasia Senegal gum is protected against stomach ulcers caused by cold stress. This gum's aqueous extract reduced bowel enzyme activity and offered protection against meloxicam-induced intestinal damage [90, 91]. Active components: Flavanoids, tannins, and phenolic chemicals are examined

6.2 *Tamarindus Indica*

It is a long-lived, lovely fruiting tree that can reach a height of 30 meters and has a dense, spreading crown. Bark can be used to treat ulcers and sores. Indolent lesions can be cleaned with leaf decoction, which encourages a favorable reaction. At doses of 100 and 200 mg/kg, this indica's seed coat methanolic extract significantly lowers the total volume of stomach juice [92, 93] active ingredients.

6.3 *Adansonia Digitata*

For indolent syphilitic ulcers, the fresh juice of the leaves combined with powdered ginger and the expressed juice of the fresh root of Salvadora indica are used with significant benefit [94] active ingredients as phenolic compounds.

6.4 *Ocimum Sanctum*

Millions of Indians have been using the fresh leaves as Prasad, or fuel, for many years. Sanctum was given intraperitoneally at dosages of 1, 2, and 3 ml/kg to rats whose ulcers were brought on by aspirin, indomethacin, alcohol, and stress [95]. This reduces the index of ulcer in a dose-dependent way [96]. Active constituents as fixed oil eugenol are taken [97].

6.5 **Garcinia Cambogia *Desr***

The extract's pharmacological characteristics, which include gastroprotective actions, have drawn attention. In rats with colitis caused by TNBS, the alcohol extract's anti-inflammatory properties were examined. The results showed that giving garcinia to colitic rats considerably reduced increases in MPO activity, COX-2, and iNOS expression while also improving macroscopic damage. Furthermore, garcinia extract administration was able to lower colonic levels of IL-1beta and PGE (2). The comet assay revealed a decrease in DNA damage in isolated colonocytes, which may be connected to these anti-inflammatory effects [98].

6.6 **Ginkgo Biloba L.**

For thousands of years, *ginkgo biloba* L, a potential antioxidant, has been utilized to treat a wide range of illnesses. In 2008, several researchers investigated the possibility of using the standardized G. biloba extract (EGb 761) as an antioxidant to prevent and treat colitis in mice. They discovered that EGb 761 can be used to both prevent and treat mice colitis because it inhibits macrophage activation [99]. Others demonstrated how EGB's regulation of inflammatory mediators and antioxidation likely reduced inflammatory damage in rats with TNBS-induced colitis [100]. The extent and severity of ulcerative colitis were assessed in relation to the possible function of *Zingiber Officinale Roscoe* (Zingiberaceae) extract. The antioxidant and anti-inflammatory qualities of ginger extract may have contributed to its beneficial effect against acetic acid-induced ulcerative colitis, according to the results [101]. Because oxidative stress and GSH (glutathione) depletion are strongly linked to the pathological mechanism of UC, the protective effects of *Angelica sinensis* (Oliv.) *Diels* (Apiaceae) polysaccharides may be partially explained. Additionally, the protective effects of AS polysaccharides are closely linked to the prevention of oxidative stress, which may occur during neutrophil infiltration in the pathological process of UC [102]. The impact of *Rheum tanguticum Maximex Balf.* (Polygonaceae) polysaccharide (RTP) on human intestinal

epithelial cell damage caused by hydrogen peroxide was investigated. It was discovered that pretreatment of the cells with RTP could considerably increase cell survival and SOD activity while lowering MDA, LDH activity, and cell apoptosis. By preventing cell necrosis and apoptosis, RTP may have cytoprotective and antioxidant effects against intestinal epithelial cell damage caused by H_2O_2. This could be one among the ways that RTP treats ulcerative colitis in rats [103].

Ulcerative colitis has been successfully treated with green tea *Camellia sinensis* (L.) Kuntze, Theaceae). Green tea extract treatment can considerably reduce both diarrhea and weight loss. The mechanism of action was linked to a notable improvement in the disturbance of the colonic architecture, as well as a notable decrease in the generation of tumor necrosis factor-alpha (TNF-alpha) and colonic myeloperoxidase (MPO). Additionally, green tea extract decreased the colon's nitrotyrosine immunoreactivity and intercellular adhesion molecule 1 (ICAM-1) up-regulation [104].

The effectiveness and safety of aloe vera (*Aloe vera* (L.) *Burm.f.,* Xanthorrhoeaceae) leaf gel for the treatment of slightly to moderately active ulcerative colitis were investigated in a randomized, double-blind, placebo-controlled experiment. According to the results, taking oral aloe vera for four weeks reduced the histology disease activity and seemed to be safe. It also generated a clinical response more frequently than a placebo [105]. Other researchers found that wheat grass (*Triticum aestivum* L., Poaceae) juice seemed safe and effective as a stand-alone or adjuvant treatment for active distal UC [106].

Furthermore, *Plantago ovata Forssk.* and Plantaginaceae (dietary fiber) seeds may be just as useful as mesalamine in keeping ulcerative colitis in remission [107]. D-002 is made up of a combination of higher aliphatic primary alcohols and is derived from beeswax. It was discovered that D-002 has strong antiulcerogenic and modest anti-inflammatory properties. Additionally, by lowering leukotriene (LTB 4) in the exudate, it protects the guinea pig against the pre-ulcerative stage of carrageenan-induced colonic ulceration. Furthermore, D-002 worked well to guard against or stop the harm caused by acetic colitis brought on by acid. When D-002 was given orally at doses of 25 and 50 mg/kg in both single and repeated experiments, the treated animals' wet weight, macroscopic damage, polymorphonuclear infiltration, and wall thickness in the colonic mucosa were significantly lower than those of the controls in both protective and therapeutic alternatives [108].

7. EFFECT OF TOTAL EXTRACTS

Alcohol (ethanol or methanol), ether, chloroform, ethyl acetate, n-butanol, and water are only a few of the solvents that have been employed to extract active ingredients from plants [109].

When the root of *Saussurea lappa* C.B. Clarke (Asteraceae) was extracted using ethyl acetate and tested for antiulcerogenic qualities at two oral doses of 200 and 400 mg/kg, it was discovered to exhibit cytoprotective action that prevented peptic ulcers [110]. At a dose of 300 mg/kg, the ethanol extract of *Zizyphus oenoplia* (L.) Mill. (Rhamnaceae) root has antiulcerogenic action with a mechanism that includes an increase in Flavonoids are likely responsible for this extract's antiulcer properties in prostaglandin production [111]. However, oral administration of aqueous extracts of its root bark (50–200 mg/kg), leaves (50–200 mg/kg), and fruits (200–400 mg/kg) produced a significant and dose-dependent inhibition to the acute ulcer caused by HCl/ethanol, indicating that *Zizyphus lotus* (L.) Lam. extracts function essentially as cytoprotective agents. However, at a dose of

200 mg/kg, the methanol, ethyl acetate, and chloroform leaf and root bark extracts significantly inhibited stomach lesions [112].

In acute ulcer induction models, the standardized extracts of *Quassia amara* L. (Simaroubaceae) bark called Lipro (4.9 to 48.9 mg/kg) and Ligas (4.0 to 39.7 mg/kg) shown a significant anti-ulcerogenic action. According to Garcia-Barrantes and Badilla (2011), their impact was linked to an increase in non-protein sulfhydril groups and gastrointestinal barrier mucus. The extraction process also employed 70% ethanol, 100% ethanol, 100% dichloromethane, and 100% HEX as additional solvents. Every extract was administered orally at a dose of 100 mg/kg. Their actions were linked to cytoprotective elements such prostaglandins and mucus [113].

The oral administration of ethanol extract of coconut seed (*Cocus nucifera* L., Arecaceae) at When compared to the control, the administration of a different dose (400 mg/kg) of the same extract enhanced the evidence of ulceration, but doses of 100 and 200 mg/kg demonstrated an ulcer inhibition of 65.4% and 67.9%, respectively [114]. The antiulcerogenic activity of an ethanol extract of the aerial portions of *Encholirium spectabile Mart.* (Bromeliaceae) was assessed following oral administration at a concentration of 100 mg/kg. The extract protected the stomach mucosa from ulcers by 53%, 75%, 52%, and 43%. that was brought on by four different models: ischemia/reperfusion, ibuprofen, ethanol/HCl, and absolute ethanol. This defense appears to be brought about via prostaglandins, the NO synthase pathway, and the activation of antioxidant mechanisms [115].

Using an aspirin-induced gastric ulcer model, the methanol extract of *Cissus quadrangularis* L., Vitaceae (CQE) was given orally to rats at a dose of 1000 mg/kg. The results showed protective benefits against stomach ulceration better than ranitidine at a dose of 30 mg/kg [116]. Rats were given oral dosages of 50, 100, 200, and 400 mg/kg of alcohol extract from the leaves of *Gynura procumbens* (Merr.), Asteraceae. It demonstrated strong defense against damage caused by ethanol. This protection was dose-dependent and peaked at 400 mg/kg [117].

Zingiber Officinale's gastroprotective properties the rhizome of *Roscoe* (Zingiberaceae) was extracted using 50% ethanol and given orally at doses of 50, 100, and 200 mg/kg. It was evaluated in rats using several stomach ulcer models, including ulcers caused by acetic acid and ethanol. The findings demonstrated that the extract inhibited the ulcer index in a dose-dependent manner and shielded the stomach mucosa from oxidative damage by preventing lipid peroxidation, lowering superoxide dismutase, and raising catalase activity [118]. Other workers proved that, the ethanol extract showed good protective effect against indomethacin-induced gastric ulcer model in the rats at doses of 100, 200 and 400 mg/kg (Anosike *et al.,* 2009). Furthermore, Agrawal *et al.* (2000) and Moshen *et al.* (2006) suggested that ginger extract possesses its anti-ulcer properties through augmentation of mucin secretion and decreased cell shedding rather than offensive acid and pepsin secretion. Petroleum ether, chloroform, ethanol, and water were used to extract the leaves of *Butea frondosa* (Roxb.), Fabaceae. The extracts were administered orally to mice at doses of 250 and 500 mg/kg. The extracts demonstrated protection against chronic gastric ulcers caused by 0.6 M HCl, with the chloroform extract exhibiting the highest activity at 250 mg/kg [119].

Three dosages (62.5, 125, or 250 mg/kg) of ethanol extract from *Parkia platycephala*

Benth. (Leguminosae) leaves shown gastroprotective efficacy against stomach damage caused by ethanol and ethanol-HCl, which may be partially mediated by the generation of nitric oxide. Additionally, it shows protection against ischemia-reperfusion-induced injuries and has an antioxidant impact by increasing catalase activity [120]. When *Anacardium humile St*. Hil. (Anacardiaceae) leaves are extracted using ethyl acetate extract and given orally to rats at a dose of 50 mg/kg, the gastric mucosa is significantly protected against absolute alcohol-induced ulcers. This protection may be caused by increased PGE2 and mucous production [121].

Red mangrove oral therapy A 500 mg/kg dosage of bark extract from *Rhizophora mangle* L. (Rhizophoraceae) resulted in a high degree of stomach protection. Proteins increased proportionately with mucus content (Sánchez *et al.,* 2001). Because of the veracity of its active principles, it possesses its activity through multiple ways. It increased PGE2 levels in a dose-dependent manner and demonstrated gastroprotective and antisecretory properties [122]. Thirunavukkarasu and colleagues employed lyophilized cold and hot water extracts at doses of 62.5 and 125 mg/kg in a model of NSAID-induced ulcer rats to investigate the gastroprotective efficacy of *Excoecaria agallocha* L. (Euphorbiaceae) bark. The findings showed that the extract improves mucosal defense and lowers acidity in the stomach regions [123].

When *Erythrina indica* L. (Febaceae) leaves were extracted using methanol and given orally to rats at doses of 125, 250, and 500 mg/kg, it was discovered that the leaves have notable antiulcer qualities. Both pylorus-ligated and indomethacin-induced ulceration models were used in the study. The presence of polyphenolic chemicals may be responsible for the observed effect [124].

Liquorice or Glycyrrhiza glabra L. (Fabaceae) leaves, roots and seeds were reported in folk medicine to possess antiulceogenic activity. The total alcohol extract of the seed given orally to rats at a dose of 200 mg/kg showed protection against alcohol mucosa damage appeared as a significant reduction in the ulcer index. In addition, ALP and TBARS were significantly reduced. Liquorice seed extracts have significant mucosal protective and antioxidant effects on the gastric mucosa in rats [125].

After pretreating mice with the ethanol extract at a concentration of 500 mg/kg orally, some researchers examined the antiulcerogenic efficacy of the resin derived from the bark of *Virola surinamensis* (Rol. ex Rottb.) *Kuntze* (Myristicaceae). When compared to mice administered with a vehicle, the extract prevented mucosal damage and decreased the development of gastric lesions caused by indomethacin, stress, and pylorus ligation (by 39%, 45%, and 31%, respectively) [126].

When the stem bark of *Combretum leprosum* Mart. & Eiche (Combretaceae) was extracted using ethanol and taken orally, it had anti-ulcerogenic and gastroprotective properties that were linked to an increase in mucosal defense factors and a suppression of stomach acid secretion [127].

Gymnosporia rothiana (Celastraceae) leaf extracts were assessed using ethanol and indomethacin-induced stomach ulcer models following oral administration of varying doses. In both experimental models, all extracts significantly decreased the ulcer lesion index while increasing the volume and pH of the stomach liquid. The most successful extracts were methanol extract (500 mg/kg) and petroleum ether extract (250 mg/kg). The petroleum ether extract works by boosting the defense of the stomach mucosa (prostaglandin and free radical scavenging), which is explained by

its high levels various terpenoids, including friedelin, lupeol, and β amyrin (Jain and Surana, 2009a). Similarly, Spathodea falcate (Bignoniaceae) bark extracts in petroleum ether, chloroform, and methanol at dosages of 250 and 500 mg/kg exhibit cytoprotective effects against the same animals and have the same mechanism of action [128].

When given orally to rats at a dose of 800 mg/kg, UlGen—a polyherbal formulation primarily made up of *Glycyrrhiza glabra* L. (Fabaceae; Root), *Saussurea lappa* C.B. Clarke (Asteraceae; Root), *Aegle marmelos* (L.) *Corr.Serr.* (Rutaceae; Fruit), and *Santalum album* L. (Santalaceae; Stem)—significantly prevented the development of ulcers caused by cold resistance stress. Additionally, it strongly prevented aspirin and alcohol-induced stomach ulcers. This product's cytoprotective impact could be explained by strengthening the defensive mechanism through improved gastric cytoprotection and acid inhibition [129].

Oral administration of *Terminalia chebula* Retz. (Combretaceae) fruit extract at doses of 250 and 500 mg/kg significantly inhibited the gastric lesions caused by pylorus ligation and ethanol-induced gastric ulcers, possibly as a result of its antisecretory effect [130]. Mice who received an oral dose of 400 mg/kg of *Matricaria chamomilla* L. (Asteraceae) flower aqueous extract did not develop stomach ulcers (Karbalay-Doust and Noorafshan, 2009). Others reported that rats given oral dosages of 1000 and 3000 mg/kg of Lasianthera Africana P. Beauv. (Icacinaceae) leaves suppressed ethanol-induced, indomethacin-induced, and reserpine-induced ulcer models in a dose-dependent manner [131].

In rats, an ethanol extract of the leaves of *Morus alba* L. (mulberry), Moraaceae, was discovered to have strong anti-ulcerogenic properties. Animals pretreated with plant extracts orally at 250 mg/kg and 500 mg/kg doses shown a significant decrease in stomach mucosal damage, edema, and leucocyte infiltration of the submucosal layer using an absolute ethanol-induced ulcer paradigm. *M. alba* extracts have a direct protective impact on damage to the stomach mucosa, and this plant's gastroprotective function may be attributed to its anti-inflammatory and antioxidant qualities [132].

The ethanol extracts of five plants, namely Croton zehntneri Pax & K. Hoffm. (Euphorbiaceae; essential oils from leaves), *Vanillosmopsis arborea* (Gardner) Baker (Asteraceae; essential oils from bark), *Caryocar coriaceum* Wittm. (Caryocaracea; oil from fruit pulp), *Himatanthus drasticus* Mart. Plumel (Apocynaceae; latex), and *Stryphnodendron rotundifolium* Mart. (Fabaceae; leaves), were tested at doses of 200 and 400 mg/kg. The findings showed revealed the extracts have anti-ulcer action, which could be linked to the plants' cytoprotective qualities or antacid effect. Additionally, tannins, terpenes, and fatty acids may be the cause of these plants' inhibitory impact (Oliveira *et al.,* 2009). Several models were used to investigate the antiulcerogenic properties of *Mentha arvensis* L. (Lamiaceae) leaves. The plant was extracted using various solvents (petroleum ether, chloroform, and water) and administered orally to rats at a dose of 375 mg/kg. In ibuprofen plus pyloric ligation, 0.6 M HCl-induced, and 90% ethanol-induced ulcer models, the results demonstrated a protective effect against acid secretion and gastric ulcers [133]. It has been suggested that the fruit of *Carica papaya* L. (Caricaceae) may be useful in treating stomach disorders. Rats were given an oral dose of 400 mg/kg of the aqueous extract, which decreased the ulcer index. Carica papaya may work by scavenging free radicals to provide gastroprotection [134].

Rats were given oral dosages of 0.5, 1, and 2 g/kg of the methanol and aqueous extracts of *Coccinia grandis* Linn. (Cucurbitaceae) leaves. The antiulcerogenic ability of these extracts was tested using an aspirin-induced gastric ulcer model. In addition to their antioxidant qualities, the extracts demonstrated a notable dose-related antiulcer effect that may be linked to increased mucus secretion (Mazumder *et al.,* 2008). However, Polyalthia longifolia (Sonn.) *Thwaites* (PL) leaves were found to have a strong anti-ulcer effect(Annonaceae) when extracted with ethanol and given to animals in various models at a dose of 300 mg/kg (aspirin plus pylorous ligation generated stomach ulcer in rats, HCl–ethanol induced ulcer in mice, and water immersion stress induced ulcer in rats) [135].

Rats with ethanol-induced stomach ulcers may benefit from the cytoprotective effects of *Linum usitatissimum Linnaeus* (flaxseed), Linaceae, oil and mucilage. The number and duration of stomach ulcers were considerably decreased in rats pretreated with oral flaxseed oil at a dose of 5.0 ml/kg and flaxseed mucilage at a dose of 10.0 ml/kg. When it came to lowering the amount of ulcers, the oil outperformed the mucilage (Dugani *et al.,* 2008). Rats were administered aqueous extract of *Strychnos potatorum* Linn (Loganiaceae) seeds at dosages of Antiulcerogenic action was demonstrated at 100 and 200 mg/kg. The aspirin plus pyloric ligation-induced gastric ulcer model was used to investigate this action. The findings demonstrated that the extract inhibited the development of ulcers by lowering acid secretory activity and raising mucin activity, which may have been caused by the presence of mucilaginous polysaccharides called mannogalactans [136].

Two plants To investigate their antiulcerogenic properties, the bark of *Ceiba pentandra* G. (Bombacaceae) and the leaves of *Helicrysum mechowianum* Klatt (Asteraceae) were extracted with water and given orally to rats at a dose of 400 mg/kg. Both extracts markedly lowered the pH and the indomethacin-induced lesion development [137].

Ethanol was used to extract clove (the dried flower buds of *Syzygium aromaticum* L. (Myrtaceae)), and n-butanol was then used to extract the ethanol extract. When administered subcutaneously to rats using an indomethacin-induced stomach ulcer model, the n-butanol part showed anti-ulcerogenic and antisecretory effects at doses of 50, 100, and 200 mg/kg. Tannins and flavonoids included in the extract enhanced the activity [138].

Ethanol extract from the leaf gel of *Aloe vera* (L.) Burm.f. (Xanthorrhoeaceae) has been shown to be beneficial for both acute and chronic stomach ulcers. The development of lesions caused by two models (indomethacin and ethanol-induced gastric lesions) is prevented by pretreatment with Aloe vera leaf gel extract (150 mg/kg). Additionally, in the treatment of chronic ulcers, the extract dramatically increased the amount of glycoprotein in gastric juice and significantly decreased the ulcer index and ulcerated area after 15 days of treatment. Defensive mucosal factors may mediate this gastroprotective action. Additionally, histological research has demonstrated the *Aloe vera* leaf gel extract's ability to treat ulcers [139].

Using HCl/ethanol-induced and indomethacin/bethanechol-induced ulcer models in mice, the flavonoid-rich fraction extracted from the methanol extract of *Orostachys japonicus* A. Berger (Crassulaceae) was investigated for its anti-ulcerogenic activities. At a dose of 100 mg/kg, the fraction significantly decreased the diameter of gastric lesion (Jung *et al.,* 2007).

Using two ulcer models (ethanol-induced and pylorus ligation plus aspirin-induced), Shrivastava and colleagues assessed the antiulcer activity of *Adhatoda vasica Nees* (Acantheceae) leaves. They concluded that the plant has enormous potential as an antiulcer agent of great therapeutic relevance (Shrivastava *et al.,* 2006). Other employees examined the *Tripleurospermum disciforme* Shultz Bip (Asteraceae) flowers are extracted hydroalcoholically. The extract demonstrated a protective effect against ulcer formation in pyloric ligation when given orally to rats at 500 and 2000 mg/kg doses, with a significant reduction in ulcer area and ulcer index. The activity did not appear to be mediated through acid reduction [140].

Iberis amara L. (Brassicaceae), *Melissa officinalis Linnaeus* (Lamiaceae), *Matricaria recutita* L. (Asteraceae), *Carum carvi* L. (Apiaceae), *Mentha piperita* (Lamiaceae), *Glycyrrhiza glabra* L. (Fabaceae), *Angelica archangelica* L. (Apiaceae), *Silybum marianum* (L.) *Gaertn*. (Asteraceae), and *Chelidonium majus* L. (Papaveraceae). Every extract generated a dose-dependent action linked to a decrease in leukotrienes, an increase in prostaglandin E_2 release, a decrease in acid production, and an increase in mucin secretion. The extracts' ability to scavenge free radicals and their flavonoid concentration may contribute to their cytoprotective action (Khayyal et al., 2001). The findings of additional research on the same product showed that STW 5 was more successful in preventing secondary hyperacidity in addition to lowering gastric acidity as effectively as commercial antacids. Additionally, STW 5 was able to diminish the generation of stomach acid while simultaneously suppressing the serum gastrin level in rats [141].

Jainu and Shyamala (2006) used cold restraint stress, indomethacin, pyloric ligation, and ethanol-induced gastric ulcer models to study the antiulcer effect of *Solanum nigrum* L. (Solanaceae) fruit extract (SNE). They also used an acetic acid-induced ulcer model in rats to assess the ulcer healing activity. They discovered that SNE had both antiulcerogenic and ulcer-healing qualities, which may be related to its antisecretory action. The stomach lesions caused in many animals were considerably reduced by oral administration of the methanol extract at doses of 200 and 400 mg/kg. By inhibiting H(+)K(+)ATPase and reducing gastrin release, the extract provides antiulcer action by preventing acid secretion. Hydroethanol was used to extract the leaves and bark of *Alchornea castaneaefolia* (Bonpl. ex Willd.) *A. Juss*. (Euphorbiaceae). The antiulcerogenic qualities of both extracts were investigated at doses of 500 and 1000 mg/kg for leaves and 1000 mg/kg for bark. The findings demonstrated that both extracts considerably lessened the severity of stomach damage formation caused by indomethacin/bethanechol in mice as well as the gastrointestinal injuries caused by the combination of HCl/ethanol. In rats with persistent stomach ulcers caused by acetic acid, leaf extract was similarly successful in accelerating the healing process. Furthermore, stomach lesions caused by HCl/ethanol and indomethacin/bethanechol were lessened by an enhanced flavonoid fraction derived from leaf extract. in mice at a dose of 100 mg/kg [142].

Several models, including ethanol, piroxicam, hypothermic restraint stress, and pylorus ligature, were used to assess the antiulcerogenic activity of *Indigofera truxillensis Kunth* (Fabaceae) in mice and rats. In every experiment, the stomach lesions were suppressed by the aerial parts' methanol extract at dosages of 250, 500, and 1000 mg/kg. The findings indicated that the presence of flavonoids found by

phytochemical analysis may be connected to the methanol extract's antisecretory and cytoprotective properties [143].

Certain plant extracts were tried to demonstrate their antiulcerogenic properties using rats with stomach ulcers caused by ethanol and aspirin. The average ulcer index was considerably reduced when *Bidens bipinnata* L. (Asteraceae), *Zygophyllum album* L. (Zygophyllaceae), *Plantago major* L. (Plantaginaceae; leaves), and *Schouwia thebaica Webb* (Brassicaceae) methanol extracts were administered orally at a dose of 400 mg/kg. Furthermore, although they were less effective, *Mentha microphylla* C. Koch (Labiatae), *Conyza linifolia* (Willd.) Těh. (Asteraceae), *Conyza dioscoridis* (Linn) Desf. (Asteraceae), *Cynanchum acutum* Linn. (Asclepiadoideae), and *Plantago major* L. (Plantaginaceae; seeds) all reduced the ulcer index [144].

When administered orally to rats at a dose of 1000 mg/kg, the hydroalcohol extract of the aerial portions of *Trixis divaricata Spreng* (Asteraceae) shown notable anti-ulcerogenic efficacy. Two models of ulcer induction indomethacin and absolute alcohol were used to demonstrate this activity. The hydroalcohol extract's phytochemical screening revealed flavonoids and tannins, which may be the cause of the impact [145].

Three distinct extracts were used to assess the antiulcerogenic action of *Byrsonima crassa Niedenzu* (IK) (Malpighiaceae) leaves: hydromethanol (80% MeOH), methanol (MeOH), and chloroform ($CHCl_3$) extracts. When these extracts were given orally to mice at doses of 250, 500, and 1000 mg/kg, the development of lesions linked to the administration of ethanol and HCl was decreased [146].

When administered orally at doses of 200, 400, 800, and 1200 mg/kg, the aerial parts of *Zataria multiflora Boiss.* (Lamiaceae) hydroalcohol extract were found to be a powerful antiulcerogenic agent, significantly reducing ulcerated area and index in a dose-dependent manner in a model of duodenum ulcers induced by cysteamine HCl (Minaiyan *et al.,* 2005). *Pausinystalia macroceras* (K. Schum.) *Pierre ex Beille* (Rubiaceae; stem-bark) methanol extract decreased the ulcer indices caused by ethanol, reserpine, and indomethacin in a dose-dependent manner (17.5–350 mg/kg). It may have an antiulcerogenic action because it blocks the H_2 receptor, protecting the rat stomach mucosa from damage caused by oxygen-derived free radicals (Nwafor et al., 2005). In an absolute ethanol-induced ulcer model, pretreatment with an aqueous extract of *Ageratum conyzoides* L. (Asteraceae) leaves at doses of 250 and 500 mg/kg considerably decreased the development of stomach lesions and markedly decreased submucosal edema [147].

When given at doses of 50, 100, and 200 mg/kg following ulcer induction, D-002 or (Abexol), a combination of higher aliphatic primary alcohols derived from beeswax, effectively healed both acute and chronic stomach ulcers [148].

Ocimum sanctum Linn. (Labiatae) fixed oil demonstrated a strong antiulcer effect; aspirin, indomethacin, and alcohol-induced ulcer models were used to study the mechanism of action, which may have been caused by the inhibition of 5-lipooxygenase. However, its antihistaminic, anticholinergic, and antisecretory qualities were responsible for the antiulcer efficacy in histamine, reserpine, and stress-induced ulcer models (Singh and Majumdar, 1999). Additionally, the same plant's ethanol leaf extract at a concentration of 100 mg/kg decreased acid output and may have increased the mucoprotective effect [149].

Rats with gastroduodenal mucosa injuries brought on by pyloric ligation, hypothermic-restraint stress, indomethacin, reserpine, and cysteamine showed notable anti-ulcerogenic

efficacy when given an oral dose of 500 mg/kg of the ethanol extract of turmeric (*Curcuma longa* Linnaeus, Zingiberaceae). It greatly raised the amount of mucus on the stomach wall and restored the amount of non-protein sulfhydryl (NP-SH) in the rats' glandular stomachs [150].

8. ANTI *H. PYLORI* NATURAL PRODUCTS

The use of synthetic antimicrobials, such as the currently approved antibiotics clarimycin and amoxicillin, to eradicate *H. pylori* has limits because of limited compliance and the possibility of resistance developing [151].Therefore, new studies on natural compounds with anti-H. pylori action have been created. The anti-*H. pylori* activity of compounds (2-methoxy-1, 4-naphthoquinone (1) and stigmasta-7,22-diene-3β-ol (2)) derived from *Impatiens balsamina* L. (Balsaminaceae) was assessed. For *H. pylori* resistant to antibiotics (clarithromycin, metronidazole, and levofloxacin), the minimum inhibitory concentrations (MICs) and minimum bactericidal concentrations (MBCs) were 0.156–0.625 and 0.313–0.625 μg ml−1, respectively, for (1) and 20–80 μg ml−1 for (2). Compound (1) had an action comparable to amoxicillin (Yuan-Chuen *et al.,* 2011). The *in vitro* growth of *H. pylori* was inhibited by the ethanol extracts of *Bixa orellana* L. (Bixaceae) seed, *Chamomilla recutita* L. (Asteraceae) inflorescence, Ilex *paraguariensis A*. (Aquifoliaceae) leaves, *Malva sylvestris* L. (Malvaceae) inflorescence & leaves, *Plantago major* L. (Plantaginaceae) aerial parts, and *Rheum rhaponticum* L. (Polygonaceae; Root) [151].

From the peel extract of *Malus domestica Borkh*., Rosaceae (Golden Delicious Apple), seven carotenoids were identified: (all-E)-luteoxanthin, (all-E)-neoxanthin, (9′Z)-neoxanthin, (all-E)-antheraxanthin, (all-E)-violaxanthin, (9Z)-violaxanthin, and (all-E)-lutein. Where only With MIC50 values of 7.9, 11, and 27 μg/mL, respectively, (all-E)-luteoxanthin, (all-E)-neoxanthin, and (9′Z)-neoxanthin demonstrated strong anti-*H. pylori* action [152].

Enantia chlorantha Oliv. (Annonaceae) stem bark aqueous extract has anti-*H. pylori* properties both in vitro and *in vivo.* The activity in vitro was dose-dependent. The extract's ability to eradicate *H. pylori in vivo* was evaluated using *H. pylori*-infected mice. Mice given *E. chlorantha* extract at dosages of antral mucus sample cultures 500 and 1000 mg/kg for 3 days did not yield any growth [153].

Nigella sativa L. (Ranunculaceae) seeds had clinically beneficial anti-*H. pylori* action when administered at a dose of 2 g/d in combination with 40 mg/d omeprazole to patients with dyspeptic symptoms who tested positive for H. pylori infection. Although the H. pylori eradication rate attained with the doses of 1 g/d and 3 g/d of *N. sativa* was comparable to that obtained with a single antibiotic, both doses were less effective (Salem *et al.,* 2010). Additionally, *N. sativa* extract demonstrated a 100% inhibition of the growth of all tested strains of H. pylori within 60 minutes in an *in vitro* research [154].

The effects of extracts from *Solanum lyratum Thunb*. (SLE), *Solanum erianthum* D. Don, and *Solanum torvum Sw.* (Solanaceae) against *H. pylori* were examined. SLE demonstrated a moderate capacity to prevent H. pylori from growing and to disrupt the bacterial attachment to host cells. Therefore, by down-regulating *H. pylori* in the affected gastric epithelium, SLE may provide a novel strategy for treating the infection. Treatment for SLE may not result in the emergence of resistant strains because it does not directly target microorganisms (Hsu *et al.,* 2010a, Hsu *et al.,* 2010b). However, Japanese apricot (Prunus mume Siebold & Zucc., Rosaceae) consumption has been shown to prevent

chronic atrophic gastritis by preventing H. pylori infection and lowering active mucosal inflammation [155].

A crude methanol extract prepared from Brassica oleracea L., Brassicaceae (fresh broccoli sprout) was extracted with hexane, chloroform, ethyl acetate, and butanol sequentially. Residual water fraction was obtained from the residual aqueous layer. The greatest inhibition zones (>5 cm) were noted for the chloroform extract followed by the hexane, ethyl acetate, butanol and the crude methanol extracts by (5.03 cm, 4.90 cm, 3.10 cm and 2.80 cm, respectively), whereas the residual water fraction did not show any inhibition zone. From the chloroform extract 18 sulforaphane, five sulforaphane-related compounds were positively identified (six amines, six isothiocyanates, and six nitriles), two amines, six isothiocyanates, and one nitrile exhibited >5 cm inhibitory zones for *H. pylori* strain [156].

When *Apium nodiflorum* L. (Apiaceae) essential oil was tested in vitro against H. pylori, the MIC value was found to be 12.5 µg/ml (Menghini *et al.,* 2010). Aceton extract from the fruit of *Feijoa sellowiana O. Berg* (Myrtaceae) has strong antibacterial properties against H. pylori. The active ingredient in *F. sellowiana* fruits was flavone, which had strong antibacterial activity against H. pylori that was noticeably greater than that of metronidazole [157].

The impact of pure mastic gum (*Pistacia lentiscus* L., Anacardiaceae) on *H. pylori* eradication in patients with an *H. pylori* infection was investigated in a randomized pilot study. Fifty-two patients were randomly assigned to receive either 350 mg of pure mastic gum three times a day (tid) for 14 days (Group A), 1.05 g of pure mastic gum tid for 14 days (Group B), pantoprazole 20 mg bid plus amoxicillin 1 g bid plus clarithromycin 500 mg bid, or pantoprazole 20 mg bid plus pure mastic gum 350 mg tid for 14 days (Group C). for ten days (Group D). Five weeks after the eradication regimen was finished, H. pylori eradication was evaluated. Four out of thirteen patients in Group A and five out of thirteen in Group B had their H. pylori eradication confirmed [158].

Every part of *Impatiens balsamina* L., Balsaminaceae, including the root, stem, leaf, seed, and pod, showed bactericidal action against H. pylori. The MIC and MBC of the pod extract were considerably lower (1.25–2.5 and 1.25–5.0 µg/ml, respectively). Strong anti-*H. pylori* activity was demonstrated by the acetone and ethyl acetate pod extracts. This activity was comparable to amoxicillin and higher than that of metronidazole [159].

Glycyrrhiza glabra L. (Fabaceae) aqueous extract (1 mg/ml) dramatically reduced *H. pylori's* ability to adhere to human stomach tissue. One pure acidic fraction was identified as the primary active polymer, and this effect was associated with the polysaccharides extracted from the extract. According to Wittschier *et al.* (2009), purified polysaccharides had no effect on hemagglutination or direct cytotoxic effects against *H. pylori*. According to a previous study, licorice extract inhibited *H. pylori* strains in vitro with a minimum inhibitory concentration (MIC) of 50–400 mg/ml (Jafarian and Ghazvini, 2007). Furthermore, three novel isoflavonoids were extracted from the methanol extract (3-arylcoumarin, pterocarpan, and isoflavan) with a pyran ring, gancaonols A–C, were isolated together with 15 known flavonoids. Among these compounds, vestitol, licoricone, 1-methoxyphaseollidin and gancaonol C exhibited anti-H. pylori activity against resistant strains [160].

Tephrosia purpurea (Linn.) Pers. (Fabaceae) methanol extract demonstrated encouraging effectiveness against standard strains and

clinical isolates of *H. pylori,* including those resistant to metronidazole. The extracts of n-hexane and chloroform showed significant activity [161].

With a minimum inhibitory concentration (MIC) of 40 µg/ml, the methanol extracts of *Desmostachia bipinnata* (L.) Stapf (Gramineae), sometimes referred to as Al-Hagnah, were found to be effective against *H. pylori*. Following the methanol extract's fractionation (using diethylether, chloroform, ethyl acetate, and butanol in that order), the ethyl acetate fraction showed outstanding anti-*H. pylori* activity. From this, a flavonoid compound (4′-methoxy quercetin-7-O-glucoside) was isolated and tested against *H. pylori*; the MIC value was 62 µg/ml[162].

9. CONCLUSION

According to a World Health Organization (WHO) estimate, between 85 and 90 percent of people worldwide use traditional herbal remedies. India's herbal health care and personal care market is thought to be worth between Rs 2500 and three thousand crores. As these numbers continue to climb, so does the number of fatalities and other adverse effects brought on by the usage of herbal remedies. In essence, pharmacognosy is the research, standardization, and verification of natural medications. It works closely with related subjects, such as toxicological screening of natural materials and phytochemistry. This review cover all the medicinal plants part traditionally used in treatment of ulcer and also elaborates the extract of plant parts which used for the antiulcer properties with the evidence present as pee literature.

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