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Review Article

SYNERGISTIC IMPACT OF HERBAL MEDICINE IN PEPTIC ULCER

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ABSCTACT

Up to 10% of people worldwide are affected by a chronic condition known as peptic ulcer. Peptic ulcer development is influenced by the pH of gastric juice and a decline in mucosal defences. *Helicobacter pylori (H. pylori)* infection and non-steroidal anti-inflammatory medicines (NSAIDs) are mucosal resistance to the damage being affected by two main elements. Conventional peptic ulcer therapy, Histamine-2 (H2) receptor antagonists, and proton pump inhibitors (PPIs) have shown negative consequences, relapses, and different medication combinations. Contrarily, therapeutic herbs and many illnesses may be prevented and treated with the help of their chemical ingredients. Hence, in this study, common medicinal plants that may be utilized for healing or preventing stomach ulcer diseases are presented.

Key words*: Helicobacter pylori* infection, Peptic ulcer therapy, Healing.

INTRODUCTION

A peptic ulcer is an acid-induced digestive tract lesion characterized by denuded mucosa with the defect spreading into the submucosa or muscularispropria. It commonly occurs in the stomach or proximal duodenum. [1]. The incidence of peptic ulcer disease occurs in 5–10% of the population [2], but recent epidemiological studies have revealed a decline in the prevalence. Peptic ulcers are linked to higher rates of hospitalization and death [3,4]. This is most likely due to the advent of new medicines and better cleanliness, both of which have resulted in a decrease in Helicobacter pylori (H. pylori) infections. Mucosal disruption has traditionally been thought to be a sign of acid peptic illness, a hypersecretory acidic environment in combination with dietary variables or stress. Nonsteroidal anti-inflammatory medications (NSAIDs) and Zollinger–Ellison syndrome are both linked to peptic ulcers [5].H. pylori infection and NSAID usage are the two primary risk factors for gastric and duodenal ulcers [6]. Individual susceptibility is crucial in the early stages of mucosal injury since only a small percentage of patients infected with H. pylori or using NSAIDs develop peptic ulcer disease. Functional polymorphisms in numerous cytokine genes have been associated to peptic ulcers. For example, polymorphisms in the interleukin 1 beta (IL1B) gene affect mucosal interleukin 1 manufacturing, resulting in H. pylori-related gastroduodenal diseases [7].

NSAID users, on the other hand, have a four-fold higher risk of peptic ulcer complications, and aspirin users have a two-fold higher risk [8].The use of anticoagulants, corticosteroids, and selective serotonin reuptake inhibitors with NSAIDs or aspirin increases the risk of upper gastrointestinal bleeding [9]. Despite the fact that many individuals who use NSAIDs or aspirin also have H. pylori infection, the involvement of these medicines in the aetiology of peptic ulcer disease is still a point of contention. NSAIDs, aspirin, and H. pylori infection all increase the risk of peptic ulcer disease, according to a meta-analysis of observational studies [10].

Pathogenesis of Peptic Ulcer:

H. pylori is still one of the most common causes of peptic ulcer disease, infecting more than half of the world's population [11].In underdeveloped nations, such as Africa, Central America, Central Asia, and Eastern Europe, the frequency of H. pylori is greater [12]. The organism is most commonly acquired during childhood in a filthy and crowded setting, most commonly in nations with lower socioeconomic standing. The inflammatory response, including neutrophils, lymphocytes, plasma cells, and macrophages, caused by H. pylori causes epithelial cell destruction and degeneration, which is especially serious in the antrum.The mechanism by which H. pylori causes distinct types of lesions in the gastroduodenal mucosa is not completely understood. Whether H. pylori infection generates hypochlorhydria or hyperchlorhydria determines the kind of peptic ulcer.H. pylori infection is mostly caused by cytokines that diminish parietal cell secretion, but it may also affect the H+/K+ ATPase -subunit, activate calcitonin gene-related peptide (CGRP) sensory neurons, and inhibit gastrin production [13].Despite the fact that hyposecretion has been associated to stomach ulcer formation,10–15 percent of H. pylori patients had increased gastric secretion as a result of hypergastrinemia and lower antral somatostatin levels [14]. This results in increased histamine release and, as a result, increased acid or pepsin secretion from parietal and stomach cells. Furthermore, H. pylori eradication causes a reduction in gastrin mRNA expression while increasing somatostatin mRNA expression [15]. In the majority of instances, gastric ulcers are associated with hypochlorhydria and mucosal atrophy. In the majority of instances, gastric ulcers are associated with hypochlorhydria and mucosal atrophy.

Mainpathophysiologicalmechanismsandthesitesofactionofantiulcertreatmentareshownin theFigure 1.

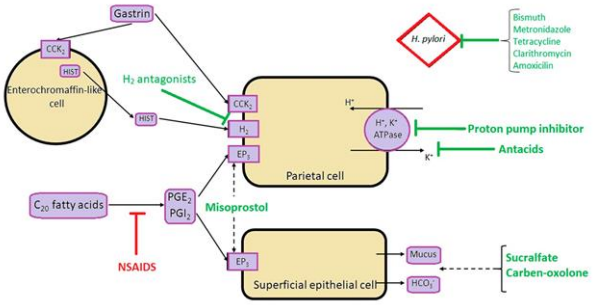

Fig.1:The primary pathophysiological pathways involved in the development of peptic ulcer disease, as well as the sites of action of the most often used pharmaceutical alternatives for treating peptic ulcer disease, are depicted schematically. CCK2 stands for cholecystokinin receptor 2; PGE2 stands for prostaglandin E2; PGI2 stands for prostaglandin I2; EP3 is for prostaglandin E receptor 3; HIST stands for histamine.

EFFICACY OF HERBAL MEDICINES

Animal Model

In animal models, herbal remedies have been demonstrated to be beneficial in treating stomach ulcers produced by NSAIDs, ethanol, cold-restraint stress, pylorus ligation, and erosive agents. Herbal medications' therapeutic efficacy varies based on how they are manufactured and utilized in each model.

NSAID-induced gastric ulcer model

The development of a stomach ulcer is a common NSAID adverse effect. As a consequence, they're often used to generate stomach ulcer, animal models. A single dose of oral indomethacin in rats may produce stomach ulcer-like damage that lasts for up to three days[16,17]. The macroscopic damage score was reduced by more than 60% after a three-day oral intake of Myristicamalabaricaextract [16]. In a rat model of indomethacin-induced stomach ulcer, oral Piper betel extract at a dosage of 2 mg/kg per day for 7 days substantially decreased ulcer index [18]. It works similarly to misoprostol, a common anti-ulcer medication. As per Mehrabani et al [19], oral Teucriumpolium extract reduced ulcer index by more than 90% in just 24 hours.Similarly, a seven-day oral therapy with Phyllanthusemblica fruit extract decreased ulcer index by 79.39%[20]. Furthermore, oral beeswax extract for 5 days dramatically in a rat model, ulcer healing was accelerated [21]. This study suggests that herbal remedies may be beneficial in the treatment of NSAID-induced stomach ulcers.Gastric ulcer model caused by acetic acid:In the acetic acid induce stomach ulcer model, oral Qualea grandiflora extract was administered.once daily for 14 days accelerated once daily for 14 days accelerated ulcer healing (ulcer area6.86 1.46 mm 2 for control, 1.13 1.3 mm 2 for Qualea grandiflora extract, and 1.63 1.11 mm 2for Cimetidine) [22]. Only 3 days of oral Centella asiatica in a dose- dependent manner, hastened ulcer healing [23]. In an acetic acid-induced stomach ulcer model, Dharmani etal[24] found that oral treatment with Ocimum sanctum Linn at a daily dose of 100mg/kg for10 days had the same ulcer healing efficiency as omeprazole medicines. Herbal medicines areeffective in terms of effectiveness and may occasionally outperform medicines.OralAlchorneaglandulosa extract was shown to be more efficacious than cimetidine at a dose of250 mg/ kg per day for 14 days [25]. Additionally, oral administration of an herbalcombination extracts enhanced ulcer healing and reduced recurrence rates [26]. In both normaland type 2 diabetes mellitus rats, oral Bacopa monniera or Azadirachtaindica extract for 5days improved stomach ulcer healing [28]. Herbal extracts' efficacy in healing ulcers varydepending on molecular size. In the treatment of acetic acid-induced stomach ulcers,Chitosan with a smaller molecular weight is more effective than chitosan with a highermolecular weight [29]. Rats were administered oral Salvia miltiorrhiza at 840mg/d for 5 days,then 410 mg/d for 25 days after a stomach ulcer was created. As a positive control, cimetidinewas utilized. Cimetidine treated rats showed a lower ulcer index than Salvia miltiorrhiza-treated rats. The ulcer has improved much more three months after treatment with Salviamiltiorrhiza [30]. Other ulcer models include:

Through oxidative stress, water immersion constraint stress causes the establishment of astomach ulcer [31, 32]. In stomach ulcer models caused by water immersion restraint stress,oral extracts of different herbal mixes for 3 hours significantly decreased ulcer indictors,according to Ohta et al [32]. Ina pylorus ligation- induced stomach ulcer model, oralcurcumin reduced ulcer indices in a dose-dependent manner [33]. These finding shows thatherbal extracts of single components or mixes can help in curing stomach ulcers.

Patients with gastric ulcer

For years, human stomach ulcers have been treated with natural remedies. In multiple controlled clinical trials, herbal drugs have been demonstrated to be effective in the treatment of human stomach ulcers. He et al[34] found that after taking a herbal mixture three times daily for six weeks, > 86 percent of patients with stomach ulcers improved. In patients with stomach ulcers, oral herbal mixes taken two or three times daily for two months resulted in a > 90% improvement[35,36].Oral herbal treatments relieved clinical symptoms in as little as three days[37]. In the treatment of stomach ulcers, herbal drugs are just as efficient as famotidine, a histamine H2-receptor blocker [38]. In investigations, herbal medicine was shown to be comparable to or superior than cimetidine in the treating of gastric [39-42] and duodenal [49,50] ulcers.Oral herbal remedies were shown to be more effective than cimetidine is used to treat ulcers in the stomach and duodenum, as well as gastritis.in one investigation.Additionally, combining herbal therapy with ranitidine has a synergistic impact in the treatment of stomach ulcers [51-53]. Herbal medications efficiently treat and prevent the recurrence of stomach ulcers. one study discovered that using oral herbal medicines results in a 62.4 percentage cure rate, with a 17.7 percent recurrence rate after a year of follow-up. Treatment with ranitidine, on the other hand, only yielded a 50.7 percent cure rate and a 54.1 percent recurrence rate [54]. Similarly, following 6 months of follow-up,when compared to omeprazole alone, an oral combo of omeprazole plus herbal treatment dramatically reduced stomach ulcer risk of recurrence (by 25%). (57.1 %) [55].These findings suggest that herbal medicines are efficient in healing stomach ulcers and avoiding recurrence when used alone. In the treatment of stomach ulcers, a synergistic effect is achieved when herbal drugs and conventional treatments are used together.

Efficacy and safety of herbal medicines for gastric ulcer

Healing effect of *Piper betel*: The rats were given ulceration caused by a single dose of indomethacin (30 mg/kg body mass, oral intubation) diluted in purified water.Before ulcer induction, the rats were given no food but were given unrestricted access to tap water for 24 hours.APCfor 7 days, oral intubation was used to administer (5, and 10 mg/kg body weight) once daily commencing 4 hours after indomethacin delivery to standardise medication dosage. Each dose was given to five rats, and the experiment was repeated three times. The macroscopic damage scores were used to determine the amount of repair.The levels of these enzymes in stomach tissue were likewise decreased after indomethacin treatment. When compared to normal control rats, SOD activity was lowered by 74%, while CAT activity was reduced by roughly 57%. Treatment with APC raised SOD activity to near normal levels (P 0.05) (21.1 U/min versus 22.2 U/min per mg protein in normal rats), whereas CAT levels recovered 90% (P 0.05). Possible mechanism through which *Piper betel* shown its effect is by increasing mucus content and due to its antioxidant effect[18].

Healing effect of*Centella asiatica*extract: As previously described luminal usage of acetic acid induced gastric kissing ulcers. Rats were deprived for 24 hours before having their stomachs exposed under ether anaesthesia. A pair of metal rings with an internal diameter of 11 mm clamped the stomach's anterior and posterior walls. A 0.12 ml acetic acid solution (60 present v/v in distil water) was injected into the strapped fraction and withdrawn 45 seconds later into the syringe. The abdomens were then closed, and the rats were given free access to water and food to recover.Rats were given CE (0.05 g/kg, 0.10 g/kg, and 0.25 g/kg) or AC (1 mg/kg, 5 mg/kg, and 10 mg/kg) in distilled water for 3 or 7 days following kissing ulcer induction, and then slaughtered on day 4 or day 8, respectively. Rats in the ulcer control group were given distilled water in the same way. The ulcers were traced onto a translucent sheet after the stomachs were removed. Measuring the number of 1mm squares covered by the ulcer tracing on grid paper was used to calculate the ulcer area. Gastric ulcer tissues were retrieved and frozen in liquid nitrogen before being stored at -70°C until utilised for bFGF Western blot analysis. The ulcerated gastric tissues were also taken and preserved in 10% buffered formalin for histological and immunohisto-chemical examination. Possible mechanism through which *Centella asiatica*show its effect is by increasing bFGF& proliferation and by decreasing MPO [23].

Healing effect of *Myristica malabarica*: The fruit rind of Myristica malabarica (Myristicaceae) (also known as rampatri, Bombay mace, or fake nutmeg) is used as an unusual spice in Indian cuisines. It is attributed with hepatoprotective, anticarcinogenic, and antithrombotic effects, and is found as an ingredient in several Ayurvedic remedies such as pasupasi, despite the lack of appropriate evidence.As previously reported, the malabaricones (designated as mal B and mal C, respectively) were extracted from a methanol extract of M. malabarica's dried fruit rind. Mal B, mal C, Omez, and misoprostol were produced as aqueous suspensions in 2 percent gum acacia as the vehicle and given to the mice orally.The mice were given a single dosage of indomethacin (18 mg/kg, p. o.) diluted in distilled water and placed in 2% gum acacia

to cause ulceration. Our research with indomethacin dosages of 5, 10, 15, 18, 20, 25, and 30 mg/kg p. o. found that the lowest doses (5 and 10 mg/kg) caused minimal ulceration after 6 hours, whereas the higher doses (25 and 30 mg/kg) caused death. The selected dosage (18 mg/kg) resulted in optimum ulceration, inflammation, and mucosal insult in mice without causing death.Overall, three days of therapy with mal B and mal C (10 mg/kg) following ulcer induction resulted in excellent ulcer healing. As a result, only mice who received mal B, mal C (each 10 mg/kg), Omez (3 mg/kg), or misoprostol (10 g/kg) for 3 days were chosen for angiogenic testing.The number of microvessels in ulcerated mice was decreased by 31.9 percent compared to normal mice (p0.05), with no effect on ulcer induction day. Treatment with mal B and mal C for 3 days increased the mucosal microvessels by 36.6 percent (p0.05) and 61.6 percent (p0.01), respectively, compared to group III mice. When compared to the ulcerated untreated animals, misoprostol treatment for three days considerably improved the parameter (16.9%). Omez (3 mg/kg 3 days) was ineffective, but at 10 mg/kg, it enhanced mucosal microvesselsby 15.6 percent (p0.05) as compared to group III mice.Possible mechanism through which *Myristica malabarica*show its effect is by ↑ EGF, ↑ VEGF, ↓ endostatin [16].

Healing effect of *Ganoderma lucidum*: G. lucidum fruiting bodies were collected, and a crude PS fraction was produced by hot water extraction. G .lucidum fruiting bodies were washed, disintegrated, and extracted two times with hot water at 70°C for three hours. The PS-enriched fractions were precipitated by adding 75 percent (vol/vol) ethanol to all of the resulting extracts.The refined fraction included glucose (61.2%), xylose (15.5%), fructose (14.4%), galactose (4.8%), and rhamnose (4.1%), all of which were connected together by -glycosidic bonds. The bicinchoninic acid technique indicated that the protein concentration was 0.35 percent. By using silica gel thin-layer chromatography and ultraviolet light shadowing, no triterpenes were found in the final extracts. Using the chromogenic Limulus amebocyte lysate test, there was no detectable quantity of endotoxin (lipopolysaccharide) in the extracted PS fractions.Before the studies, the animals were fasted for 24 hours and given unrestricted access to drinking water until 1 hour before the test. Rats (n = 6) were treated with acetic acid according to the previously disclosed modified procedure.Rats were sedated with halothane and had their stomachs exposed through coeliotomy. Glacial acetic acid (10 M, 100 L) was administered for 1 minute via a plastic tube to the surface of the serosa at the confluence of the gastric fundus and antrum, and then rinsed with sterile saline. To avoid infection, a few drops of penicillin G (1 105 U/mL) were sprayed into the surgical site. The rats were subjected to their individual treatments after an hour of recuperation.G. lucidum PSs (0.1, 0.5, or 1.0 g/kg) or an equivalent amount of water (as the control) or atropine sulfate (10 mg/kg; utilized as a positive control) were given intragastricallyonce a day for 14 days to five groups of rats in a parallel design. All rats were slain by an overdose of halothane following the treatment period, and the stomach was removed after clamping the esophagus. After that, the stomach was opened and the larger curvature was rinsed in sterile saline before being viewed under a 3X dissecting microscope. The ulcer index (percentage) was calculated by dividing the total ulcer area by the total stomach area.Additional rats (n = 6) were anaesthetized, the abdomen was incised, and the sur- the face of the serosa at the intersection of the gastric fundus and the antrum was treated for 1 minute with 10 M glacial acetic acid (10 M, 100 L). G. lucidum PS (1.0 g/kg) was subsequently given to the rats through intragastric intubation for 3, 7, 10, or 14 days. We picked 1.0 g/kg as the dosage since it achieved maximal ulcer healing with minimal side effects. The glandular segment and gastric corpus tissues were extracted and kept at -80°C until analysis.Treatment with G. lucidum PS at 0.1 g/kg/day for 14 days had no effect on ulcer healing (P >.05), while oral administration had no effect. administration of the PS portion of G. lucidum at 0.5 or 1.0 g/kg/day for t he rate of change was significantly accelerated (P.01) after 14 days. 40.1 percent and 55.9%, respectively, of ulcer healing. Administration- Atropine sulphate administration was likewise shown to be substantially (P.05) in- acetic acid-induced gastrointestinal mucosal lesions in mice were inhibited 82.8 percent of rats G. lucidum PS (0.5 and 1.0) has a healing effect. The atropine treatment dose (1.0 g/kg) was much lower. (P < .01).Possible mechanism through which *Ganoderma lucidum*shows its effect is by ↑ Mucus content, ↑ PGE2 [56].

Anti-ulcer Effect of Tea Catechin: Catechins are the primary ingredient of green tea and are chemically classified as polyphenols. The four main catechins in green tea are -epicatechin (EC), epicatechin gallate (ECg), epigallocatechin (EGC), and epigallocatechin gallate (EGCg). These catechins have strong antioxidant properties. 10) As a result, catechins and the antioxidants listed above are thought to have antiulcer properties.*Tea catechin* [EGCg 50%, ECg13%, 92 percent as polyphenols [Teaflan 90S] was employed in the study.The test chemicals were suspended in a 1% gum Arabic solution. Absolute ethanol was given to rats in the stomach at a volume of 1 ml per 100 g of body weight after they had fasted for 24 hours. At 1 h before ethanol delivery, each test chemical was administered orally in a volume of 1 ml per 100 g of body weight. Instead of each test chemical, a vehicle (1 percent gum arabic) was used as a control.The animals were killed under ether anaesthesia one hour after receiving the necrotizing drug, and the stomach was removed and opened along the larger curvature. The length (mm) and breadth (mm) of hemorrhagic erosions in the stomach mucosa were examined using a stereoscopic microscope to determine the degree of gastric mucosal lesions, and the area of each erosion (mm2) was estimated a lesion index is used to indicate the overall area of each erosion (mm2).After fasting for 24 hours, rats were given 1 ml per 100 g of body weight of a test chemical or a vehicle (1 percent gum arabic) as a control. These animals were held in a stress cage and submerged in 23 °C water one hour after receiving the test substance or vehicle. 12) The animals were killed by ether anaesthesia six hours after the stress load, and the stomach was evacuated and opened along the larger curvature. As described in the assessment of ethanol-induced stomach mucosal damage, the amount of gastric mucosal injury was quantified as the mucosal lesion index (mm2).Gastric ulcers were produced in these rats using Takagi et al.14's approach of injecting 20 percent (v/v) acetic acid in a volume of 0.05 ml into the submucosal layer at the fundus-antrum junction. Each test ingredient was administered orally twice daily for 14 days (*tea catechin* and sucralfate: 9:30 a.m. and 5:30 p.m. twice; omeprazole: 11:30 a.m. once) following the acetic acid injection. Instead of the test substance, the vehicle was given to the control animals. On the 15th day, the animals were decapitated quickly. The stomachs were removed, filled with 5 mL of 10% formalin, and left for 5 minutes before being sliced open along the larger curvature. With a stereoscopic microscope and a micrometre, the longitudinal and abscissa lengths of the upper-opened region of the ulcer were measured, and the product of both lengths (mm2) was represented in terms of the ulcer index. Following the measurement of the ulcer size, the stomach tissue was submerged in 10% formalin for further 24 hours.1 hour after intragastric instillation of ethanol, the effects of test compounds on absolute ethanol-induced gastric mucosal damage were assessed. Control rats were given 100% ethanol intragastrically, which resulted in a significant hemorrhagic damage in the glandular stomach. At oral dosages of 50, 100, and 200 mg/kg, *tea catechin* reduced stomach mucosal damage by 49, 70, and 100%, respectively (Fig. 3). Both comparator medications, omeprazole at 50 mg/kg and sucralfate at 500 mg/kg, entirely avoided the harm in 92 and 99 percent of the cases, respectively. Tea catechins have antioxidant properties, which is the reason for their anti-ulcer properties [57].

Healing effect of *Cochinchina momordica*: Cochinchinamomordica is the dried mature seed of Momordica cochinchinensis. Chemical investigation reveals that the cochinchina Momordica seeds include fatty acids, saponins, proteins, a-spinasterol, oleanolic acid, and Momordica acid, among other chemicals. Momordica saponin I, glycoside, a triterpenoid saponin with a disaccharide chain, is a key active component among these substances.One kilogramme of sugar was mixed with five litres of aqueous ethanol solution. (dry weight) of Momordica cochinchinensis, Extraction was carried out at 80°C for 4 hours.This procedure was repeated twice. A filter was applied to the extractthen utilising a rotating concentrator at 60°C under decreased pressureevaporator. After the solvent has been completely removed in a vacuum,60 g powdered ethanol extract in the oven (SK-MS10)was acquired The carboxymethylcellulose was used to dissolve SK-MS10 during the experiment, (CMC) was used.Male Spraque-Dawley rats aged seven weeks were kept in a pathogen-free environment at a temperature of 23°C and 12/12-hour light/dark cycles.The trials were conducted on 8-week-old rats weighing 250-300 g after a week of adaption. Before the studies, the rats were famished but given water for 12 hours.After inducing gastric ulcers with acetic acid, the fasting rats

were sedated with an intramuscular injection of 80 mg/kg ketamine, and their stomachs were exposed through a midline incision. A microsyringe was used to inject acetic acid (20%, 30 mL) into the subserosal layer near the intersection of the anterior wall of the antrum and the corpus. After that, the abdominal incision was sutured shut. The rats were given SK-MS10 (200 mg/kg) or a vehicle by gavage starting on day 1 following ulcer induction. On day 7 or 14, the rats were sacrificed.By days 7 and 14, SK-MS10 had considerably accelerated ulcer healing. That is, by days 7 and 14 following ulcer induction, the mean ulcer size in the SK-MS10-treated group was considerably less than in the vehicle-treated group. The ulcer area was 33.2 mm2 and 9.3 mm2 after 7 and 14 days after SK-MS10 therapy, respectively, which was less than the 52.6 mm2 and 32.3 mm2 of the vehicle-treated group.According to the findings, SKMS10 accelerates the healing of acetic acid-induced stomach ulcers in rats via increasing angiogenesis and the production of the angiogenic growth factor VEGF [58].

Anti-Ulcer activity of *Plantago lanceolata*:The effect of Plantago lanceolata L. (Plantaginaceae) leaf extract on gastric secretion and cytoprotection was investigated using various gastroduodenal ulcer models, including acetic acid-induced chronic gastric ulcer, indomethacin-induced gastric ulcer, cysteamine-induced duodenal ulcer, and pylorus ligation-induced gastric ulcer. For mice and rats, the aqueous extract was given at 200 mg/kg and 400 mg/kg, and 140 mg/kg and 280 mg/kg, respectively, and was compared to vehicle or the standard, ranitidine (50 or 70 mg/kg) or misoprostol (280 g/kg). In addition, the action of mucilage (172 mg/kg) was tested in chronic stomach ulcers caused by acetic acid. Except for pylorus ligation, when the intraduodenal route was employed, the administration was done orally. Higher dosages of the extract and the mucilage offered superior protection in all instances, indicating a dose-dependent impact. While greater dosages of the extract resulted in improved ulcer healing and protection in the indomethacin and pylorus ligation models, the cysteamine model revealed actions that were less potent than ranitidine. These data suggest that the larger dosages used in this trial gave generally greater protection against gastroduodenal ulcers than the usual medicines used in previous studies, which worked via antisecretory and cytoprotective mechanisms [59].

Anti-Ulcer activity of *Bupleurum falcatum*: The effect of*Bupleurum falcatum L.*(Umbelliferae) root extract on gastric secretion was investigated using various gastroduodenal ulcer models, Male wistar rats were used. The rats were starved for 20 hours but given free access to water.Takagi et almodified .'s approach was used to create this ulcer model (1969). Coeliotomy was performed on rats under diethyl ether anesthesia to expose the stomach. Through a plastic tube (6 mm ID), 100 mL glacial acetic acid was administered to the surface of the serosa at the intersection of the fundus and antrum on the abdominal side of the glandular stomach for 1 minute, and then the serosa of the stomach was rinsed with 0.9 percent NaCl. The surgical wound region was treated with 3 drops of penicillin G solution (1 X 105 U/mL) before colporrhaphy to avoid bacterial infection. The rats were given unrestricted access to water and food after the procedure. Rats with ulcers were administered BR-2 or atropine sulfate, as a positive control, intragastrically twice a day (9:00–10:00 a.m. and 5:00–6:00 p.m.) in a volume of 1.0 mL/100 g of body weight for 14 days, beginning on the day (day 1) following the acetic acid treatment. Water was given to the control group as a vehicle (1.0 mL/100 g of body weight). On day 15, the rats were killed by an overdose of diethyl ether. The stomach was taken out and incised along the larger curvature, then gently rinsed with 0.9 percent NaCl. Each ulcer's longitudinal and abscissa lengths were swiftly measured using a stereoscopic microscope, and the ulcer index was calculated using the multi-plied product.When rats were given BR-2, it was discovered that it helped cure an acetic acid-induced ulcer. The ulcer healing was significantly accelerated by 43.1 percent, 41.2 percent, and 51.9 percent, respectively, after 14 days of oral administration of BR-2 at dosages of 50, 100, and 200 mg/kg twice a day. Atropine sulphate, given orally at a dose of 10 mg/kg, considerably aided the healing of the acetic acid-induced ulcer. A microscopic research also revealed that administering BR-2 had a considerable healing impact.The findings support the use of herbal prescriptions including B. falcatum for the treatment of peptic ulcers, indicating that the polysaccharide from B. falcatum L. may be responsible for antiulcer action [60].

Anti-Ulcer activity of *Allium Sativum*

Allium sativum was primarily used for its medical characteristics throughout history, and the health advantages of garlic have been thoroughly established. The major constituents of Allium sativum's bioactivity are known to be its organosulfur components, notably S-allyl-L-cysteine (SAC) sulfoxides and -glutamyl S-allyl-L-cysteine. It is simple to transform raw Allium sativum into bioactive form. As a result, multiple varieties of its extract have been created with various bioactive component compositions, and their efficiency has been seen and assessed in numerous investigations [61]. By scavenging reactive oxygen species, Allium sativum extract has been shown to have a significant antioxidant effect.Reducing the serum glucose-induced activation of antioxidant enzymes and preventing lipoprotein oxidation. Additionally, it demonstrated a suppressive impact on stomach inflammation brought on by H. pylori in vivo [62] and an anti-tumorigenic effect by encouraging apoptosis and cell cycle arrest [63]. In vitro studies have shown that the development of H. pylori was inhibited by allicin and allyl-methyl plus methyl-allyl thiosulfinate from acetonic Allium sativum extracts [64].

SAFETY

Although interactions between herbs and medicines have raised safety concerns [65,66] and some herbs may have major adverse effects[67,68] herbal remedies used to treat stomach ulcers have been confirmed to be safe in both animal models and humans. A mouse model of indomethacin-produced stomach ulcer of *Myristicamalabarica* extract was given a daily dose of 40 mg/kg of indomethacin, which accelerated ulcer healing[69]. Mice administered oral *Myristicamalabarica* extract at a dose of 500 mg/kg per day for one month showed no evidence of toxicity. The liver and kidney histology and function in mice were likewise normal[16]. Similarly, a dose of 500 mg/kg of Gualeagrandiflora extracts taken orally for 14 days healed 83 percent of acetic acid-induced stomach ulcers[70]. When mice were administered Gualeagrandiflora extract at a dose of 5 g/kg per day for 14 days, the weight of the heart, liver, kidneys, and lungs showed no significant differences when compared to the control group. None of the treated mice died throughout the 14-day observation period. Methanolic extract of Alchorneaglandulosa at a dose of 250 mg/kg per day was shown to be more efficient than cimetidine in treating acetic acid-induced stomach ulcers[71]. The weight of numerous organs, including the liver, kidneys, heart, lungs, and spleen, was unaffected by oral Alchorneaglandulosa at a dosage of 5 g/kg per day for 14 days. In addition, there were no significant differences in hepatic or renal function between the control and herbal treatment groups[71]. Furthermore, a daily oral Solanumnigrum extract dose of 200 mg/kg for 7 days substantially decreased ulcer index (10.1 0.91 for herbal extract vs 16.9 1.4 for controls)[72]. After 14 days of oral treatment of Solanumnigrum extract at a dose of 4 g/kg per day, no changes in red blood cell count, white blood cell count, hemoglobin, hematocrit, or mean corpuscular volume were observed. Finally, multiple clinical studies have shown that herbal drugs are safe for human usage. Even thoughthe fact that these studies indicate that herbal treatments are safe for treating stomach ulcers, herbal medicines should be taken with care owing to possible adverse effects and drug-herb interactions.

CONCLUSION

The use of herbal remedies in addition to conventional anti-gastric ulcer medications may have a synergistic impact in the fight against H. pylori and gastric ulcer disease and enhance the prognosis for patients with stomach ulcers. It is advised to carry out further clinical research with bigger sample sizes on the effectiveness and safety of medicinal plants with antiulcer activity since there are so few human studies available. Designing research to look into and clarify the mechanisms of action of medicinal plants used in the treatment or prevention of peptic ulcers would also be useful.

Finally, in order to improve their safety and quality and to guarantee that randomised controlled studies evaluate the requirements of their potential usefulness, herbal products used for therapeutic reasons need licence. Despite an increase in reports of herb-drug interactions, there is still an issue with inadequate study in this area and no steps have been done to fix it. Therefore, whether used alone or in conjunction with other herbal

preparations or regular conventional medicine, pharmacists and physicians should be particularly mindful of the hazards connected with the use of herbal preparations.

CONFLICT OF INTERESTS

The authors declare that they have no conflict of interest

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