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Herbal Treatment of Peptic Ulcer: Guilty or Innocent

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1. Introduction

Normally there is a balance between the protective factors (e.g. mucus, bicarbonate, prostaglandins, nitric oxide and normal blood flow) and aggressive factors (e.g. acid plus pepsin, active oxidants, leukotrienes, endothelins, bile or exogenous factors including nonsteroidal anti-inflammatory drugs). Peptic ulcer develops when aggressive factors overcome the protective mechanisms (Borrelli & Izzo, 2000). *Helicobacter pylori*, nonsteroidal anti-inflammatory drugs and acid-pepsin hypersecretion are the major factors that disrupt this equilibrium. There is other type classified as idiopathic and may be related to defective mucosal defence mechanisms due to tobacco use, psychological stress (stress gastritis), rapid gastric emptying or genetics (Calam & Baron, 2001).

Drug treatment of peptic ulcers is targeted at either counteracting aggressive factors or stimulating the mucosal defences (Tepperman & Jacobson, 1994). The ideal aims of treatment of peptic ulcer disease are to relieve pain, heal the ulcer and delay ulcer recurrence (Borrelli & Izzo, 2000).

2. Aim of the work

The aims of this chapter are to review data about their herbs current usage by patients with peptic ulcer, evidence for their efficacy, the mechanisms by which they might act, and, lastly, their adverse effects on the body.

3. Herbal treatment of peptic ulcer

Tyler defines herbal medicines as “crude drugs of vegetable origin utilized for the treatment of disease states, often of a chronic nature, or to attain or maintain a condition of improved health (Tyler, 1994).

In spite of the progress in conventional chemistry and pharmacology in producing effective drugs, the herbal medicine might provide a source of treatment by many people in the world. In many cultures herbal knowledge was said to have been handed down from the gods. Herbs had been used by all cultures throughout history because patients are often

unaware of the potential problems caused by herbal medicines. In addition, their physicians commonly lack knowledge about these compounds. This factor results in the perception by physicians that herbal drugs are ineffective placebos that can simply be ignored. Some physicians view use of these products as a threat to their paternalistic role and sternly admonish their patients or angrily label them as being crazy (Crone & Wise, 1998).

3.1 Examples of herbs used in treatment of peptic ulcer

Solanum nigrum (family: Solanaceae) commonly known as black nightshade, deadly nightshade, sunberry, makoy, fragrant tomato, duscle, Hound's berry, petty Morel, wonder berry, popolo or wonder cherry. It is effective in treatment of peptic ulcers. The raw juice of its leaves is given either separately or in conjunction with other beneficial juices (Akhtar & Munir, 1989).

A condensed tannin, polyflavonoid tannin, catechol-type tannin non-hydrolyzable tannin or flavolan has been isolated and their anti-peptic and anti-ulcer activity confirmed experimentally (Vasconcelos et al., 2010). When a low concentration of tannin is applied to the mucosa, only the outermost layer is tanned, becoming less permeable and affording an increased protection to the subjacent layers against the action of bacteria, chemical irritation, and, to a certain extent, against mechanical irritation. Tannins may promote a mechanic barrier that protects the stomach from ulcer formation and facilitates ulcer healing (Borrelli & Izzo, 2000).

Saponins (family: Sapindaceae) are so-called because of their soap-like effect, which is due to their surfactant properties. Saponins isolated from the rhizome of *panax japonicas*, the fruit of *kochia scoparia* (which contain approximately 20% of saponins) some oleanolic acid oligoglycosides extracted from *P. japonicas*, *K. scoparia* and a methanol extract of *P. japonicus* rhizome have been demonstrated to possess gastro-protective properties (Matsuda et al., 1998).

Licorice or *glycyrrhiza glabra* (family: Leguminosae) also known as lacrisse (German), licorice root, liquorice, reglisse (French), regolizia (Italian), suessholz, sweet licorice, sweet wood. It is one of the most widely used medicinal plants in the world, commonly used in European, Arabian and Asian traditional medicine systems. Licorice is very effective in the treatment of stomach ulcers. It soothes the irritation of the inner lining of the stomach caused due to excessive acids. Its root is taken, dried and then soaked overnight in water. This is taken in an infusion with rice gruel. This is such an effective treatment that it is used in conventional allopathic medicine also (Hayashi & Sudo, 2009).

Plants containing mucilages traditionally used in several countries in the treatment of gastric ulcer include *althaea officinalis* (marshmallow), *cetraria islandica* (Iceland moss), *malva sylvestris* (common mallow), *matricaria chamomilla* (chamomile) and aloe species (Capasso & Grandolini, 1999). Myrrh (meaning bitter), an oleo-gum-resin obtained from *commiphora molmol*, contains up to 60% gum and up to 40% resin (Newall et al., 1996). Myrrh pre-treatment produced a dose-dependent protection against the ulcerogenic effects of different necrotizing agents (Al-Harbi et al., 1997). The protective effect of myrrh is attributed to its effect on mucus production or increase in nucleic acid and non-protein sulphhydryl concentration, which appears to be mediated through its free-radical scavenging, thyroid-stimulating and prostaglandin-inducing properties. Also aloe seems to be able to speed wound healing by improving blood circulation through the area and preventing cell death around a wound (Borrelli & Izzo, 2000).

3.2 Potential benefits and mechanism of action

Experimental studies have demonstrated that the herbs have gastroprotective activity against gastric mucosal injury induced by ethanol (Souza et al., 2007), ischemia reperfusion (El-Abhar et al., 2002), indomethacin (Souza et al., 2007), alcohol toxicity (Kanter et al., 2005) or stress (Khaled, 2009) in rat.

The mechanism of herb-induced gastroprotection varies according to the nature and chemical constituents of the herbs. The main functions including; inhibition of acid plus pepsin secretion (Baggio et al., 2007), cytoprotective (by enhancement of epidermal growth factor content in gastric juice, nitric oxide and H⁺, K⁺-ATPase inhibitory activity in gastric tissue, PGE₂ in plasma, inhibition of endothelin in plasma, an increase in mucosal thickness (Fan et al., 2007) and mucus content in the gastric mucosa) (Kamath et al., 2008), bactericidal activity, inhibition of the growth and activity of *helicobacter pylori* (Mahady et al., 2002) and antioxidant activities (and the ability to scavenge reactive oxygen species) (Souza et al., 2007), isolated or in combination, are responsible for gastric mucosal protection (Zaidi, et al., 2009). Moreover, plantextract- induced gastroprotection is probably related to the enhancing effect on NOS inhibitor expression, gastric microcirculation (Al Mofleh, 2010). Herbs could protect the gastric mucosa by increasing the bioavailability of arachidonic acid, resulting in biosynthesis of the cytoprotective prostaglandins in the stomach (Tsuji et al., 1990). Moreover, herbs have also been reported to produce a marked inhibition on the release of leukotrienes, which cause mucosal tissue injury and hypoxemia (Mansour, 1990).

3.3 Risks of herbal treatment of peptic ulcer

It is important to acknowledge that all conventional drugs have potential toxicities. However, in contrast to herbal products, conventional drugs undergo trials and postapproval surveillance that define these toxicities, giving practitioners data on that to weigh risks and benefits of treatment. The therapeutic window and dosage are also defined, as are the constituents of the medicine. Because of rigorous quality control, each pill has the same ingredients as another. Adverse reactions to herbal medicines are probably underrecognized and underreported (D'Arcy et al., 1991). Herbal medicines can produce unwanted side effects, toxicity and herbal drug interaction caused by their pharmacologic properties.

A-Side-effects and toxicity of herbal therapy

i. Direct side-effects and toxicity of herbal therapy

Nausea, diarrhea, and skin reactions are common side effects of a wide variety of herbal medicines (tannins, mucilages, saponins and solanum nigrum). Also there is a serious side effects of herbal remedies on the liver (tannins and Licorice) include liver injury, acute and chronic hepatitis, hepatic failure and possibly hepatic tumours (Chandler, 1987). While most of the adverse effects on the digestive tube are self-limiting and relatively trivial, the same is not true of herb-induced hepatotoxicity, in which fatalities have been reported with alarming frequency (Chitturi & Farrell, 2000). More serious side effects of herbal medicines may include hypertension, heart failure (licorice), anaphylaxis (matricaria chamomilla), and lupus-like symptoms (D'Arcy et al., 1991). Ventricular arrhythmias, intravascular hemolysis, hemorrhage, renal failure, and pulmonary hypertension have all been linked to the active chemical components found in herbal remedies (Larrey et al., 1992). Psychoactive effects in several herbal medicines have produced behavioural, cognitive, mania and emotional

disturbances (Capwell, 1995). Most of these herbs are not recommended for woman with pregnancy or breast feeding (Roulet et al., 1988).

Black nightshade is UNSAFE. It contains a toxic chemical called solanin. At higher doses, it can cause severe poisoning. Signs of poisoning include irregular heartbeat, trouble breathing, dizziness, drowsiness, twitching of the arms and legs, cramps, diarrhea, paralysis, trembling, paralysis, coma, and death (Duke, 1985).

In sensitive individuals, a large intake of tannins may cause bowel irritation, kidney irritation, liver damage, irritation of the stomach and gastrointestinal pain. A correlation has been made between esophageal or nasal cancer in humans and regular consumption of certain herbs with high tannin concentrations (Lewis, 1977). Tannins interfere with iron absorption through a complex formation with iron when it is in the gastrointestinal lumen which decreases the bioavailability of iron. There is an important difference in the way in which the phenolic compounds interact with different hydroxylation patterns (gallic acid, catechin, chlorogenic acid) and the effect on iron absorption. The content of the iron-binding galloyl groups may be the major determinant of the inhibitory effect of phenolic compounds. However, condensed tannins do not interfere with iron absorption (Brune et al., 1989).

Saponins are harmful if swallowed or inhaled. They cause irritation to skin, eyes and respiratory tract. Symptoms include redness, itching, and pain. Saponin inhalation causes sneezing and may irritate the respiratory tract. They cause haemolysis of RBC's if reach the blood. Frequent ingestion of small amounts of saponin results in chronic githagism (a disease, similar to lathyrism, that results in pain, burning and prickling sensations in lower extremities, and increasing paralysis) (Hostettmann and Marston, 2005).

Excessive consumption of licorice is known to be toxic to the cardiovascular system and may produce oedema (van Uum, 2005). Comparative studies of pregnant women suggest that licorice can also adversely affect both IQ and behaviour traits of offspring (De Smet, 2002). In large amounts, licorice containing glycyrrhizin can cause high blood pressure, salt and water retention, and low potassium levels, which could lead to heart failure (Blumenthal et al., 2000).

Mucilage side effects include bloating, abdominal pain, flatulence and oesophageal obstruction. *Matricaria chamomilla* (chamomile) causes symptoms of an allergic reaction such as rash, itching, swelling, dizziness and trouble breathing (Andres et al., 2009). *Althaea officinalis* is generally regarded as safe. However, the potential for marshmallow to cause allergic reactions or low blood sugar, genotoxicity, carcinogenicity and/or reproductive and developmental toxicity has been noted anecdotally (Büechli et al., 2005). Taking aloe by mouth is unsafe, especially at high doses. There is some concern that some of the chemicals found in aloe latex might cause cancer. Additionally, aloe latex is hard on the kidneys and could lead to serious kidney disease and even death (Poppenga, 2002).

ii. Indirect Side-Effects and Toxicity of Herbal Therapy

The use of herbal therapy may be complicated by several indirect adverse effects. People initially consulting herbal practitioners may suffer from misdiagnosis and consequent delay in obtaining effective conventional treatment (Angell & Kassirer, 1998). Others may delay or forego appropriate conventional options in favour of ineffective unconventional ones. When expectations of alternative therapy are high, failure to obtain relief from symptoms, particularly if treatment has been expensive, could also be construed as an adverse effect (Langmead & Rampton, 2001).

B-Drug–herb Interactions

A pharmacodynamic interaction occurs when substances act at the same receptor, site of action or physiologic system. Pharmacodynamic interactions result in an antagonistic or additive drug effect (Anastasio et al., 2000). A drug or substance that accentuates or interferes with the absorption, distribution and elimination of a second drug or substance produces a pharmacokinetic interaction. This mechanism is the most frequent cause of adverse interactions, commonly caused by altered drug elimination. Induction of elimination can result in a decreased therapeutic benefit whereas inhibition of drug elimination can produce excessively increased dose related toxicity (Nicole & Mitchell, 2003).

Saponins and mucilage can interfere with the absorption of other medicines within the gut if they are taken at the same time (Mohammed, 2009).

Several medications may cause potentially negative drug interactions with licorice. Some of these medications include blood pressure medications (beta blockers, calcium channel blockers, and nervous system inhibitors), certain diuretics (such as bumetanide, chlorothiazide, chlorthalidone, ethacrynic acid, furosemide, hydrochlorothiazide, metolazone and torsemide), hypoglycemics and corticosteroids (D'Arcy et al., 1991). These licorice drug interactions can result in serious problems, such as low blood potassium and low blood calcium (Blumenthal et al., 2000). Licorice should not be taken concurrently with corticosteroid treatment (Poppenga, 2002). Concurrent use of furosemide may potentiate development of acute renal failure. Potassium loss due to other drugs, e.g. thiazide diuretics, can be increased. With potassium loss, sensitivity to digitalis glycosides increases (D'Arcy et al., 1991). Licorice should not be administered in conjunction with spironolactone or amiloride (Poppenga, 2002).

It is mentioned in some literature sources (Barnes et al. 2002, Poppenga, 2002) that absorption of concomitantly administered medicines can be delayed due to mucilage protecting layer. Potential risks of chamomile include interference with warfarin and infant botulism in very young children (Biancoa et al., 2008). Aloe may increase K⁺ loss and potentiate cardiac glycosides and antiarrhythmic agents such as quinidine. Increased K⁺ loss when used with other drugs, such as diuretics, with similar effect on K⁺. Laxative effect may reduce absorption of other drugs (Poppenga, 2002).

4. Conclusion

Herbal medicine is prescribed by the herbalists symptomatically—based on signs and symptoms alone—rather than as a result of a full understanding of the underlying disease. Proper diagnosis is totally absent. As any plant, medicinal herbs contain many chemicals that are subjected to change with changing conditions of the environment, especially storage. The discriminate and proper use of some herbal products is safe and may provide some therapeutic benefits, but the indiscriminate or excessive use of herbs can be unsafe and even dangerous (Borrelli & Izzo, 2000).

There is an urgent need for further scientific assessment of the potential benefits and dangers of the huge range of herbal medications available. Herbal preparations used for medicinal purposes should require licensing by an independent national body in order to improve their quality and safety, and to ensure that claims of efficacy are validated by randomized controlled trials.

The general public, as well as pharmacists, general practitioners and hospital doctors, should be aware, particularly, of the risks associated with the use of herbal remedies,

whether on their own or in combination with other herbal or conventional medicines. The incorporation of a short course on alternative and complementary therapy in medical school curricula would help achieve this end.

Lastly, because of the potential for side effects, toxic reactions, and unwanted drug-drug interactions, it is essential for physicians to ascertain if their patients are taking herbal medications. So if you are thinking about using herbal medicine it would be a good idea to check with your physician about possible adverse reactions and interactions with medications you may be taking before starting (D'Arcy et al., 1991).

IF YOU NEED ONE WORD "Do not take herbs internally except under the supervision of a qualified professional".

Herbs you're guilty until proven innocent by researchers!

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Peptic ulcer disease is one of the most common chronic infections in human population. Despite centuries of study, it still troubles a lot of people, especially in the third world countries, and it can lead to other more serious complications such as cancers or even to death sometimes. This book is a snapshot of the current view of peptic ulcer disease. It includes 5 sections and 25 chapters contributed by researchers from 15 countries spread out in Africa, Asia, Europe, North America and South America. It covers the causes of the disease, epidemiology, pathophysiology, molecular-cellular mechanisms, clinical care, and alternative medicine. Each chapter provides a unique view. The book is not only for professionals, but also suitable for regular readers at all levels.

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