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Role of Natural Antioxidants in Gastritis

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1. Introduction

Gastritis represents an inflammation of the stomach lining in response to injury. It is either acute or chronic, and has many underlying causes which can be diagnosed and classified histologically where endoscopic appearances such as redness are often misleading. Gastritis is seldom if ever symptomatic, but usually have important clinical sequelae, principally duodenal and gastric ulceration, gastric adenocarcinoma and primary gastric lymphoma (El-Zimaity, 2007; Thirumurthi & Lanza 2010). The three most important causes of gastritis are categorized as Helicobacter pylori infection, prolonged use of aspirin, non-steroidal anti inflammatory drugs (NSAIDs) and autoimmunity (Dohil & Hassall, 2011).

1.1 Acute gastritis

Acute gastritis, is usually a diffuse and intense mucosal alteration, mostly is characterized by a sudden onset of symptoms and rapid resolution after the underlying aetiological mechanisms or agents (either chemical or physical) have been corrected. The patients can present with an acute gastroenteritis-like illness, or other symptoms which may be overshadowed by their general physical condition. Broadly speaking, acute gastritis arises when there is an acute imbalance between mucosal injury and repair mechanisms (Fig. 1) and can be organized in three groups based on the aetiologies: (i) infectious gastritis (ii) secondary to caustic injury; and (iii) ulcero-haemorrhagic (Srivastava & Lauwers, 2007).

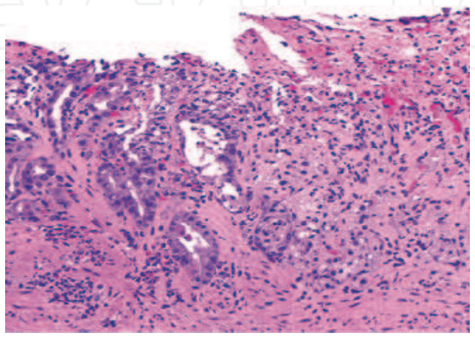

Fig. 1. Acute gastritis. Erosion and complete effacement of the epithelium is observed. The residual glands, on the left, display regenerative changes with basophilic epithelium.

No correlation may be exist between microscopic inflammation (histologic gastritis) and the presence of gastric symptoms (eg, abdominal pain, nausea, vomiting). In fact, most patients with histologic evidence of acute gastritis (inflammation) are asymptomatic. The diagnosis is usually obtained during endoscopy performed for other reasons. Acute gastritis may present with an array of symptoms, the most common being nondescript epigastric discomfort. Other symptoms include nausea, vomiting, loss of appetite, belching, and bloating. Fever, chills may be present. The diagnosis of acute gastritis may be clarified from the patient's history and can be confirmed histologically by biopsy specimens taken at endoscopy. Epidemiologic studies reflect the widespread incidence of gastritis (Ford et al., 2010).

1.1.1 Pathophysiology

Acute gastritis has a number of causes, including certain drugs; alcohol; bile; ischemia; bacterial, viral, and fungal infections; acute stress (shock); radiation; allergy, food poisoning; and direct trauma. The common mechanism of injury is an imbalance between the aggressive and the defensive factors that maintain the integrity of the gastric mucosal lining (mucosa) (Kasper et al., 2006).

Acute erosive gastritis can result from the exposure to a variety of agents or factors, referred to as reactive gastritis. These agents/factors include nonsteroidal anti-inflammatory medications (NSAIDs), alcohol, cocaine, stress, radiation, bile reflux, and ischemia. The gastric mucosa exhibits hemorrhages, erosions, and ulcers. NSAIDs, such as aspirin, ibuprofen, and naproxen, are the most common agents associated with acute erosive gastritis, mostly attributed to therapeutic. Major injury is attributed to reduced prostaglandin synthesis. Prostaglandins are chemicals responsible for maintaining mechanisms that result in the protection of the mucosa from the injurious effects of the gastric acid.

Bacterial infection is another cause of acute gastritis. The corkscrew-shaped bacterium called H. pylori is the most common cause of gastritis. Complications result from a chronic infection rather than from an acute infection. The prevalence of H. pylori in otherwise healthy individuals varies depending on age, socioeconomic class, country of origin where the infection is usually acquired in childhood. In the Western world, the number of people infected with H pylori increases with age. Evidence of H. pylori infection can be found in 20% of individuals younger than 40 years and in 50% of individuals older than 60 years. Transmission is likely from person to person through the oral-fecal route or through the ingestion of contaminated water or food. This is why the prevalence is higher in lower socioeconomic classes and in developing countries. H pylori is associated with 60% of gastric ulcers and 80% of duodenalulcers (Andersen, 2007).

H. pylori gastritis typically starts as an acute gastritis in the antrum, causing intense inflammation, and over time, it may extend to involve the entire gastric mucosa resulting in chronic gastritis. The acute gastritis encountered with H. pylori is usually asymptomatic. The bacterium imbeds itself in the mucous layer, a protective layer that coats the gastric mucosa. It protects itself from the acidity of the stomach through the production of large amounts of urease, an enzyme that catalyzes the breakdown of urea to the alkaline ammonia and carbon dioxide. The alkaline ammonia neutralizes the gastric acid in the immediate vicinity of the bacterium conferring protection. H. pylori also has flagella that enable it to move and help it to penetrate the mucous layer so that it comes into contact with gastric epithelial cells. It also has several adhesions that help it to adhere to these cells. It produces

inflammation by activating a number of toxins and enzymes that activate IL-8, which eventually attracts polymorphs and monocytes that cause acute gastritis (Fig. 2) (Das & Paul, 2007).

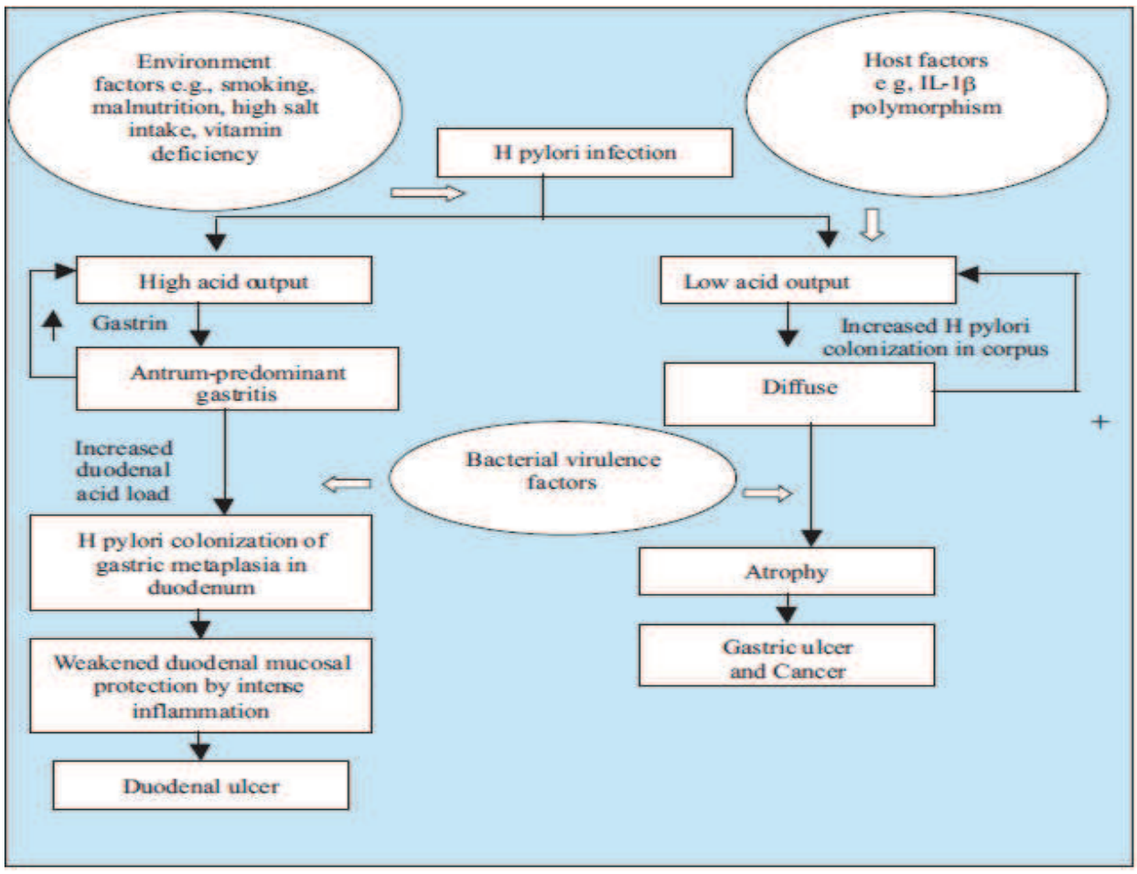

Fig. 2. Proposed interaction between host, environment and H. pylori infection in the development of gastric and doudenal ulcers.

Antigen-presenting cells activate lymphocytes and other mononuclear cells that lead to chronic superficial gastritis. The infection is established within a few weeks after the primary exposure to H. pylori. The intense inflammation can result in the loss of gastric glands responsible for the production of acid and mostly referred to as atrophic gastritis consequently production of gastric acid drops. The virulence genotype of the microbe is an important determinant for the severity of the gastritis of intestinal metaplasia transformation of gastric epithelium which can lead to gastric cancer (Soltermann et al., 2007).

Reactive gastropathy is the second most common diagnosis made on gastric biopsy specimens after H. pylori gastritis. It is now considered to represent a nonspecific response to a variety of other gastric irritants (Owen, 2003).

Tuberculosis is a rare cause of gastritis and generally associated with generally associated pulmonary or disseminated disease (Marshall, 1993) where secondary syphilis of the stomach is a rare cause of gastritis (Chen et al., 2006).

Phlegmonous gastritis is an uncommon form of gastritis (rare) caused by numerous bacterial agents, including streptococci, staphylococci, Proteus species, Clostridium species,

and Escherichia coli. Phlegmonous gastritis usually occurs in individuals who are debilitated. It is associated with a recent large intake of alcohol, a concomitant upper respiratory tract infection, and AIDS. Phlegmonous means a diffuse spreading inflammation of or within connective tissue. In the stomach, it implies infection of the deeper layers of the stomach (submucosa and muscularis).

Viral infections can cause gastritis either localized or diffuse and cytomegalovirus (CMV) is a common viral cause. It is usually encountered in individuals who are immunocompromised, including those with cancer, immunosuppression, transplants, AIDS with a localized or diffuse involvement to the gastric tissuesand AIDS (Bonnet et al., 2001; Sepulveda & Patil, 2008).

Fungal infections that cause gastritis include Candida albicans and histoplasmosis. Gastric phycomycosis is another rare lethal fungal infection. The common predisposing factor is immunosuppression. C albicans rarely involves the gastric mucosa and when isolated in the stomach, the most common locations tend to be within a gastric ulcer or an erosion bed and it is generally of little consequence. Disseminated histoplasmosis can involve the stomach. The usual presenting clinical feature is bleeding from gastric ulcers or erosions on giant gastric folds (Lauwers et al., 2010).

Parasitic infections are rare causes of gastritis. Anisakidosis is caused by a nematode that embeds itself in the gastric mucosa along the greater curvature. Anisakidosis is acquired by eating contaminated sushi and other types of contaminated raw fish. It often causes severe abdominal pain that subsides within a few days and this nematode infection is associated with gastric fold swelling, erosions, and ulcers (Kim et al., 2003).

Ulcero-hemorrhagic gastritis is most commonly seen in patients who are critically ill and it is believed to be secondary to ischemia related to hypotension and shock or to the release of vaso constrictive substances but the etiology is often unknown. The gastric mucosa reveals multiple petechiae, mostly in the fundus and body, or exhibits a diffusely hemorrhagic pattern. The gross pathology may resemble that of NSAID- or other ingestion-induced gastritis except that the location of injury is different. This form of gastritis can be life-threatening if the patient experiences hemorrhaging and may even require emergency gastrectomy (Chamberlain, 1993).

Microscopic evidence of acute gastritis can be seen in patients with Crohn disease, though clinical manifestations are rare (occurring in only about 2-7% of patients with Crohn disease). Focally enhancing gastritis is now recognized as a condition seen in both Crohn disease and ulcerative colitis (Xin & Greenson, 2004).

Eosinophilic gastritis is often seen in conjunction with eosinophilic gastroenteritis but can be associated with various disorders, including food allergies (eg, cow milk, soy protein), collagen vascular diseases, parasitic infections, gastric cancer, lymphoma, Crohn disease, vasculitis, drug allergies, and H. pylori infections. An eosinophilic infiltrate is seen involving the gastric wall or epithelium (Rothenberg, 2004).

1.2 Chronic gastritis

Chronic gastritis is caused mainly by Helicobacter pylori infection, and nonatrophic gastritis progresses to atrophic gastritis for a long period. It is characterized by the presence of chronic inflammatory infiltrate in the gastric mucosa (Fig. 4). H. pylori-atrophic gastritis is strongly associated with gastric cancers, and its diagnosis is very important. It is diagnosed histologically according to the Updated Sydney System, which is now widely used in the world (Satoh et al., 2008). Chronic gastritis can be classified on the base of the underlying etiologic agent (eg, Helicobacter pylori, bile reflux, nonsteroidal anti-inflammatory drugs

[NSAIDs], autoimmunity, allergic response) and the histopathologic pattern, which may suggest the etiologic agent and clinical course (eg, H pylori –associated multifocal atrophic gastritis). Other classifications are based on the endoscopic appearance of the gastric mucosa (eg, varioliform gastritis) (Rugge & Genta, 2005).

1.2.1 Pathophysiology

The pathophysiology of chronic gastritis complicating a systemic disease, such as hepatic cirrhosis, uremia, or another infection is described in the relevant disease (Boulton et al., 2011). The pathogenesis of the most common forms of gastritis is described as follows.

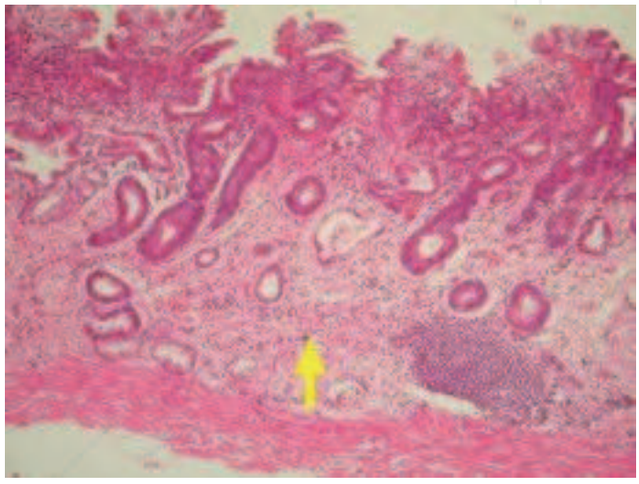

Fig. 3. Chronic gatritis showing inflammation of mucosa linning

The host response to H. pylori and bacterial products is composed of T- and B-cell lymphocytes, denoting chronic gastritis, followed by infiltration of the lamina propria and gastric epithelium by polymorphonuclear leukocytes that eventually phagocytize the bacteria. The presence of polymorphonuclear leukocytes in the gastric mucosa is diagnostic of active gastritis. The interaction of H pylori with the surface mucosa results in the release of proinflammatory cytokine interleukin (IL)-8, which leads to recruitment of polymorphonuclear cells and may begin the entire inflammatory process. Gastric epithelial cells express class II molecules, which may increase the inflammatory response by presenting H pylori antigens, leading to further cytokine release and more inflammation. High levels of cytokines, particularly tumor necrosis factor-a (TNF-α) and multiple interleukins (eg, IL-6, IL-8, IL-10), are detected in the gastric mucosa of patients with H. pylori gastritis (Zalewska-Ziob et al., 2009).

In subsequent or joining such inflammation pattern is an increase in oxidative damage due to high level of ROS and increased apoptosis level in human gastric mucosa (obst et al., 2000; cover et al., 2003). Infection also leads to the expression of inducible nitric oxide synthase (iNOS) in host macrophage and polymorphnuclear leukocytes (Tari et al., 2003). NO produced by these cells infiltrating the gastric mucosa may damage DNA. Interaction between NO and superoxide anion can form peroxinitrite, potent nitrating agent leading to apoptosis in a variety of cell types (yue et al., 2001).

Prostaglandins especially PGE2 in the stomach play an important role in the maintenance of gastric mucosal integrity via several mechanism including regulation of gastric mucosal blood flow, kinetic of epithelial cells, synthesis of mucous, inhibition of gastric acid secretion and referring to its protective potential to gastric mucosa (Takeeda et al., 2004).

Patients having Hpylori infection demonstrate significant gastremia which is mostly attributed to intragastric increase of H pylori inducing corpus atrophy and G cells damage in the antrum part. It may be also depends on alkalinization in G cells environment caused by H pylori urease (walsh et al., 1976; shacter et al., 2002).

Serum pepsinogens (1&11) are higher also and specifically in patient category having IgM positive as compared to others (IgM-ve). This may be attributed to a polypeptides secreted by HP during earlier infection which stimulates chief cells directly and promote pepsinogen synthesis (Takeeda et al., 2004; kist, 1991; Elseweidy et al., 2010 a;b).

This led certain study (Kekki et al., 1991) to consider serum pepsinogen level-as a non endoscopic blood test in the diagnosis of atrophic gastritis, HP eradication and, a screening tool for high risk subjects having atrophic gastritis rather than a test for cancer itself.

Generally known Hp infection is associated with special local and systemic immune response. Early after 18 days of infection IgM response is detectable while IgG, IgA response occurs later after 60 days of infection at which time IgG titers decline. IgG, IgA serology is widely used as an accurate test for the diagnosis of Hp infection but those 2 immunoglobulins remains detectable after eradication of HP and d'not demonstrate the infection status (acute, chronic or previously treated infection). Therefore the use of IgM test would allow for direct screening of the sample and serve as a diagnostic tool for establishing active or recent infection (Alem et al., 2002, Elseweidy et al 2010).

Accordingly many authors concluded that diagnosis of atrophic gastritis using test panel of seum gastrin 17, pepsinogen 1, HP antibodies were in good agreement with endoscopic and biopsy findings, considering such panel a non endoscopic diagnostic and screening tool (vaananen et al., 2003).

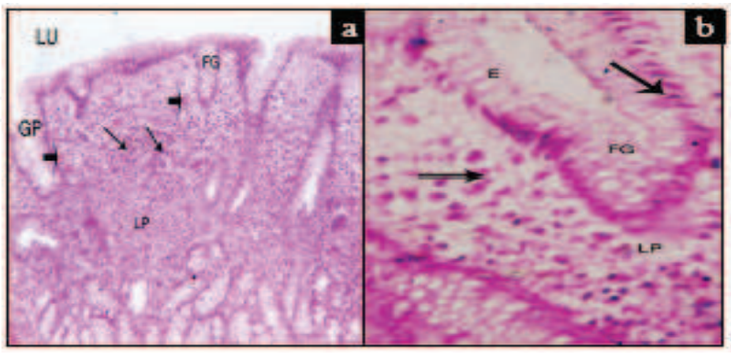

Fig. 4. Histological section of human fundic gland of patient suffering from gastritis with anti H. pylori IgM positive group showing (a) x100 irregular short fundic gland (FG), wide gastric pit (GP), multiple inflammatory cells (arrows) and blood vessels (double arrows) filling lamina propria (LP), (b) x400 showing irregular simple columnar epithelium (E), small pyknotic nuclei (arrows) of cells lyning fundic gland (FG) and multiple inflammatory cells (double arrows) filling lamina propria (LP) (Elseweidy et al., 2010 a).

2. Natural products used in treating gastritis

Phenolic compounds, which include tannins and flavonoids, are apparently related to the interesting anti-inflammatory, woundhealing, antioxidant and antiulcerogenic properties to several medicinal plants (Moleiro et al., 2009).

Tannins are potent scavengers of peroxyl radicals and can also interact with mucus proteins, improving their cytoprotective effect by forming a protein lining over the gastrointestinal mucosa (Okuda, 2005; Moleiro et al., 2009).

Fresh fruit and vegetables have been reported to exert multiple biological effects on the mucosa of the gastrointestinal tract due to their antioxidant contents (La Vecchia & Tavani, 1998). In particular, a diet rich in vegetable is associated with a lower incidence of gastric tumours (Roukos et al., 2003).

Apart from their action as radical scavengers, phenolic compounds also have several indirect effects; they can inhibit lipoxygenase (Laughton et al., 1991), reduce platelet aggregation (Ferro-Luzzi & Ghiselli, 1993) and reduce the bioavailability of food carcinogens (Stavric, 1994). Certain flavonoids or compounds with flavonoid-like properties have antiulcer activity and can prevent gastric mucosal lining lesions brought about by a number of ulcerogens (Alarcon de la Lastra et al., 2002).

Certain polyphenolics can exert a preventive action on gastric injury in rats. Research topics her have focussed on the antiulcer activity of polyphenol from grape seed (Saito et al., 1998), cacao liquor (Osakabe et al., 1998), curcuminoids and Black seed oil (Elseweidy et al., 2008) or from Opuntia ficus indica (Galati et al., 2003). This activity was mainly explained by the strong antioxidant power and/or by some other factors, such as strong protein-binding capacity (Saito et al., 1998), modulation of leukocyte function (Osakabe et al., 1998), mucus production and restoration (Galati et al., 2003). It is believed that the antioxidant activity of polyphenols is an important factor to combat the potential of free radicals.

2.1 Morinda citrifolia aqueous fruit extract

Morinda citrifolia L. (Rubiaceae), commonly known worldwide as “Noni” or so called in Thai as “Yor” is regularly consumed as food, additionally as medicinal plants used in primary health care. The decoction or infusion of roasted mature unripe fruits is recommended to relieve the symptoms of nausea and vomiting, if it is not too severe. According to the claimed efficacies in Thai traditional textbooks, the fruit is also used for treatment of various gastrointestinal disorders as a carminative, appetite stimulant, and reliever of gum diseases, heartburn or stomachache. Nevertheless, experimental studies demonstrated the preventive activity of an ethyl acetate extract of the fruit against acute gastric lesions induced by ethanol, aspirin and pyloric ligation; and acute duodenal ulcer induced by cysteamine in rats (Muralidharan & Srikanth, 2009). This extract was claimed to exhibit potent antioxidant properties and the active components are thought to be non-polar lignans (Kamiya et al., 2004). Previous studies of the effect of an aqueous fruit extract on gastrointestinal motility reported controversial results with increase (Chuthaputti et al., 1996) and delay (Pu et al., 2004) gastric emptying action.

It has been claimed also that aqueous extract have anti-inflammatory (McKoy et al., 2002) and antioxidative activities (Ikeda et al., 2009) in several in vitro test systems. Among a number of major components identified in the aqueous fruit juice, scopoletin, a coumarin derivative, as one of the main compounds that has known pharmacological activities especially an ability to control the serotonin level in the body (Levand and Larson, 1979),

together with anti-inflammatory (Deng et al., 2007; Moon et al., 2007) and antioxidative activities (Ikeda et al., 2009). Scopoletin is also recommended as a marker constituent for the quality control and pharmacokinetic study of Noni products (Samoylenko et al., 2006).
This aqueous fruit extract as well as its biomarker: scopoletin, may be beneficial as a potential preventive and therapeutic agent for gastro-esophageal inflammation. This is mainly through its antisecretory and prokinetic activities including its ability to enhance the mucosal defensive mechanisms. Their efficacy was compared with a standard potent antisecretory proton pump inhibitor (lansoprazole) and referring to its stronger prokinetic efficacy in accelerating gastric emptying and intestinal transit in rats. These observed beneficial effects of AFE may be accounted for by one of its major active biological components scopoletin (Mahattanadul et al., 2011).

2.2 Quercetin-3-O-β-D-glucuronopyranoside (QGC), isolated from Rumex Aquaticus herb

It is well known that flavonoids which have anti-inflammatory, antioxidant, antiallergic, hepatoprotective, antithrombotic, antiviral, and anticarcinogenic activities. As reported before the anti-inflammatory activities of flavonoids demonstrate their candidacy as therapeutic agents (Lewis, 1989). The flavonoids are typical phenolic compounds that act as potent metal chelators, antioxidants and free radical scavengers, which modulate intracellular signaling caused by upstream binding partners, such as, regulatory kinases and receptors (Williams et al., 2004a).
Such flavonoid is a natural flavone with various bioactivities and was found to be highly efficient to scavenge free radicals in cell-free systems (Rice-Evans et al., 1996), as compared to traditional antioxidants like vitamin C and E (Geetha et al., 2005). Gerritsen et al., (1995) found that flavonoids, especially an apigenin, blocked the cytokine-induced expressions of intercellular adhesion molecule-1 (ICAM-1), vascular cell adhesion molecule-1 (VCAM-1), and E-selectin on human endothelial cells.
Regarding gastric secretion, the oral administration of QGC reduced gastric content significantly, dose-dependently, and prevented the development of reflux esophagitis. These results suggest that QGC has inhibitory effects on reflux esophagitis and gastritis in rats. Furthermore, in feline esophageal epithelial cells, QGC was found to have a protective effect on ethanol induced cell damage by inhibiting ROS generation, activation downstream of ERK (Min et al., 2009), and downstream signal transduction induced by interleukin-1 beta (Lee et al., 2009a).

2.3 The aqueous decoction of mango flowers (Mangifera indica L.)

Mangifera indica L. (Anacardiaceae) is a large tree that grows in tropical and subtropical regions. The Caribbean population used aqueous decoction from M. indica flowers for the treatment of gastritis and gastric ulcer. Phytochemical research from different parts of M. indica has demonstrated the presence of phenolics, triterpenes, flavonoids, phytosterols and polyphenols (Selles et al., 2002; Singh et al., 2004).
Garrido et al., (2004) reported the antinociceptive and anti-inflammatory activities of Vimang®, an aqueous extract obtained from M. indica. They attributed these activities to their inhibitory influence on the prostaglandin synthesis through arachidonic acid metabolism additionally production of reactive oxygen species. Tordera et al., (1994) demonstrated the influence of several anti-inflammatory flavonoids present in M. indica on mast cell degranulation and arachidonic acid release in rats.

M. indica is also described as an antioxidant agent (Sanchez et al., 2003). Oxygen-derived free radicals have been postulated to play an important role in the pathogenesis of acute gastric mucosal injuries such as those induced by stress (Hariganesh & Prathiba, 2000), ethanol (Salim, 1990) and NSAIDs (Pihan et al., 1987) and scavenging of these radicals can stimulate the healing process. This was illustrated before in experimental model induced by acetic acid and attributed mainly to their high content of flavonoids (Naito et al., 1995).

2.4 Abarema cochliacarpos

Several medicinal plants including species of the Brazilian Cerrado biome as well as plants of the "Caatinga" biome contain phenolic compounds like tannins and flavonoids that have anti-inflammatory, antioxidant and antiulcerogenic properties (Almeida et al., 2005; Moleiro et al., 2009).

Catechins (flavan-3-ols) such as catechin, epicatechin, epigallocatechin, epicatechin gallate and epigallocatechin gallate, are particularly abundant in the bark of the species of Mimosaceae family (Santos et al., 2002). These compounds has anti-inflammatory and anti cholesterolemic effects additionally protective agent against cytotoxicity owing to their antioxidant properties (Williams et al., 2004b).

Araujo et al. (2008) studied plants with elevated levels of phenolic compounds within specific groups of plants for further therapeutic applications. They concluded that Caatinga medicinal plants, which are known and/or used for their wound-healing or anti-inflammatory properties, tend to have high tannin contents. Moreover, these compounds appear markedly elevated in some species, such as Abarema cochliacarpos, that are intensively used by the local communities (Monteiro et al., 2006).

Abarema cochliacarpos is a plant native to Brazil, occurring mainly in the Atlantic Forest and in the Caatinga biomes. It is a tree species of the legume family Mimosaceae (International Union for Conservation of Nature "IUCN", 2009), which is popularly known as "barbatimao". In this community, the decoction of the bark is utilized to wash external ulcers while its tincture, (bark immersed in white wine) "cachaca", or ingested form is used against inflammation and gastric ulcers, among other uses (Silva et al., 2006). Other authors also observed similar applications in different traditional communities (Agra et al., 2008).

As to pharmacologic effects, the hydroalcoholic extract from the bark of Abarema cochliacarpos showed antimicrobial activity. Both crude aqueous and methanol extracts also showed antinociceptive effects (Silva et al., 2009). Butanolic fraction of the methanolic extract was tested recently in a model of acute experimental trinitrobenzene sulfonic acid (TNBS)-induced colitis and showed anti-inflammatory effects (Silva et al., 2010a).

It has been suggested that Abarema cochliacarpos (Gomes) Barneby & Grimes extracts exerts gastroprotective effects and wound healing properties in the ethanol-induced ulcer model. The safety and efficacy in the healing of gastric ulcers is based on its ability to activate the expression of COX-2, vascular-endothelial growth factor (VEGF) and stimulate proliferative factors like HSP-70 that re-establish the gastric mucosa integrity (Silva et al., 2010b).

2.5 Apple polyphenol extracts

Eberhardt and colleagues (2000) illustrated the antiproliferative effect of apple extract in vitro using tumor cells and attributed such effect to the presence of phytochemicals (phenolic acids and flavonoids) other than ascorbic acid. Therefore, dietary antioxidants play a crucial role in the maintenance of gastric homeostasis by counteracting the potentially

mucosal damage exerted by ROS. This may explain the role of dietary antioxidants as scavenger of oxygen, nitrogen free radicals and breaking lipid peroxisdation reactions. Phenolic compounds are one of the major classes of dietary antioxidants and apple phenolic compounds represent 22 percent of such total (Le Marchand et al., 2000).
In vitro and in vivo studies demonstrated the protective effect of apple juice regarding gastric mucosa of rat. This was markedly observed in gastric injury model induced by aspirin and independently of its inhibition to gastric acid. Therefore it might be of therapeutic benefit in prophylaxis of aspirin- related gastropathy (D' argenio et al., 2008). Accordingly a diet rich in apple antioxidants might exert a beneficial effect in gastric diseases associated with generation of reactive oxygen species (Graziani et al., 2005).

2.6 Foeniculum vulgare (Fennel)

Foeniculum vulgare (FVE) is a well-known umbelliferous plant. For centuries, FVE fruits have been used as traditional herbal medicine in Europe and China. It is native to southern Europe and the Mediterranean area. The seeds of this plant have been used to regulate menstruation, alleviate the symptoms of female climacteric syndrome, and increase libido (Albert-Puleo, 1980). FVE also possesses emnenagague, galactagogue and antispasmodic properties additionally in folk remedies for treatment of dysmenorrheal, also as diuretic and wound dressing in Turkish traditional medicine (Savino et al., 2005).
It contains 1%-3% of a volatile oil, which is composed of 50%-85% of anethole and about 20% of d-fenchone (Dadalioglu & Evrendilek, 2004). Other compunds present in FVE are d-a-pinene, d-a-phellandrene, dipentene, methyl chavicol, feniculun, anisaldehyde, and anisic acid (Mimica-Dukic et al., 2003).
Previous studies proved that anethole possesses significant antioxidant, anti-inflammatory and ulcer healing activity in experimental models (Freire et al., 2005). Additionally, flavonoids, sterols, tannins and coumarins of some plants are also known to possess antiulcer activity (Khalil, 2006). Therefore, the presence of flavonoids content and other bioactive compounds in FVE may be beneficial in ulcer therapy. Its gastro protective effect has been also observed before in certain gastric mucosal lesion induced by ethanol, attributed mostly to its antioxidant activity and reduction of lipid peroxidation cascade.
Therefore it may be a new alternative for clinical management of gastric ulcer diseases and/or an antioxidant against oxidative stress (Birdane et al., 2007).

2.7 Flavonoids isolated from Piper carpunya Ruiz & Pav

The leaves of Piper carpunya Ruiz & Pav. (syn Piper lenticellosum C.D.C.) (Piperaceae), known with the popular name of "guaviduca" in Ecuador are widely used in folk medicine in tropical and subtropical countries of South America, as an anti-inflammatory, anti-ulcer, anti-diarrheal and anti-parasitical remedy as well as an ailment for skin irritations. The antiinflammatory activity has been confirmed in rat models like the carrageenan-induced paw edema and the results obtained can support its use in the traditional medicine of Ecuador (De las Heras et al., 1998). Recently, this plant has been shown to protect against gastric ulcers induced by non-steroidal anti-inflammatory drugs (NSAID) in rats (Trabadela et al., 2009).
Numerous plant remedies have shown to be active against Helicobacter pylori infection, such as the oil extract of Chamomilla recutita (Shikov et al., 2008), the ethanolic extract of Cuminum cyminum L., Propolis (Nostro et al., 2005) as well as the methanolic extract of

Alchornea triplinervia (Spreng.) Mull. Arg., which exhibited anti-secretory, anti-Helicobacter pylori and gastroprotective effects (Lima et al., 2008).
Several mechanisms of action have been proposed to illustrate its anti-inflammatory effects. This may be explained through other properties such as anti-oxidant activity, inhibition of eicosanoid generating enzymes or as modulator for proinflammatory molecules. Recent studies have also shown that some flavonoids are modulators of proinflammatory gene expression (Garcia-Lafuente et al., 2009). Gastro protective activity of flavonoids may be through reducing gastric acid secretion and inhibition of gastric H+, K+-ATPase. One example is Baccharis illinita D.C., which is also used in folk medicine, and whose anti-secretory activity is attributable to the flavonoid luteolin (Freitas et al., 2008).
Furthermore, some flavonoids have also demonstrated inhibitory effects on Helicobacter pylori growth and vacuolation. Helicobacter pylori induces gastric epithelial cell apoptosis via secreted mediators such as the VacA cytotoxin and lipopolysacccharides which damage epithelial acid-secreting parietal cells (Neu et al., 2002). Several flavonoids have inhibitory influence on the apoptotic signaling induced by Helicobacter pylori VacA toxin (Xiao et al., 2007). Antimicrobial compounds from plants may inhibit bacterial growth by different mechanisms and could therefore be useful in case of resistance state to antibiotics. In this way, Castillo-Juarez et al., (2007) found that the petroleum ether fraction from Amphipterygium adstringens (Schltdl.) Standl. had significant anti-microbial activity against Helicobacter pylori. From this fraction, the authors isolated a mixture of anacardic acids and three known triterpenes: masticadienonic acid, 3-alpha-hydroxymasticadienonic acid, 3-epi-oleanolic as well as the sterol ß-sitosterol.
Previous study suggested that the flavonoids (vitexin, isovitexin, rhamnopyranosylvitexin and isoembigenin), nervogenic acid and geranylbenzoate isolated from the ethanolic extract of Piper carpunya may contribute to the anti-myeloperoxidase activity, as well as to their anti-Helicobacter pylori effect. These flavonoids may also be responsible for the important inhibition of H+, K+-ATPase pathway, additionally the obtained phytosterols and phytol could be involved in these gastroprotective activities (Quilez et al., 2010).

2.8 Quassia amara

Quassia is a plant that grows typically in the American tropical regions (from Mexico to the Brazilian Amazona) below 500 m altitude, especially in the Caribbean side of Central America and the Pacific coast of Costa Rica and Panama. The plant prefers very humid environments, but it can be found in the dry forest next to a riverbank (López and Pérez, 2008).
Quassia amara L. is one of the most mentioned plants in ethnomedicine for the treatment of malaria, mainly in Surinam, Guyana and French Guyana, where tea cups are carved from the wood and the addition of hot water forms an infusion in them (Odonnea et al., 2007). There only exist a few studies on the gastrointestinal, digestive and secretagogue activity of Quassia amara L. extracts. The results point to an increase of bile secretion with a standardized extract, inhibition of ulcer induction with crude extracts, accompanied by a slight decrease in pH and peptic activity of gastric juice additionally an enhancement of cytoprotective factors like gastric mucus (Toma et al., 2002).
The biological activity of Quassia amara L. has been attributed mainly to its high content of quassinoids. These metabolites are oxygenated triterpenes derived from euphol and are exclusive to the Simaroubaceae family. The most important quassinoids in Quassia amara L. are quassin and neoquassin. Quassin is one of the most bitter substances known, it

represents 0.1% of the dried weight of wood and bark, and it is present in larger quantities when the plant is grown in the shade (Guo et al., 2005).
Quassia amara L. bark standardized extracts, Lipro® and Ligas®, which were standardized to its quassinoid content, showed an important anti-ulcerogenic and gastroprotective potential in acute ulcer induction models. Their effect was related to an increase in gastric barrier mucus and non protein sulfhydril groups (Garcia-Barrantes & Badilla, 2011). Gastric barrier mucus is an important factor in gastroprotection (Kaunitz, 1999). Animals treated with Ligas® showed substantial mucus production. Prostaglandins I2, E2 and F2 are some of the main stimuli for the production of gastric and duodenal mucus (Dharmani et al., 2005). The increase in mucus could be a signal of the role of prostaglandins in the anti-ulcerogenic properties of the extracts.

2.9 Gardenia jasminoides Ellis ethanol extract

Gardenia jasminoides Ellis (GJE), has been used in traditional oriental medicine for the treatment of jaundice, fever, hypertension, and ulcers of a skin (Tseng et al., 1995). It has been reported that the crude extract of GJE fruit has biological and pharmacological activities. In the phytochemical studies of GJE, genipin, chlorogenic acid, rutin, and ursolic acid were detected in GJE extracts (He et al., 2006). Genipin is an aglycone derived from an iridoid glycoside called geniposide present in fruit of GJE, and is an excellent natural cross-linker for proteins, collagen, gelatin, and chitosan cross-linking. It has been also used for pharmaceutical purposes, such as choleretic action for liver diseases control, and the relief of type 2 diabetes symptoms. Ursolic acid is a pentacyclic triterpene acid, used in cosmetics (Shishodia et al., 2003), and as inhibitor for various types of cancer cells by inhibiting the STAT3 activation pathway (Pathak et al., 2007) and human fibrosarcoma cells by reducing the expression of matrix metalloproteinase-9 by the glucocorticoid receptor.
Gastric cancer is the second commonest cause of death from malignant disease worldwide (Neugut et al., 1996). Antioxidant compounds, such as vitamin C and E, have a key role for prevention and termination of development of gastric cancer (Block, 1991). It has been recognized that chronic infections of the gastric mucosa by Helicobater pylori (H. pylori) plays a pivotal role in gastric carcinogenesis. Such infection usually causes acute and chronic inflammation cell infiltrate, leading to an increase of reactive oxygen species (ROS), which are highly reactive compounds. The latter may combine with DNA in a number of potentially genotoxic ways, subsequently accumulated in H. pylori gastritis. Therefore it may be possible to prevent carcinogenesis through reduction of ROS damage to cellular constituents, especially DNA, additionally the eradication of H. pylori can lead to a reduction in ROS activity in the gastric mucosa (Drake et al., 1998).
Lee et al., (2009b) in confirm indicated that the ethanolic extracts of GJE exerted protective activities against potential gastritic diseases like gastritis and gastric cancer. This action might be due to antioxidant activity, anti-H. pylori activity of ursolic acid and genipin that counteract free radicals exerting anti-ulcer activity.

2.10 Curcumin

Curcumin, the polyphenolic yellowish pigment of the rhizome Curcuma longa Linn, is known to possess anti-inflammatory, antioxidant, wound-healing, and antiallergic activities (Das& Das, 2002). Several investigators have also reported the antiulcerogenic activity of the ethanolic extract of the rhizome of C. longa in acute gastric mucosal lesion (Rafatullah et.,

1990), but not in chronic ulcer models. More recently, it has been considered that curcumin exerts a variety of pharmacological actions through inhibition of inducible nitric oxide synthase (iNOS) as well as its potential as radical scavenger (Elseweidy et al., 2008) Thus, the previously proposed mechanisms for antiulcerogenic effect of curcumin (Yano et al., 2000), such as inhibitory effect on gastric secretion, cytoprotection, antioxidant activity and inhibition of mast-cell degranulation, need to be evaluated again.

Curcumin, exerted its preventive effect on gastric lesion formation, although it possesses anti-inflammatory activity resulting from a blockade of all branches of the arachidonic acid pathway (Ammon et al., 1993). This effect is consistent with the findings reported by several authors that the inhibition of prostaglandins synthesis is unlikely to be the mechanism responsible for the inflammatory ulceration formation. Curcumin therefore may exert this through its antioxidant activity and its inhibition of nuclear factor kappa B activation which up-regulates many genes involved in inflammation and immunity, including its potent suppressive effect on mast-cell degranulation (Jobin et al., 1999). Although there is a potential increase of gastric acid secretion with a high dose of curcumin, gastric acid secretion has been found to play little role in the pathogenesis of this model (Ohta et al., 1999).

Apparent healing – promoting effect of curcumin was also observed in gastric ulcer model, induced by acetic acid with an enhancement of mucosal layer regeneration. This effect was not seen in a dose-related fashion, presumably through some curative mechanisms differently modified by curcumin dosage. Accordingly, it is conceivable that the effect of curcumin occurs at least partly through its inhibition of the cytokine-mediated inflammatory mechanism, suppression of iNOS activity and antioxidant activity as mentioned above. In addition, the curative properties and ulcer healing might result from the elevation of epidermal growth factor and transforming growth factor-beta-1, as shown in acceleration of cutaneous wound healing in rats, guinea pigs and mice (Sidhu et al., 1998). Another study attributed such preventive and curative effects of curcumin to an increase in the mucosal defensive mechanism through its antioxidant property, increase in mucin secretion and inhibition of NO or cytokine-mediated inflammation (Mahattanadul et al., 2006).

2.11 Artichoke leaf extract

Artichoke (Cynara Scolymus L.) is a plant that is widely grown in Mediterranean countries, including southern France and California in the United States. In general, the dried extract consisting of leaves and not flowering heads of artichoke has been eluted with water in European countries and the main components are caffeoylquinic acid derivatives (cynarin and chlorogenic acid), flavonoids (luteolin and apigenin) and bitters (cynaropicrin) (Joy & Haber, 2007). Artichoke leaf extract has been used for hepatoprotective and cholesterol reducing (Aktay et al., 2000) purposes. Based on in vitro (Perez-Garcia et al., 2000) and in vivo (Speroni et al., 2003) studies, it is believed that artichoke leaf extract is very effective as an antioxidant and its leaf extract contains cynaropicrin and chlorogenic acid as the main components. It is currently used in Germany and Switzerland as a remedy for indigestion. And its better compounds such as cynariopicrin as inflammatory agents due to its inhibitory influence on inflammatory mediators (Holtmann et al., 2003).

Previous results indicated that artichoke leaf extract is effective against acute hemorrhagic gastritis and its beneficial effect is due to that of cynaropicrin. The gastric mucus-increasing

action of artichoke leaf extract may be, at least in part, related to the anti-gastritic action of the extract (Ishida et al., 2010).

2.12 Pear (Pyrus communis L.) procyanidins

Some European pear (Pyrus communis L.) cultivars have been reported to contain significant amounts of polyphenols, such as chlorogenic acid, flavan-3-ols and arbutin. procyanidins are reported to have many beneficial properties, such as potent antioxidant activity (Zhu et al., 2002), free radical scavenging activity (Arteel & Sies, 1999), antiinflammatory activity and anti-influenza viral activity (Hamauzu et al., 2005).

It has been shown that procyanidins extracted from pear (Winter Nelis) fruit had a very high mean degree of polymerization (mDP), indicating that these compounds may interact with mucosa proteins. Accordingly the mechanism of mucosa protection by pear procyanidins may be both physical and chemical. By binding strongly to the mucosa, procyanidins build a protective layer against injury, reducing leukocyte migration, and then exerting its local antioxidant protection against free radicals (Hamauzu et al., 2007).

2.13 Sesame lignan sesamol

Sesamol (3,4-methylenedioxyphenol), the lignan of sesame oil, is a potent antioxidant and anti-inflammatory agent in various oxidative systems, including endotoxin and iron intoxication (Hsu et al., 2007). Recent study has confirmed its effect in gastric haemorrhage model and mucosal ulcer induced in rats by aspirin. Sesamol her significantly reduced gastric mucosal lipid peroxidation, nitric oxide production, gastric mucosal proinflammatory cytokines (tumor necrosis factor-a and interleukin 1-ß levels), and the activity of gastric mucosal myeloperoxidase. This was attributed to an inhibition of neutrophil infiltration, subsequent gastric mucosal inflammation and oxidative stress in rats (Hsu et al., 2009a). It seems likely that sesamol protective influence on gastric mucosal injury may be at least partially through an inhibition of mucosal reactive nitrogen species and subsequent lipid peroxidation.

Inhibition of neutrophils activation and their infiltration into gastric mucosa may be sesamol's anti-inflammatory and antioxidative mechanism. Neutrophil activation and infiltration are crucial in the pathogenesis of NSAID-induced gastric inflammation and oxidative stress (Souza et al., 2008). Activating neutrophils results in the expression of proinflammatory genes and the overproduction of proinflammatory mediators, including TNF-α and IL-1ß, which initiates an inflammatory response (Jaeschke & Hasegawa, 2006). Overproduction of proinflammatory mediators can upregulate nitric oxide production leading to an increase of reactive nitrogen species, lipid peroxidation, and cell damage (Hayes and McLellan, 1999). Similar effect for Sesamol was also observed in the gastric mucosa of aspirin-treated rats preventing inturn gastric injury. This may be attributed to certain combination between sesamol and aspirin, inhibiting inturn neutrophil infiltration, mucosal inflammation and oxidative stress (Hsu et al., 2009a).

Daily consumption of sesame or sesame oil may be beneficial in protecting against gastric mucosal damage induced by long-term use of NSAID. Sesame lignan sesamol is one of the important antioxidative components in sesame in addition to some other antioxidants such as sesamin, sesamolin, and gamma-tocopheral (Tokusoglu et al., 2003). All of them could attenuate NSAID initiated gastric mucosal oxidative stress. Therefore, we suggested that daily consumption of sesame or sesame oil could protect against NSAID-induced gastric mucosal damage. However, more investigations will be needed to confirm this.

Also, pretreatment of sesame oil, significantly decreased acidified ethanol-induced mucosal ulcer formation and luminal hemorrhage. Sesame oil her reduced mucosal lipid peroxidation, as well as glutathione and nitric oxide production in experimental rats model attenuating in turn oxidative stress and gastric mucosal injury (Hsu et al., 2009b).

3. Conclusion

Gastritis represents an inflammation of the stomach lining in response to injury.It is either acute or chronic and has many underlying causes ,however the most important of them are Helicobacter pylori (HP) infection, Autoimmunity additionally prolonged uptake of certain drugs ,specifically aspirin and nonsteroidal antiinfilammatory drugs (NSAIDs).The common mechanism of an injury is an imbalance between the aggressive and defensive factors that maintain the integrity of the gastric lining (mucosa). In subsequent or joining such inflammation pattern an increase in oxidative damage due to high level of reactive oxygen species (ROS) , higher gastrin, pepsinogen, expression of inducible nitric oxide synthase (iNOS) leading to corpus atrophy and G cells damage. Interaction of NO and can form peroxynitrite, leading finally to apoptosis in a variety of cell types.

Tannins and flavonoids (phenolic compounds) are commonly found in several medicinal plants. Certain therapeutic properties mainly anti-inflammatory, wound healing, antioxidant and anti ulcerogenic are mostly attributed to these plant constituents.

Tannins are potent scavengers of per oxi radicals and can interact with mucus proteins, improving their cytoprotective effect by forming a protein lining over the gastrointestinal mucosa, additionally involved in wounds treatment. Fresh fruits and vegetables have been reported to exert multiple biological effects on the mucosa of gastrointestinal tract due to their antioxidants content. Certain flavonoids or compounds with flavonoid-like properties have antiulcer activity, prevent gastric mucosal lesions brought about by a number of ulcerogens. This had been illustrated before on polyphenol from grape seed, aqueous fruit extract of morinda citrifolia, Quarcetin, apple extract, curcumin, black seed oil, quassin, artichoke and others. It is conceivable that some of these plant constituents exerted their effects through the inhibition of cytokine-mediated inflammatory mechanism, suppression of iNOS, antioxidant activities and healing of the produced ulcer.

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5. References

Agra, M.F.; Silva, K.N.; Basilio, I.J.L.D.; Freitas, P.F.& Barbosa-Filho, J.M. (2008). Survey of medicinal plants used in the region northeast of Brazil. *Brazilian Journal of Pharmacognosy*, Vol. 18, No. 3, (2008), pp. 472–508, ISSN 0102-695X.

Alarcon de la Lastra, C.; Barranco, M.D.; Martin, M.J.; Herrerías, J& Motilva, V. (2002). Extra-virgin olive oil enriched diets reduce indomethacin-induced gastric oxidative damage in rats. *Dig Dis Sci*, Vol. 47, No. 12, (December 2002), pp. 2783–2790, ISSN 1573-2568.

Albert-Puleo M. (1980). Fennel and anise as estrogenic agents. J. Ethnopharmacol., Vol. 2, No. 4, (December 1980), pp. 337-344, ISSN 0378-8741.

Alem, M.; Alem, N.; Cohen, H.; England, T.; Hamedi, N.; Moussazadeh, M.; Roth, J.A.& Shen, G.Q. (2002). Diagnostic value of detection of IgM antibodies to Helicobacter pylori. *Exp Mol Pathol.*, Vol. 72, No. 1, (February 2002), pp. 77-83, ISSN 0531-5522.

Almeida, C.F.C.B.R.; Lima e Silva, T.C.; Amorim, E.L.C.; Maia, M.B.S.& Albuquerque, U.P. (2005). Life strategy and chemical composition as predictors of the selection of medicinal plants from the Caatinga (Northeast Brazil). *Journal of Arid Environments*, Vol. 62, No. 1, (July 2005), pp. 127–142, ISSN 1095-922X.

Ammon, H.P.T.; Safayhi, H.; Mack, T.& Sabieraj, J. (1993). Mechanism of anti-inflammatory actions of curcumin and boswellic acids. *J. Ethnopharmacol.*, Vol. 38, No. 2-3, (March 1993), pp. 113–119, ISSN 0378-8741.

Andersen, L.P. (2007). Colonization and infection by Helicobacter pylori in humans. *Helicobacter*, Vol. 12, No. 12, (November 2007), pp. 12-15, ISSN 1523-5378.

Arauȯjo, T.A.S.; Alencar, N.L.; Amorim, E.L.C.& Albuquerque U.P. (2008). A new approach to study medicinal plants with tannins and flavonoids contents from the local knowledge. Journal of Ethnopharmacology, Vol. 120, No. 1, (August 2008), pp. 72–80, ISSN 0378-8741.

Arteel, G. E., & Sies, H. (1999). Protection against peroxynitrite by cocoa polyphenol oligomers. *FEBS Letters*, Vol. 462, No. (1-2), (November 1999), pp. 167–170, ISSN 0014-5793.

Binmoeller, K.F.& Benner, K.G. (1992). Emphysematous gastritis secondary to gastric infarction. *Am. J. Gastroenterol.*, Vol. 87, No. 4, (April 1992), pp. 526–529, ISSN 0002-9270.

Birdane, F.M.; Cemek, M.; Birdane, Y.O.; Gülçin, İ.& Büyükokuroğlu, M.E. (2007). Beneficial effects of Foeniculum vulgare on ethanol-induced acute gastric mucosal injury in rats. *World J. Gastroenterol.*, Vol. 13, No. 4, (January 2007), pp. 607-611, ISSN 1007-9327.

Block, G. (1991). Vitamin C and cancer prevention: the epidemiologic evidence. *Am. J. Clin. Nutr.*, Vol. 53, No. 1, (January 1991), pp. 270S–282S., ISSN 1938-3207.

Bonnet, F.; Neau, D.; Viallard, J.F.; Morlat, P.; Ragnaud, J.M.; Dupon, M.& et al. (2001). Clinical and laboratory findings of cytomegalovirus infection in 115 hospitalized non-immunocompromised adults. *Ann. Med. Interne.*, Vol. 152, No. 4, (June 2001), pp. 227-235, ISSN 0003-410X.

Boulton, R.; Hodgson, H.& Gupta, S. (2011). *Chronic gastritis*, Manson, ISBN 978-1-48067-068-2, Corringham road, London.

Castillo-Juarez, I.; Rivero-Cruz, F.; Celis, H.& Romero, I. (2007). Anti-Helicobacter pylori activity of anacardic acids from Amphipterygium adstringens. *Journal of Ethnopharmacology,* Vol. 114, No. 1, (July 2007), pp. 72–77, ISSN 0378-8741.

Chamberlain, C.E. (1993). Acute hemorrhagic gastritis. *Gastroenterol. Clin. North. Am.*. Vol. 22, No. 4, (December 1993), pp. 843–873, ISSN 0889-8553.

Chen, C.Y.; Chi, K.H.; George, R.W.; Cox, D.L.; Srivastava, A.; Rui Silva, M.& et al. (2006). Diagnosis of gastric syphilis by direct immunofluorescence staining and real-time PCR testing. *J. Clin. Microbiol.*, Vol. 44, No. 9 (September 2006), pp. 3452–3456, ISSN 1098-660X.

Chuthaputti, A.; Pattaloong, P.N.; Permpipat, U.& Techadamrongsin, Y. (1996). Study on antiemetic activity of Morinda citrifolia Fruits. *Thai Journal of Pharmaceutical Sciences*, Vol. 20, No. 3, (1996), pp. 195–202, ISSN 1948-2124.

Cover, T.L.; Krishna, U.S.; Israel, DA& Peek, R.M. Jr. (2003). Induction of gastric epithelial cell apoptosis by Helicobacter pylori vacuolating cytotoxin. *Cancer Res.*, Vol. 63, No. 5, (March 2003), pp. 951-957, ISSN 1538-7445.

Dadalioglu, I.& Evrendilek, G.A. (2004). Chemical compositions and antibacterial effects of essential oils of Turkish oregano (Origanum minutiflorum), bay laurel (Laurus nobilis), Spanish lavender (Lavandula stoechas L.), and fennel (Foeniculum vulgare) on common foodborne pathogens. *J. Agric. Food Chem.*, Vol. 52, No. 26, (December 2004), pp. 8255-8260, ISSN 1520-5118.

Dharmani, P.; Mishra, P.K.; Maurya, R.; Chauhan, V.S.& Palit, G. (2005). *Allophylus serratus*: A plant with potential anti-ulcerogenic activity. *Journal of Ethnopharmacol*, Vol. 99, No. 3, (July 2005), pp. 361-366, ISSN 0378-8741.

D'Argenio, G.; Mazzone, G.; Tuccillo, C.; Grandone, I.; Gravina, A.G.; Graziani, G.; Fogliano, V.& Romano, M. (2008). Apple polyphenol extracts prevent aspirin-induced damage to the rat gastric mucosa. *Br. J. Nutr.*, Vol. 100, No. 6, (December 2008), pp. 1228-1236, ISSN 1475-2662.

Das, K.C.& Das, C.K. (2002). Curcumin (diferuloylmethane), a singlet oxygen (1O2) quencher. *Biochem. Biophys. Res. Commun.*, Vol. 295, No. 1, (July 2002), pp. 62–66, ISSN 0006-291X.

Das, J.C.& Paul, N. (2007). Epidemiology and pathophysiology of Helicobacter pylori infection in children. Indian *Journal of Pediatrics*, Vol. 47, No., (March 2007), pp. 287-290, ISSN 0973-7693.

De las Heras, B.; Slowing, K.; Benedi, J.; Carretero, E.; Ortega, T.; Toledo, C.; Bermejo, P.; Iglesia, S.I.; Abad, M.J.; Gomez-Serranillos, P.; Liso, P.A.; Villar, A.& Chiriboga, X. (1998). Anti-inflammatory and antioxidant activity of plants used in traditional medicine in Ecuador. *Journal of Ethnopharmacology*, Vol. 61, No. 2, (June 1998), pp. 161–166, ISSN 0378-8741.

Deng, S.; Palu, A.K.; West, B.J.; Su, C.X.; Zhou, B.N.& Jensen, J.C. (2007). Lipoxygenase inhibitory constituents of the fruits of Noni (Morinda citrifolia) collected in Tahiti. *Journal of Natural Products*, Vol. 70, No. 5, (March 2007), pp. 859–862, ISSN 1520-6025.

Dohil, R.& Hassall, E. (2011). Gastritis, gastropathy and ulcer disease. In: *Pediatric Gastrointestinal and Liver Disease*, Kindle, pp. 277-292, ISBN 0721639240.

Drake, I.M.; Mapstone, N.P.; Schorah, C.J.; White, K.L.; Chalmers, D.M.; Dixon, M.F.& Axon, A.T. (1998). Reactive oxygen species activity and lipid peroxidation in Helicobacter pylori associated gastritis: relation to gastric mucosal ascorbic acid concentrations and effect of H. pylori eradication. *Gut*, Vol. 42, No. 6, (June 1998), pp. 768–771, ISSN 1468-3288.

Elseweidy, M.M.; Younis, N.N.; Amin, R.S.; Abdallah, F.R.; Fathy, A.M.& Yousif, Z.A. (2008). Effect of some natural products either alone or in combination on gastritis induced in experimental rats. *Dig Dis Sci.*, Vol. 53, No. 7, (March 2008), pp.1774-1784, ISSN 1573-2568.

Elseweidy, M.M.; Taha, M.M.; Younis, N.N.; Ibrahim, K.S.; Hamouda, H.A.; Eldosouky, M.A.; Soliman, H.& Ghate, S. (2010a). Pattern of gastritis as manipulated by current

state of Helicobacter pylori infection. *International journal of biology and biomedical engineering,* Vol. 4, No. 1, (2010), pp. 1-9, ISSN 1998-4510.

Elseweidy. M.M.; Taha, M.M.; Younis, N.N.; Ibrahim, K.S.; Hamouda, H.A.; Eldosouky, M.A.& Soliman, H. (2010b). Gastritis induced by Helicobacter pylori infection in experimental rats. *Dig Dis Sci.*, Vol. 55, No. 10, (January 2010), pp. 2770-2777, ISSN 1573-2568.

El-Zimaity, H.M.T. (2007). Recent advances in the histopathology of gastritis. *Current Diagnostic Pathology,* Vol.13, No.4, (2007), pp. 340–348, ISSN 0968-6053.

Ferro-Luzzi, A.& Ghiselli, A. (1993). Protective aspects of the Mediterranean diet. *Adv. Exp. Med. Biol.*, Vol. 348, (1993), pp. 137–144, ISSN 0065-2598.

Ford, A.C.; Marwaha, A.; Lim, A.& Moayyedi, P. (2010). What is the prevalence of clinically significant endoscopic findings in subjects with dyspepsia? Systematic review and meta-analysis. *Clin. Gastroenterol. Hepatol.*, Vol. 8, No. 10, (October 2010), pp. 830-837, ISSN 1542-3565.

Freire, R.S.; Morais, S.M.; Catunda-Junior, F.E.& Pinheiro, D.C. (2005). Synthesis and antioxidant, anti-inflammatory and gastroprotector activities of anethole and related compounds. *Bioorg. Med. Chem.*, Vol. 13, No. 13, (July 2005), pp. 4353-4358, ISSN 0968-0896.

Freitas, C.S.; Baggio, C.H.; Finau, J.; Anginoni, M.; Pizzolatti, M.G.; Santos, A.R.& Marques, M.C. (2008). Inhibition of H+/K+ ATPase in the gastroprotective effect of Baccharis illinita DC. *Journal of Pharmacy and Pharmacology*, Vol. 60, No. 8, (August 2008), pp. 1105–1110, ISSN 2042-7158.

Galati, E. M.; Mondello, M. R.; Giuffrida, D.; Dugo, G.; Miceli, N.; Pergolizzi, S.& Taviano MF. (2003). Chemical characterization and biological effects of Sicilian Opuntia ficus indica (L.) Mill. fruit juice: antioxidant and antiulcerogenic activity. *Journal of Agricultural and Food Chemistry*, Vol. 51, No. 17, (August 2003), pp. 4903-4908, ISSN 1520-5118.

Garcia-Barrantes, P.M.& Badilla, B. (2011). Anti-ulcerogenic properties of *Quassia amara* L. (Simaroubaceae) standardized extracts in rodent models. *J Ethnopharmacol*, (Epub ahead of print), (February 2011), ISSN 0378-8741.

Garcia-Lafuente, A.; Guillamon, E.; Villares, A.; Rostagno, M.A.& Martinez J.A. (2009). Flavonoids as anti-inflammatory agents: implications in cancer and cardiovascular disease. *Inflammation Research*, Vol. 58, No. 3, (March 2009), pp. 537–552, ISSN 1420-908X.

Geetha, T.; Malhotra, V.; Chopra, K.& Kaur, I.P. (2005). Antimutagenic and antioxidant /prooxidant activity of quercetin. *Indian J Exp Biol*, Vol. 43, No. 1, (January 2005), pp. 61−67, ISSN 0019-5189.

Gerritsen M.E., Carley W.W., Ranges G.E., Shen C.P., Phan S.A., Ligon G.F., Perry C.A. (1995). Flavonoids inhibit cytokine-induced endothelial cell adhesion protein gene expression. *Am J Pathol*, Vol. 147, No. 2, (August 1995), pp. 278−292, ISSN 0887-8005.

Graziani, G.; D'Argenio, G.; Tuccillo, C.; Loguercio, C.; Ritieni, A.; Morisco, F.; Del Vecchio Blanco, C.; Fogliano, V.& Romano, M. (2005). Apple polyphenol extracts prevent damage to human gastric epithelial cells in vitro and to rat gastric mucosa *in vivo*. *Gut* Vol. 54, No. 2, (February 2005), pp. 193–200, ISSN1468-3288.

Guo, Z.; Vangapandu, S.; Sindelar, R.W.; Walker, L.A.& Sindelar, R.D. (2005). Biologically active quassinoids and their chemistry: potential lads for drug design. *Current Medicinal Chemistry*, Vol. 12, No. 2, (2005), pp. 173-190, ISSN 0929-8673.

Hamauzu, Y.; Forest, F.; Hiramatsu, K.& Sugimoto, M. (2007). Effect of pear (Pyrus communis L.) procyanidins on gastric lesions induced by HCl/ethanol in rats. *Food Chemistry*, Vol. 100, No. 1, (2007), pp. 255–263, ISSN 0308-8146.

Hamauzu, Y.; Yasui, H.; Inno, T.; Kume, C., & Omanyuda, M. (2005). Phenolic profile, antioxidant property, and anti-influenza viral activity of Chinese quince (Pseudocydonia sinensis Schneid.), quince (Cydonia oblonga Mill.), and apple (Malus domestica Mill.) fruits. *Journal of Agricultural and Food Chemistry*, Vol. 53, No. 4, (February 2005), pp. 928–934, ISSN 1520-5118.

Hariganesh, K.& Prathiba, J. (2000). Effect of dimethylglycine on gastric ulcers in rats. *Journal Pharmacy and Pharmacology*, Vol. 52, No. 12, (December 2000), pp. 1519–1522, ISSN 2042-7158.

Hayes, J. D., & McLellan, L. I. (1999). Glutathione and glutathione-dependent enzymes represent a co-ordinately regulated defense against oxidative stress. *Free Radical Research*, Vol. 31, No. 4, (October 1999), pp. 273–300, ISSN 1029-2470.

He, M.L.; Cheng, X.W.; Chen, J.K.& Zhou, T.S. (2006). Simultaneous determination of five major biological active ingredients in different parts of Gardenia jasminoides fruits by HPLC with diode-array detection. *Chromatographia*, Vol. 64, No. 11-12, (2006), pp. 713–717, ISSN 1612-1112.

Holtmann, G.; Adam, B.; Haag, S.; Collet, W.; Grunewald, E.& Windeck, T. (2003). Efficacy of artichoke leaf extract in the treatment of patients with functional dyspepsia: a six-week placebo-controlled, double-blind, multicentre trial. *Aliment. Pharmacol. Ther.*, Vol. 18, No. 11-12, (December 2003), pp. 1099-1105, ISSN 1365-2036.

Hsu, D. Z.; Chien, S. P.; Chen, K. T., & Liu, M. Y. (2007). The effect of sesamol on systemic oxidative stress and hepatic dysfunction in acutely iron-intoxicated mice. *Shock*, Vol. 28, No. 5, (November 2007), pp. 596–601, ISSN 1540-0514.

Hsu, D.-Z.; Chu, P.-Y.; Chandrasekaran, V.R.M.& Liu, M.-Y. (2009a). Sesame lignan sesamol protects against aspirin-induced gastric mucosal damage in rats. *Journal of functional foods*, Vol. 1, No. 4, 1 (2009) pp. 349–355, ISSN 1756-4646.

Hsu, D.Z.; Chu, P.Y.& Liu, M.Y. (2009b). Effect of sesame oil on acidified ethanol-induced gastric mucosal injury in rats. *JPEN J. Parenter Enteral Nutr.*, Vol. 33, No. 4, (February 2009), pp. 423-427, ISSN 1941-2444.

Ikeda, R.; Wada, M.; Nishigaki, T.& Nakashima, K. (2009). Quantification of coumarin derivatives in Noni (Morinda citrifolia) and their contribution of quenching effect on reactive oxygen species. *Food Chemistry*, Vol. 113, No. 4, (April 2009), pp. 1169–1172, ISSN 0308-8146.

Ishida, K.; Kojima, R.; Tsuboi, M.; Tsuda, Y.& Ito, M. (2010). Effects of Artichoke Leaf Extract on Acute Gastric Mucosal Injury in Rats. *Biol. Pharm. Bull.*, Vol. 33, No. 2, (February 2010), pp. 223-229, ISSN 1347-5215.

IUCN (2009). IUCN Red List of Threatened Species. Version 2009.1. <www.iucnredlist.org> (accessed 11.10.09).

Jaeschke, H., & Hasegawa, T. (2006). Role of neutrophils in acute inflammatory liver injury. *Liver International*, Vol. 26, No. 8, (October 2006), pp. 912–919, ISSN 1478-3231.

Jobin, C.; Bradham, C.A.; Russo, M.P.; Juma, B.; Narula, A.S.; Brenner, D.A.& Sartor, R.B. (1999). Curcumin blocks cytokine mediated NF-KB activation and proinflammatory gene expression by inhibiting inhibitory factor I-KB kinase activity. *J. Immunol.*, Vol. 163, No. 6, (Sep 1999), pp. 3474–3483, ISSN 1550-6606.

Joy, J.F.& Haber, S.L. (2007). Clinical uses of artichoke leaf extract. *Am. J. Health Syst. Pharm.*, Vol. 64, No. 18, (September 2007), pp. 1906-1909, ISSN 1079-2082.

Kasper, D.L.; Braunwald, E.; Fauci, A.& et al. (2006). Disorders of the gastrointestinal system. In: *Harrison's Principles of Internal Medicine: Companion Handbook*, McGraw-Hill, pp. 1855-1872, Retrieved from <http://books.mcgraw hill.com/medical/harrisons/index.html>.

Kaunitz, J.D. (1999). Barrier function of gastric mucus. *Keio Journal of Medicine*, Vol. 48, No. 2, (June 1999), pp. 63-68, ISSN 1880-1293.

Kekki, M.; Samloff, I.M.; Varis, K.& Ihamäki, T. (1991). Serum pepsinogen I and serum gastrin in the screening of severe atrophic corpus gastritis. *Scand J Gastroenterol*, Vol. 186, (1991),pp. 109-116 ISSN 1502-7708.

Khalil, M.L. (2006). Biological activity of bee propolis in health and disease. *Asian Pac. J. Cancer Prev.*, Vol. 7, No. 1, (January-March 2006), pp. 22-31, ISSN 1513-7368.

Kim, J.; Joo, H.S.; Kim, D.H.; Lim, H.; Kang, Y.H.& Kim, M.S. (2003).A case of gastric strongyloidiasis in a Korean patient. Korean. J. Parasitol., Vol. 41, No. 1, (March 2003), pp. 63–67, ISSN 0023-4001.

Kist M. (1991). Immunology of Helicobacter pylori in: Bj marshall , *HP in peptic ulceration and gastritis* . Blackwell.Sci.Boston 1991 :92-110, ISBN 04445-31815.

Laine, L.; Curtis, S.P.; Cryer, B.; Kaur, A.& Cannon, C.P. (2010). Risk factors for NSAID-associated upper GI clinical events in a long-term prospective study of 34 701 arthritis patients. *Aliment. Pharmacol. Ther.*, Vol. 32, No. 10, (November 2010), pp. 1240-1248, ISSN 1365-2036.

Lauwers, G.Y.; Fujita, H.; Nagata, K.& Shimizu, M. (2010). Pathology of non-Helicobacter pylori gastritis: extending the histopathologic horizons. *J. Gastroenterol.*, Vol. 45, No. 2, (December 2010), pp. 131–145, ISSN 1435-5922.

La Vecchia, C.& Tavani, A. (1998). Fruit and vegetables, and human cancer. *Eur. J. Cancer Prev.*, Vol. 7, No. 1, (February 1998), pp. 3–8, ISSN 1473-5709.

Lee, S.E.; Jang, H.S.; Song. H.J.; Hwang, W.K.; Sohn, U.D. (2009a). M1904 Downstream Signal Transduction Induced By Interleukin-1 Beta-Stimulated ROS Generation and Anti-Oxidative Effects of Quercetin-3-O-[beta]-D Glucuronopyranoside (QGC) in Feline Esophageal Epithelial Cells. *Gastroenterology*, Vol. 136, No. 5, (May), pp. A442−443, ISSN 0016-5085.

Lee, J.-H.; Lee, D.-U.& Jeong, C.-S. (2009b). Gardenia jasminoides Ellis ethanol extract and its constituents reduce the risks of gastritis and reverse gastric lesions in rats. *Food and Chemical Toxicology*, Vol. 47, No., 6 (February 2009), pp. 1127–1131, ISSN 0278-6915.

Le Marchand, L.; Murphy, S.P.; Hankin, J.H.; Wilkens LR, Kolonel LN. (2000). Intake of flavonoids and lung cancer. J. Natl. Cancer Inst., Vol. 92, No. 2, (January 2000), pp. 154–160, ISSN 0027-8874.

Levand, O.& Larson, H.O. (1979). Some chemical constituents of Morinda citrifolia. *Planta Medica*, Vol. 36, No. 2, (June 1979), pp. 186–187, ISSN 0032-0943.

Lewis D.A. (1989). Anti-inflammatory drugs from plant, marine sources. *Agents Actions*, Vol. 27, (1989), pp., Suppl 27: 3−373, 1989, ISSN 0065-4299.

Lima, Z.P.; Calvo, T.R.; Silva, E.F.; Pellizzon, C.H.; Vilegas, W.; Brito, A.R.; Bauab, T.M.& Hiruma-Lima, C.A. (2008). Brazilian medicinal plant acts on prostaglandin levels and Helicobacter pylori. *Journal of Medicinal Food*, Vol. 11, No. 4, (December 2008), pp. 701–708, ISSN 1557-7600.

López, J.A.& Pérez, J. (2008). Etnofarmacología y actividad biológica de *Quassia amara* (Simaroubaceae): estado de la cuestión. *Boletín Latinoamericano y del Caribe de Plantas Medicinales y Aromáticas*, Vol. 7, (2008), pp. 234-246, ISSN 0717-7917.

Mahattanadul, S.; Reanmongkol, W.; Yano, S.; Panichayupakaranant, P.; Phdoongsombut, N.& Tungsinmunkong, K. (2006). Preventive and curative effects of curcumin on the development of gastric inflammatory diseases in rats. *J. Nat. Med.*, Vol. 60, No. 3, (2006), pp. 191–197, ISSN 1861-0293.

Mahattanadul, S.; Ridtitid, W.; Nima, S.; Phdoongsombut, N.; Ratanasuwon, P.& Kasiwong, S. (2011). Effects of Morinda citrifolia aqueous fruit extract and its biomarker scopoletin on reflux esophagitis and gastric ulcer in rats. *Journal of Ethnopharmacology*, Vol. 134, No. 2, (December 2010), pp. 243-250, ISSN 0378-8741.

Marshall, J.B. (1993). Tuberculosis of the gastrointestinal tract and peritoneum. *Am. J. Gastroenterol.*, Vol. 88, No. 7, (July 1993), pp. 989–999, ISSN 0002-9270.

Mimica-Dukic, N.; Kujundzic, S.; Sokovic, M.& Couladis M. (2003). Essential oil composition and antifungal activity of Foeniculum vulgare Mill obtained by different distillation conditions. Phytother. Res., Vol. 17, No. 4, (April 2003), pp. 368-371, ISSN 1099-1573.

Min Y.S.; Lee S.E.; Hong S.T.; Kim H.S.; Choi B.-C.; Sim S.S.; Kyun W.W.& Sohn U.D. (2009). The Inhibitory Effect of Quercetin-3-O-β-D-Glucuronopyranoside on Gastritis and Reflux Esophagitis in Rats. Korean J Physiol Pharmacol., Vol. 13, No. 4, (August 2009), pp. 295-300, ISSN 1226-4512,

Moleiro, F.C.; Andreo, M.A.; Santos, R.C.S.; Moraes, T.M.; Rodrigues, C.M.; Carli, C.B.A.; Lopes, F.C.M.; Pellizzon, C.H.; Carlos, I.Z.; Bauabe, T.M.; Wagner Vilegas, W.& Hiruma-Lima, C.A. (2009). Mouriri elliptica: validation of gastroprotective, healing and anti-Helicobacter pylori effects. *Journal of Ethnopharmacology*, Vol. 123, No. 3, (April 2009), pp. 359–368, ISSN 0378-8741.

Monteiro, J.M.; Albuquerque, U.P.; Neto, E.M.F.L.; Araٜujo, E.L.; Albuquerque, M.M.& Amorim, E.L.C. (2006). The effects of seasonal climate changes in the Caatinga on tannin levels in Myracrodruon urundeuva (Engl.) Fr. All. and Anadenanthera colubrina (Vell.) Brenan. *Brazilian Journal of Pharmacognosy*, Vol. 16, (2006), pp. 338–344, ISSN 0102-695X.

Moon, P.D.; Lee, B.H.; Jeong, H.J.; An, H.J.; Park, S.J.; Kim, H.R.; Ko, S.G.; Um, J.Y.; Hong, S.H.& Kim, H.M. (2007). Use of scopoletin to inhibit the production of inflammatory cytokines through inhibition of the IkB/NF-kB signal cascade in the human mast cell line HMC-1. *European Journal of Pharmacology*, Vol. 555, No. 2-3, (October 2006), pp. 218–225, ISSN 0014-2999.

Muralidharan, P.& Srikanth, J. (2009). Antiulcer activity of Morinda citrifolia Linn fruit extract. *Journal of Scientific Research*, Vol. 1, No. 2, (2009), pp. 345–352, ISSN 2070-0245.

Naito, Y.; Yoshikawa, T.; Matsuyama, K.; Yagi, N.; Arai, M.; Nakamura, Y.; Nishimura, S.; Yoshida, N.& Kondo M. (1995). Effects of oxygen radical scavengers on the quality

of gastric ulcer healing in rats. *Journal of Clinical Gastroenterology*, Vol. 1, (1995), pp. S82–S86, ISSN 1539-2031.

Neu, B.; Randlkofer, P.; Neuhofer, M.; Voland, P.; Mayerhofer, A.; Gerhard, M.; Schepp, W.& Prinz, C. (2002). Helicobacter pylori induces apoptosis of rat gastric parietal cells. *American Journal of Physiology-Gastrointestinal and Liver Physiology*, Vol. 283, No. 2, (August 2002), pp. G309–G318, ISSN 1522-1547.

Nostro, A.; Cellini, L.; Di Bartolomeo, S.; Di Campli, E.; Grande, R.; Cannatelli, M.A.; Marzio, L.& Alonzo V. (2005). Antibacterial effect of plant extracts against Helicobacter pylori. *Phytotherapy Research*, Vol. 19, No. 3, (March 2005), pp. 198–202, ISSN 1099-1573.

Obst, B.; Wagner, S.; Sewing, K.F.& Beil, W. (2000). Helicobacter pylori causes DNA damage in gastric epithelial cells. *Carcinogenesis*, Vol. 21, No. 6, (June 2000), Vol. 21, No. 6, pp. 1111-1115, ISSN 1460-2180.

Odonnea, G.; Bourdy, G.; Beauchene, J.; Houel, E.; Stien, D.; Chevolot, L.& Deharo, E. (2007). From tonic-cups to bitter-cups: Kwasi bita beker from Suriname determination, past and present use of an ancient galenic artifact. *Journal of Ethnopharmacology*, Vol. 110, No. 2, (October 2006), pp. 318–322, ISSN 0378-8741.

Ohta, Y.; Kobayashi, T.& Ishiguro, I. (1999). Role of endogenous serotonin and histamine in the pathogenesis of gastric mucosal lesions in unanaesthetised rats with a single treatment of compound 48/80, a mast cell degranulator. *Pharmacol. Res.*, Vol. 39, No. 4, (April 1999), pp. 261–267, ISSN 1043-6618.

Okuda T. (2005). Systematics and health effects of chemically distinct tannins in medicinal plants. *Phytochemistry*, Vol. 66, No. 17, (September 2005), pp. 2012–2031, ISSN 0031-9422.

Osakabe, N.; Sanbongi, C.; Yamagishi, M.; Takizawa, T., & Osawa, T. (1998). Effects of polyphenol substances derived from Theobroma cacao on gastric mucosal lesion induced by ethanol. *Bioscience, Biotechnology and Biochemistry*, Vol. 62, No. 8, (August 1998), pp. 1535–1538, ISSN 1347-6947.

Owen, D.A. (2003). Gastritis and carditis. Mod. Pathol. Vol. 16, No. 4, (April 2003), pp. 325–341, ISSN 0893-3952.

Pathak, A.K.; Bhutani, M.; Nair, A.S.; Ahn, K.S.; Chakraborty, A.; Kadara, H.; Guha, S.; Sethi, G.& Aggarwal, B.B. (2007). Ursolic acid inhibits STAT3 activation pathway leading to suppression of proliferation and chemosensitization of human multiple myeloma cells. *Mol. Cancer Res.*, Vol. 5, No. 9, (September 2007), pp. 943–955, ISSN 1557-3125.

Perez-Garcia, F.; Adzet, T.& Canigueral, S. (2000). Activity of artichoke leaf extract on reactive oxygen species in human leukocytes. *Free Radic. Res.*, Vol. 33, No. 5, (November 20000), pp. 661-665, ISSN 1029-2470.

Pihan, G.; Regillo, C.& Szabo, S. (1987). Free radicals and lipid peroxidation in ethanol- or aspirin-induced gastric mucosal injury. *Digestion Disease Science*, Vol. 32, No. 12, (December 1987), pp. 1395–1401, ISSN 1573-2568.

Pu, H.F.; Huang, W.J.; Tseng, W.M.; Wang, S.W.; Liu, Y.W.; Doong, M.L.& Wang, P.S. (2004). Effects of juice from Morinda citrifolia (Noni) on gastric emptying in male rats. *Chinese Journal of Physiology*, Vol. 47, No. 4, (December 2004), pp. 169–174, ISSN 1469-7793.

Quilez, A.; Berenguer, B.; Gilardoni, G.; Souccar, C.; de Mendonca, S.; Oliveira, L.F.S.; Martin-Calero, M.J.& Vidari, G. (2010). Anti-secretory, anti-inflammatory and anti-Helicobacter pylori activities of several fractions isolated from Piper carpunya Ruiz & Pav. *Journal of Ethnopharmacology*, Vol. 128, No. 3, (February 2010), pp. 583–589, ISSN 0378-8741.

Rafatullah, S.; Tariq Al-Yahya, M.A.; Mossa, J.S.& Ageel, A.M. (1990). Evaluation of turmeric (Curcuma longa) for gastric and duodenal antiulcer activity in rats. *J. Ethnopharmacol.*, Vol. 29, No. 1, (April 1990), pp. 25–34, ISSN 0378-8741.

Rice-Evans, C.A.; Miller, N.J.& Paganga, G. (1996). Structure-antioxidant activity relationships of flavonoids and phenolic acids. *Free Radic Biol Med*, Vol. 20, No. 7, (1996), pp. 933−956, ISSN 0891-5849.

Rothenberg, M.E. (2004). Eosinophilic gastrointestinal disorders (EGID). *J. Allergy Clin. Immunol.*, Vol. 113, No. 1, (January 2004), pp. 11–28, ISSN 0091-6749.

Roukos, D.H.; Paraskevaidis, E.; Agnantis, N.J.; Kappas AM. (2003). Fruits and vegetables: do they protect from gastric cancer? *Gastroenterology*, Vol. 124, No. 7, (June 2003), pp. 2006–2007, ISSN 0016-5085.

Rugge, M.& Genta, R.M. (2005). Staging and grading of chronic gastritis. *Hum. Pathol.*,Vol. 36, No. 3, (March 2005), pp. 228-233, ISSN 0046-8177.

Saito, M.; Hosoyama, H.; Ariga, T.; Kataoka, S., & Yamaji, N. (1998). Antiulcer activity of grape seed extract and procyanidins. *Journal of Agricultural and Food Chemistry*, Vol. 46, No. 4, (March 1998), pp. 1460–1464, ISSN 1520-5118.

Salim A.S. (1990). Removing oxygen-derived free radicals stimulates healing of ethanol-induced erosive gastritis in the rat. *Digestion,* Vol. 47, No. 1, (1990), pp. 24–28, ISSN 0012-2823.

Samoylenko, V.; Zhao, J.; Dunbar, D.C.; Khan, I.A.; Rushing, J.W.& Muhammad, I. (2006). New constituents from Noni (Morinda citrifolia) fruit juice. *Journal of Agricultural and Food Chemistry*, Vol. 54, No. 17, (August 2006), pp. 6398–6402, ISSN 1520-5118.

Sanchez, G.M.; Rodriguez, H.M.A.; Giuliani, A.; Nunez Selles, A.J.; Rodriguez, N.P.; Leon Fernandez, O.S.& Re, L. (2003). Protective effect of *Mangifera indica* L. extract (Vimang) on the injury associated with hepatic ischaemia reperfusion. *Phytotherapy Research*, Vol. 17, No. 3, (March 2003), pp. 197–201, ISSN 1099-1573.

Santos, C.S.; Costa, W.F.; Ribeiro, J.P.; Guimarães, D.O.; Ferri, P.H.; Ferreira, H.D.; Seraphin, J.C. (2002). Tannin composition of barbatimao species. *Fitoterapia*, Vol. 73, No. 4, (July 2002), pp. 292–299, ISSN 0367-326X.

Satoh, K.; Osawa, H.; Yoshizawa, M.; Nakano, H.; Hirasawa, T.; Kihira, K.& Sugano K. (2008). Assessment of Atrophic Gastritis Using the OLGA System. *Helicobacter*, Vol. 13, No. 3, (June 2008), pp. 225–229, ISSN 1523-5378.

Savino, F.; Cresi, F.; Castagno, E.; Silvestro, L.& Oggero, R. (2005). A randomized double-blind placebo-controlled trial of a standardized extract of Matricariae recutita, Foeniculum vulgare and Melissa officinalis (ColiMil) in the treatment of breastfed colicky infants. *Phytother. Res.*, Vol. 19, No. 4, (April 2005), pp. 335-340, ISSN 1099-1573.

Selles, N.A.J.; Castro, H.T.V.; Aguero-Aguero, J.; Gonzalez, J.; Nadeo, F.; De Simone, F.& Rastelli, L. (2002). Isolation and quantitative analysis of phenolic antioxidants, free sugars, and polyols from mango (*Mangifera indica* L.) stem bark aqueous decoction

used in Cuba as a nutritional supplement. *Journal of Agriculture Food and Chemistry*, Vol. 50, No. 4, (February 2002), pp. 762–766, ISSN 1520-5118.

Sepulveda, A.R.& Patil, M. (2008). Practical approach to the pathologic diagnosis of gastritis. *Arch. Pathol. Lab. Med.*, Vol 132, No. 10, (October 2008), pp. 1586-1593, ISSN 0003-9985.

Shacter, E.& Weitzman, S.A. (2002). Chronic inflammation and cancer. *Oncology (Williston Park)*, Vol. 16, No. 2, (February 2002), pp. 217-226, 229; discussion 230-232, ISSN 0354-7310.

Shishodia, S.; Majumdar, S.; Banerjee, S.& Aggarwal, B.B. (2003). Ursolic acid inhibits nuclear factor-kappaB activation induced by carcinogenic agents through suppression of IkappaBalpha kinase and p65 phosphorylation: correlation with down-regulation of cyclooxygenase 2, matrix metalloproteinase 9, and cyclin D1. *Cancer Res.*, Vol. 63, No. 15, (August 2003), pp. 4375–4383, ISSN 1538-7445.

Sidhu, G.S.; Singh, A.K.; Thaloor, D.; Banaudha, K.K.; Patnaik, G.K.; Srimal, R.C.& Maheshwari, R.K. (1998). Enhancement of wound healing by curcumin in animals. *Wound Repair Regen.*, Vol. 6, No. 2, (March-april 1998), pp. 167–177, ISSN 1524-475X.

Silva, M.S.; Antoniolli, A.R.; Batista, J.S.& Mota, C.N. (2006). Plantas medicinais usadas nos distuo̊rbios do trato gastrintestinal no povoado Colônia Treze, Lagarto, SE, Brasil. *Acta botanica brasilica,* Vol. 20, (2006), pp. 815–829, ISSN 1677-941X.

Silva, N.C.B.; Esquibel, M.A.; Alves, I.M.; Velozo, E.S.; Almeida, M.Z.; Santos, J.E.S.; Campos-Buzzi, F.; Meira, A.V.& Cechinel-Filho V. (2009). Antinociceptive effects of Abarema cochliacarpos (B.A. Gomes) Barneby & J. W. Grimes (Mimosaceae). *Brazilian Journal of Pharmacognosy*, Vol. 19, No. 1A, (February 2009), pp. 46–50, ISSN 0102-695X.

da Silva, M.S.; Sanchez-Fidalgo, S.; Elena Talero, E.; Cardeno, A.; da Silva, M.A.; Vilegas, W.; Souza Brito, A.R.M.& de La Lastra, C.A. (2010a). Anti-inflammatory intestinal activity of Abarema cochliacarpos (Gomes) Barneby & Grimes in TNBS colitis model. *Journal of Ethnopharmacology*, Vol. 128, No. 18, (January 2010), pp. 467–475, ISSN 0378-8741.

da Silva, M.S.; de Almeida, A.C.A.; de Faria, F.M.; Luiz-Ferreira, A.; da Silva, M.A.; Vilegas, W.; Pellizzon, C.H.& Souza Brito A. R. M. (2010b). Abarema cochliacarpos: Gastroprotective and ulcer-healing activities. *Journal of Ethnopharmacology*, Vol. 132, No. 1, (August 2010), pp. 134–142, ISSN 0378-8741.

Shikov, A.N.; Pozharitskaya, O.N.; Makarov, V.G.& Kvetnaya, A.S. (2008). Antibacterial activity of Chamomilla recutita oil extract against Helicobacter pylori. *Phytotherapy Research*, Vol. 22, No. 2, (February 2008), pp. 252–253, ISSN 1099-1573.

Singh, U.P.; Singh, D.P.; Singh, M.; Maurya, S.; Srivastava, J.S.; Singh, R.B.& Singh, S.P. (2004). Characterization of phenolic compounds in some Indian mango cultivars. *International Journal of Food Science and Nutrition*, Vol. 55, No. 2, (March 2004), pp. 163–169, ISSN 1465-3478.

Soltermann, A.; Koetzer, S.; Eigenmann, F.& Komminoth, P. (2007). Correlation of Helicobacter pylori virulence genotypes vacA and cagA with histological parameters of gastritis and patient's age. *Mod. Pathol.*, Vol. 20, No. 8, (August 2007), pp. 878-883, ISSN 0893-3952.

Souza, M. H.; Mota, J. M.; Oliveira, R. B., & Cunha, F. Q. (2008). Gastric damage induced by different doses of indomethacin in rats is variably affected by inhibiting iNOS or

leukocyte infiltration. Inflammation Research, Vol. 57, No. 1, (January 2008), pp. 28–33, ISSN 1420-908X.

Speroni, E.; Cervellati, R.; Govoni, P.; Guizzardi, S.; Renzulli, C.& Guerra, M.C. (2003). Efficacy of different Cynara scolymus preparations on liver complaints. J. Ethnopharmacol., Vol. 86, No. 2-3 , (June 2003), pp. 203-211, ISSN 0378-8741.

Srivastava, A.& Lauwers, G.Y. (2007). Pathology of non-infective gastritis. *Histopathology* Vol.50, No.1, (2007), pp. 15–29, ISSN 1365-2559.

Staroverov, V.V.; Kisel, A.T.; Sumarokov, U.A.& Kachanova, T.N. (2001). A case of phlegmonous gastritis diagnosed by echography. *Eur. J. Ultrasound*., Vol. 13, No. 3 , (July 2001), pp. 197–200, ISSN 0929-8266.

Takeeda, M.; hayahic, Y.; murkams, M.& Takeuchi, K. (2004). roles of endogenous prostaglandins , cycloxygenase enzyme in mucosal defense of inflamed rat stomach. *J. physiology and pharmacology*, Vol. 55, No. 1, (2004), pp. 193-205, ISSN 0867-5910.

Tari, A.; Kodama, K.; Kitadai, Y.; Ohta, M.; Sumii, K.& Kajiyama, G. (2003). Is apoptosis in antral mucosa correlated with serum nitrite concentration in Japanese Helicobacter pylori-infected patients? *J Gastroenterol Hepatol*., Vol. 18, No. 5, (May 2003), pp.498-504, ISSN 1440-1746.

Thirumurthi, S.& Lanza, F.L. (2010). Gastritis, In: *GI/Liver Secrets Plus* ,Peter R. McNally,pp. 63-67, Mosby Elsevier, ISBN 978-0-323-06397-5, Philadelphia.

Tokusoglu, O.; Yildirim, Z., & Yemis, F. (2003). Some functional properties as gelation, water and oil absorption, emulsion capacity, and foaming stability of sesame seed (Sesamum indicum L.) spreads. *Turkish Journal of Field Crops*, Vol. 8, (2003), pp. 15–21, ISSN 1303-6173.

Toma, W.; Gracioso, J.; Pezzuto, F.D.; Hiruma-Lima, C.A.; Vilegas, W.& Monteiro, A.R. (2002). Antiulcerogenic activity of four extracts obtained from the Bark Wood of *Quassia amara* L. (Simaroubaceae). *Biological & Pharmaceutical Bulletin*, Vol. 25, No. 9, (September 2002), pp. 1151-1155, ISSN 1347-5215.

Tordera, M.; Ferrandiz, M.L.& Alcaraz, M.J. (1994). Influence of antiinflammatory flavonoids on degranulation and arachidonic acid release in rat neutrophils. *Zeitschrift fur Naturforschung [C]*, Vol. 49, No. 3-4, (March-April 1994), pp. 235–240, ISSN 0932-0784.

Trabadela, C.; Sanchez-Fidalgo, S.; Mino, P.; Berenguer, B.; Quilez, A.; de la Puerta, R.& Martin, M.J. (2009). Gastroprotective effects of Piper carpunya against diclofenac-induced gastric lesions in rats. *Pharmaceutical Biology*, Vol. 46, No. 12, (February 2009), pp. 829–837, ISSN 1744-5116.

Tseng, T.H.; Chu, C.Y.; Huang, J.M.; Shiow, S.J.& Wang, C.J. (1995). Crocetin protects against damage in rat primary hepatocytes. *Cancer Lett.*, Vo. 97, No. 1, (October 1995), pp. 61–67, ISSN 0304-3835.

Väänänen, H.; Vauhkonen, M.; Helske, T.; Kääriäinen, I.; Rasmussen, M.; Tunturi-Hihnala, H.; Koskenpato, J.; Sotka, M.; Turunen, M.; Sandström, R.; Ristikankare, M.; Jussila, A.& Sipponen, P. (2003). Non-endoscopic diagnosis of atrophic gastritis with a blood test. Correlation between gastric histology and serum levels of gastrin-17 and pepsinogen I: a multicentre study. *Eur J Gastroenterol Hepatol.*, Vol. 15, No. 8, (August 2003),pp. 885-891, ISSN1440-1746.

Walsh, J.H.; Isenberg, J.I.; Ansfield, J.& Maxwell, V. (1976). Clearance and acid-stimulating action of human big and little gastrins in duodenal ulcer subjects. *J Clin Invest.*, Vol. 57, No. 5, (May 1976), pp. 1125-1131, ISSN 0021-9738.

Weck, M.N.; Gao, L.& Brenner, H. (2009). Helicobacter pylori infection and chronic atrophic gastritis: associations according to severity of disease. *Epidemiology*, Vol. 20, No. 4, (July 2009), pp. 569-574, ISSN 1531-5487 .

Williams, R.J.; Spencer, J.P.& Rice-Evans, C. (2004a). Flavonoids: antioxidants or signalling molecules? *Free Radic Biol Med*, Vol. 36, No. 7, (April 2004), pp. 838−849, ISSN 0891-5849.

Williams, R.J.; Spencer, J.P.E.& Rice-Evans Catherine (2004b). Serial review: flavonoids and isoflavones (Phytoestrogens): absorption, metabolism, and bioactivity. flavonoids: antioxidants or signalling molecules? *Free Radical Biology & Medicine*, Vol. 36, No. 11, (August 2004), pp. 838–849, ISSN 0891-5849.

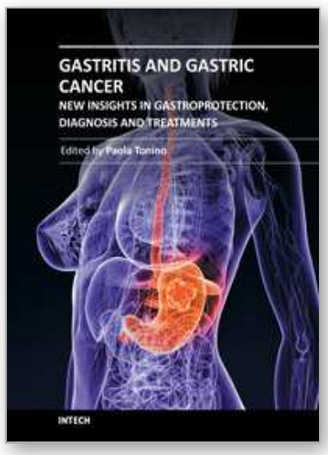
Xiao, Z.P.; Shi, D.H.; Li, H.Q.; Zhang, L.N.; Xu, C.& Zhu, H.L. (2007). Polyphenols based on isoflavones as inhibitors of Helicobacter pylori urease. *Bioorganic & Medicinal Chemistry*, Vol. 15, No. 11, (June 2007), pp. 3703–3710, ISSN 0968-0896.

Xin, W.& Greenson, J.K. (2004). The clinical significance of focally enhanced gastritis. *Am. J. Surg. Pathol.*, Vol. 28, No 10., (October 2004), pp. 1347–1351, ISSN 1532-0979.

Yano, S.; Terai, M.; Shimizu, K.L.; Futagami, Y.; Horie, S.; Tsuchiya, S.; Ikegami, F.; Sekine, T.; Takamoto, K.; Saito, K.; Ueno, K.& Watanabe, K. (2000). Antiallergic activity of Curcuma longa (II) features of inhibitory actions on histamine release from mast cells. *Nat. Med.*, Vol. 54, No. 6, (2000), pp. 325–329, ISSN1861-0293.

Yue, G.; Lai, P.S.; Yin, K.; Sun, F.F.; Nagele, R.G.; Liu, X.; Linask, K.K.; Wang, C.; Lin K.T.& Wong, P.Y. (2001). Colon epithelial cell death in 2,4,6-trinitrobenzenesulfonic acid-induced colitis is associated with increased inducible nitric-oxide synthase expression and peroxynitrite production. *J Pharmacol Exp Ther.,* Vol. 297, No. 3, (June 2001), pp. 915-925, ISSN 1521-0103.

Zalewska-Ziob, M.; Adamek, B.; Strzelczyk, J.K.; Gawron, K.; Jarzab, B.; Gubala, E.; Kula, D.; Krakowczyk, Ł.; Sieroń, A.& Wiczkowski, A. (2009). TNF-alpha expression in gastric mucosa of individuals infected with different virulent Helicobacter pylori strains. *Med. Sci. Monit.*, Vol. 15, No. 6, (June 2009), pp. BR166-171, ISSN 1643-3750.



Gastritis and Gastric Cancer - New Insights in Gastroprotection, Diagnosis and Treatments

Edited by Dr. Paola Tonino

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This book is a comprehensive overview of invited contributions on Helicobacter pylori infection in gastritis and gastric carcinogenesis. The first part of the book covers topics related to the pathophysiology of gastric mucosal defense system and gastritis including the gastroprotective function of the mucus, the capsaicin-sensitive afferent nerves and the oxidative stress pathway involved in inflammation, apoptosis and autophagy in H. pylori related gastritis. The next chapters deal with molecular pathogenesis and treatment, which consider the role of neuroendocrine cells in gastric disease, DNA methylation in H. pylori infection, the role of antioxidants and phytotherapy in gastric disease. The final part presents the effects of cancer risk factors associated with H. pylori infection. These chapters discuss the serum pepsinogen test, K-ras mutations, cell kinetics, and H. pylori lipopolysaccharide, as well as the roles of several bacterial genes (cagA, cagT, vacA and dupA) as virulence factors in gastric cancer, and the gastrokine-1 protein in cancer progression.

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