



Herbal plants as potent candidate for Anti-ulcer drug development

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Abstract

Peptic ulcer is a common disorder that affects the lives of millions of people every year. The predominant causes of peptic ulcer are infection with the bacterium called *Helicobacter pylori* (*H. pylori*) and the use of Nonsteroidal Anti-Inflammatory Drugs (NSAIDs). Chemical drugs used in the treatment of peptic ulcer produces side effects on long term use. Extensive research has been carried out in the area of treatment of ulcers through medicinal plants. Many medicinal plants have been reported to possess antiulcer activity. Effective plant extracts, screened by cytotoxic, genotoxic, toxicological parameters will lead to establishment as potent candidate for antiulcer drug development.

Keywords: Antiulcer activity, herbal plants, drug, peptic ulcer

Introduction

The human gastrointestinal tract is inhabited by a complex and dynamic population of around 500-1000 of different microbial species which remain in a complex equilibrium. It has been estimated that bacteria account for 35–50% of the volume content of the human colon. These include *Bacteroides*, *Lactobacillus*, *Clostridium*, *Fusobacterium*, *Bifidobacterium*, *Eubacterium*, *Peptococcus*, *Peptostreptococcus*, *Escherichia* and *Veillonella* (Ley *et al.*, 2006). The bacterial strains with identified beneficial properties include mainly *Bifidobacterium* and *Lactobacillus* species. The dominant microbial composition of the intestine have been shown to be stable over time during adulthood and the microbial patterns are unique for each individual (Zoetendal *et al.*, 2004). The intestinal tract of newborn appears sterile but immediately after birth a microbial community starts to establish (Salminen *et al.*, 2005). The intestine is one of the main surfaces of contact with exogenous agents (viruses, bacteria, allergens) in the human body. It has a primary role in the host defense against external aggressions by means of the intestinal mucosa, the local immune system,

and the interactions with the intestinal microbiota (resident and in transit bacteria). Gut microbiota influences human health through an impact on the gut defense barrier, immune function, and nutrient utilization and potentially by direct signaling with the gastrointestinal epithelium (Hooper *et al.*, 2001). A balance among microbial groups present in human gut is crucial for maintaining health. When this balance is disturbed, the host–microbe relationship can progress towards a disease state. In addition, it has been described that microbiota deviations are associated with enhanced risk of specific diseases including inflammatory bowel diseases, irritable bowel disease and antibiotic associated diarrhea and it has been associated with allergy, obesity and diabetes (Kalliomäki *et al.*, 2001). Thus, the maintenance of microbiota equilibrium is important to preserve and to promote health. Herbal drugs are prescribed widely even when their biologically active components are unknown because of their effectiveness, fewer side effects and relatively low cost. Human beings are utilizing plant resources for therapeutic purposes. Herbal drug are traditional method of treating the disease in worldwide as the plant has the ability to treat the diseases (medicinal plant). Several types of medicinal plants are present in the nature and

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effective in different type of diseases (Saurabh *et al.*, 2012).

Peptic Ulcer

Peptic ulcer is a common disorder that affects the lives of millions of people every year (Ramakrishnan *et al.*, 2007). It is also called as *ulcus pepticum* Peptic Ulcer Disease (PUD). Peptic ulcer is a sore on the lining of the gastrointestinal tract caused due to mucosal erosions (Bethesda *et al.*, 2010). It can be classified as gastric, duodenal, esophageal and Meckel's Diverticulum ulcers (Wolfsthal, 2008). Gastric ulcer is a peptic ulcer that develops in the stomach. Duodenal and esophageal ulcers occur in the duodenum and esophagus respectively. Meckel's Diverticulum ulcer is a less common type of ulcer that develops in the Meckel's Diverticulum (a vestigial remnant in the form of a small bulge in the small intestine). A person can suffer from two or more type of peptic ulcers at the same time. The predominant causes of peptic ulcer are infection with the bacterium called *Helicobacter pylori* (*H. pylori*) and the use of Nonsteroidal Anti-Inflammatory Drugs (NSAIDs) such as aspirin and ibuprofen (Goroll, 2009). Cell linings of the gastrointestinal tract are susceptible to hydrochloric acid and pepsin and leads to the formation of ulcer. *H. pylori* infection alone is the major causative factor (95% of the duodenal ulcer and 80% of gastric ulcers) (Sravani *et al.*, 2011). Factors related with lifestyle such as smoking, alcohol, spicy foods and stress are also associated with peptic ulcer formation. Cancerous or noncancerous tumors in the stomach, duodenum or pancreas can also cause ulcers.

Epigastric discomfort is the most common symptom of peptic ulcer disease (Anthony *et al.*, 2002). The patient perceives a gnawing and burning pain in the abdomen between the sternum and the navel. Duodenal ulcers are typically relieved by food intake while gastric ulcers are exacerbated by it. Epigastric pain is often accompanied with nausea, vomiting, loss of appetite, abdominal bloating and fullness. In case of bleeding ulcer the patient may suffer from weakness and tiredness. Complications associated with peptic ulcer are bleeding, perforation and obstruction (Meyer *et al.*, 2006). Bleeding may result due to disruption of blood vessels in the lining of the gastrointestinal tract. Gastrointestinal bleeding may also cause

vomiting of blood (hematemesis). Perforation is caused when peptic ulcer burrows completely through the sto-mach or duodenal wall. This can lead to spillage of stomach or intestinal content into the abdominal cavity. Peptic ulcer may even obstruct the passage of food in the gastrointestinal tracts.

Antiulcer drug development of natural origin

Chemical drugs such as Proton Pump Inhibitors (PPIs) and H2 blockers used in the treatment of peptic ulcer produces side effects on long term use. Extensive research has been carried out in the area of treatment of ulcers through medicinal plants. Many medicinal plants have been reported to possess antiulcer activity.

Till date hundreds of herbal plants have been explored with different constituents having antiulcer activity like *Zingiber officinale* (Ginger), *Aloe barbadensis miller* (*Aloe vera*), *Lycopodium cernuum*, Tamrabhasma, *Asparagus racemosus* (Satavari), *Curcuma longa* (turmeric), *Ocimum sanctum*, *Mangifera indica* (mango), *Commiphora molmol*, *Elettaria cardamomum* (cardamom), *Pyrena canthastaudtii*, *Davillarugosa*, *Jasminum grandiflorum*, *Sapindus saponaria*, *Thymus caramanicus*, *Piper carpunya Ruiz & pav.*, *Apium graveolens* (celery), *Apium nodiflorum*, *Enantia chlorantha*, *Calophyllum brasiliense camb.*, *Solanum lyratum.*, *Solanum torvum etc.* (Sravaniet *al.*, 2011; Lawande *et al.*, 2012; Saurabh *et al.*, 2012). Patents has been obtained on antiulcer herbal phytoconstituents, herbal composition for gastrointestinal disorders, method for treating stomach ulcers with herbal extracts composition, medicament for treating gastric ulcer, composition for the prevention and treatment of gastritis diseases and ulcer (Solanki, 2010). Though there are several published reports on the plants having antiulcer activities along with their analyzed phytoconstituents but still our therapeutic treasure is lacking with an effective and safe plant based antiulcer drug. Major problems associated with herbal medicine are the lack of standardization, consistency, toxicity, safety, quality, and in some countries, regulations. The correct identification of herbal materials and pharmacologically active constituents, standardization, pharmacological basis of efficacy, toxicity, clinical and nonclinical trials, adopting Good Agricultural Practices (GAP), Good



Sourcing Practices (GSP), Good Manufacturing Practices (GMP), and strict implementation of regulation are needed to improve the acceptability, quality, and possible integration of herbal medicines with modern medicine for the effective management of health problems.

Thus, there is an urgent need to check the efficacy, safety and translational guidelines for a potent herb to be used as a safe, effective drug. Current ICH Harmonised Tripartite Guidelines, current step 2 version, 2008 may be followed to study parameters like Cytotoxicity test, Hematological test, Comet assay, Biochemical analysis (SGPT, SGOT, ALP, cholesterol, bilirubin, glucose etc.), Histopathological study, Cytotoxicity assay (MTT test), Genotoxicity assay, carcinogenicity assay, percent protection test in challenged animal models.

Conclusion

Peptic ulcer is a common disorder. As compared to chemical drugs, medicinal/herbal plants present an effective and safer way in disease management. Lots of medicinal plants have shown significant anti-ulcer activity. These plants provide leads to find therapeutically useful compounds and combination of traditional and modern knowledge can produce better drugs for the treatment of peptic ulcer. Identification of active principal, screening of biomedical properties by appropriate in vitro assays, investigation of toxicological effects as per the regulatory guidelines will lead to establishment as a potent candidate for anti-ulcer drug development.

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