International Journal of Pharmacognosy and Herbal Drug Technology (IJPHDT)
ISSN: 3049-1630 | Vol. 03, Issue 05, May-August-2026 | pp. 01-14

ORIGINAL ARTICLE https://www.aktpublication.com/index.php/ijphdt

Role of Herbal Medicine and Nutraceuticals like Licorice and Aloe Vera in the Management of Peptic Ulcer

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Abstract:

Peptic ulcer disease is a most common gastrointestinal ailment that cause mucosal erosion in the stomach or duodenum is most commonly induced by Helicobacter pylori infection, NSAIDs, stress, and lifestyle. Conventional therapies, including antibiotics and proton pump inhibitors effective, but causes potential side effects and recurrence risks. More focus has shifted towards complementary and alternative medicines, with special emphasis on herbal drugs and nutraceuticals because of their safety profile, cost-effectiveness, and comprehensive health benefits. Of these, Licoricey (Glycyrrhiza glabra) and Aloe vera have been shown to possess highly effective anti-ulcer effect. Licoricey contains autoprotective, anti-inflammatory, and anti-H. pylori activities, whereas Aloe vera provides wound healing, antioxidant, and cytoprotective actions to the gastric mucosa. This review discusses the mechanism, effectiveness, and possible therapeutic applications of these natural compounds in the treatment of peptic ulcers, noting their synergistic potential with standard treatments.

Keywords: Nonsteroidal Anti-Inflammatory Drugs, Peptic Ulcer, Gastrointestinal Tract, Acute and Chronic Diseases.

Received: May. 21, 2026 **Revised:** June. 25, 2026 **Accepted:** July 25, 2026 **Published:** August 01, 2026

DOI: https://doi.org/10.64063/3049-1630.vol3.issue5.000247

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1. Introduction

1.1 Definition and prevalence of peptic ulcers

Incidence calculations: Crude incidence is the number of new cases of perforated peptic ulcer in our population per 10,00,0 persons per year. The adjusted rates of incidence are the crude incidence age- and sex-adjusted to the total Norwegian population based on Statistics Norway. The crude

death rate is the number of deaths in the study population per 10,00,00 persons per year. Adjusted mortality rate is the age- and sex-standardized crude death rate to the whole population of Norway according to Statistics Norway [1]. Peptic ulcers, being the most frequent in the stomach and proximal duodenum, may produce intense acute upper abdominal pain or have an insidious onset and become subsequently a chronic disease with periods of symptomatic and asymptomatic episodes. Symptomatic stage may present as epigastric pain, bloating, nausea and early satiety. Regardless of the duration of the disease, acute and fulminating complications like bleeding, perforation or gastric outlet obstruction may arise. Furthermore, chronic gastric ulcer disease also threatens patients with gastric cancer. Those serious complications are likely to be expensive medically and socially [2.] Pressure ulcers are injuries that occur as localized areas of skin and deeper tissue soft tissue necrosis. They typically occur in bony prominences and predominantly in nonmobile patients. These old wounds are estimated to add more than a billion dollars a year to health care costs, potentially occurring predominantly at the time of a person's life when they are most likely to need health care resources. Pressure ulcers, like other chronic wounds, can contribute to compromised quality of life, longer hospital stays, and increased morbidity and mortality [3].

1.2 Etiology:

Over the last 20 years, ulcer pathogenesis has increasingly moved away from psychosocial causes; enormous efforts are now being directed toward Helicobacter pylori infection and nonsteroidal anti-inflammatory drugs. Enthusiasm for H. pylori infection as the final pathogenic cause of peptic ulcer disease needs to be balanced by three facts. First, although knowledge about the pathogenesis of peptic ulcer disease has increased, the declining prevalence of H. pylori infection among Western populations, and the greater availability of efficacious treatments, the burden of disease remains significant. Second, most individuals infected with never develop peptic ulcer disease. Third, 5% to 20% of patients develop peptic ulcer disease in the absence of any other recognized organic risk factor. The widespread enthusiasm with which H. pelorias been embraced as an ethology of peptic ulcer disease has also led us to realize that this infection might neither be sufficient nor necessary for ulcer disease development [4]. An acid is a chemical that has aqueous solutions distinguished by an unpleasant taste, the capacity to change blue litmus to red, and the ability to react with bases and some metals to form salts. Acidity means a pathological condition where the fluid in the stomach converts into excess acid. The English term "ulcer" originated from the Latin term ulus which mean "sore, wound, or an ulcer" and therefore peptic ulcer literally translates to tissue corrosion of the digestive tract. Gastroesophageal Reflux Disease is an illness in which the liquid material in the form of acidic digestive juices inside the stomach flows back into the esophagus. A peptic ulcer is "an ulcer of the alimentary mucosa, located in the stomach the first portion of the small intestine is called the duodenum. "The English word "peptic" is derived from the Latin word peptics are an abbreviation for "to digest" or provoking digestion. An ulcer is erosion or a sore which develops when the lining of the digestive tract colored by corrosive digestive juices secreted by the stomach cells while a peptic ulcer is a hole or a wound on the lining of the stomach or duodenum or the esophagus. Peptic ulcer is a rupture of the stomach lining, duodenum, or esophagus while an ulcer is a sore or erosion which develops as a consequence of the lining of the digestive tract being consumed by corrosive digestive juices. Peptic ulcers that develop in the stomach are known as gastric ulcers and in the in the duodenum

are known as duodenal ulcers and ulcer of the esophagus is known as an esophageal ulcer Reflux esophagitis is due to occurred due to reflux of stomach acid into the esophagus [5]. In the case of gastric ulcer, usually acid secretion is normal or reduced, whereas impaired mucosal defense (mainly compromised mucus and bicarbonate secretion) has a more pronounced role. In duodenal ulcer, acid secretion is elevated in approximately half of the patients but normal in the remainder. Regardless of whether production of acid is normal or elevated, it does play a part in ulceration as an aggressive agent, decreased in the primary method of treating ulcers. Knowledge of mechanism and regulation of gastric acid secretion will explain targets of antisecretory drug action [6].

1.3 Overview of conventional treatments and their limitations

The long-standing increase in cancer fatalities, together with the risks inherent in current therapy and its harmful side effects, underscores the necessity of more effective and more individualized therapies. Largely owing to their cost and prevalence, however, traditional therapy continues to be the most widely used, even in the face of new interventions like immunotherapy and gene therapy. Thus, repeated efforts towards improving and progressing conventional cancer treatments like surgery, radiotherapy, chemotherapy, and hormonal therapy are even important, as exemplified. This review aims to provide a comprehensive overview of the development and limitations of these ancient therapies. By discussing their status quo, evolutionary progress, and ongoing challenges, we try to outline areas of need and highlight potential future research directions and innovation [7]. Major depressive disorder is a disabling disease that happens in 10%–15% of the population every year. Despite advances in the understanding of psychopharmacology and biomarkers of major depression and the introduction of some new antidepressant classes, only 60%–70% of patients with depression respond to treatment with antidepressants. Of the nonresponses, 10%–30% have resistant symptoms along with social and occupational dysfunctioning physical health worsening, ideation of suicide, and increased use of health care. Treatment-resistant depression is a dilemma for health care providers. Major depression with a poor or unsatisfactory response to two optimal (optimal dosage and duration) trials of two diverse antidepressant classes has been proposed as an operational definition of treatment-resistant depression [8].

1.4 Need for alternative and complementary therapies

We are at a point in health care where it is no longer reasonable to assume that complementary therapies are useless in the delivery of health care. In this editorial, I give a modern overview of the problems in the application of complementary therapies and consider that their application has now achieved a level where they can be held to be an integral component of health care in offering an invasive and holistic complement to health care [9]. Alternative and complementary medicine is defined by the National Center for Complementary and Alternative Medicine as "a group of diverse medical and health care systems, practices, and products that are not generally considered to be part of conventional medicine". NCCAM further classifies CAM into five broad categories alternative medical systems, mind–body interventions, biologically based therapies, manipulative and body based methods energy therapies [10].

1.5 Introduction to herbal medicines and nutraceuticals.

Phytomedicines have been a major drug source since ancient times, though their use has been increased due to their therapeutic property and lower side effects than the other drugs. Developing and developed countries are counting on the popularity of herbal drugs mainly due to their natural origin and lowest side effects. The fast-evolving nanotechnologies have given a lot of help towards the establishment of innovative novel herbal drugs. Nutraceuticals are foodstuffs and food ingredients that have health benefits beyond normal nutrition, but most of the nutraceuticals exhibit poor bioavailability. Nanotechnology applications have provided to eliminate the challenges and technical hurdles associated with the solubility, bioavailability, stability and delivery of bioactive from foods. Spontaneous advancement in nutraceutical nanotechnology has immense scope to provide new and effective functional foods as a preventive approach as well as possible cure for certain non-communicable diseases. Different studies are already showcased in different forms of preparative methods of nanomaterials in nanotechnology for herbal drug delivery and nutraceuticals.

The current review highlights the application of nanotechnology in herbal medicines and nutraceuticals to nanomedicine and functional food. It is also emphasizing significant and quick progress in biomedical and food technology [11]. Various plants are poisonous to those who consume them. But man (or more probably woman) had the ingenuity to use fire (and later food) to break down the noxious effects of plant poisons. As man climbed, societies established what plants were safe to eat, what plants seemed to have medicinal uses and what plants were simply poisonous. Most of the plants that possessed medicinal value were hallucinogens, which gave the giver the authority to trance, but not necessarily heal or cure, the patient [12].

1.6 Objective of the review: to explore the therapeutic potential of licorice and aloe vera in PUD management.

Ulcers are penetrating ulcers that pass through the complete thickness of the gastro intestinal tract mucosa and muscularis mucosa. Peptic ulcers is a collective name which covers ulcers of the digestive system either in the stomach or in the duodenum. Current research has proven that this ulcer was caused by aggressive factors. Bacterial infection Helicobacter pylori or response to specific drugs as nonsteroidal anti-inflammatory drugs is the etiologic agent of the disease [13]. It requires carrying out a proper evaluation of natural products and how far they can be beneficial in GERD because of the continued difficulties in managing the disease. There is a need to fully assess alternative treatment continuously. There are possibilities that some herbal extracts, polyphenols, probiotics, and some other naturally occurring agents may potentially modify or influence the pathophysiological mechanisms of gastroesophageal reflux disease. Such pathologic mechanisms include enhanced inflammation and gastric acid secretion, and reduced mucosal defenses. While their potential is significant, these mechanisms and efficiencies of such natural products remain to be detailed fully, especially when in the context of standard medicines. This review will thus attempt to investigate in depth the natural products being used in the treatment of GERD, their known mechanism of action, clinical efficiency, and capacity to be incorporated into established models of therapy. The purpose of this review is to venture into current literature, wherein gaps in related information will be plugged and novel directions for study and therapy will be suggested This would enable more effective control and the creation of new, more inclusive, and safer therapeutic alternatives [14]. Nutraceutical is a word coined from "nutrition" and "pharmaceutics."

The term refers to those products that are derived from herbal products, dietary supplements, special diets, and processed foods like cereals, soups, and drinks that aside from nutrition are employed as medicine [15].

2.Pathophysiology of Peptic Ulcer

2.1 Mechanisms of ulcer formation:

In the present article we discuss the cellular and molecular pathways of healing of gastric ulcer emphasizing the pivotal role played by growth factors in healing. Gastric ulcer is a deep mucosal defect of the gastric wall extending through the entire mucosa and the muscularis mucosae [16]. Tissue hypoxia will result in a number of clinical presentations, ranging from erosion to ulcer, when similar lesion happens in the stomach. Peptic ulcer is one of the most common presentations [17].

2.2 Gastric acid and pepsin activity

Pepsin needs an acidic environment in order to break down protein. Therefore, it works optimally at a pH of approximately 1.5 to 2. Low pH allows pepsinogen to autoclave and form active pepsin. After it arrives in the duodenum, however, it is inactivated as pH rises above 6. However, protein breakdown continues throughout the small intestines by means of pancreatic enzymes: trypsin, chymotrypsin, elastase, and carboxypeptidase. Thus, pepsin is not vital to life, and protein digestion remains possible without pepsin. It should be noted that pepsin structurally persists up to at least a pH of 8. Thus, it can always be reactivated provided pH is less than 8. This property becomes significant in the pathophysiology of laryngopharyngeal reflux, as will be elaborated later in the article [18]. Two sets of experiments were conducted at different pH with CA suspensions as well as with EWP solutions. The first one was utilized to trace kinetics of protein hydrolysis for 2 h digestion at high time resolution using the pH-STAT method. The degree of hydrolysis in the end sample was measured by the ortho-thioaldehyde method. The second set of experiments was utilized to determine the initial rate of the hydrolysis reaction (3 min after) using the OPA method [19].

2.3 Mucosal defense disruption

The intestinal mucosal barrier is mainly made up of a mechanical barrier, a chemical barrier, a microbial barrier and an immune barrier. The intestinal mucosal barrier will play a significant role to prevent invasion by pathogens such as Candida species. The most common pathogenic Candida species in man is C. albicans. It is widely believed that the most significant reservoir for [20]. Distributionally, the mucosal immune system lies mostly in the upper respiratory, lower respiratory, gastrointestinal, and urogenital tracts. Furthermore, the mucosal immune system exists in other mucosal tissue-bearing locations such as the conjunctival and lacrimal glands of the eye, middle ear, salivary glands, and mammary glands. Respiratory virus infection routes were strongly correlated with mucosal immune system distribution, indicating their intimate relationship [21].

2.4 Role of Pylori

Helicobacter pylori is a gram-negative rod that is worldwide in distribution, infecting more than 50% of the world's population, with a high prevalence in developing nations compared to

industrialized countries. The major mode of transmission is the inter-human. Low socio-economic status is a major risk factor. Though being worldwide diffused, the infection occurs in only 10%-20% of patients complicated by clinical symptoms [22]. This review has set out to identify recent developments in H. pylori pathogenesis, particularly the bacterial and host factors that contribute to the host-pathogen interaction during chronic colonization. It also emphasizes the host immune response to H. pylori colonization and its impact on varied clinical outcomes, particularly on progression towards GC [23].

2.5 NSAID-induced mucosal damage

The GI injury produced by NSAIDs may be mitigated in several manners - best by withdrawal of the drug by selecting one less toxic by supplementation with a second drug prophylactically or following a complication. The identification of the cyclooxygenase preferential towards the end of the 1990s promised to revolutionize therapy with sparing, and therefore efficacious control of inflammation, with fewer ulcers and bleeding complications. These drugs were widely used until evidence of cardiovascular side effects, including an increased risk of myocardial infarction, gradually began to emerge, and some of the COX-2 NSAIDs were subsequently taken out of widespread use in North America and Europe [24]. NSAID-induced damage of gastric and duodenal mucosa has been extensively researched. The upper GI side effects are troublesome symptoms with or without mucosal damage, asymptomatic mucosal injury, and severe complications, including death [25].

2.6 Oxidative stress and inflammation

Inflammation is a fundamental biological process which is taking center stage in the pathogenesis of an overwhelming majority of acute and chronic diseases. Complex inflammatory systems with billions of cellular and humoral components are responsible for main characteristics of such highly disparate diseases as myocardial infarction, diabetes, rheumatoid arthritis, sepsis, cancer, or Alzheimer's disease to name but a few. As a direct sequela, clinical and basic studies on the subject of inflammation have been increasing steadily, evidenced by the results of a Medline search employing the term 'inflammation [27].

3. Herbal Medicine and Nutraceuticals: An Overview

3.1 Definition of herbal medicines and nutraceuticals

A herbal medicinal product means any medicinal product which contains solely as active ingredients one or more herbal substances or one or more herbal preparations, or one or more such herbal substances combined with one or more such herbal preparations [28]. A nutraceutical has been otherwise defined as 'a functional food that assists in the prevention and cure of disease and or disorders. The author of this definition explained that he had singled out to be ruled out 'since most of the functional foods do something or the other as exception to anemia a clear-cut distinction between the two terms, functional food and nutraceutical', with the bewildering rider that 'a functional food for one consumer may function as a nutraceutical for another consumer [29].

3.2 Historical and cultural context of plant-based ulcer remedies

Pandemics have painted the history of mankind, and plants were mostly the first available medicament. Egyptian evidence of plant remedies dates to, further elaborated by Greeks and

Romans, and well documented in official drugs books named Pharmacopoeias. Even in our times, traditional medicines based primarily on plants are the sole therapeutic option for most people in developing nations [30].

3.3 Licorice use in Peptic Ulcer Management

Glycyrrhiza glabra L. is used in folk medicine to treat stomach ailments like peptic ulcers. Hydroalcoholic extract of Glycyrrhiza glabra L. was investigated for antiulcerogenic effect as well as acute toxicity profile in mice. Doses ranging from 50 to 200 mg/kg were administered orally to animals of different groups. Omeprazole and cimetidine doses of 30 and 100 mg/kg were used as positive controls, respectively. Greater curvature of stomach was opened then ulceration index was determined examining inner lining of stomach [31].

4.Pharmacological Actions Relevant to PUD

4.1 Anti-*H. pylori* activity

Helicobacter pylori chronically colonize the gastric epithelium of approximately half the population of the world. Colonization can cause development of gastric and duodenal ulcers, mucosa-associated B-cell lymphoma, and gastric adenocarcinoma. H. pylori infection, if not treated, can progress to gastric cancer in as high as 3% of infections. H. pylori infection is cured by total eradication of the organism from the host. The effectiveness of currently available drug regimens has fallen considerably over the years. Clarithromycin-resistant H. pylori was designated as a priority pathogen for research on by the World Health Organization, indicative of the compelling need for novel anti-H. pylori treatment [32.]

4.2 Mucosal protective effect

GC is the most common type of cancer and the second most common cause of cancer-related death globally And the occurrence of gastric carcinoma is an evolutionary process of histopathology, starting from chronic gastritis, GPL, such as chronic atrophic gastritis intestinal metaplasia, dysplasia, even carcinoma Therefore, additional study of GPL, a margin of gastric cancer, is necessary for the prevention of the generation and formation of gastric carcinoma [33.]

4.3Anti-inflammatory and antioxidant effects

Autonomic nervous system has been known to have an important part to play in the overall health. Chronic stress associated with an unhealthy way of life in modern societies is responsible for ANS dysfunction, which is involved in the etiology of neuroendocrine, cardiovascular, respiratory, digestive and psychiatric illness. Physical exercise has been shown to affect health in general, but high-intensity exercise's adverse impact is less well documented. The oxidative stress induced by these types of physical exercise is important in impacting. In this review, we first introduce briefly the network and its correspondences with the hypothalamic–pituitary–adrenal axis. We then provide an overview of the key roles in health and disease, focusing especially on inflammation and oxidative stress [34].

4.4 Stimulating mucus and prostaglandin production

The discovery of a link between infection with Helicobacter pylori as well as gastric ulcer disease increased the focus on mucosal defernce mechanisms. This was motivated especially by the observation that only a minority of patients (~15%) with this infection will go on to develop an ulcer, and therefore host factors must be a dominant factor in deciding whether an ulcer will develop or not [34].

5. Evidence from Studies

5.1 In vitro studies

Among numerous GI disorders, functional dyspepsia is a most common and costly clinical entity in family medicine practices. Dyspepsia not associated with clinically discernible, structural GI lesions is termed functional dyspepsia or nonnuclear dyspepsia. Upper abdominal fullness, epigastric pain, belching, bloating, early satiety, nausea, vomiting, regurgitation, heartburn, and appetite loss are general symptoms of functional dyspepsia [35]. We hypothesized that the new variety of Glycyrrhiza Wonga exhibited antiallergic effects because Wonga contains only one Glycyrrhiza species and because of the well-documented effects against allergy of its constituents. Its promising effects led us to study the mechanisms of action of Wonga as an antiallergic agent free of side effects. It is the first research that attempted to investigate the antiallergic effects of Wonga extract both in vivo and in vitro. For elucidation of the antiallergic activity of Wonga, we utilized an in vivo compound-48/80-induced anaphylaxis mouse model and in vitro cells. WG was observed to alleviate allergic markers through modulation of mast-cell-dependent allergic reactions [36].

5.2 Animal models

As a result, numerous trials have been done for several decades in an effort to find anti-asthmatic medication candidates that are less harmful and more effective. Many have specifically tried to create asthma medications by researching the processes and/or modes of action of conventional prescriptions and drugs. In Korea, Jun Huh put together Dangriga, a medical encyclopaedia, some 600 years ago. It was a medical and remedy-related encyclopaedia. One of the medications prescribed in the Dangriga for the treatment of pulmonary diseases is socheongryongtang [37].

5.3 Clinical trials

Nothing is there to give full guidance to avoid from corona virus but some advice was given by WHO and ECDC. Essentially, these are advice for health profession to establish during the treatment of infected patient. Because lots of evidence was given by studies regarding human-to-human transmission of corona from Wuhan, China. Another study was narrating about air bone transmission of virus whereas no one was giving the solid evident [38.]

5.4 Comparative studies with standard drug

Ulcers are a diverse collection of ulcerative disease of upper gastrointestinal tract. Ulcer is a wound, that is, which is painful or distressful. Peptic Ulcer Disease (PUD) refers to the erosion of duodenum or stomach lining (lining composed of gastric acid secreting cells and mucosa that protects stomach cells against gastric secretions) [39].

6. Safety and Toxicity Concerns

Glycyrrhizin and glycyrrhizin acid were found to induce interferon.24 Induction of interferon results in powerful antiviral effects, since interferons attach to cell membranes, where they trigger synthesis of intracellular proteins that inhibit transcription of viral DNA. Induction of interferon is also followed by macrophage activation and enhancement of natural killer cell activity [40].

6.1 Risks of chronic use (e.g., pseudoaldosteronism, hypokalemia)

Liquorice has the metabolite glycyrrhizin acid which exerts its effect to inhibit 11βHSD2 via competitive inhibition and decreased gene expression. It thus permits unopposed activation of the mineralocorticoid receptors due to cortisol, resulting in apparent mineralocorticoid excess but in a context of suppressed or normal serum aldosterone [41].

7. Aloe Vera use in Peptic Ulcer Management

Aloe vera is also referred to as the "plant of immortality" and is one of the most therapeutically used plants in traditional medicine around the globe. Out of 420 aloe species, it is the most bioactive species. It is found to contain at least approximately 75 biologically active chemicals such as vitamins, enzymes, minerals, sugars, steroids, hormones, saponins, amino acids, and phenolic compounds. It has anti-inflammatory, antioxidant, cytoprotective, immunomodulatory, wound healing, and anti-tumor activities. Based on these biological activities, Aloe vera may be applied in GU healing [42].

7.1 Pharmacological Actions

Prostaglandins are autocoids and powerful vasodilator and are derived from arachidonic acid and unsaturated fatty acid. Prostaglandins are mainly secreted into the gut human under vagal and hormonal stimulation. The endogenous prostaglandins are involved in the maintenance of mucosal integrity, control of mucosal, control of mucosal blood flow, protection against harmful agents, inhibition of acid synthesis increase secretion of protective mucus and protection against ulcer gastric injury, ulcer healing and cytoprotective agent [43].

7.2Anti-inflammatory and healing properties

Diet rich in antioxidants has a beneficial effect against gastric diseases because of their promotion of gastric mucosal protection. Antioxidants reduce gastric mucosa oxidative damage because they protect the free radical fatty acids of the cell membrane and suppress gastritis-induced inflammatory cascade Other bioactive molecules with an anti-inflammatory effect in gastric lesions include different polyphenolic molecules. Quercetin at 50 mg/kg decreased the malondialdehyde levels on ethanol-induced gastric injury in Wistar rats and significantly elevated the activity of antioxidant enzymes [44].

7.3 Antibacterial effect against H. pylori

H. Pylori was provided by aim shams university hospital, Cairo, Egypt as a proven organism to perform these experiments. In vitro anti-h. Pylori activities were detected using a well agar diffusion method under the following protocol: a suspension of 100 all of the suspension colony-forming units of h. Pylori was inoculated in Mueller Hinton agar with 10% blood and blood products and plated. Upon solidification, a 6 mm diameter hole was aseptically drilled using a sterile corn borer. Ninety-nine µl of flower extract of a. Nilotica was placed in the well. The well containing demos was employed as a negative control, and the well containing clarithromycin as a positive control. Inoculated plates containing specific conditions and temperature (37 °c) were incubated for three days. Then, the diameter of the inhibition zone that was visualized was identified [45].

7.4 Antioxidant action

These include glutathione peroxidase, superoxide reductase, catalase, glutathione-reductase, and superoxide dismutase. Among these antioxidants superoxide dismutase, glutathione peroxidase and catalase are considered as first-line antioxidants against [46].

8 . Evidence from Studies

8.1 Laboratory and animal model studies

The significance of AV, as the entire leaf extract, the gel, and the latex, for health maintenance by modulating a number of biological activities has been well documented across the globe. The most prevalent and recent studies are enumerated below. Specifically, surveys concerning extracts derived from the plant and single compounds extracted from AV are reported, and investigations on commercially available single compounds of AV [47].

8.2Clinical research and trials

Aloe vera gel has been attempted in the management of radiation burns. Healed radiation ulcers were observed in two patients who were given Aloe vera cream, but the new gel was better than the cream. Complete resolution was noted, following treatment with the fresh gel, in two patients having radiation burns. Twenty-seven patients having partial thickness burns were treated with the gel in a placebo-controlled trial. Lesions treated with the gel healed earlier than petroleum jelly gauze treated burns a difference which has statistical significance [48].

8.3 Aloe vera as monotherapy or adjunct therapy

Aloe vera leaf and gel extracts were tested for ant sickling activity. The measurement of the ant sickling activities of the extracts was to inhibit polymerization of sickle cell and change the Fe2+/fe3+ ratio of Hank's Balanced Salt solution in the presence of the extracts. The comparative percentage inhibition of the polymerization of sickle hemoglobin by the extract varied from 77.93% in crude aqueous extract of the gel to 80.86% of that of the leaves. [49].

9. Safety and Toxicity Concerns

9.1 Laxative effect at high doses

Among many species of Aloe, Aloe vera has been the strongest, economically viable and studied plant by researchers. The plant tissues contain about 75 nutrients and 200 active ingredients such as amino acids, sugars, enzymes, vitamins, minerals, saponins, anthraquinones, lignin and salicylic acid. Volatile oils and ascorbic acid are found in flowers while ascorbic acid, polysaccharides, lignin, pectin, hemicellulose and cellulose are found in rind. Again, the leaves are the source of many organic acids, enzymes, phenolic compounds, minerals and vita Boudreau and Beland, 2006a, Boudreau and Beland, 2006b [50].

10. Comparative Efficacy and Synergistic Potential

10.1 Licorice vs. aloe vera in terms of:

10.2 Healing time

Gastroesophageal reflux disease is a condition disease caused by an intersection of multiple factors. Gastric acid overproduction, compromised esophageal defense, and persistent inflammation are some of the emphasized factors already established Hydrochloric acid, the main constituent of gastric acid, also plays an important part to contribute in causing esophageal mucosa injury in GERD Gastroesophageal reflux disease is a disease condition resulting from a convergence of various factors. Overproduction of gastric acid, impaired esophageal defense, and continued inflammation are among the highlighted factors already known Hydrochloric acid, the chief component of gastric acid, also has a crucial role to play in esophageal mucosa injury in GERD HCl-triggered injury induces inflammation that enhances damage to tissues and makes a chronic condition. In addition, bile acids and pepsin stimulate esophageal injury and extend the period of injury. Recent studies have shown that gut microbiome imbalances are another driver of GERD. It fosters the advancement of and resultant effects like Barrett's esophagus and esophageal carcinoma. Systematic evaluation of GERD pathogenesis contributing factors, including those that seek to restore microbial balance, may provide insights to accessible treatment methods which cut down inflammation and prevent esophageal injury [51].

11. Future Directions

Data were extracted and quality was assessed independently by four researchers. Data were aggregated utilizing standardized and pre-piloted forms along following categories: (1) characteristics of studies, such as the first author's last name, year of publication, design, diagnosis type, age of the subject, dose, duration of the intervention, preparation type, and country; and (2) mean FBG and SD of the control and the intervention groups. Disagreement in extraction was solved by discussion. Qualitatively and quantitively, a rigor score was utilized to appraise the quality of the study. For each study, an 8-item scale plus 1 item concerning the sample size (≥30 participants) was utilized. Each criterion of assessment was allotted a score as 1 (one) if "yes" and 0 (zero) if "no". Otherwise, we tried to access the original data source from the authors to predict the uncertain or incomplete data.[52-54]

12. Conclusion

Herbal medicines and nutraceuticals such as Licorice and Aloe vera offer significant potential in the management of peptic ulcer disease. Their multifaceted mechanisms—ranging from enhancing mucosal defense and reducing gastric acidity to exerting antimicrobial and antioxidant effects—make them valuable adjuncts or alternatives to conventional treatment. Licorice, particularly in its deglycyrrhizinated form (DGL), and Aloe vera have demonstrated efficacy in both experimental and clinical settings, supporting mucosal healing and symptom relief. However, despite their therapeutic promise, further large-scale, well-controlled clinical trials are needed to establish standardized dosing, long-term safety, and efficacy profiles. Integrating these natural agents into modern treatment paradigms may pave the way for more holistic and patient-centered approaches to peptic ulcer management.

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