

Review Of Conventional And Herbal Treatment For Peptic Ulcer Disease

SAURABH KUMAR YADAV , Mrs. JAYA SINGH , Dr. AMARJEET SINGH

Department of Pharmaceutics, Innovative College of Pharmacy, Knowledge Park II, Greater Noida, Uttar Pradesh, 201308.

Abstract

It is believed that 10 percent of the world's population suffers from peptic ulcer disease in one form or another. The existence of gastric juice pH as well as a reduction in mucosal defences are both factors that contribute to the formation of peptic ulcers. The infection caused by H. pylori and the use of nonsteroidal anti-inflammatory drugs (NSAIDs) are the two most important factors that influence mucosal resistance to injury. One of the most common issues affecting the digestive system is an ulcer in the stomach. For many patients, the current treatment strategy includes a significant amount of time spent on traditional Western medicine. In both human patients and animal models of stomach ulcers, herbal treatments have been found to be effective in healing the ulcers through a variety of different mechanisms. This study, which incorporates recent discoveries, provides an up-to-date analysis of the efficacy and safety of herbal medicines for the treatment of gastric ulcers, as well as the mechanisms by which these medicines act in both animals and people. In humans or animal models, a number of studies have demonstrated that herbal drugs can be just as effective as, or even better than, prescription treatments such as omeprazole or cimetidine in terms of their therapeutic value. Anti-oxidant qualities, a reduction in acid output, and inhibition of the H⁺/K⁺-ATPase enzyme activity are all natural treatments for stomach ulcers. Other natural cures for stomach ulcers include these. There are a number of different herbal treatments that also include antibacterial properties. People who suffer from stomach ulcers may find that treating the condition with herbal medicine is an effective treatment option that has few adverse effects.

Keywords: Peptic ulcer, NSAIDS, Herbal medicine, Antiulcer activity.

Introduction

Gastric ulcers are a common clinical presentation in the United States and regularly result in costs that run into the millions of dollars for medical treatment. Perforations are known to occur when there is a breach in the mucosal barrier of the stomach lining that extends to the muscularis mucosa and has a diameter that is greater than 5 millimetres. It is important to be aware that this illness process can in fact be remedied as well as prevented. Patients may require a different type of treatment for their stomach ulcers if the ulcers were caused by a different factor. The mucosa lining of the stomach is shielded from the harshly acidic environment of the gastric lumen by the natural defence mechanisms of the body. In the event that these defences are breached in any way, alterations to the gastric mucosa can result in erosion and, eventually, ulceration. The mucosa of the stomach is kept healthy by the

presence of prostaglandins, mucus, growth hormones, and enough blood flow. A number of factors, including smoking, hydrochloric acid, ischemia, nonsteroidal anti-inflammatory drug use (NSAIDs), hypoxia, alcohol consumption, and an infection with *Helicobacter pylori*, have been demonstrated to be deleterious to the integrity of this barrier.

Etiology & Pathology

The most prevalent causes of PUD are *H. pylori* infection and the use of nonsteroidal anti-inflammatory drugs (NSAIDs), but not everyone who has either of these factors will develop the illness. About half of the people on the planet have the *H. pylori* bacteria in their stomachs. It is during childhood that most people become infected with the disease, and it does not leave the body unless it is treated. Conditions that are overcrowded or dirty, in addition to a lower socioeconomic status, are risk factors for sickness. There are some racial and ethnic groupings that are more prone to getting infected with *H. pylori* than others. During the last five years, there has been a general decline in the prevalence of *H. pylori* in the United States among people of all ages. There is a significant difference in the infection rate across populations of different ethnicities. The infection rate among Mexican Americans is sixty percent, but the infection rate among non-Hispanic whites is thirty percent lower. The inflammatory response that is brought on by *H. pylori* in the mucosal layer of the stomach is what leads to the degeneration and destruction of epithelial cells. Although it is normal for the antrum to be more inflamed than the corpus, this is not always the case. Sometimes the inflammation is more concentrated in the corpus. It is important to conduct screenings on people who suffer from peptic ulcers to verify that they do not carry the *H. pylori* bacteria.

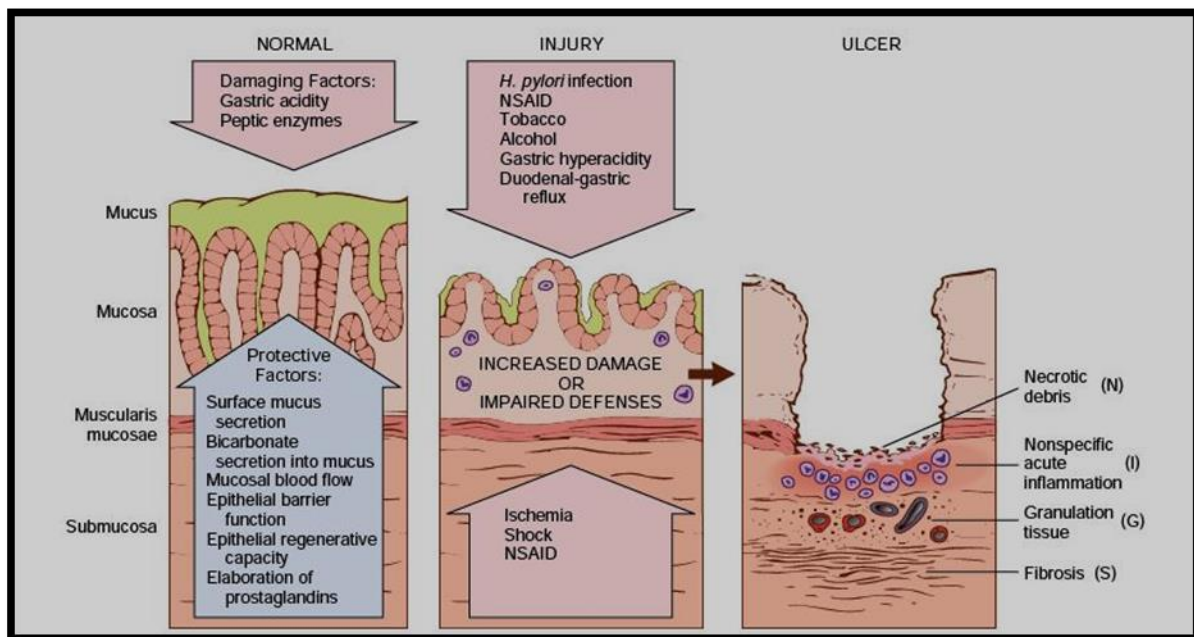


Fig:1 Patho-Physiology of Peptic ulcer

Treatment

The treatment plan for a patient's peptic ulcer will be determined by the underlying cause of the condition. If you have the letter H. pylori, you will need to eliminate it, cut back on your use of NSAIDs or stop taking them altogether, and take medication to assist in the healing of your ulcer.

Antibiotic medications to kill H. pylori If your physician determines that you have H. pylori in your stomach, he or she may advise you to take a series of medications in order to eradicate the bacteria. A number of examples include levofloxacin, amoxicillin, clarithromycin, metronidazole, and tinidazole. Tetracycline and tetracycline are also included. If you live in a region where there is a high rate of antibiotic resistance, the treatments that your doctor will prescribe to you will be determined by those characteristics. Antibiotics for a full two weeks, a proton pump inhibitor, and likely bismuth subsalicylate will be administered in an effort to bring the patient's stomach acid levels down (Pepto-Bismol).

Medications that block acid production and promote healing. These medications, which are referred to as proton pump inhibitors (PPIs), are effective because they hinder the normal functioning of cells that produce acid. Prilosec, Lansoprazole, Prevacid, Rabeprazole, Aciphex, Esomeprazole, and Pantoprazole are all examples of drugs that belong to this category. These medications are available both with and without a doctor's prescription. Prilosec, Lansoprazole Prevacid Rabeprazole (Protonix). It is possible that your risk of hip fracture, wrist fracture, and spine fracture will increase if you take proton pump inhibitors for an extended period of time, and especially if you take substantial dosages of these medications. Talk to your primary care provider to find out whether or not taking a calcium supplement will help lower your risk.

Medications to reduce acid production. Acid blockers, which are also known as histamine (H-2) blockers, reduce the quantity of stomach acid that is released into your digestive tract. This alleviates the discomfort associated with ulcers and assists in the healing process. Pepcid AC (Famox) and nizatidine (Tagamet HB) are two examples of acidity-blocking medications that can either be obtained through a doctor's prescription or bought over the counter (Axid AR).

Antacids that neutralize stomach acid. Your doctor might recommend taking an antacid for your stomach upset. Because they reduce the amount of acid produced in the stomach, antacids are an effective way to treat stomach pain rapidly. It is possible that one of the side effects will be either constipation or diarrhoea, but this will depend on the primary chemicals.

Medications that protect the lining of your stomach and small intestine. In certain circumstances, your physician may recommend that you take cytoprotective medications, which are medications that assist protect the tissues that line your stomach and small intestine.

Some Indian herbs used in treatment of ulcer

In spite of the widespread use of these plants in traditional Indian medicine, relatively little is known about the pharmacological effects of certain well-known medicinal plants. These plants are among the

most commonly utilised in Indian medicine. Research was conducted on the antiulcer and acute toxic effects of medicinal plants. The medicinal herbs that we researched were shown to be capable, according to the findings of our study, of preventing ulcers in rats in a dose-dependent manner. Histological tests revealed that the medicinal plants under investigation did not exhibit any signs of acute toxicity. During the initial phase of the photochemical analysis of this medicinal plant, secondary metabolites like flavonoids and tannins were found. Although it has been suggested that a great number of botanical components possess antiulcer characteristics, the majority of published research has been on the effects of medicines on animals. Because aloe, licorice, and chilli pepper are the only phytochemical compounds for which there is clinical evidence to support their use as gastro-protective drugs, there is a paucity of data regarding their efficacy and safety. In spite of this, there are a number of botanical chemicals that have the potential to be used in therapeutic applications due to their high efficacy and low toxicity. Compounds with antiulcer activity, such as flavonoids, aescin, aloe gel, and many others, are of particular relevance because the majority of anti-inflammatory medications used in contemporary medicine cause ulcers. The findings of the experiment are presented in Table 1.

Table: 1 Some Potentially Ulcer-Active Plants

Botanical Name	Parts used	Active Constituents	Medicinal uses
Azadirachta indica	Leaves	Phenolic Compounds, Saponins, Flavonoids	Anti-ulcer, Wound healing
Curcuma longa	Rhizome	Phenolic Compounds, Flavonoids, Tanins	Anti-ulcer, Wound healing, Anti inflammatory
Nigella sativa	Seed	Alkaloids, Phenolic Compounds, Saponins, Flavonoids	Diuretic, anti tumor
Ginseng	Root, Leaves, Stem	Triterpenoids, Volatile-oil, Peptides, amino acids	Anti-cancer, anti obesity, anti ageing

Basella rubra	Leaf	Protein, saponins,flavonoids	Anti ulcer
----------------------	------	---------------------------------	------------

Mechanism of Action of herbal in treatment of peptic ulcer

Researchers have discovered that herbal treatments for stomach ulcers act through a variety of mechanisms, including antioxidants, mucosal stimulation, suppression of acid formation and secretion, improved production of mucus, and inhibition of inflammatory processes (Figure 2).

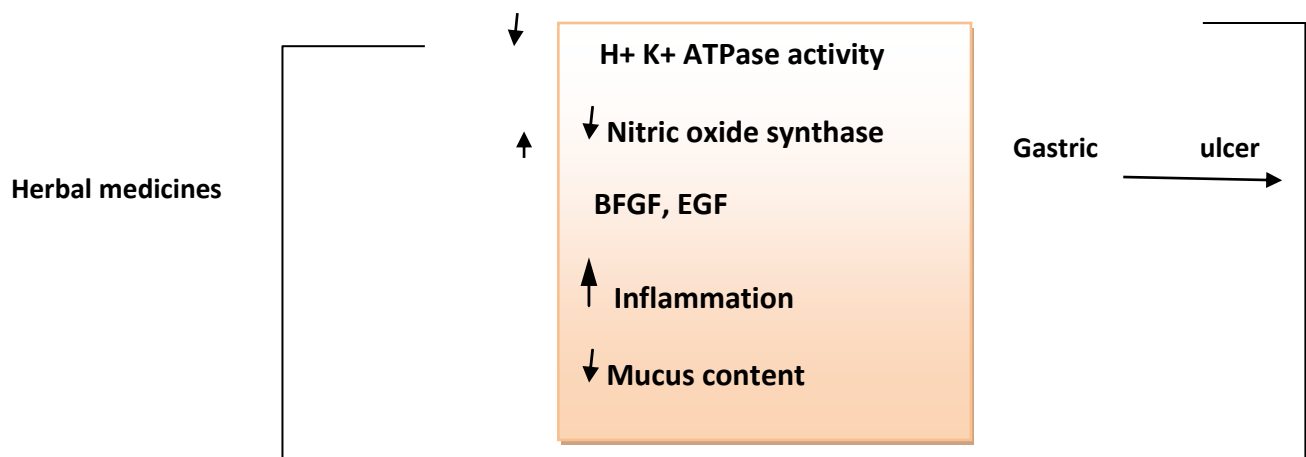


Fig: 2 Herbal medicine used in treatment of peptic ulcer

Anti-oxidant Activity:

In Brazil's Amazon and Northeastern regions, where traditional medicine is practised, the fruits of the *Libidibia ferrea* tree are traditionally employed as a treatment for gastrointestinal disorders. On the other hand, documentation of this pharmacological activity has never been done before. The dry extract of the *L. ferrea* pods, also known as DELfp, has been the subject of a number of research, all of which have shown that it is effective in the treatment of peptic ulcers. The phytochemicals of the plant were investigated with the use of HPLC/MS. For the purpose of determining in vitro antioxidant activity, DPPH, ABTS, phosphomolybdenum, and superoxide radical scavenging activities were utilised. It was investigated to see whether or not -SH and NO compounds had an impact on the antiulcerogenic activity of DELfp, as well as the drug's capacity to prevent gastric ulcers and boost mucus production. The healing activity was evaluated using a model consisting of an acetic acid-induced chronic ulcer. The effectiveness of the anti-*H. pylori* medication was examined. DELfp was analysed using HPLC/MS, and the results revealed the presence of two phenolic substances: gallic acid and ellagic acid. The extract was shown to possess anti-oxidant capabilities through the use of in vitro testing. The effective dose (ED50) of DELfp in ulcers generated by pure ethanol was 113 mg/kg, whereas the ED50 in ulcers caused

by acidified ethanol was 185.7 mg/kg. Inhibition of indomethacin-induced lesions was achieved at a percentage of 66.7, 70.6, and 65.8 percent, respectively, when DELfp was administered at dosages of 100, 200, and 400 mg/kg. DELfp at a dose of 200 mg/kg was able to lower gastric secretion as well as the concentration of hydrogen ions in the stomach contents. This effect was found to be independent of NO and dependent on sulfhydryl compounds. The gastric mucosa was protected as a result. In the model of chronic ulceration, administration of DELfp resulted in a smaller ulceration of the stomach. In addition to this, it was discovered that DELfp possessed anti-H. pylori capabilities. As a consequence of this, it was shown that DELfp possessed healing and antiulcerogenic actions in addition to antioxidant and gastroprotective capabilities. It is believed that anti-H. pylori activity and sulfhydryl compounds each play a part in the process that underlies these effects; however, these effects appear to be mediated by distinct systems. For the sake of all of these potential benefits, it is recommended that this species be utilised in the medical treatment of stomach ulcers.

Phenolic Compounds

Secondary metabolites and phenolic compounds are widespread in plants and can be found in all parts of the plant, from the roots to the seeds. Tannins and lignins are two examples of the polymeric aromatic chemicals that are ubiquitous in the natural world. Tannins are found in plants, and lignins are found in wood. Polyphenols can be broken down into two distinct categories based on their chemical make-up: flavonoids and non-flavonoids. There are several different types of flavonoid polyphenols, including anthocyanins, catechins, flavanones, flavones, flavonols, and isoflavones. Not to be confused with flavonoid polyphenolic acids, non-flavonoid polyphenolic acids include polyphenolic acids and hydroxycinnamic acids. The majority of a plant's polyphenol content is comprised of hydrolyzable tannins and phenylpropanoids, such as lignin, flavonoids, and condensed tannins.

The phenolic compounds of pharmaceutical interest are simple phenolic compounds (catechol, eugenol, vanillin, caffeic acid, ferulic acid, and salicin), flavones (apigenin, tangeritin, tangerine, and luteolin), isoflavones (genistein, daidzein, and glycitein), isoflavonoids (rotenone and genistin), flavonols (quercetin, gingerol, kaempferol, myricetin, and rutin), flavanones (hesperetin, naringenin, and eriodictyol), anthocyanidins (cyanidin, delphinidin, malvidin, and petundin), anthocyanins (haematien), coumarins (umbelliferone, aesculetin, and scopoletin), tannins (gallic acids, ellagitannins, catechins, gallitannins, and catechins), lignans (silymarin, matairesinol, pinosresinol, lariciresinol, and secoisolariciresinol), and lignins.

In the 1990s, flavonoids and several other polyphenols received a great deal of attention; nevertheless, the beginning of serious study on these compounds did not occur until 1995. A rush of study is presently being conducted on polyphenols in an effort to investigate the possible health advantages of these compounds. Antioxidants, such as polyphenols, are vital in the prevention of heart disease, some types of cancer, and diabetes, in addition to a range of other conditions that are associated with ageing. Polyphenols are an example of an antioxidant. In terms of their physiology, they exhibit a diverse variety of activities. These chemicals have been reported to possess antiviral, anti-allergic, antiplatelet,

antiestrogen, anticancerogenic, antiinflammatory, antiproliferative, antiangiogenic, and antioxidant effects, and their administration typically produces very little or no damage. It has also been suggested that polyphenolic chemicals, which are believed to be effective in the treatment of stomach ulcers due to the fact that phenols are believed to stimulate the creation of PGE₂, are beneficial. It appears that the addition of polyphenols has a beneficial effect on oxidative stress indicators. Some of these potentially beneficial effects have been linked to their antioxidant characteristics, such as their ability to interrupt chain processes involving free radicals, their ability to directly decrease levels of peroxides, and their ability to increase antioxidative defence enzyme activity.

It has been demonstrated that several different flavonoids have effects on the gastrointestinal tract, some of which include antispasmodic, antisecretory, antidiarrheal, and antiulcer properties. It has been demonstrated time and again that flavonoids, which belong to the cytoprotective chemical class, have an anti-ulcerogenic function. Their anti-ulcerogenic properties, which include the ability to scavenge free radicals and function as antioxidants, increased mucus production, antisecretory activity, and the prevention of the growth of *Helicobacter pylori*, all contribute to the preservation of healthy mucosa in the stomach. Tannins prevent ulcers by precipitating proteins and constricting blood vessels, both of which are necessary for ulcer formation. As a result of their astringency, they serve to precipitate microproteins at the ulcer site, which results in the generation of an impermeable covering that protects the lining of the gastrointestinal tract and reduces the ulcer scores in rats, as seen by the gut secretions.

Herbal & Drug Interaction

Even though it is based primarily on a nonholistic, bug-killing, target-focused approach that ultimately results in future adverse effects, modern medicine has emerged as the primary treatment option for virtually all health-related issues. This is despite the fact that modern medicine is built on an approach that kills bugs (notable in case of chronic disorders such as cancer, diabetes, arthritis, etc). When patients with such chronic diseases receive therapy in a combined or multimodal approach, the likelihood of herb–drug interactions increases, regardless of whether the patients are aware of this fact or not (HDIs). According to the MD Anderson Cancer Center in the United States, over 52 percent of cancer patients reported utilising some form of complementary and alternative medicine (CAM), and approximately 77 percent of these patients reported making use of herbs. According to the findings of the World Health Organization (WHO) and other studies, more than 80 percent of the world's population relies on complementary and alternative medicine (CAM) for their medical needs. Because healthcare professionals often do not question about herbal remedies when prescribing them, and patients do not volunteer that they are taking them, concurrent use of herbs and conventional medicines across the globe could potentially be significantly higher than it is currently. This issue has surfaced as a critical impediment or challenge in our journey toward integrative health care, and it is important to note that the potential problem of HDIs develops when herbs/CAM and conventional medications are used together (IM). The term "integrative medicine" (IM) refers to the practise of treating patients using a combination of conventional and complementary therapies and medicines that are supported by scientific evidence. This is done with the goal of giving each patient the highest level of care that is reasonably achievable. IM makes use of all of the various approaches of improving one's

health that are available. Integrative oncology practitioners have, for some time now, acknowledged the usefulness of *Withania somnifera* as a novel alternative treatment for cancer patients. *W. somnifera* is beneficial in the fight against cancer and the difficulties that arise from it due to its antioxidant, anti-inflammatory, immune-modulating, and antistress properties, as well as its function in reducing the size and growth of tumours. *W. somnifera* may also improve the efficacy of radiation therapy and chemotherapy while simultaneously lowering the risk of adverse effects associated with such treatments. Both Patil et al. and Borse et al. came to the conclusion that *Tinospora cordifolia* or *Asparagus racemosus* might be used as a novel additional therapy for integrative oncology care, and they came to the same conclusion. The number of procedures involving IM and care is rising at a startling rate all across the world. Integrative medicine can be seen in action at places such as the Osher Center for Integrative Medicine, the Arizona Center for Integrative Medicine, and a great number of other establishments located all over the world (IM). Despite the fact that enormous research efforts are being done all over the world, it is significantly more challenging to manage the condition in a holistic manner due to the risk associated with HDIs. Because complementary and alternative medicine (CAM) practises are becoming more common, it is important to be aware of the potential interactions that can occur between herbs and medications. Due to the fact that herbal remedies, even single-herb formulations, frequently contain pharmacologically active components, it is essential to emphasise that HDIs are more likely than drug–drug interactions. In order to properly integrate both conventional and complementary alternative medical systems, a comprehensive understanding of the many outcomes that could be caused by HDIs is required. These HDIs have the potential to be beneficial, harmful, or even lethal. The current overview of HDIs, which covers the various types of HDIs, tools, and methodologies for studying HDIs, as well as methods for predicting HDIs, places a significant emphasis on the interactions between drug metabolising enzymes (DMEs) and transporters. This is because these interactions are crucial to the process of drug metabolism. The interactions between two or more things can result in one or more of the things having an effect on the functioning of the other object or things. The interaction between DME and transporters has the ability to influence the pharmacokinetics and safety of a herb or medicine, in addition to the pharmacodynamics and pharmacokinetics of the herb or drug. Taking all of this into consideration, the essay goes on to address the potential for drug-disease-herb interactions in the future by centering its attention on background endogenous players and methods for predicting these interactions in order to achieve the outcomes that are wanted.

Despite the prevalence of pharmaceuticals containing one or a few chemically defined active components, herbal remedies are popular in industrialised countries and are even becoming more significant. This is despite the fact that pharmaceuticals include one or a few active chemicals. According to the findings of several polls, somewhere between 15 and 45 percent of patients in various countries make use of herbal remedies in addition to their prescribed medication for the sake of healthcare. Women of childbearing age and senior citizens have a higher propensity than other age groups to seek alternative treatment options like herbal and nutritional supplements. According to the findings of several studies, those who suffer from chronic diseases are more prone to use dietary supplements. Many patients feel that because they are "natural," they are "less risky" and have less or no negative effects. However, this is not the case. Therefore, if you do not inquire about them, it is possible that they

are not considered medicines or medicinal items and that they have not been reported to health specialists. When patients combine conventional pharmaceuticals with herbal medical products (HMP) or herbal supplements, they put themselves at risk for adverse responses that are not predicted.

Plant products that are used for medical purposes provide a convoluted legal landscape inside the European Union. Herbal products can be authorised for sale on the market at a variety of different levels, from dietary supplements, which are governed by food law, to cosmetics, which are governed by legislation pertaining to herbal medicinal products (HMP). Evaluation of applications for authorisation to sell something takes place in light of these monographs. Products that have been documented as having "traditional use" or "well-established usage" status can be brought to market because the process has been expedited. The analysis that was carried out by Bilia and Céu Costas offers a more in-depth look at the regulatory landscape in Europe as well as the effects that it has had in the real world.

Even though HMPs and other botanicals are subject to a number of rules, there is not enough evidence to designate any of them inactive. This is the case despite the fact that HMPs are botanicals. It is a sign that, in most circumstances, we are less aware of the positive and negative aspects of the position that we are now in. Because food supplements are often used in lower daily amounts than pharmaceutical prescriptions, they are commonly considered to be safe for consumption. However, factors such as age or renal impairment, medication, and consumer-driven dose fluctuations can affect a person's sensitivity to side effects and/or combinations with other drugs. This suggests that all herbal products, irrespective of the legal position in which they exist, should be evaluated for the sake of risk assessment. This review will encompass any and all plant-derived items, such as extracts, powdered plants, and teas, that are used systemically for the purpose of improving one's health or treating illness, regardless of whether or not they are considered to be lawful. Goods intended for topical use were excluded from this investigation because, in comparison to other types of products, they pose a lower risk of potentially harmful interactions with systemic medications. For example, allergies are a greater cause for concern when it comes to topical herbal products. Patients who are using phototoxic drugs should exercise extreme caution when in the presence of plants that also have the potential to be phototoxic. Some examples of these plants include citrus species and chamomile. Traditional homoeopathic medicines are highly diluted, therefore it is unlikely that they will react negatively with other chemicals. This renders them generally safe. Practitioners need to be careful of products with low potency dilutions (D6 and smaller) as well as original tinctures that have not been diluted. They are capable of delivering relevant concentrations of plant metabolites to the recipient. The potential interactions that could arise between vitamins, minerals, and items originating from animals are not covered in this article (such as glucosamine). You'll find an overall summary in here somewhere.

Which species of herbal medicine are utilised most frequently in a specific region is largely determined by the availability of said medicine as well as by local customs. The curiosity that Westerners have regarding alternative medical practises such as Traditional Chinese Medicine and Ayurveda is expanding. Nevertheless, Westerners continue to have limited access to a significant number of the herbs and other botanicals used in these systems. Due to time and space constraints, this article will not be able to

discuss all of the medicinal plants that are widely used around the world. This article focuses mostly on plants that have their origins in Europe or that have a long history of use in Europe as well as the rest of the Western Hemisphere.

In chronic inflammatory illnesses such as rheumatoid arthritis (RA) and chronic inflammatory bowel disease, intricate immune-mediated pathways are responsible for the perpetuation of inflammation as well as the destruction of physical tissues (IBD). Even though there has been a lot of progress made in the pathophysiology and therapy over the past few decades, there is still the possibility of failure in both areas. Medication that has cytostatic-like actions or that modifies the immune system is regularly used in treatment regimens. These drugs frequently have narrow therapeutic windows and a considerable risk of adverse effects.

There are secondary inflammatory pathways that, when activated, speed up the degenerative process of osteoarthritis and other common diseases. Nevertheless, even if non-pharmacological approaches are the predominant mode of treatment for these individuals, analgesic medication is routinely used, and in most cases for an extended period of time.

Conclusion

Studies have demonstrated that treating *H. pylori* and gastric ulcer illness with a mix of traditional herbal treatments and contemporary anti-gastric ulcer medications may be beneficial to patients. Because there have only been a handful of studies conducted on humans to determine the efficacy and safety of medicinal plants that have an antiulcer function, it is recommended that more clinical trials be conducted with larger sample sizes. It would also be beneficial to do research on the mechanisms of action of medicinal plants that are used for the treatment or prevention of peptic ulcers. Not least, herbal products that are used for medicinal reasons are required to be licenced in order to improve product safety and quality, as well as to ensure that randomised controlled trials confirm expectations regarding the likely usefulness of the product. Even though there have been increasing reports of herb–drug interactions, there has not been nearly enough research conducted in this field, and there have been no initiatives done to rectify this problem. Because of this, both pharmacists and medical professionals should be aware of the potential risks associated with the use of herbal medicines, regardless of whether they are taken on their own or in combination with other herbal or conventional treatments.

References

1. Kwok, C.S.; Arthur, A.K.; Anibueze, C.I.; Singh, S.; Cavallazzi, R.; Loke, Y.K. Risk of clostridium difficile infection with acid suppressing drugs and antibiotics: Meta-analysis. *Am. J. Gastroenterol.* 2012, 107, 1011–1019.

2. Deshpande, A.; Pasupuleti, V.; Thota, P.; Pant, C.; Mapara, S.; Hassan, S.; Rolston, D.D.; Sferra, T.J.; Hernandez, A.V. Acid-suppressive therapy is associated with spontaneous bacterial peritonitis in cirrhotic patients: A meta-analysis. *J. Gastroenterol. Hepatol.* 2013, 28, 235–242.
3. Haigh, C.R.; Attwood, S.E.; Thompson, D.G.; Jankowski, J.A.; Kirton, C.M.; Pritchard, D.M.; Varro, A.; Dimaline, R. Gastrin induces proliferation in Barrett’s metaplasia through activation of the CCK2 receptor. *Gastroenterology* 2003, 124, 615–625. [
4. Laine, L.; Ahnen, D.; McClain, C.; Solcia, E.; Walsh, J.H. Review article: Potential gastrointestinal effects of long-term acid suppression with proton pump inhibitors. *Aliment. Pharmacol. Ther.* 2000, 14, 651–668.
5. Lam, J.R.; Schneider, J.L.; Zhao, W.; Corley, D.A. Proton pump inhibitor and histamine 2 receptor antagonist use and vitamin B12 deficiency. *JAMA* 2013, 310, 2435–2442.
6. Koivisto, T.T.; Rautelin, H.I.; Voutilainen, M.E.; Heikkinen, M.T.; Koskenpato, J.P.; Färkkilä, M.A. First-line eradication therapy for *Helicobacter pylori* in primary health care based on antibiotic resistance: Results of three eradication regimens. *Aliment. Pharmacol. Ther.* 2005, 21, 773–782.
7. . Lew, E.A. Review article: Pharmacokinetic concerns in the selection of anti-ulcer therapy. *Aliment. Pharmacol. Ther.* 1999, 13 (Suppl. S5), 11–16.
8. Gilard, M.; Arnaud, B.; Le Gal, G.; Abgrall, J.F.; Boschard, J. Influence of omeprazol on the antiplatelet action of clopidogrel associated to aspirin. *J. Thromb. Haemost.* 2006, 4, 2508–2509.
9. Ghebremariam, Y.T.; Lee, J.C.; LePendu, P.; Erlanson, D.A.; Slaviero, A.; Shah, N.H.; Leiper, J.M.; Cooke, J.P. Response to letters regarding article, “unexpected effect of proton pump inhibitors: Elevation of the cardiovascular risk factor asymmetric dimethylarginine”. *Circulation* 2014, 129, e428.
10. Merwat, S.N.; Spechler, S.J. Might the use of acid-suppressive medications predispose to the development of eosinophilic esophagitis? *Am. J. Gastroenterol.* 2009, 104, 1897–1902.
11. Lanas, A. We are using too many PPIs, and we need to stop: A European perspective. *Am. J. Gastroenterol.* 2016, 111, 1085–1086.
12. Kumar, R., Saha, P., Kumar, Y., Sahana, S., Dubey, A., & Prakash, O. (2020). A Review on Diabetes Mellitus: Type1 & Type2. *World Journal of Pharmacy and Pharmaceutical Sciences*, 9(10), 838-850.
13. KUMAR, A. (2019). The Scenario of Pharmaceuticals and Development of Microwave Assisted Extraction Techniques.

14. Hui DS, I Azhar E, Madani TA, et al.. The continuing 2019-nCoV epidemic threat of novel coronaviruses to global health—the latest 2019 novel coronavirus outbreak in Wuhan, China. *Int J Infect Dis.* 2020;91:264–266.
15. Wiersinga WJ, Rhodes A, Cheng AC, et al.. Pathophysiology, transmission, diagnosis, and treatment of coronavirus disease 2019 (COVID-19): a review. *JAMA.* 2020;324:782–793.
16. KUMAR, R., SAHA, P., SARKAR, S., RAWAT, N., & PRAKASH, A. (2021). A REVIEW ON NOVEL DRUG DELIVERY SYSTEM. *IJRAR-International Journal of Research and Analytical Reviews (IJRAR)*, 8(1), 183-199.
17. Saha, P., Nyarko, R. O., Lokare, P., Kahwa, I., Boateng, P. O., & Asum, C. (2022). Effect of Covid-19 in Management of Lung Cancer Disease: A Review. *Asian Journal of Pharmaceutical Research and Development*, 10(3), 58-64.
18. Kumar, R., Saha, P., Pathak, P., Mukherjee, R., Kumar, A., & Arya, R. K. EVOLUTION OF TOLBUTAMIDE IN THE TREATMENT OF DIABETES MELLITUS. *Jour. of Med. P'ceutical & Alli. Sci*, 9.
19. Kumar, R., Jain, A., Tripathi, A. K., & Tyagi, S. (2021, January). Covid-19 outbreak: An epidemic analysis using time series prediction model. In *2021 11th international conference on cloud computing, data science & engineering (Confluence)* (pp. 1090-1094). IEEE.
20. Nyarko, R. O., Saha, P., Kumar, R., Kahwa, I., Boateng, E. A., Boateng, P. O., ... & Bertram, A. (2021). Role of Cytokines and Vaccines in Break through COVID 19 Infections. *Journal of Pharmaceutical Research International*, 33, 2544-2549.
21. PURABISAHA, R. K., RAWAT, S. S. N., & PRAKASH, A. (2021). A REVIEW ON NOVEL DRUG DELIVERY SYSTEM.
22. Nyarko, R. O., Boateng, E., Kahwa, I., Boateng, P. O., & Asare, B. (2020). The impact on public health and economy using lockdown as a tool against COVID-19 pandemic in Africa: a perspective. *J Epidemiol Public Health Rev*, 5(3).
23. Raj, A., Tyagi, S., Kumar, R., Dubey, A., & Hourasia, A. C. (2021). Effect of isoproterenol and thyroxine in herbal drug used as cardiac hypertrophy. *Journal of Cardiovascular Disease Research*, 204-217.
24. Daharia, A., Jaiswal, V. K., Royal, K. P., Sharma, H., Joginath, A. K., Kumar, R., & Saha, P. (2022). A Comparative review on ginger and garlic with their pharmacological Action. *Asian Journal of Pharmaceutical Research and Development*, 10(3), 65-69.
25. Nyarko, R. O., Kumar, R., Sharma, S., Chourasia, A., Roy, A., & Saha, P. (2022). ANTIBACTERIAL ACTIVITY OF HERBAL PLANT-TINOSPORA CORDIFOLIA AND CATHARNTHUS ROSEUS.

26. Singh, M. K., Kumar, A., Kumar, R., Kumar, P. S., Selvakumar, P., & Chourasia, A. (2022). Effects of Repeated Deep Frying on Refractive Index and Peroxide Value of Selected Vegetable Oils. *International Journal for Research in Applied Sciences and Biotechnology*, 9(3), 28-31.
27. Kumar, R., & Dubey, A. PHYTOCHEMICAL INVESTIGATION AND HEPTOPROTECTIVE EVALUTION ACACIA RUBICA EXTRACT ISONIZED AND PARACETAMOL INDUSED ANIMAL TOXICITY. *Turkish Journal of Physiotherapy and Rehabilitation*, 32(3).
28. Nyarko, R. O., Prakash, A., Kumar, N., Saha, P., & Kumar, R. (2021). Tuberculosis a globalized disease. *Asian Journal of Pharmaceutical Research and Development*, 9(1), 198-201.
29. Nyarko, R. O., Boateng, E., Kahwa, I., & Boateng, P. O. (2020). A comparison analysis on remdesivir, favipiravir, hydroxychloroquine, chloroquine and azithromycin in the treatment of corona virus disease 2019 (COVID-19)-A Review. *World J. Pharm. Pharm. Sci*, 9, 121-133.
30. Sahana, S., Kumar, R., Nag, S., Paul, R., Chatterjee, I., & Guha, N. (2020). A REVIEW ON ALZHEIMER DISEASE AND FUTURE PROSPECTS.
31. Sahana, S. (2020). Roshan kumar, Sourav nag, Reshmi paul, Nilayan guha, Indranil Chatterjee. A Review on Alzheimer disease and future prospects. *World Journal of Pharmacy and Pharmaceutical science*, 9(9), 1276-1285.
32. Saha, P., Kumar, R., Nyarko, R. O., Kahwa, I., & Owusu, P. (2021). HERBAL SECONDARY METABOLITE FOR GASTRO-PROTECTIVE ULCER ACTIVITY WITH API STRUCTURES.
33. Saha, P., Kumar, R., Nyarko, R. O., Kahwa, I., & Owusu, P. (2021). HERBAL SECONDARY METABOLITE FOR GASTRO-PROTECTIVE ULCER ACTIVITY WITH API STRUCTURES.
34. Dubey, A., Yadav, P., Verma, P., & Kumar, R. (2022). Investigation of Proapoptotic Potential of Ipomoea carnea Leaf Extract on Breast Cancer Cell Line. *Journal of Drug Delivery and Therapeutics*, 12(1), 51-55.
35. Bind, A., Das, S., Singh, V. D., Kumar, R., Chourasia, A., & Saha, P. Natural Bioactives For The Potential Management Of Gastric Ulceration. *Turkish Journal of Physiotherapy and Rehabilitation*, 32(3).
36. Kumar, R., Saha, P., Lokare, P., Datta, K., Selvakumar, P., & Chourasia, A. (2022). A Systemic Review of Ocimum sanctum (Tulsi): Morphological Characteristics, Phytoconstituents and Therapeutic Applications. *International Journal for Research in Applied Sciences and Biotechnology*, 9(2), 221-226.
37. Sahana, S. (2020). Purabi saha, Roshan kumar, Pradipta das, Indranil Chatterjee, Prasit Roy, Sk Abdur Rahamat. A Review of the 2019 Corona virus (COVID-19) *World Journal of Pharmacy and Pharmaceutical science*, 9(9), 2367-2381.

38. Kumar, R., Saha, P., Lokare, P., Datta, K., Selvakumar, P., & Chourasia, A. (2022). A Systemic Review of *Ocimum sanctum* (Tulsi): Morphological Characteristics, Phytoconstituents and Therapeutic Applications. *International Journal for Research in Applied Sciences and Biotechnology*, 9(2), 221-226.
39. Roshan, K. (2020). Priya damwani, Shivam kumar, Adarsh suman, Suthar Usha. An overview on health benefits and risk factor associated with coffee. *International Journal Research and Analytical Review*, 7(2), 237-249.
40. Umama, Y., Venkatajah, G., Shourabh, R., Kumar, R., Verma, A., Kumar, A., & Gayoor, M. K. (2019). Topic-The scenario of pharmaceuticals and development of microwave as; sisted extraction technique. *World J Pharm Pharm Sci*, 8(7), 1260-1271.
41. Awuchi, C. G., Amagwula, I. O., Priya, P., Kumar, R., Yezdani, U., & Khan, M. G. (2020). Aflatoxins in foods and feeds: A review on health implications, detection, and control. *Bull. Environ. Pharmacol. Life Sci*, 9, 149-155.
42. SHAFQAT ZAIDI, R. K. MEHRA, Dr. SACHIN TYAGI, ROSHAN KUMAR ANUBHAV DUBEY.(2021). Effect of Kalahari Cactus Extract on Appetite, Body Weight And Lipid Profile In Cafeteria Diet Induced Obesity In Experimental Animal. *Annals of the Romanian Society for Cell Biology*, 25(6), 13976-13987.
43. Roshan Kumar, & Purabi Saha. (2022). A Review on Artificial Intelligence and Machine Learning to Improve Cancer Management and Drug Discovery. *International Journal for Research in Applied Sciences and Biotechnology*, 9(3), 149–156. <https://doi.org/10.31033/ijrasb.9.3.26>
44. IUPAC-IUB Joint Commission on Biochemical Nomenclature (JCBN). The nomenclature of steroids. Recommendations 1989. *Eur J Biochem*. 1989;186:429–58.
45. Goel RK, Sairam K. Anti-ulcer drugs from indigenous sources with emphasis on *Musa sapientum*, *Asparagus racemosus* and *Zingiber officinale*. *Indian J Pharmacol*. 2002;34:100–10.
46. Mazumder PM, Farswan M, Parcha V, Singh V. Hypoglycaemic and antioxidant activity of an isolated compound from *Ficus arnottiana* bark. *Pharmacologyonline*. 2008
47. Veitch GE, Beckmann E, Burke BJ, Boyer A, Maslen SL, Ley SV. Synthesis of azadirachtin: A long but successful journey. *Angew Chem Int Ed Engl*. 2007;46:7629–32.
48. Senthil NS, Kalaivani K, Murugan K, Chung G. The toxicity and physiological effect of Neem limonoids on *Cnaphalocrocis medinalis* (Guenée) the rice leaf folder pesticide. *Biochem Physiol*. 2005;81:113.
49. Nathan SS, Kalaivani K, Murugan K. Effects of neem limonoids on the malaria vector *Anopheles stephensi* Liston (Diptera: Culicidae) *Acta Trop*. 2005;96:47–55.

50. Anonymous. The wealth of India. A Dictionary of Indian Raw Materials and Industrial Products. 1998;2(B):49–52.
51. Pharmacopoeia of India. Vol. 2. New Delhi: Controller of Publication, Ministry of Health and Family Welfare, Govt. of India; 1996. Anonymous; pp. A53–4.
52. The Merck index: An encyclopedia of chemicals, drugs, and biological. 11th ed. Merck: United States pharmaceutical company Merck & Co; 1989. p. 4386. ISBN 091191028X.
53. Brito-Arias M. Synthesis and characterization of glycosides. New York: Springer; 2007. p. ISBN 978-0-387-26251-2.
54. Lindhorst TK. Essentials of carbohydrate chemistry and biochemistry. Wiley: VCH; 2007. p. ISBN 978-3527315284.
- 55.** Hornick CA, Sanders LI, Lin YC. Effect of carpaine, a papaya alkaloid, on the circulatory function in the rat. Res Commun Chem Pathol Pharmacol. 1978;22:277–89.