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ROLE OF HERBS IN MANAGEMENT OF DIABETES, HYPERTENSION AND PEPTIC ULCERS

M. Mahadeswar Babu[1], R. Kesava Naik[1], Ch. Lalitha[2], Angilicam Avinash*[3] and Dr. M. Sreenivasulu[4]

[1]B.Pharm 4th Year, Narayana Pharmacy College, Chintharedy palem, Nellore, Andhra Pradesh-524002, India.

[2]Assistant Professor, Dept. of Pharmaceutical Chemistry, Narayana Pharmacy College, Chintharedy palem, Nellore, Andhra Pradesh-524002, India.

[3]Assistant Professor, Dept. of Pharmaceutics, Narayana Pharmacy College, Chintharedy palem, Nellore, Andhra Pradesh-524002, India.

[4]Principal, Narayana Pharmacy College, Chintharedypalem, Nellore, Andhra Pradesh, India-524002.

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***Corresponding Author**
Prof. Angilicam Avinash
Assistant Professor, Dept. of Pharmaceutics, Narayana Pharmacy College, Chintharedy palem, Nellore, Andhra Pradesh-524002, India.

ABSTRACT

Major life threating diseases now days are hypertension, Diabetes and peptic ulcer. Many drugs are available for the management of these diseases. All the drugs are chemical substances. These review focus on the use of herbal drugs in treatment of these disease. Hypertension (HTN) is the medical term for high blood pressure. It is dangerous because it makes the heart work too hard and contributes to atherosclerosis (hardening of arteries), besides increasing the risk of heart disease and stroke. HTN can also lead to other conditions such as congestive heart failure, kidney disease, and blindness. Conventional antihypertensives are usually associated with many side effects. About 75 to 80% of the world population use herbal medicines, mainly in developing countries, for primary health care because of their better acceptability with human body and lesser side effects. In the last three decades, a lot of concerted efforts have been channeled into researching the local plants with hypotensive and antihypertensive therapeutic values. Diabetes mellitus is a dreadful disease found in all parts of the world and is becoming a serious threat to mankind health. Diabetes mellitus is a group of metabolic diseases characterized by high blood sugar (glucose) levels that result from

defects in insulin secretion, or action, or both. The World Health Organization (WHO) has listed 21,000 plants, which are used for medicinal purposes around the world. Herbal medicines have been highly esteemed source of medicine throughout the human history. Alternative to synthetic agents, plants provide a potential source of hypoglycemic drugs and are widely used to prevent diabetes. In the present review, an attempt has been made to summarize some of the herbal plants having anti-diabetic activity which are beneficial for the mankind. An ulcer is erosion in the lining of the stomach and duodenum. There are two types of ulcers -gastric and duodenal ulcer. Together, they are called peptic ulcer. There are many herbs and plant products that have been found to play a role in protecting or helping to heal stomach and peptic ulcers. In recent years, gastric ulcer has also been associated with infection of gastrointestinal mucosal tissue by *Helicobacter pylori.* Herbal plants are considered as safe for peptic ulcer treatment with fewer side effects.

INTRODUCTION

Nature always stands as a golden mark to exemplify the outstanding phenomena of symbiosis. Natural products from plant, animal and minerals have been the basis of the treatment of human disease. Today estimate that about 80 % of people in developing countries still relays on traditional medicine based largely on species of plants and animals for their primary health care. Herbal medicines are currently in demand and their popularity is increasing day by day.[1] About 500 plants with medicinal use are mentioned in ancient literature and around 800 plants have been used in indigenous systems of medicine. India is a vast repository of medicinal plants that are used in traditional medical treatments. The various indigenous systems such as Siddha, Ayurveda, Unani and Allopathy use several plant species to treat different elements. The use of herbal medicine becoming popular due to toxicity and side effects of allopathic medicines. This led to sudden increase in the number of herbal drug manufactures.[2] In Herbal medicines as the major remedy in traditional system of medicine have been used in medical practices since antiquity. The practices continue today because of its biomedical benefits as well as place in cultural beliefs in many parts of world and have made a great contribution towards maintaining human health. In India around 20,000 medicinal plant species have been recorded recently but more than 500 traditional communities use about 800 plant species for curing different diseases.[3] Currently 80% of the world population depends on plant-derived medicine for the first line of primary health care for human alleviation because it has no side effects. Plants are important sources of medicines and presently about 25% of pharmaceutical prescriptions in the United States

contain at least one plant-derived ingredient. In the last century, roughly 121 pharmaceutical products were formulated based on the traditional knowledge obtained from various sources.[4]

MANAGEMENT OF DIABETES

Diabetes is a chronic disorder of carbohydrate, fat and protein metabolism characterized by increased fasting and post prandial blood sugar levels. The global prevalence of diabetes is estimated to increase, from 4% in 1995 to 5.4% by the year 2025.[5] WHO has predicted that the major burden will occur in developing countries Studies conducted in India in the last decade have highlighted that not only is the prevalence of diabetes high but also that it is increasing rapidly in the urban population. It is estimated that there are approximately 33 million adults with diabetes in India. This number is likely to increase to 57.2 million by the year 2025.[6]

Diabetes mellitus is a complex metabolic disorder resulting from either insulin insufficiency or insulin dysfunction. Type I diabetes (insulin dependent) is caused due to insulin insufficiency because of lack of functional beta cells. Patients suffering from this are therefore totally dependent on exogenous source of insulin while patients suffering from Type II diabetes (insulin independent) are unable to respond to insulin and can be treated with dietary changes, exercise and medication. Type II diabetes is the more common form of diabetes constituting 90% of the diabetic population. Symptoms for both diabetic conditions may include: (i) high levels of sugar in the blood; (ii) unusual thirst; (iii) frequent urination; (iv) extreme hunger and loss of weight; (v) blurred vision; (vi) nausea and vomiting; (vii) extreme weakness and tiredness; (viii) irritability, mood changes etc. Though pathophysiology of diabetes remains to be fully understood, experimental evidences suggest the involvement of free radicals in the pathogenesis of diabetes and more importantly in the development of diabetic complications Free radicals are capable of damaging cellular molecules, DNA, proteins and lipids leading to altered cellular functions. Many recent studies reveal that antioxidants capable of neutralizing free radicals are effective in preventing experi- mentally induced diabetes in animal models as well as reducing the severity of diabetic complications. For the development of diabetic complications, the abnor- malities produced in lipids and proteins are the major etiologic factors. In diabetic patients, extra-cellular and long lived proteins, such as elastin, lamina, and collagen are the major targets of free radicals. These proteins are modified to form glycoproteins due to hyperglycemia. The

modification of these proteins present in tissues such as lens, vascular wall and basement membranes are associated with the development of complications of diabetes such as cataracts, microangiopathy, atherosclerosis and nephropathy. During diabetes, lipoproteins are oxidized by free radicals. There are also multiple abnormalities of lipoprotein metabolism in very low density lipoprotein (VLDL), low density lipoprotein (LDL), and high density lipoprotein (HDL) in diabetes. Lipid peroxidation is enhanced due to increased oxidative stress in diabetic condition. Apart from this, advanced glycation end products (AGEs) are formed by non-enzymatic glycosylation of proteins. AGEs tend to accumulate on long-lived molecules in tissues and generate abnormalities in cell and tissue functions. In addition, AGEs also contribute to increased vascular permeability in both micro and macro vascular structures by binding to specific macrophage receptors. This results in formation of free radicals and endothelial dis- function. AGEs are also formed on nucleic acids and histones and may cause mutations and altered gene expression. As diabetes is a multifactorial disease leading to several complications, and therefore demands a multiple therapeutic approach. Patients of diabetes either do not make enough insulin or their cells do not respond to insulin. In case of total lack of insulin, patients are given insulin injections. Whereas in case of those where cells do not respond to insulin many different drugs are developed taking into consideration possible disturbances in carbohydrate-metabolism. For example, to manage post-prandial hyper-glycaemia at digestive level, glucosidase inhibitors such as acarbose, miglitol and voglibose are used. These inhibit degradation of carbohydrates thereby reducing the glucose absorption by the cells. To enhance glucose uptake by peripheral cells biguanide such as metphormine is used. Sulphonylureas like glibenclamide is insulinotropic and works as secretogogue for pancreatic cells. Although several therapies are in use for treatment, there are certain limitations due to high cost and side effects such as development of hypoglycemia, weight gain, gastrointestinal disturbances, liver toxicity etc. Based on recent advances and involvement of oxidative stress in complicating diabetes mellitus, efforts are on to find suitable ant diabetic and antioxidant therapy.

Indian Medicinal Plants with Antidiabetic and Related Beneficial Effects

There are many herbal remedies suggested for diabetes and diabetic complications. Medicinal plants form the main ingredients of these formulations.

Acacia arabica: It is found all over India mainly in the wild habitat. The plant extract acts as an antidiabetic agent by acting as secretagouge to release insulin. It induces hypoglycemia in

control rats but not in alloxanized animals. Powdered seeds of Acacia arabica when administered (2, 3 and 4 g/kg body weight) to normal rabbits induced hypoglycemic effect by initiating release of insulin from pancreatic beta cells.

Aegle marmelos: Administration of aqueous extract of leaves improves digestion and reduces blood sugar and urea, serum cholesterol in alloxanized rats as compared to control. Along with exhibiting hypoglycemic activity, this extract also prevented peak rise in blood sugar at 1h in oral glucose tolerance test.

Allium cepa: Various ether soluble fractions as well as insoluble fractions of dried onion powder show anti-hyperglycemic activity in diabetic rabbits. Allium cepa is also known to have anti-oxidant and hypolipidaemic activity. Administration of a sulfur containing amino acid from Alliumcepa, S-methyl cysteine sulphoxide (SMCS) (200 mg/kg for 45 days) to alloxan induced diabetic rats significantly controlled blood glucose as well as lipids in serum and tissues and normalized the activities of liver hexokinase, glucose 6-phosphatase and HMG Co A reductase. When diabetic patients were given single oral dose of 50 g of onion juice, it significantly controlled post-prandial glucose levels.[7]

Allium sativum: Allicin, a sulfur-containing compound is responsible for its pungent odour and it has been shown to have significant hypo-glycemic activity. This effect is thought to be due to increased hepatic metabolism, increased insulin release from pancreatic beta cells and/or insulin sparing effect Aqueous homogenate of garlic (10 ml/kg/day) administered orally to sucrose fed rabbits (10 g/kg/day in water for two months) significantly increased hepatic glycogen and free amino acid content, decreased fasting blood glucose, and triglyceride levels in serum in comparison to sucrose controls. S-allyl cystein sulfoxide (SACS), the precursor of allicin and garlic oil, is a sulfur containing amino acid, which controlled lipid peroxidation better than glibenclamide and insulin. It also improved diabetic conditions. SACS also stimulated in vitro insulin secretion from beta cells isolated from normal rats Apart from this, Allium sativum exhibits anti-microbial, anticancer and cardio protective activities.[8]

Aloe Vera and Aloe barbadensis: Extracts of aloe gum effectively increases glucose tolerance in both normal and diabetic rats Treatment of chronic but not single dose of exudates of Aloe barbadensis leaves showed hypoglycemic effect in alloxanized diabetic rats. Single as well as chronic doses of bitter principle of the same plant also showed

hypoglycemic effect in diabetic rats. This action of Aloe vera and its bitter principle is through stimulation of synthesis and/or release of insulin from pancreatic beta cells This plant also has an anti-inflammatory activity in a dose dependent manner and improves wound healing in diabetic mice.[9][10]

Azadirachta indica: Hydroalcoholic extracts of this plant showed anti-hyperglycemic activity in streptozotocin treated rats and this effect is because of increase in glucose uptake and glycogen deposition in isolated rat hemidiaphragm Apart from having anti-diabetic activity, this plant also has anti-bacterial, antimalarial, antifertility, hepatoprotective and antioxidant effects.[11]

Table 1. Indian medicinal plants with anti-diabetic and related beneficial properties

Plant Name	Ayurvedic/common name	Antidiabetic and other beneficial effects in traditional medicine
Annona squamosal	Sugar apple	Hypoglycemic and, Increased plasma insulin level
Areca catechu	Supari	Hypoglycemic
Beta vulgaris	Chukkander	Increases glucose tolerance in OGTT
Bombax ceiba	Semul	Hypoglycemic
Butea monosperma	Palasa	Antihyperglycemic
Camellia sinensis	Tea	Anti-hyperglycemic activity, antioxidant
Capparis decidua	Karir or Pinju	Hypoglycemic, antioxidant, hypolipidaemic
Coccinia indica	Bimb or Kanturi	Hypoglycemic
Emblica officinalis	Amla	Decreases lipid peroxidation, antioxidant, hypoglycemic
Eugenia uniflora	Pitanga	Hypoglycemic, inhibits lipase activity
Ficus bengalenesis	Bur	Hypoglycemic, antioxidant
Gymnema sylvestre	Gudmar or Merasingi	Anti-hyperglycemic effect, hypolipidemic
Hibiscus rosasinesis	Gudhal or Jasson	Initiates insulin release from pancreatic beta cells
Ipomoea batatas	Sakkargand	Reduces insulin resistance
Musa sapientum	Banana	Antihyperglycemic, antioxidant
Punica granatum	Anar	Antioxidant, anti-hyperglycemic effect
Salacia reticulate	Vairi	Inhibitory activity against sucrase, α-glucosidase inhibitor
Swertia chirayita	Chirata	Stimulates insulin release from islets
Terminalia chebula	Hirda	Antibacterial, hypoglycemic
Vinca rosea	Sadabahar	Anti-hyperglycemic

MANAGEMENT OF HYPERTENSION

Introduction

Hypertension (HTN) is the medical term for high blood pressure. It is dangerous because it makes the heart work too hard and contributes to atherosclerosis (hardening of arteries), besides increasing the risk of heart disease and stroke. HTN can also lead to other conditions such as congestive heart failure, kidney disease, and blindness. Conventional antihypertensives are usually associated with many side effects. About 75 to 80% of the world population use herbal medicines, mainly in developing countries, for primary health

care because of their better acceptability with human body and lesser side effects. In the last three decades, a lot of concerted efforts have been channeled into researching the local plants with hypotensive and antihypertensive therapeutic values. The hypotensive and antihypertensive effects of some of these medicinal plants have been validated and others disproved. However, ayurvedic knowledge needs to be coupled with modern medicine and more scientific research needs to be done to verify the effectiveness, and elucidate the safety profile of such herbal remedies for their antihypertensive potential.[12]

PATHOPHYSIOLOGY

Most of the mechanisms associated with secondary HTN are generally fully understood. However, those associated with essential (primary) HTN are far less understood. What is known is that cardiac output is raised early in the disease course, with normal total peripheral resistance (TPR). Over time, cardiac output drops to normal levels, but TPR is increased. The following three theories have been proposed to explain this:

- Inability of the kidneys to excrete sodium, resulting in natriuretic factors such as atrial natriuretic factor being secreted to promote salt excretion with the side effect of raising TPR.
- An overactive renin-angiotensin system leads to vasoconstriction and retention of sodium and water. The increase in blood volume leads to HTN.[13]
- An overactive sympathetic nervous system, leading to increased stress responses
- It is also known that HTN is highly heritable and polygenic (caused by more than onegene) and a few candidate genes have been postulated in the etiology of this condition.

Recently, work related to the association between essential HTN and sustained endothelial damage has gained popularity among HTN scientists. It remains unclear however whether endothelial changes precede the development of HTN or whether such changes are mainly due to long-standing elevated BPs. HTN is a major independent risk factor for coronary artery disease, stroke, and kidney failure. Each increase of 20 mmHg in systolic BP and 10 mmHg in diastolic BP, over the range of 115/75 to 185/115 mmHg, doubles the risk of a fatal coronary event.[14]

List of naturally occurring medicinal plants, herbs having hypotensive/antihypertensive potential

Agathosma betulina: It is a South African medicinal plant and has been used by the indigenous people of the area for centuries to treat wider ailments. It is an effective diuretic and anti-inflammatory agent. Early Dutch settlers used buchu to make a brandy tincture, which is still used today to treat many disorders.[15]

Allium sativa: Garlic has long been used for a variety of cardiovascular conditions, especially hyperlipidemia. It has also been reported to have hypotensive action. It is thought to increase nitric oxide production, resulting in smooth muscle relaxation and vasodilatation. One of the primary active compounds that gives garlic its characteristic odor and many of its healing benefits is called allicin. Meta-analysis of randomly chosen literary data has demonstrated that garlic is related to decrease of BP in patients with increased systolic pressure, but not in patients without increased systolic pressure Garlic preparations have been found to be superior to placebo in reducing BP in individuals with HTN The ant oxidative and antihypertensive effect of garlic has been observed in 20 patients with HTN compared to 20 patients with normal pressure, who have been receiving garlic pearls preparation for a period of two months. The results have revealed decreased BP, significant reduction of 8-hydroxy-2-deoxyguanosin, level of nitric oxide, and lipid peroxidation, and an increased level of ant oxidative vitamins (C and E). This study points to the beneficial cardio protective action of garlic in essential HTN.[16]

Annona muricata: A. muricata is a member of the family of custard apple trees called Annonaceae and a species of the genus Annona, known mostly for its edible fruits Annona. The tree grows natively in the Caribbean and Central America. The leaf extract of the plant has been reported to lower an elevated BP by decreasing the peripheral vascular resistance.

Apium graveolens: According to Chinese theory, Celery is effective for HTN because it acts upon the liver; one type of HTN is associated with liver. In Mainland China, celery was useful in reducing HTN in 14 of 16 patients. The juice was mixed with equal amount of honey and about 8 ounces were taken orally three times each day for up to one week It has also been reported to reduce systolic and diastolic BP. The difference of BP in human beings before and after treatment has been found to be significant ($P<0.05$), indicating that seeds of A. graveolens can be used as a safe and effective treatment of high BP. Fresh celery juice

can be mixed with vinegar to relieve dizziness and headache and shoulder pain associated with HTN. It is also administered in HTN associated with pregnancy and climacteric.[17]

Artocarpus altilis: The plant is native to the Malay Peninsula and western Pacific islands. A study has shown that the leaf extract of the plant decreased the tension of phenylephrine-stimulated isolated guinea pig aorta rings by 15 to 35%.[18]

Avena sativa: A diet containing soluble fiber-rich whole oats can significantly reduce the need for antihypertensive medication and improve BP control. Considering the lipid and glucose improvements as well, increased consumption of whole oats may significantly reduce cardiovascular disease risk. The addition of oat cereals to the normal diet of patients with HTN has been found to significantly reduce both systolic and diastolic BP. Soluble fiber-rich whole oats may be an effective dietary therapy in the prevention and adjunct treatment of HTN.[19]

Blond psyllium: Preliminary clinical research shows that taking a B. psyllium (Plantago species) supplement 15 g daily can modestly lower BP; systolic by about 8 mmHg and diastolic by 2 mmHg.

Camellia sinensis: There are many potential health benefits from drinking tea. There is lots of interest among researchers on the effect of tea on cardiovascular disease. Research on tea and HTN is contradictory. Research on black tea (fermented tea) (Camellia sinensis) shows no effect on BP in people with HTN. Population research links consumption of green tea (unfermented) (Camellia sinensis) and oolong tea (partially fermented) (Camellia sinensis) with a decreased risk of developing HTN.[20]

Capris cartilaginea: It is a prostrate or scrambling shrub found in rocky ground, sometimes hanging from cliffs. It has been reported that crude extract of C. cartilaginea produces a dose-dependent decrease in BP and slight bradycardia in anesthetized rats.

Carum copticum: The crude extract of C. copticum (1-30 mg/kg) produces a fall in BP and heart rate (HR) of anesthetized normotensive (NMT) rats. Hypotension produced is very brief and returns to normal within a minute. At the low dose (up to 1 mg/kg), the crude extract produces negligible change in the HR. However, bradycardia has been reported at the higher doses (10-30 mg/kg).

Cassia absus: This plant is found in the tropical region and is found everywhere in India. It has been reported that an intravenous administration of a crude extract of C. absus produces a dose-related (1-30 mg/kg) decrease in BP, accompanied with a decrease in HR at the higher doses (10 and 30 mg/kg). Repeated injections of the same dose of the crude extract have been seen to produce tachyphylaxis. A sustained fall in BP of anesthetized animals and weak antiacetylcholine effect has been reported.[21]

Cassia occidentalis: It is a small tree growing 5 to 8 m in height. The leaf of this plant is used in local folk medicine as an antihypertensive agent. In vitro studies of the leaf extract have shown a relaxant effect on the aortic rings. The studies revealed that cassia extract may be relaxing smooth muscle and reducing BP by inhibiting Ca2+ influx through receptor-operated channel and voltage-sensitive channel, showing its non-selectivity on these Ca2+ channels.

Castanospermum austral: Crude extract of C. australe has been reported to cause a fall in systolic as well as diastolic BP in a dose-dependent manner (1-100 mg/kg). This fall in BP has been attributed to the saponin fraction and medicogenic acid glucoside present in the crude extract.[22]

Coleus forskohlii: The pharmacological properties of coleonol, a diterpene, isolated from C. forskohlii, have been investigated. Its predominant effect has been to lower the BP of anesthetized cat and rat as well as of the spontaneously hypertensive rat due to relaxation of the vascular smooth muscle. In small doses, it has a positive inotropic effect on isolated rabbit heart as well as on cat heart in vivo. Coleonol also exhibits nonspecific spasmolytic activity on smooth muscle of the gastrointestinal tract in various species, but not on bronchial musculature of guinea pig. Large doses of coleonol have a depressant action on the central nervous system.[23]

Commelina virginica: It is a perennial herbaceous plant in the dayflower family. It is native to the mideastern and southeastern United States. Whole plant extract has been reported to decrease the tension of phenylephrine-stimulated isolated guinea pig aorta rings by 15 to 35%.

Crataegus pinnatifida: It has been used in China as a decoction for treatment of HTN for thousands of years. Pharmacological and clinical trials have shown that it lowers BP. The two

main substances that contribute to hawthorn's beneficial effects on heart are flavonoids and oligomeric procyanidins, which are potent antioxidant agents. Rhynchophylline, an alkaloid in cat's claw, has demonstrated an ability to inhibit platelet aggregation and thrombosis, which suggests that it may be useful in preventing strokes and reducing the risk of heart attack by lowering BP, increasing circulation, and inhibiting both the formation of plaque on arterial walls and formation of blood clots in the brain, heart, and arteries. In experiments with anesthetized rabbits, intravenous administration of the extract preparation lowered the BP for up to 3 hours. Grataegic acid was identified as the hypotensive principle. Mechanisms of action of Crataegus postulated to date reveal a remedy with potentially broad-based influence on the cardiovascular system. These effects include a hypotensive activity through vasorelaxation resulting from nitrous oxide stimulation, significant antioxidant activity, and a tonic action on cardiac myocytes.[24]

Crinum glaucoma: C. glaucum used traditionally in Western Nigeria for treatment of asthma was investigated for its effects on respiratory and cardiovascular functions. Increasing doses of the aqueous extract caused an increase in tidal volume (increase in ventilatory rate and depth) and a corresponding decrease in both systolic and diastolic pressures.

Cuscuta reflexa: Crude extract of C. reflexa has been reported to cause a decrease in systolic and diastolic BP as well as HR in anesthetized rats. The antihypertensive activity and bradycardia produced were found to be dose-dependent, but the decrease in HR was observed at slightly higher doses. Pretreatment with atropine (1 mg/kg) did not abolish the cardiovascular responses to C. reflexa.

Daucus carota: It has been used in traditional medicine to treat HTN. Activity-directed fractionation of aerial parts of D. carota resulted in the isolation of two coumarin glycosides coded as DC-2 and DC-3. Intravenous administration of these compounds caused a dose-dependent (1–10 mg/kg) fall in arterial BP in NMT anesthetized rats. In the in vitro studies, both compounds caused a dose-dependent (10–200 μg/ml) inhibitory effect on spontaneously beating guinea pig atria as well as on the K+ -induced contractions of rabbit aorta at similar concentrations. These results indicate that DC-2 and DC-3 may be acting through blockade of calcium channels, and this effect may be responsible for the BP-lowering effect of the compounds observed in the in vivo studies. Two new guaiane-type sesquiterpene terpenoids containing an interesting epoxy unit, daucuside and daucusol, have been isolated from fruits of D. carota

Fuchsia magellanica: This plant is native to Southern Argentina and Chile. Infusion of the leaf extract reduces body temperature, acts as a diuretic, and lowers BP Schmeda-Hirschmann et al. investigated the ethanol/aqueous extracts of this species in NMT rats and found a moderate to strong reduction in the mean arterial pressure.

MANAGEMENT OF PEPTIC ULCERS

Introduction

Ulcer are sore means open and painful wounds and the peptic ulcer are erosion of lining of stomach (the lining is a wrinkly bag that holds acid to help digest food) or the duodenum[25] still the etiology of peptic ulcer is not clearly known but it has been well established that peptic ulcers occurrence takes place due to the imbalance between the aggressive factors (like acid, pepsin, bile & H.pyroli infection) and defensive factors (like gastric mucosa bi carbonates secretion prostaglandin's nitric oxide and innate resistance of the mucosal cell) in gastric ulcers acid secretion may be normal or low while in duodenal ulcer, volume of acid secretion is high in half life of patient and may be normal in rest to mucosal cell death results from increase in H^+ concentration in its immediate environment (decrease PH).[26]

Complications

Gastrointestinal bleeding is the most common complication. Sudden large bleeding can be life-threatening. It occurs when the ulcer erodes one of the blood vessels, such as the gastroduodenal artery. Perforation (a hole in the wall) often leads to catastrophic consequences. Erosion of the gastro-intestinal wall by the ulcer leads to spillage of stomach or intestinal content into the abdominal cavity. Perforation at the anterior surface of the stomach leads to acute peritonitis, initially chemical and later bacterial peritonitis. The first sign is often sudden intense abdominal pain. Posterior wall perforation leads to pancreatitis; pain in this situation often radiates to the back.[27] Penetration is when the ulcer continues into adjacent organs such as the liver and pancreas. Scarring and swelling due to ulcers causes narrowing in the duodenum and gastric outlet obstruction. Patient often presents with severe vomiting. Cancer is included in the differential diagnosis (elucidated by biopsy), Helicobacter pylori as the etiological factor making it 3 to 6 times more likely to develop stomach cancer from the ulcer.

Cause of Peptic Ulcer

Helicobacter pylori: A major causative factor (60% of gastric and up to 90% of duodenal ulcers) is chronic inflammation due to Helicobacter pylori that colonizes the antral mucosa.

The immune system is unable to clear the infection, despite the appearance of antibodies. Thus, the bacterium can cause a chronic active gastritis (type B gastritis), resulting in a defect in the regulation of gastrin production by that part of the stomach, and gastrin secretion can either be decreased (most cases) resulting in hypo- or achlorhydria or increased. Gastrin stimulates the production of gastric acid by parietal cells and, in H. pylori colonization responses that increase gastrin, the increase in acid can contribute to the erosion of the mucosa and therefore ulcer formation.[28]

NSAIDs: Another major cause is the use of NSAIDs (see above). The gastric mucosa protects itself from gastric acid with a layer of mucus, the secretion of which is stimulated by certain prostaglandins. NSAIDs block the function of cyclooxygenase 1 (cox-1), which is essential for the production of these prostaglandins. COX-2 selective anti-inflammatories (such as celecoxib or the since withdrawn rofecoxib) preferentially inhibit cox-2, which is less essential in the gastric mucosa, and roughly halve the risk of NSAID-related gastric ulceration. As the prevalence of H. pylori-caused ulceration declines in the Western world due to increased medical treatment, a greater proportion of ulcers will be due to increasing NSAID use among individuals with pain syndromes as well as the growth of aging populations that develop arthritis. The incidence of duodenal ulcers has dropped significantly during the last 30 years, while the incidence of gastric ulcers has shown a small increase,[29] mainly caused by the widespread use of NSAIDs. The drop in incidence is considered to be a cohort-phenomenon independent of the progress in treatment of the disease. The cohort-phenomenon is probably explained by improved standards of living which have lowered the incidence of H. pylori infections [30]. A study of peptic ulcer patients in a Thai hospital showed that chronic stress was strongly associated with an increased risk of peptic ulcer, and a combination of chronic stress and irregular mealtimes was a significant risk factor.

Smoking: Studies show that cigarette smoking can increase a person's chance of getting an ulcer. Smoking also slows the healing of existing ulcers and contributes to ulcer recurrence.

Caffeine: Beverages and foods that contain caffeine can stimulate acid secretion in the stomach. This can aggravate an existing ulcer, but the stimulation of stomach acid can't be attributed solely to caffeine.

Alcohol: While a link hasn't been found between alcohol consumption and peptic ulcers, ulcers are more common in people who have cirrhosis of the liver, a disease often linked to heavy alcohol consumption.

Genetic factor: People with blood group O appear to be more prone to develop peptic ulcer than those with other blood groups. Genetic influences appear to have greater role in duodenal ulcers as evidence by their occurrence in family's monozygotic twins and association with HLB-B5 antigen.[31]

Plant Used for Treating Peptic Ulcer

There are many herbs, nutrients, and plant products that have been found to play a role in protecting or helping to heal stomach and peptic ulcers. Few human trials are available, but many have shown good potential in animal or in vitro studies. Except for a few phytogenic compounds (i.e. aloe, liquorice and chilly), limited clinical data are available to support the use of herbs as gastro-protective agents and thus, the data on efficacy and safety are limited. Despite this, there are several botanical products with potential therapeutic applications because of their high efficacy and low toxicity. Finally, it should be noted that substances such as Flavonoids, aescin, aloe gel and many others, that possess antiulcer activity are of particular therapeutic importance as most of the anti-inflammatory drugs used in modern medicine are ulcerogenic. Active principles of antiulcer activity are Flavonoids, terpenoids and tannins.

Table No. 2: Some medicinal plants used in the treatment of ulcer

Ficus arnottiana ,	Gymnosporia motana
Alstonia Scholari	Azadirachta indica
Asparagus racemosus,	Berberis asiatica
Bauhinia variegate	Aloe vera
Butea frondosa,	Hibiscus rosa sinensis
Carica papaya	Astragalus membranaceus
Annona squamoza,	Rheum emodi,
Benincasa hispida	Curcuma longa
Eruca sativa,	Uncaria tomentosa
Angelica sinensis	Ulmus rubra
Emblica officinalis,	Althaea officinalis
Tinospor cordifolia	Brassica oleracea
Withania somnifera,	Glycyrrhiza glabra
Centella asiatica	Crataeva nurvala
Moringa oleifera,	Musa paradisca
Garcinia cambogia	Panax ginseng

Plant profiles

Asparagus racemosus: Asparagus racemosus (Shatavari) is recommended in Ayurvedic texts for prevention and treatment of gastric ulcers, dyspepsia and as a galactogogue. Generally the root is employed in diarrhoea as well as in chronic colic and dysentery problems. Root boiled with some bland oil, is applied in various skin diseases. Root is boiled in milk and the milk is administered to relieve bilious dyspepsia and diarrhoea and to promote appetite; root is also used in rheumatism. Tubers are candied and taken as a sweetmeat.Fresh root juice is given with honey as a demulcent. Boiled leaves smeared with ghee are applied to boils, smallpox, etc., in order to prevent their confluence. Juice of this drug taken with milk is useful in gonorrhea. Asparagus racemosus has been shown to mitigate the discomfort due to Amlapitta (Acid dyspepsia with or without ulcer) on 109 cases in a clinical Study at Central Research Institute for Ayurveda, New-Delhi.[32]

Eruca sativa: Extract possesses anti-secretary, cytoprotective, and anti-ulcer activities against experimentally-induced gastric lesions. The anti-ulcer effect is possibly through prostaglandin-mediated activity and/or through its anti-secretory and antioxidant properties.**Panax ginseng:** Ginseng shows anti-ulcer activity due to the presence of ginsenoside Rb1. Both American ginseng (Panax quinquefolius) and Asian ginseng (Panax ginseng) roots are taken orally as adaptogens, aphrodisiacs. A polysaccharide fraction of the leaves from Panax ginseng prevented gastric ulcer formation in rats after administration of necrotizing agents (Hall-ethanol, ethanol) and after pylorus ligation. This effect was observed not only after oral, but also after systemic administration, suggesting a non-local effect. Rats administered tissue cultured and cultivated ginseng had reduced gastric secretion and acid output. However, pepsin activity was not affected. Specifically, the cultivated ginseng blocked histamine induced acid secretion.

Carica papaya: The effects of Carica papaya Linn on exogenous ulcer and histamine-induced acid secretion were studied in rats. The latex of the unripened fruit of C. papaya was effective in protecting the exogenous ulcer. It significantly lessened the acid secretion induced by intravenous infusion of histamine in chronic gastric fistulated rats. Crystalline papain was also effective in protecting the exogenous ulcer and in decreasing the histamine-induced acid secretion in rats. The conclusion is that papain is the active principle in C. papaya that exerts the ulcer-protective effect.[33]

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