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Pharmacology of Traditional Herbal Medicines and Their Active Principles Used in the Treatment of Peptic Ulcer, Diarrhoea and Inflammatory Bowel Disease

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1. Introduction

The endocrine, exocrine and paracrine secretions of the gastrointestinal (GI) tract play a pivotal role in the digestion and absorption of food and orally administered drugs. The secretion of mucus by mucus-secreting cells protects the erosion of the gastric mucosa from the highly acidic gastric juice. The secretion of hydrochloric acid from parietal cells is regulated by acetylcholine, histamine and gastrin. Disturbances in secretory functions of the gastrointestinal tract can lead to several GI complications. Conventional therapies employ a range of drugs that have been pharmacologically well characterised. While these drug molecules are proven to be beneficial, the adverse effects and drug-drug interactions highlight the need for better treatment modalities for GI tract disorders.

Since ancient times, herbal medicines have been traditionally used to treat several diseases. The gastroprotective properties of these herbs and their active constituents have been experimentally demonstrated (Al Mofleh, 2010). Asian traditional medicine systems have identified several herbs and spices to treat GI tract disorders (Langmead & Rampton, 2006; Sengupta et al., 2004). In support of these traditional claims, several preclinical and clinical studies have provided the scientific basis for the effectiveness of herbal extracts (e.g. *Glycyrrhiza glabra*) and their active constituents (e.g. flavonoids) in treating GI tract disorders (Borrelli & Izzo, 2000). The discovery and development of anti-ulcer agents such as carbenoxolone from *Glycyrrhiza glabra* and gefarnate from cabbage further highlight the presence of pharmacologically active components in herbal extracts and suggests their use as an alternative therapy to treat GI tract disorders.

The effectiveness and the mechanisms of action of crude herbal extracts vary according to the composition of their chemical constituents. Herbal medicine seems to fill this gap, especially when employing high manufacturing standardised forms of herbal medicine with regard to the quality and quantity of ingredients (Suzuki et al., 2009). In addition, well characterised herbal formulations may lead to the production of reliable clinical data on efficacy and safety. As several studies have shown that herbal medicines may produce adverse reactions and herb-

drug interactions, the common assumption that 'herbal products are natural, they are safe' is no longer valid. Safety and quality data of herbal medicines should be made available to medical practitioners and other healthcare professionals to avoid these unwanted effects.

Several plants have been used by traditional healers around the world to treat various gastrointestinal tract diseases. Centuries ago the reliance on nature to cure human ailments was developed by great efforts of dedicated professionals by keen observation and trial and error method. This important knowledge is updated constantly and passed from generations to generations. Today traditional healing systems play important roles in several parts of the world, especially where modern pharmaceuticals are less accessible. Modern scientific research methods are invaluable to support traditional claims and also to develop traditional remedies as a viable alternative to mainstream pharmaceuticals. In recent years, a number of research papers have been published on herbal medicines to provide the experimental evidence for their traditional claims. Given the multitude of these research publications, it is not possible to cover all of them. In this chapter, we only attempted to provide the experimental (animal and human studies) evidence for the plants that have been traditionally used to treat most notable gastrointestinal diseases, namely, peptic ulcer, diarrhoea and inflammatory bowel syndrome.

2. Peptic ulcer

2.1 Animal models of gastric ulcer

Rats are commonly used animals to induce ulcers that resemble the human condition by various noxious chemical agents. NSAIDs (eg. Indomethacin and Aspirin) cause gastrointestinal ulceration, due to their ability to suppress cytoprotective prostaglandin synthesis (Wallace, 2001). The NSAIDS-induced ulcer model is important to identify mechanisms of action of plants that maintain the gastric mucosa integrity by balancing the toxic effects of NSAIDs. The widely used ethanol-induced gastric ulcer model is suitable to study gastric protective and free radical scavenging properties of plants. Stress induced gastric lesions in rats are useful to study gastric mucosal barrier strengthening properties (eg. increased mucus production) of potential plant extracts and their actives. Pylorus ligation in rats helps to screen plants for their antisecretory properties.

2.2 Plants used in the treatment of peptic ulcer

- *Diodia sarmentosa* (Rubiaceae), *Cassia nigricans* (Celsapinaceae), *Ficus exasperate* (Moraceae) and *Synclisia scabrida* (Menispermaceae) are the most popularly used antiulcer recipes in Nigeria. In vivo studies in mice and rats revealed their anti-ulcer activities by decreasing the ulcer index in aspirin-induced ulcerogenesis, delayed intestinal transit, increased pH, and decreased volume and acidity of gastric secretion (Akah et al., 1998).
- *Eruca sativa*, commonly known as Rocket, is a commonly used leaf vegetable in Unani, Ayurveda and Arab traditional medicine systems. Rocket is shown to possess significant anti-secretory, anti-ulcer and cytoprotective properties in rats (Alqasoumi et al., 2009). Pretreatment with ethanolic extract of Rocket attenuated gastric ulceration induced by ethanol, indomethacin and hypothermic stress. In pylorus ligated rats, Rocket dose-dependently reduced gastric acid secretion. In addition, the extract

significantly replenished gut wall mucous and reduced malondialdehyde (an indicator of lipid peroxidation) levels in ethanol treated rats. Gastroprotective effects of Rocket are attributed to the presence of flavonoids, sterols and triterpines.

- *Turnera ulmifolia* or 'chanana' (Turneraceae) is a small herb with wide geographical distribution ranging from Guyana to the North Eastern region of Brazil. It is a widely used folk medicine for its anti-inflammatory properties. The hydroalcoholic extract of *T. ulmifolia* inhibited gastric lesions induced by pylorus ligation, by indomethacin and by ethanol, but stress mediated lesions remained unaffected. As histamine plays a role in ulcerogenesis in pylorus ligation, it was postulated by the study authors that *T. ulmifolia* exerts gastroprotective actions by inhibiting histamine. The inhibition of gastric ulcers induced by indomethacin and ethanol indicate that gastroprotective effects of *T. ulmifolia* could be due to an enhancement of mucosal defensive factors such as gastric mucus (Antônio & Souza Brito, 1998).
- *Dodonaea viscosa* is a stiff bushy plant. Tribes who reside in the forest regions of South India (Kerala) use leaves of this plant for headaches and backaches. The hexane extract of *Dodonaea viscosa* dose dependently inhibited ethanol and indomethacin induced gastric lesions. Gastric secretion studies showed significant decrease of total acid in gastric juice (Arun & Asha, 2008). Furthermore, it decreased total acid content and increased gastric glutathione levels in ethanol and indomethacin treated rats.
- *Azadirachta indica* is a native tree to the Indian subcontinent. To the Indian it is commonly known as Neem and regarded as a 'village dispensary' due its multiple therapeutic properties. It has been extensively used in Ayurveda, Siddha, Unani and other local Indian folklore medicine systems (Brahmachari, 2004). Standardized aqueous extract of Neem exhibited remarkable anti-ulcer activity in restraint-cold stress and indomethacin induced gastric ulcers in rats. Animal studies suggest that the major gastroprotective effect of Neem bark extract against ulcer is mediated through inhibition of acid secretion by H⁺-K⁺-ATPase and prevention of oxidative damage (Bandyopadhyay et al., 2002).
- The aqueous extract of Neem bark when administered for 10 days at 30 mg dose twice daily significantly inhibited gastric acid secretion in patients with chronic gastric acid problem. The bark extract completely healed the duodenal ulcers at the dose of 30-60 mg twice daily for 10 weeks (Bandyopadhyay et al., 2004). Some important blood parameters for organ toxicity such as sugar, urea, creatinine, serum glutamate oxaloacetate transaminase, serum glutamate pyruvate transaminase, albumin, globulin, hemoglobin levels and erythrocyte sedimentation rate remained unaffected upon Neem exposure.
- *Pteleopsis suberosa* is traditionally used in Mali for the treatment of gastric ulcers. The aqueous extract of *P. suberosa* exhibited protective effects on gastric mucosa in ethanol and indomethacin treated rats (De Pasquale et al., 1995). It has also been shown that *Pteleopsis suberosa* decoction containing triterpenoid saponins and tannins is effective against *Helicobacter pylori* (Germano` et al., 1998).
- *Calligonum comosum* is a shrub distributed throughout Arabia and growing in sandy deserts. It is used by the local healers to treat stomach ailments. Pre-treatment with the 10% ethanolic extract displayed a significant and dose-dependent inhibition of acute gastric ulcers induced by NSAIDs (phenylbutazone and indomethacin) and necrotic agents (0.2 N NaOH and 80% ethanol) (Liu et al., 2001).
- *Solanum torvum*, a small tree, is widely used in African folk medicine to treat various diseases including gastric ulcer (Noumi et al., 2000). Aqueous and methanolic extracts from

- leaves of *Solanum torvum* produced significant anti-ulcer activity in HCl/ethanol, indomethacin, pylorus ligation and cold-restraint stress induced gastric ulcers in rats. The authors proposed that the cytoprotective activity of extracts could be due to strengthening of the mucosal barrier through the increase of mucus production (Nguelefack et al., 2008).
- *Tetrapleura tetraptera* and *Guibourtia ehie* Leonard are native trees to Ghana. The Ghanaian ethnomedical system employs these plant extracts in the management of stomach ulcers. In support of their traditional use, aqueous extracts of the barks of *Tet. Tetraprera* and *G. ethie* dose dependently inhibited HCl/ethanol induced gastric ulcers (Noamesi et al., 1994).
 - *Glycyrrhiza glabra* is a legume native to southern Europe and parts of Asia. It is a well-known folk medicine for gastric ulcer (Aly et al., 2004). Gastric mucosal damage induced by NSAIDs is markedly reduced by *G. glabra* (Aly et al., 2004). Clinical data on *Gycrrhiza glabra* is inconsistent. In a double-blind clinical trial, administration of deglycyrrhizinized liquorice thrice daily at the dose of 760 mg for four weeks significantly accelerated the healing of gastric ulcer. In contrast, a cross over study at the same dose and treatment time reported no improvement in ulcer healing (Engqvist et al., 1973). A similar result was shown in a double-blind placebo- control study with administration of deglycyrrhizinized liquorice for one month at the dose of 380 mg thrice daily (Feldman et al., 1971). No side effects are reported in subjects who received deglycyrrhizinized liquorice extract in these studies.

Plant	Scientific Evidence	Active Constituent(s)	Reference
<i>Diodia sarmentosa</i>	Pre-clinical	Unknown	Akah et al
<i>Cassia nigricans</i>	Pre-clinical	Flavonoids	Akah et al
<i>Ficus exasperate</i>	Pre-clinical	Gallic acid & ellagic acid	Akah et al ; Sirisha et al
<i>Synclisia scabrida</i>	Pre-clinical	Alkaloids & flavonoids	Akah et al ; Orisakwe et al ; Obi et al
<i>Eruca sativa</i>	Pre-clinical	Flavonoids, sterols & triterpines	Alqasoumi et al
<i>Turnera ulmifolia</i>	Pre-clinical	Flavonoids	Antônio et al
<i>Dodonaea viscosa</i>	Pre-clinical	Flavonoids, saponins, bitter principles & phenols	Arun et al
<i>Azadirachta indica</i>	Pre-clinical & clinical	Phenolic glycoside	Bandyopadhyay et al
<i>Pteleopsis suberosa</i>	Pre-clinical	Triterpenoid saponins & tannins	De Pasquale et al ; Germanò et al
<i>Calligonum comosum</i>	Pre-clinical	Unknown	Liu et al
<i>Solanum torvum</i>		Flavonoids, sterols & triterpenes	Nguelefack et al
<i>Tetrapleura tetraptera</i>	Pre-clinical	Unknown	Noamesi et al
<i>Guibourtia ehie</i>	Pre-clinical	Unknown	Noamesi et al
<i>Glycyrrhiza glabra</i>	Pre-clinical & clinical	Unknown	Aly et al, Rees et al ; Engqvist et al; Feldman et al

Table 1. Plants and their active constituents with anti-ulcer activity

3. Diarrhoea

3.1 Experimental models

Rodents are commonly used to induce experimental diarrhea and to study mechanisms of action of plants and their active principles. Castor oil, Prostaglandin E2 (PG-E2) and heat-labile enterotoxin are commonly used agents to induce diarrhea in animals. The diarrhoeal effect of castor oil is mediated through ricinoleic acid which causes irritation and inflammation of intestinal mucosa, and consequently leads to the stimulation of intestinal motility and increased secretion of fluid and electrolytes. This model is ideal to study the antisecretory and antimotility potential of medicinal plants. Prostaglandin E2 causes enteropooling by stimulating fluid secretion and increasing propulsive activity in the colon (Pierre et al., 1991). Heat-labile enterotoxin (LT) is the virulent factor of *Escherichia coli* and diarrhea by accumulation of salt and water in the intestinal lumen (Spangler., 1992). Therefore, the LT-induced diarrhoeal model is suitable to study inhibitory effects of plant extracts on bacterial toxins. In addition, the charcoal meal test and charcoal-gum acacia-induced hyperperistalsis in animals are helpful to identify the effect of potential medicinal plants on intestinal motility.

3.2 Plants tested for antidiarrheal activity in animal models of diarrhoea

- *Ficus bengalensis*, *Eugenia jambolana*, *Ficus racemosa* and *Leucas lavandulaefolia* are commonly used folk medicine to treat diarrhoea by the people who live in Khatra region of West Bengal, India. Ethanolic extracts of *Ficus bengalensis* (hanging roots), *Eugenia jambolana* (bark), *Ficus racemosa* (bark) and *Leucas lavandulaefolia* (aerial parts) significantly inhibited castor oil induced diarrhoea and PGE2 induced enteropooling in rats. In addition, these extracts also showed a significant reduction in gastrointestinal motility in charcoal meal tests in rats (Mukherjee et al., 1997).
- *Geranium mexicanum* plant is a commonly used medicinal plant in Traditional Mexican Medicine for the treatment of diarrhoea. Methanolic extract of *Geranium mexicanum* (roots) remarkably inhibited charcoal-gum acacia-induced hyperperistalsis in rats. However the authors suggested that this medicinal plant should be used with care to avoid toxic effects (Clazada et al., 2009).
- *Galla chinensis* and *Chaenomeles speciosa* have been traditionally used in China to treat gastrointestinal disorders. These plant extracts significantly inhibited heat-labile enterotoxin-induced diarrhoea in the mouse (Chen et al., 2006, Chen et al., 2007).
- *Satureja hortensis* is an annual herb that is traditionally used in Iran for treating stomach and intestinal disorders. Essential oil isolated from *S. hortensis* exhibited antispasmodic activity in isolated rat ileum. In addition, it also inhibited castor oil-induced diarrhea in mice (Hajhashemi et al., 1999).
- *Thespesia populnea*, a large tree found in tropical regions and coastal forests of India, is traditionally used in India to treat several disorders including diarrhea and dysentery. Residue fraction of aqueous extract of *T. populnea* significantly inhibited castor oil and prostaglandin E2 (PGE₂)-induced diarrhea induced diarrhea in rats. In addition, it also inhibited intestinal motility in the charcoal meal test (Viswanatha et al., 2011).
- *Mitragyna speciosa* is an indigenous tree to Thailand, where it is commonly called kratom. In folk medicine, it is often used to treat diarrhea. Methanolic extract of *M. speciosa* dose dependently inhibited castor oil-induced diarrhea and intestinal transit in rats (Chittrakarn et al., 2008).

- *Punica granatum* is a deciduous shrub or small tree that is native to the Himalayas in north Pakistan and Northern India. Bark, rind of the fruit and seeds of this plant are used in folk medicine to treat diarrhea. Methanol extract of seeds of *P. granatum* dose dependently reduced castor oil induced diarrhea. It also significantly inhibited gastrointestinal motility and PGE₂ mediated enteropooling in rats (Das et al., 1999).

Plant	Scientific Evidence	Active Constituent(s)	Reference
<i>Ficus bengalensis</i>	Pre-clinical	Tannin	Mukherjee et al
<i>Eugenia jambolana</i>	Pre-clinical	Tannin	Mukherjee et al
<i>Ficus racemosa</i>	Pre-clinical	Tannin	Mukherjee et al
<i>Leucas lavandulaefolia</i>	Pre-clinical	Tannin	Mukherjee et al
<i>Geranium mexicanum</i>	Pre-clinical	(-)-epicatechin, tyramine	Calzada et al
<i>Galla chinensis</i>	Pre-clinical	Gallic acid	Chen et al
<i>Chaenomeles speciosa</i>	Pre-clinical	Oleanolic acid, ursolic acid & betulinic acid	Chen et al
<i>Satureja hortensis</i>	Pre-clinical	Carvacrol	Hajhashemi et al
<i>Thespesia populnea</i>	Pre-clinical	Unknown	Viswanatha et al
<i>Mitragyna speciosa</i>	Pre-clinical	Mitragynine & other alkaloids	Chittrakarn et al
<i>Punica granatum</i>	Pre-clinical	Tannin	Das et al

Table 2. Plants and their active constituent(s) with anti-diarrheal activity

4. Inflammatory Bowel Diseases (IBD)

4.1 Animal models of IBD

In IBD oxidative stress mediates disease progression by disrupting epithelial cell integrity. Acetic acid-induced colitis is helpful to screen herbs which can inhibit cytotoxic effects of reactive oxygen species (ROS). Dextran sulphate sodium (DSS)-induced colitis is also a frequently used animal colitis model in ethnopharmacological studies. This model is useful to test the effect of herbs on inflammatory cytokines mediated cellular injury (Dieleman et al., 1998). The transgenic rat model (HLA-B27) with overt chronic gastrointestinal tract inflammation also serves to screen medicinal herbs to treat IBD.

- *Zingiber officinale* is traditionally used to treat inflammatory gastrointestinal disorders. Ethanolic extract of dried rhizomes of ginger displayed protective effects against acetic acid-induced ulcerative colitis in rats (El-Abhar et al., 2008).
- *Cordia dichotoma* is a deciduous tree with many medicinal uses in Ayurveda. Traditionally bark of the plant is reported for the treatment of ulcerative colitis. Methanolic extract of *C. Dichotoma* improved lesions and reduced colonic myeloperoxidase (MPO) and malondialdehyde (MDA) in acetic acid induced UC in male swiss mice (Ganjare et al., 2011).
- *Patrinia scabiosaefolia* is a commonly used herbal medicine in Korea. It is used traditionally to treat colonic inflammations. Methanolic extract of *P. Scabiosaefolia* significantly attenuated dextran sulfate sodium induced colitis in mice. In addition, it

- also suppressed colonic MPO accumulation and pro-inflammatory mediators (TNF α , IL-1, IL-6 and nitric oxide) (Cho et al., 2011).
- *Vitex negundo* is a shrub that grows in Southeast Asia. Traditionally its roots are used in the treatment of ulcerative colitis in India. Ethanolic extract of *V. negundo* significantly inhibited acetic acid ulcerative colitis and reduced colonic MPO and MDA levels in mice (Zaware et al., 2011).
 - *Pistacia lentiscus* is a dioecious shrub that grows in the Mediterranean region. Oleogum resin from *P. Lentiscus* is used in traditional Iranian medicine to treat IBD. Treatment with oleogum resin from *P. Lentiscus* improved the symptoms of dextran sulfate sodium (DSS) induced colitis in mice (Kim & Neophytou, 2009). A pilot study conducted in mild to moderate Crohn's disease patients demonstrated that mastic (resin) from *P. Lentiscus* significantly reduced disease activity index, plasma IL-6 and C-reactive protein (Kaliora et al., 2007a) and TNF α in peripheral blood mononuclear cells (Kaliora et al., 2007b). In addition, total antioxidant potential was significantly increased. No side effects are observed in mastic treated patients (Kaliora et al., 2007a). A double-blind clinical trial in patients with duodenal ulcers exhibited symptomatic relief in 80% patients on mastic and 50% patients on placebo, while endoscopically proven healing occurred in 70% patients on mastic (Al-Habbal et al., 1984).
 - *Plantago ovata* is a well-known medicinal plant in the treatment of IBD. *P. ovata* seeds ameliorated the development of colonic inflammation in transgenic rats as evidenced by an improvement of intestinal cytoarchitecture, significant decrease in some of the pro-inflammatory mediators and higher production of short-chain fatty acids (Rodríguez-Cabezas et al., 2003). An open label, parallel-group, multicenter, randomized clinical trial in patients with ulcerative colitis concluded that *Plantago ovata* seeds (dietary fiber) might be as effective as mesalamine to maintain remission in ulcerative colitis (Fernández-Bañares et al., 1999).
 - *Boswellia serrata*, a tree which grows in the hilly areas of India, is an efficacious remedy for IBD in traditional Iranian medicine and also it has been used in the Ayurvedic medicine for the treatment of inflammatory diseases. Despite its traditional claims, *Boswellia* extracts are ineffective in ameliorating colitis in DSS-induced colitis in mice (Kiela et al., 2004). In contrast to animal studies, a double-blind, randomized, placebo-controlled, multicenter trial in colitis patients showed higher remission in *Boswellia serrata* extract treated group than in the placebo group (Madisch et al., 2007). However, a recent double-blind, placebo-controlled, randomized, parallel study in patients with Crohn's disease has shown no difference between the *Boswellia* treated group and control group in disease remission (Holtmeier et al., 2011).

5. Quality, efficacy and safety of herbal medicines

5.1 Quality

The quality of herbal medicines is important to ensure their safe use and efficacy. In contrast to well characterized conventional medicine, assurance of the quality of herbal medicine is a major concern. The problems associated with the herbal products include deliberate or accidental inclusion of prohibited or restricted ingredients, substitution or adulteration of herbal materials, contamination with toxic substances and differences between labelled and actual contents (Barnes et al., 2nd ed). However, increased consumer awareness and

Plant	Scientific Evidence	Chemical Constituents	Reference
<i>Zingiber officinale</i>	Pre-clinical	Gingerols	El-Abhar et al ; Minaiyan et al
<i>Cordia dichotoma</i>	Pre-clinical	Apigenin	Ganjare et al
<i>Patrinia scabiosaeifolia</i>	Pre-clinical	Oleanonic acid, oleanolic acid & ursolic acid	Cho et al
<i>Vitex negundo</i>	Pre-clinical	Unknown	Zaware et al
<i>Pistacia lentiscus</i>	Pre-clinical & clinical	Oleanolic acid	Kim et al; Kaliora et al; Al-Habbal
<i>Plantago ovata</i>	Pre-clinical & clinical	Unknown	Rodriguez-Cabezas et al ; Fernandez- Banares et al
<i>Boswellia serrata</i>	Pre-clinical & clinical	Boswellia acids	Kiela et al ; Madisch et al ; Holtmeier et al

Table 3. Plants and their active constituents for treatment of ulcerative colitis/IBD

regulatory agencies’ strict guidelines on the quality and stability of herbal products has led to significant improvements in the quality control of herbal medicines. Recently the herbal manufacturing industry has focused on improving its quality assurance and quality control mechanisms to guard against the frequent episodes of substandard quality and possible adulterations. Use of high-performance liquid chromatograms, thin-layer chromatography, atomic absorption spectroscopy, gas chromatography and where necessary more sophisticated techniques such as NMR and LC/MS has now become common in complementary medicines manufacturing industries to ensure the quality of plant materials and final product (Rosenbloom et al., 2011). The emphasis on good manufacturing practice has steadily increased over years. In addition, new regulatory laws are now in place on product stability to support its shelf life. With the steady progress on different herbal quality control fronts, it is now possible to apply almost the same set of quality standards as for conventional medicines. As most of the traditional herbs listed in this chapter are not commercially manufactured, the data on the quality of these plant medicines is scarce.

5.2 Efficacy

Herbal medicines have a long history of traditional use. However, from today’s stand point, traditional claims need to be verified. A well-designed randomized controlled trial is essential to determine the efficacy and safety of herbal medicines. The use of standardized herbal extracts in clinical trials is important to obtain reproducible data on the efficacy and safety of herbal medicines. Standardization of herbal extracts has become a common practice in phytomedicines. It allows the establishment of reproducible pharmaceutical quality by comparing a product with established reference substances and by defining the

specific quantity of one or several compounds. As the herbs are of natural origin, their chemical composition is affected by several factors (climate, growing conditions, time of harvesting, storage conditions and processing). Therefore, the use of standardized herbal extracts in preclinical and clinical research is helpful to develop evidence based traditional therapies. Although rigorous clinical investigations are lacking at present for many herbs used in GIT disorders, there is a vast literature on the *in vitro* and *in vivo* pharmacological effects of medicinal plants. These pre-clinical observations provide a rationale for further investigation of such plants.

5.3 Safety

The positive attitude towards herbal medicines is based on the testimony that herbs have been used since antiquity and the belief that they have the advantage of being 'natural' rather than 'synthetic'. Traditional healing systems employed herbal medicines for the symptomatic management of diseases. However, these herbs are now being used extensively for health promotion and disease prevention not only in underdeveloped and developing nations, but also increasingly in developed nations. As little is known regarding adverse effects of herbal medicines and their frequencies, the chronic exposure of these herbal ingredients may pose health risks. In particular, when herbs are extracted and purified, their toxicity might be increased due to increased concentration of potential toxic compounds. Therefore, the common assumption that herbal medicines are by inference 'safe' may not be valid by today's health standards.

Generally, traditional herbal medicines lack the following pharmacological data in humans:

- pharmacologically active chemical constituents and their metabolites
- mechanisms of action of active constituents/whole extract
- pharmacokinetics
- toxicology
- adverse effects and their frequencies
- drug-herb and food-herb interactions
- use in vulnerable individuals: children, elderly, individuals with renal or hepatic disease, gender effects, individuals with a different genetic profile
- contraindications

Phytochemical and pharmacological (preclinical and clinical) studies are important to address the above issues. The majority of the herbs mentioned in this chapter are tested only in animals. The main focus of these studies has been determining the efficacy of herbal extracts to support their traditional claims. However, it is a common procedure in these animal studies to measure toxic dose of herbal extracts. These toxicological studies are important to provide *in vivo* data in a whole animal situation on the dose and adverse effects of herbal extracts which may be relevant when tested in humans. None of these studies have reported any major adverse events in the experimental models of various GI disorders.

6. Conclusion

The use of plants in treating diseases is a very old human tradition. This knowledge, derived from observations and experiences, has been handed over from generation to generation

verbally and also in the form of ancient texts. Medicinal plants are the foundations for modern therapeutic agents. Herbal medicines are an important part of the health care system in many developing countries. The use of herbal medicines, as health promoting agents, in developed countries has also increased and this trend is continuing. Healthcare professionals need to be aware of the pharmacology of these herbal medicines in order to provide well informed advice to patients. The traditional herbal medicines field is very vast. In this chapter we attempted to provide scientific evidence for the herbs with historical use in three major GIT disorders namely: peptic ulcer, diarrhoea and IBD. Researchers successfully reproduced these human disorders in animals by employing a range of chemical agents and scientific procedures. In some cases, these models not only have supported the traditional claims, but also provided important information on the mechanism of action of the plant extracts and in some cases their components. The majority of these preclinical studies established the scientific evidence to traditional herbal medicines. Unfortunately, very few clinical trials are conducted to translate animal data into humans. As clinical trials are important to furnish efficacy and safety data, the lack of clinical data has become the main impediment in developing traditional herbal remedies into mainstream medicines. Recent progress in the quality control of herbal products is very promising in gaining consumer confidence and promoting consideration of herbal medicines as complementary and in some cases alternative approaches to conventional therapies. Medicinal plants listed in this chapter have the potential to treat peptic ulcer, diarrhoea and IBD. Additional studies on quality, efficacy and safety in animals and humans will be required to integrate them in mainstream medicine.

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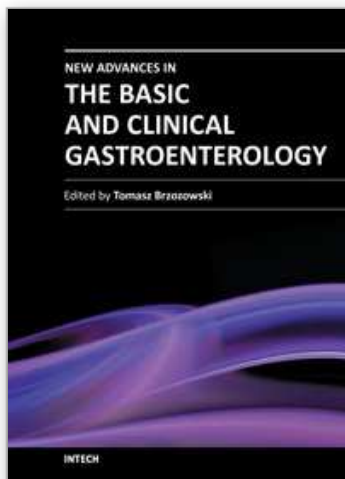
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The purpose of this book was to present the integrative, basic and clinical approaches based on recent developments in the field of gastroenterology. The most important advances in the pathophysiology and treatment of gastrointestinal disorders are discussed including; gastroesophageal reflux disease (GERD), peptic ulcer disease, irritable bowel disease (IBD), NSAIDs-induced gastroenteropathy and pancreatitis. Special focus was addressed to microbial aspects in the gut including recent achievements in the understanding of function of probiotic bacteria, their interaction with gastrointestinal epithelium and usefulness in the treatment of human disorders. We hope that this book will provide relevant new information useful to clinicians and basic scientists as well as to medical students, all looking for new advancements in the field of gastroenterology.

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