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A Comprehensive Analysis of Commercially Available Polyherbal Antiulcer Formulations

Chetna Kothari [1], Shirish P Jain [2]

[1]Research Scholar, Sunrise University Alwar

[2] Research Supervisor, Sunrise University Alwar

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Corresponding author: Chetna Kothari

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Abstract:

Peptic ulcers occur when there is an imbalance between the protective and aggressive elements in the gastrointestinal system. The use of allopathic medications is common in modern ulcer treatment prescriptions. However, the search for new, safer drugs has been prompted by a number of drawbacks, including side effects, discordance, and changed physiological characteristics. Ayurveda has a long history of using herbal remedies to cure ulcers. Several benefits, such as synergistically enhanced positive effects, improved patient compliance, and reduced dosage of individual medications without compromising therapeutic effects, are shown by combining such herbs, which is called polyherbal formulation. Improved Ayurvedic medicine has been used in treatment settings in recent years thanks to this priceless traditional knowledge of the therapeutic properties of plants and modern value-added innovations. Over the last 20 years, several polyherbal combinations have been researched and tested for their ability to alleviate ulcer symptoms. Thanks to developments in analytical technologies, phytoconstituents from crude herbal medications have been isolated and examined for their therapeutic advantages. The primary objective of this study is to provide a thorough synopsis of the ingredients used in various polyherbal formulations sold as antiulcer medications, as well as an analysis of the preclinical models used to demonstrate the gastroprotective effects of these products.

Keywords: Antiulcer, Ulcer, Phytoconstituents, and Polyherbal formulations

INTRODUCTION

Worldwide, a large percentage of the population suffers from peptic ulcers, the most prevalent gastrointestinal tract disorder. The treatment of ulcers and its consequences has increased the societal and financial burden.1 Damage to the areas of the digestive system that are exposed to acid and pepsin is what is seen as an ulcer.2 It is believed that the imbalance between the protective and harmful components of the gastrointestinal tract underlies the pathophysiology of ulcers.1 Mucus secretion, proper tissue blood supply, endogenous nitric oxide, bicarbonate, and gastroprotective prostaglandin are the defensive components. Acid, free radicals, pepsin, aberrant motility, bile salts, nonsteroidal anti-inflammatory drugs (NSAIDs), alcohol, and Helicobacter pylori are all aggressive variables.2 Prolonged

lesions increase the risk of complications including gastrointestinal bleeding, obstruction, and damage.3 For the treatment of peptic ulcers, there is now an increased push for the use of antibiotics, proton pump inhibitors, histamine receptor antagonists, antacids, ulcer protectives, and anticholinergics.2,4 Prolonged use of these medications has been associated with serious adverse effects including impotence, nephrotoxicity, hepatotoxicity, and thrombocytopenia. There is a growing need for safer and more effective alternatives to these side effects in the treatment of ulcers.4 The use of phytopharmaceuticals as a complementary and alternative medicine modality has been on the rise recently. Traditional herbs with antiulcer properties and phytoconstituents include Balsamodendron mukul, Aegle marmelos, Azadirachta indica, Carica papaya, Allium sativum, Acacia arabica, and Azadirachta indica.5 The Ayurvedic text Sharangdhar Samhita traditionally recognises the medicinal value of herb-herb combinations. A large number of polyherbal formulations (PHFs) have been created and have been recommended for treatment against various illnesses for quite some time.6 The separation of many phytoconstituents, including 7,8-dihydro-8-hydroxypalmatine, Atropine, Cocaine, Matrine,7 Thymoquinone,8 Costunolide, and others, has allowed researchers to assess their therapeutic potential in peptic lesions, thanks to developments in analytical methods. The use of a single herb or a mixture of herbs are two primary ideas that underpin Ayurvedic compositions.9 These days, the majority of Ayurvedic remedies are polyherbal, meaning they include extracts from many plants rather than just one. The interaction of herbs, which results in synergism, is the most important advantage of combining them. The individual herbs may only have trace amounts of certain components, but when combined, they may have a synergistic effect that makes them more effective. In addition, it is worth mentioning that several phytoconstituent actions were enhanced when combined with another plant, but had no impact when used alone. As a result of synergy, reducing the amount of one PHF component also reduces the undesirable side effects. The patient's comfort is also enhanced by eliminating the need for them to take many medications at once, which implies better compliance and healing benefits. Because of these benefits, PHFs have become more common than single herb formulations. On the other hand, polyherbal formulations have their own set of restrictions. Incompatibility among the components—whether quantitative, energetic, or functional—is the main problem. Interactions between herbs and allopathic medications are possible. Herbal remedies may make it difficult to achieve clinical response repeatability.9 Traditionally, Ayurvedic medications were either made by the doctors themselves or prescribed to local villagers who would then gather medicinal plants for use in treatment, prevention, and correction. Medicated oils, bhasma, churna, asava-arista, sindoor extract, Vati, decoction, gutika, and decoction were the traditional dosing forms of Ayurvedic medicines. Capsules, syrups, pills, and salves derived from Ayurvedic formulas were not available until the contemporary era, thanks to a game-changing improvement in industrial infrastructure.10

Herb-Herb Combination

Traditional medicine has long made use of both raw and processed plant components for their ethnomedicinal value. Because individual herbs do not have sufficient therapeutic benefits, herbal mixtures are preferred over employing only one herb in treatment. It would indicate that there are

probable interconnections present in the formulation of the ethnobiological components. These relationships would arise as a result of cooperative efforts, competitive threats, complementary strengths, and complementary weaknesses.12 Incompatibility, potentiation, reinforcement, restraint, counteraction, and detoxification are some of the negative outcomes that might result from these interactions.13

Benefits of Herb-Herb Combination

Polyherbal formulations designed by the combination of multiple herbs exhibit ample advantages over a single herb and allopathic medicine. This resulted in the emerging trend in herbal drug therapy worldwide.

- High therapeutic effectiveness against a vast number of afflictions is exerted owing to the presence of numerous phytoconstituents. Factual assessments show an inclination for herbal preparations due to their adequacy and promising outcomes of the treatment.9
- The existence of multi-components in the combination serves to potentiate the action of one drug by another. This enhancement in activity may not be attainable by individual components when utilized alone.10
- Polyherbal formulations have a widespread therapeutic window. Being viable indeed at a lower dose and harmless at a higher dose, most of them have a predominant risk-to-benefit ratio.9
- Due to synergism, polyherbal preparations are desirable. They can be prescribed at a lower dose to accomplish the required pharmacological action. This results in decreasing the possibility of harmful side effects as compared to allopathic medication.9,10
- By abolishing the need to administer more than one single herbal formulation at a time, polyherbal preparations bring enhanced convenience for patients. As the administration of multiple herbs as one formulation shows better convenience, it indirectly marks improved patient compliance.10
- Herbal combinations with a number of constituents simultaneously act on diverse targets to elicit intensive alleviation. The presence of distinctive types of constituents remedies the affliction by distinctive mechanisms to provide a complete treatment against an illness.10
- Having a natural source, developing a polyherbal formulation is economical and it is easily available. Global demand for PHF has increased due to accessibility and affordability, especially in developing countries.9
- Synergism could be attained at the pharmacokinetic or pharmacodynamic level. Pharmacokinetic synergism is seen when the absorption, distribution, metabolism, and elimination of one herb are facilitated by another in the combination. Pharmacodynamic synergism is achievable by targeting active principles from multiple components toward common physiological systems.[9,10]

Limitations of Herb-Herb Combination

A combination of herbs may not always be superior to a single herb in that certain situations may exert antagonistic effects.

- Possible chemical incompatibility might be exhibited by the combination of herbs which may lead to instability and consequently loss of therapeutic benefits.10
- Inappropriate use or preparation of Ayurvedic formulation may lead to adverse effects, as reported in Charaka Samhita. Concomitant use of the allopathic drug along with the Ayurvedic preparation has been increasing, which is unknown to the medical practitioner. Such use of medication of diverse origins might result in possible drug- herb interactions to accelerate harmful impacts on the patient's well-being.9
- It is difficult to achieve clinical reproducibility with Ayurvedic PHFs. Despite the standards available, several factors such as habitat, harvesting conditions, the season in which the

herbs grow, storage conditions, and diverse manufacturing processes can affect the lack of reproducibility in the quality of the finished product. Therefore, batch-to-batch variation is a common occurrence, and it affects the safety and efficacy of the preparation.9

- Toxicity is another concern with respect to the presence of heavy metals like mercury, even in trace amounts. Hepatotoxic, nephrotoxic, hematotoxic and neurotoxic consequences have been reported due to these elements.[9]

The present review is a compilation of some marketed polyherbal formulations. The components and their antiulcer models, along with the parameters considered, are talked about in brief (Table 1).

PHFS WITH ANTIULCER POTENTIAL

Yelathy Chooranam

Seven drugs—Taxus buccata, Piper nigrum, Eletaria cardamomum, Syzygium aromaticum, Cinnamomum zeylanicum, Zingiber officinale, and Curcuma angustifolia (Arrowroot)—make up the Yelathy Chooranam Polyherbal antiulcer Siddha composition. Within the Siddha medical system, the components' various therapeutic functions have been described. The antiulcer potential of the polyherbal formulation's components has been shown in many animals. Both the aspirin- and ethanol-induced acute ulcer models were shown to be strongly suppressed by petroleum ether fractions and methanolic extracts of Eletaria cardamomum. Syzygium aromaticum showed a reduction in ethanol-induced lesions. Ferula foetida and Piper nigrum, when given orally, reduced cysteamine-induced duodenal lesions in rats in a dose-dependent manner. The indomethacin-induced ulcer rat models showed less severe ulceration when treated with a Cinnamomum zeylanicum suspension. The lignan components of Taxus buccata showed anti-inflammatory and antinociceptive effects by reducing the production of TNF and cytokines. Zingiber officinale demonstrated its gastroprotective efficacy by reducing indomethacin-induced stomach damage. Yelathy Chooranam's antiulcer benefits were recovered by the writers.14

NR-ANX-C

Organic Remedies Pvt. Ltd. of Bangalore, India, sells NR-ANX-C, a PHF made of Camellia sinensis, Withania somnifera, shilajit, and Triphala. These components have shown significant antioxidant effects. Ayurvedic Rasayana makes use of Ocimum sanctum and Withania somnifera because of their anti-ulcerative properties. The practice of gastrointestinal care has benefited greatly by triphala. Additionally, the polyherbal formulation was tested for its ability to prevent ulcers, taking into consideration the role that free radicals, acidity, and the breakdown of mucosal defences play in ulcerations. Aspirin and pyloric ligation gastric lesion assays were part of the experimental methodology, which also involved measuring ulcer index, malondialdehyde (MDA), gastric pH, gastric volume, total acidity, and adherent gastric mucus. The standards for the assays were ranitidine (27 mg/kg p.o.) and omeprazole (1.8 mg/kg p.o.). Findings showed that MDA levels, gastric juice volume, and total stomach acidity were all significantly reduced at higher dosages of the PHF (25 and 50 mg/kg p.o.), with the decrease being dose-dependent. As a result of the formulation, stomach pH and adhering gastric mucus both increased noticeably. Furthermore, the PHF shown greater adequacy in reducing stomach ulcers compared to the norm. Research found that NR-ANX-C's antiulcer effectiveness was due to its antioxidant, cytoprotective, and antisecretory properties.15

Livina

Solanum nigrum, Holarrhena antidysenterica, Tephrosia purpurea, Andrographis paniculata, Phyllanthus niruri, Tinospora cordifolia, Terminalia chebula, Asteracantha longifolia, Alstonia scholaris, Berberis aristata, Cichorium intybus, and Picrorhiza kurroa are all parts of the Livina polyherbal capsule made by Dey's Medical Stores (Mfg.) Ltd. Antiulcer efficacy against ethanol-induced ulcers was assessed using the polyherbal formulation. Ethanol is known to irritate the stomach mucosa, but the exact pathogenic pathways are still a mystery. Free radicals produced by ethanol cause lipid peroxidation, which in turn causes oxidative damage. The experimental design used dose levels of 50, 100, and 200 mg/kg p.o. of Livina powder methanol extract to measure ulcer index, total acid, free acid, stomach volume, and gastric juice pH. A petechial lesion and lengthy haemorrhage bands were shown by the morphological examination, which revealed an apparent large mucosal lesion. Very little lesions with interstitial haemorrhage or no lesions at all were seen prior to Livina therapy. Both the ethanol-treated and Livina pre-treated animals showed significant microscopic alterations. In the submucosa, there was a lot of swelling, stomach epithelial necrosis, mucosal haemorrhage, and edoema. In contrast, the pre-treated rats showed little loss of mucosal epithelial cells. By comparing the ethanol-induced ulcer index, total acid, free acid, and stomach volume with the standard, Ranitidine (50 mg/Kg p.o.), Livina (200 mg/kg p.o.) showed a substantial reduction. A substantial increase in pH was also seen in comparison to the group that was treated with ethanol.16

Rumi Herbal Research Institute Private Limited of Chennai markets RO12, a PHF. Aegles marmelos, Glycyrrhiza glabra, Eletteria cardomum, Citrous aurantifolia, and Saccharum officinarium are all included in its water-based extracts. Aegles marmelos, Citrous aurantifolia, and Glycyrrhiza glabra have all been known to have antiulcer effects in the past. Antioxidant activity has been found in Eletteria cardomum and Glycyrrhiza glabra, according to research. We conducted preliminary phytochemical evaluations on the PHF aqueous extract. Acute toxicity testing was conducted in accordance with OECD guideline 423 and found that doses up to 2000 mg/kg were safe. Pyloric ligation- and ethanol-induced ulcers were used to test the antiulcer efficacy of high and low dosages of PHF (400 mg/kg and 200 mg/kg p.o., respectively). Mucosal barrier collapse, decreased blood flow, and autodigestion by gastric fluids all play a role in ulcer induction after pylorus ligation. Results showed a statistically significant reduction in ulcer score and index compared to the control group given Ranitidine (50 mg/kg p.o.). Total acidity, free acidity, total protein, and pepsin levels were significantly reduced by the 200 m/kg dosage of RO12 aqueous extract. On the other hand, total protein content increased while pepsin and free acidity levels decreased with the high dosage. Hematoxylin and eosin were used to stain and fix slices of stomachs for microscopic examinations in histopathology. The research proved that PHF's gastroprotective effects are due to its antisecretory, antioxidant, cytoprotective, bicarbonate-raising, and blood-circulating properties.17

Avipattikar Churna

In Nepal, a product called Avipattikar churna is sold as a PHF. It contains the following ingredients: Vida Lavana, Terminalia chebula, Operculina terpethum, Cyperus rotundus, Embelia ribes, Syzgium aromaticum, Cinnamomum tamala, and Sharkara. The antiulcer activity of each component has been confirmed. When applied to the stomach mucosa, Piper

nigrum, Terminalia chebula, and Piper longum all show cytoprotective effects. Research on Zingiber officinale has shown that it reduces stomach output, increases mucosal resistance, and strengthens the gastric mucosa's protective properties. In addition to increasing gastric mucus production, Syzgium aromaticum helps maintain blood flow to the stomach mucosa. Gastric ulcers were created in this investigation by use of Shay's pyloric method. Avipattikar churna was tested for its gastroprotective effects by comparing two oral dosages of the drug—500 mg/Kg and 750 mg/kg—to a conventional dose of ranitidine—25 mg/kg. Gastric content volume, acidity, pH, ulcer score, ulcer length, ulcer count, curative ratio, gastric irritancy size, and gastric irritancy index are some of the parameters that have been researched. A person's gastric irritancy size was determined as the total length of their ulcers. An ulcer's stomach irritancy index was the product of its size and the number of ulcers. The control group's stomach tissue was found to have fibrinopurlent exudates, dead neutrophils, and pus formation upon histological testing. Groups treated with Avipattikar churna showed signs of ulcer healing with little inflammatory cell involvement. The group that received ranitidine showed less deformation in the architecture of the stomach mucosa. When compared to the control group, the research found that the lower dosage of churna had a substantial antisecretory and gastroprotective effect. There was no statistically significant difference between the churna-treated and Ranitidine-treated groups.18

VRC/AS/014 Syrup

Vasu Research Centre, Vadodara, makes and sells a polyherbal syrup called VRC/AS/014 syrup. It contains Emblica officinalis, Asparagus racemosus, Glycyrrhiza glabra, Hemidesmus indicus, Centella asiatica, Terminalia chebula, Terminalia belerica, Ipomoea turpethum, Sodii carbonas, and black salt. Despite claims that several of these ingredients have antiulcer properties, there has been no preclinical testing of the mixture. The formulation underwent acute toxicity assessment using a step-up, step-down technique in accordance with OECD guideline 423. To assess the acid-neutralizing and antiulcer potential, several in-vitro and in-vivo investigative models were used. We tested its astringent qualities, prokinetic activity, and ability to neutralise acids in vitro. The antiulcer potential of the PHF (2 and 4 mL/kg p.o.) was tested using an aspirin plus pylorus ligation induced ulcer model. The model included evaluation of parameters such as ulcer index, total acidity, volume of gastric secretion, and gastric wall mucus content. The gastroprotective benefits were shown by an increase in mucus content and a reduction in ulcer index. Similar to the conventional Sucralfate (300 mg/kg p.o.), the larger dosage (4 mL/kg) exhibited substantial antiulcer and antisecretory effects. Preclinical scientific evidence supporting the foundation for the clinical usage of VRC/AS/014 syrup was supplied by the current work's results. Furthermore, the formulation does not include aluminium or magnesium, which are often found in antacids. This means that it has little effects on absorption and digestion.19

Digitrall

The Kolkata-based pharmaceutical company M/s. S. C. Pharmaceuticals Ltd. sells Digitrall. Aqueous extracts of many plants, including Amomum sabulatum, Foenieulum vulgar, Zingiber officinale, Piper nigram, Berberis aristata, Ptychotis ajowan, and Carica papaya, make up its makeup. The purpose of this research was to determine if Digitrall was effective in preventing stomach ulcers. The indomethacin-induced

stomach mucosal damage was significantly reduced when Digitrall was administered orally at dosages of 1, 2, and 4 mL/kg compared to the normal dose of Ranitidine (50 mg/kg). The anti-cycloxygenase action of indomethacin increases 5-lipoxygenase and leukotriene synthesis. These have a mediating role in the development of ulcers. The stomach lining is damaged by reactive oxygen species such hydroxyl radicals, hydrogen peroxide, and superoxide anion, which further complicates matters. The research that was cited to showed that in the stomach mucosal tissue, there was a drop in MDA that was dose-dependent, an increase in SOD levels, and a decrease in glutathione levels. The component of antiulcer effect that Digitrall may have, according to the scientists, is its antioxidant activity.20

Pepgard Syrup

Developed and manufactured in Vadodara by Vital Care Pvt. Ltd., Pepgard syrup is an exclusive Ayurvedic PHF. The syrup contains the following ingredients: Glycyrrhiza glabra, Asparagus racemosus, Astoneman indicum, Centella asiatica, Emblica officinale, Ipomoea turpethum, Syzygium aromaticum, Fumaria officinalis, and Coriandrum sativum. Many people use it as an antacid for conditions such drug-induced gastritis, heartburn, GERD, and non-ulcer dyspepsia. In order to determine the test dosage, we extrapolated the human dose relative to body surface area using the standard table of Paget and Barnes. It was thought that coordinated hits or release of reactive species constituted the basic pathophysiology of Aspirin-induced ulcerogenic damage. Modifications to the gastrointestinal mucosa were seen in response to impedances with defensive capabilities, including mucus formation, bicarbonate synthesis, and blood circulation. The DPPH and H2O2 scavenging techniques were used to measure the antioxidant activity of the formulation's alcoholic extract. The effectiveness of the formulation's alcoholic extract as an antiulcer agent was assessed using the Aspirin-induced ulcers model. Doses of 1, 2, and 4 mL administered orally were considered. The results showed that increasing the amount of Pepgard syrup alcohol extract and ascorbic acid significantly reduced the levels of DPPH and H2O2 radicals. A dose-dependent increase in the antiulcer potential was also seen when compared to the standard, Ranitidine (100 mg/kg p.o.). Pepgard syrup's cytoprotective properties may be due in part to its phytobiological components, which the authors identified as include terpenoids, alkaloids, tannins, saponins, flavonoids, and glycosides. Someone brought up the idea that antioxidant activity could interfere with the gastroprotective effects.21

Amlapitta Mishran Suspension

Phyllanthus emblica, Adhatoda vasica, Tinospora cordifolia, Azadirachta indica, Swertia chirata, Eclipta alba, Glycyrrhiza glabra, Terminalia chebula, Terminalia belerica, Shouktik bhasma, and Fumaria indica are the active ingredients in Amlapitta Mishran, a herbo-mineral suspension made by Shree Dhootapapeshwar Limited, Mumbai. Each component has shown antiulcer efficacy in animal studies. To help scavenge reactive species caused by ulcers, Fumaria indica has shown antioxidant activity. The antiulcer potential of polyherbal suspension was tested using an indomethacin-induced ulcer model. Doses of 1.35 and 2.7 mL/kg p.o. were administered, with 100 mg/kg p.o. of ranitidine serving as the reference. It may be concluded that the Amlapitta Mishran suspension has great gastroprotective potential based on the results of the % inhibition and decrease in ulcer index. Amlapitta Mishran may be able to prevent ulcers by increasing the synthesis of prostaglandins.22

Hingwashtak Churna

Piper nigrum, Nigella sativa, Ferula foetida, Zingiber officinale, Cuminum cyminum, Piper longum, Trachyspermum ammi, and Saindhava lavana are the components of Hingwashtak churna, a PHF-type blend. Astringent, digestive, carminative, and antacid are some of its uses. Citrous aurantium, Zingiber officinale, Ferula foetida, Nigella sativa, and Piper nigrum were shown to be powerful antioxidants. Reports indicated that Zingiber officinale, Ferula foetida, and Piper longum increased mucus production and decreased stomach cell shedding. An antioxidant activity test using DPPH, nitric oxide, lipid peroxidation, and 2,2'-azino-bis(3- ethylbenzothiazoline-6-sulfonic acid (ABTS) was performed on the chloroform water extract (750 mg/kg p.o.) of the formulation. Multiple dosage levels were tested for acute toxicity. Neurological, autonomic, and behavioural alterations in the mice were continuously monitored over 2 hours. We noticed any harmful effects within three days. The gastroprotective research of the extract was evaluated using ibuprofen- and ethanol-induced ulcer models, with Ranitidine (2.5 mg/kg p.o.) serving as the benchmark. The findings indicated that the antioxidant property of the PHF was dose-dependent, according to the scientists. It was shown that 10,000 mg/kg of the formulation was the safe amount. Hingwashtak churna showed a strong antiulcer effect when evaluated using criteria including ulcer number, ulcer size, and ulcer index. One possible explanation for the protection against harm is the presence of antioxidants and an elevated prostaglandin level.23

Qarahine

Hamdard Laboratories in Pakistan created Qarahine, a polyherbal compound that contains Glycyrrhiza glabra Linn., Cochlospermum gossypium DC., Lapis lazuli, Koalinum ponderosum, Pistacia terebinthus Linn., silicate of magnesia, magnesium silicate, ferrum, and other ingredients. For the treatment of amoebic and bacillary dysentery, acute and chronic gastritis, diarrhoea, and other gastrointestinal issues, the PHF is recommended. Glycyrrhiza glabra, one of the components, has antiulcerogenic potential. Models of ulcers caused by aspirin and ethanol were used to assess the antiulcer potential. Using One-way ANOVA, we compared the pH and ulcer index of Qarahine (250, 500, and 1000 mg/kg p.o.) with conventional Omeprazole (20 mg/kg p.o.). At a dosage of 500 mg/kg, the research found that ulcer index significantly decreased and stomach content pH increased, providing optimum protection. Both versions demonstrated the same level of protection against ulceration. Significant reductions in injury severity, ulcer index, and number of lesions were seen as compared to the control group.24

Phy-Blica-D

Glycyrrhiza glabra, Aegle marmelos, Phyllanthus emblica, Terminalia arjuna, Terminalia bellirica, Cyperus rotundus, Maerua siamensis, Terminalia citrina, Piper retrofractum, Zingiber officinale, Alpinia galanga, Solanum torvum, Allium sativum, and Tinospora crispa are the ingredients of Phy-Blica-D, a traditional Thai polyherbal infusion. The revitalising Phy-Blica-D formula has a high concentration of flavonoids and phenols, making it an effective antioxidant, and THP-R016 or Phy-Blica-O. The original, powerful recipe had a number of drawbacks, including an unpleasant smell and a strong bitter taste. The antioxidant effect was unaffected by the minor formula changes that improved the sensory appeal. To determine the antioxidant capability of the Phy-Blica-D water extract, the oxygen radical antioxidant capacity

(ORAC) test was used as an in vitro antioxidant activity approach. An omeprazole standard of 20 mg/kg p.o. was used to evaluate the efficacy of Phy-Blica-D aqueous extract at 500 and 1000 mg/kg p.o. against Ethanol-induced acute gastric lesions in terms of ulcer activity. Both PHF dosages substantially reduced the stomach ulcer index (UI), according to the study's results. Although the gastric juice pH remains same, the levels of glutathione (GSH), superoxide dismutase (SOD), and catalase (CAT) significantly increase. Both MDA activity and iNOS levels were significantly lower in the extract pre-treatment group compared to the vehicle control group. The scientists deduced that Phy-Blica-D's gastroprotective action may be due to its ability to mask oxidative damage and increase antioxidant activity. Previous research indicated that the phytoconstituents have gastroprotective and free radical scavenging activities, which may explain the formulation's therapeutic value.25

Normacid Syrup

Normacid syrup (marketed by Ayurlab herbals Pvt. Ltd., Vadodara) is composed of Ficus glomerata Roxb., Fagonia Arabica L., Vetiveria zizanioides Stapf., Santalum album L., Andrographis paniculata Nees., Melia azadirachta L., Terminalia bellerica Roxb., Emblica officinalis Gaertn., Terminalia chebula Retz., Adhatoda vasica Nees., Trichosanthes dioica Wall., Fumaria officinalis L., Tinospora cordifolia Miers., Kapardika bhasma, Praval bhasma, and Shauktik bhasma. Because of their antioxidant and antiulcer characteristics, these substances found their way into the innate pharmaceutical system for the treatment of stomach ulcers. Acute oral toxicity experiments were conducted on mice for 14 days in accordance with OECD guideline 423 to confirm the syrup's safety. Up to a dosage of 5000 mg/Kg, the formulation exhibited no symptoms of toxicity or death. We used the Pylorus ligation model and the Diclofenac-induced ulcer model to assess the antiulcer potential of Normacid syrup (250 and 500 mg/kg p.o.), with Ranitidine (20 mg/kg p.o.) serving as the benchmark. Volume of gastric juice, pH, total acid, free acid, mucus secretion, ulcer index, and sulphur, hydrogen, and peroxidase levels are among the parameters measured. Results showed that gastric juice volume, total acid, free acid, ulcer index, and malondialdehyde levels all dropped significantly. On the other hand, pH, mucin secretion, and nitrite, SOD, CAT, and GSH levels all rose. Normacid syrup treatment reduced histological alterations, normalised the stomach mucosa, and eliminated ulcerations. The scientists reasoned that mucosal nitrite and mucin may have a self-protective role or that Normacid syrup's scavenging activity on reactive oxygen species may be responsible for its cytoprotective effects. 26

Shivaksharpachan Churna

Each of the following herbs—Ferula foetida, Cuminum cyminum Linn., Terminalia chebula Retz., Trachyspermum ammi Linn., and Piper longum Linn.—and Zingiber officinale Roscoe make up one component of Shivaksharpachan Churna. In order to validate the phytoconstituents, a preliminary phytochemical analysis was performed. The recommended dosage, according to acute toxicity studies, is 2000 mg/kg. We compared the antiulcer potential of the formulation (50, 100, and 200 mg/kg p.o.) to that of Ranitidine (100 mg/kg p.o.) using pylorus ligation and ethanol-induced ulcer models. Antioxidant activity was evaluated in ulcer models using parameters including LPO, CAT, and SOD. Saponins, flavonoids, bitter principles, steroids, and phenols were identified in the extract by the qualitative phytochemical evaluation. We observed that compared to the control group, pre-treatment with the extract dramatically decreased lipid

peroxidation and increased CAT and SOD levels. The researchers came to the conclusion that the formulation's ingredients may have an antioxidant effect, which might explain the gastroprotective effects.27

Gasteon Syrup

Shankha Bhasma, Kapardika Bhasma, Hedychium spicatum, Asparagus racemosus, and Glycyrrhiza glabra are the ingredients of Gasteon syrup. Antisecretory and antiulcer effects have been shown in Glycyrrhiza glabra and Asparagus racemosus. The histamine-induced ulcer model was protected against by Hedychium spicatum. Dysentery, hypoacidity, lack of appetite, duodenal ulcer, and alkaline Shankha Bhasma's antiulcer action are its indications. It is clear that Kapardika Bhasma and Kamadudha Rasa have an acidic effect. The mice were examined for 14 days after acute oral toxicity was administered according to OECD guideline 425. The gastropare syrup No-Observed-Adverse-Effect-Level (NOAEL) was found to be 2000 mg/kg. As a benchmark, ranitidine (27 mg/kg) was used to generate ulcer lesion using the Pylorus ligation procedure. Acidity, volume, pH, ulcer index, and total acidity were all measured after administering 25 mg/kg of syrup. The impact on SOD, catalase, and LPO-MDA, which are indicators of oxidative stress, was also assessed. The experimental group showed a considerable increase in catalase, superoxide dismutase, and pH activity. The following parameters were recorded: reduced stomach content volume, ulcer index, lipid peroxidation, free acidity, and total acidity. An antioxidant effect may have a part in the ulcer healing process, according to the positive results of stress indicators.28

Laghusoothshekhar

Nav Samhita states that Laghusoothshekhar is made with three ingredients: Zingiber officinale, Piper betle, and Suvarna gairik. Zingiber officinale has shown promise in treating gastritis and ulcers. Additionally, it showed anti-H. pylori action in vitro. The amount of mucus that adheres to the stomach mucosal membrane was improved by Piper betle. Additionally, it prevented the pathophysiology of ulcers by inhibiting free radicals. A variety of vomiting, burning sensations, bleeding problems, abdominal ailments, and emesis may be effectively treated with suvarna gairik, an iron oxide. This laid the groundwork for the verification of preventive activity against lesions that cause ulcers. Animals in the lab had ulcers induced using Shay's pyloric method. Comparisons were made between the control group and groups treated with Laghusoothshekhar (50 and 100 mg/kg) or Ranitidine (25 mg/kg, standard) with respect to ulcer index and percentage protection. Results from statistical analyses of the data demonstrated that rats given 100 mg/kg as a pre-treatment had effects similar to Ranitidine. The authors asserted that the formulation's components worked together synergistically. Its unique preparation method, Bhavana, is also essential to its enhanced efficacy.29

Amukkara Choornam

The Erode-based SKM Siddha and Ayurvedic Medicines India (P) Ltd markets Amukkara choornam, a Siddha PHF. For TB, enlarged spleen, hiccups, leucorrhea, stomach ulcers, and anaemia, it's a mixture of spices and herbs. This recipe calls for cane sugar and a blend of spices including cinnamon, ginger, cloves, cardamom, and withania somnifera (Duncan), as well as syzygium aromaticum (Linn.), cinnamon bark (Blume), and cinnamon (Piper nigrum). In their protective effects against ulcers, these components display a variety of methods, as shown by the literature review. Researchers have shown that Withania somnifera has antistressor function, Cinnamomum wightii has urease activity,

Elettaria cardamomum inhibits gastric ulcers, Zingiber officinale inhibits acid and pepsin secretory action, and Syzygium aromaticum stimulates mucus formation. The presence of steroids, bitter components, flavonoids, saponins, and phenols was confirmed by phytochemical screening of the formulation. The formulation had a high concentration of piperine, eugenol, and trans-caryophyllene, as shown by the HPTLC examination. These components may have anti-H. pylori effects, aid in tissue healing, protect mucus membrane integrity, and scavenge free radicals. The antioxidant capability of the formulation was determined by conducting DPPH scavenging activity. Antioxidant activity was measured using ethanol-induced and pylorus ligation procedures to further determine the formulation's favourable benefits on stomach protection. After that, we examined the activities of catalase, SOD, and ulcer-inducing LPO at 50, 100, and 200 mg/kg of formulation, with 100 mg/kg of ranitidine serving as the benchmark. Both models showed dose-dependent protective benefits against very harmful outcomes, according to the cited research. This provide credence to the comprehensive approach of treating ulcers with Amukkara choornam.30

Ulcerene

Ingredients of PHF Ulcerene include Bambusa arundinacea, Coriandrum sativum, Elettria cardamomum, Foeniculum vulgare, Rosa damascene, Mineral bezoar triturated, and Pistacia lentiscus. The powder was left to macerate at room temperature for three days in a solvent that was 70% water and 30% methanol. The resulting extract was then tested for the presence of several types of phytochemicals. In terms of phytochemicals, the results showed that there were tannins, carbs, proteins, alkaloids, phenols, and saponins present. Various techniques were used to produce ulcers, including those using ethanol, aspirin, and stress. The three models' respective standards were 100 mg/kg of Sucralfate, 50 mg/kg of Ranitidine, and 50 mg/kg of Ulcerene extracts, whereas the test groups received 50 and 100 mg/kg of Ulcerene extracts, respectively. On histopathological evaluation, the control group showed signs of hyperplasia, localised erosion, infiltration of inflammatory cells, congestion in lamina propria, and persistent superficial gastritis. Animals given conventional medication showed only little or no changes to their stomach mucosa. Ulcerene at its highest dosage (100 mg/kg) produced less gastritis, infiltration, and congestion when contrasted with its lower dose (50 mg/kg). Both the ulcer score and index decreased in a dose-dependent manner after using Ulcerene. When comparing several models, it was shown that the PHF was the most efficient in reducing lesions caused by ethanol.31

CONCLUSION

Because of its alarming global frequency, peptic ulcer is a condition that deserves serious attention. Presently, ulcer therapy with allopathic methods is associated with unpleasant and often debilitating side effects. Herbal remedies for ulcers were therefore developed as a result of the ongoing quest for better alternative therapies. Synergism, ease of use, high efficacy, a broader therapeutic window, and cost-effectiveness are some of the benefits of polyherbal formulations that have recently been recognised. As a result, there has been a surge in the usage of PHFs for ulcer therapy. The PHFs included in this study have promising antiulcer properties, which gives them a solid scientific foundation for their widespread usage in society. Nevertheless, there is a great deal of need for more clinical and pharmacological research on these PHFs.

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