BOLETIN LATINOAMERICANO Y DEL CARIBE DE PLANTAS MEDICINALES Y AROMÁTICAS
© / ISSN 0717 7917 / www.blacpma.ms-editions.cl

Revisión / Review

Antioxidant rich medicinal plants as a potential candidate to treat gastric ulcer

[Plantas medicinales ricas en antioxidantes como candidatas potenciales para tratar la úlcera gástrica]

Sidra Altaf[1], Rao Zahid Abbas[2], Tayyaba Akhtar[3], Faisal Siddique[4], Muhammad Shahid Mahmood[5], Muhammad Kasib Khan[2], Khurram Ziaf[6], Muhammad Rafay[7], Muhammad Azam Khan[8], Asghar Abbas[9], Tauseef ur Rehman[10], Liliana Aguilar Marcelino[11], Muhammad Zia[12], Hanem Fathy Khater[13], Nahla Muhammad Saeed[14] & Karim Yar Abbasi[6]

[1]Department of Pharmacy, University of Agriculture, Faisalabad, Pakistan
[2]Department of Parasitology, University of Agriculture, Faisalabad, Pakistan
[3]KBCMA College of Veterinary and Animal Sciences, Narowal, Sub campus UVAS-Lahore, Pakistan
[4]Department of Microbiology, Faculty of Veterinary Science, Cholistan University of Veterinary and Animal Sciences, Bahawalpur
[5]Institute of Microbiology, University of Agriculture, Faisalabad, Pakistan
[6]Institute of Horticultural Sciences, University of Agriculture, Faisalabad, Pakistan
[7]Department of Forestry, Range and Wildlife Management, The Islamia University of Bahawalpur, Pakistan
[8]Department of Horticulture, PMAS-Arid Agriculture University, Rawalpindi, Pakistan
[9]Department of Veterinary and Animal Sciences, Muhammad Nawaz Shareef University of Agriculture Multan, Pakistan
[10]Department of Parasitology, Faculty of Veterinary and Animal Sciences, The Islamia University of Bahawalpur, Pakistan
[11]Department of Helminthology CENID-Animal Health and Inocuidad, INIFAP. Cuernavaca, Jiutepec, Morelos, Mexico
[12]Department of Anesthesia, Faisalabad Medical University, Faisalabad, Pakistan
[13]Department of Parasitology, Faculty of Veterinary Medicine, Benha University, Moshtohor, Toukh, Egypt
[14]Department of Microbiology, College of Veterinary Medicine, University of Sulaimani, Sulaymaniyah, Iraq

Reviewed by:
Marcelo L. Wagner
Universidad de Buenos Aires
Argentina

Edmundo Venegas
Universidad Nacional de Trujillo
Peru

Correspondence:
Rao Zahid ABBAS
raouaf@hotmail.com

Section Review

Received: 15 June 2022
Accepted: 22 August 2022
Accepted corrected: 27 November 2022
Published: 30 September 2023

Citation:
Altaf S, Abbas RZ, Akhtar T, Siddique F, Mahmood MS, Khan MK, Ziaf K, Rafay M, Khan MA, Abbas A, Rehman T, Marcelino LA, Zia M, Khater HF, Saeed NM, Abbasi KY
Antioxidant rich medicinal plants as a potential candidate to treat gastric ulcer
Bol Latinoam Caribe Plant Med Aromat
22 (5): 560 - 580 (2023).
https://doi.org/10.37360/blacpma.23.22.5.41

Abstract: Oxidative stress is a key cause of gastrointestinal disorders, primarily stomach ulcers. Multiple intrinsic and extrinsic mechanisms caused the body to produce reactive oxygen species (ROS). The body's antioxidant defense system protects against these reactive species. When the degree of ROS production exceeds the normal range, the body's natural defense system fails to neutralize these dangerous free radicals, necessitating need for an exogenous source of natural antioxidants. Natural herbal remedies have been widely employed as antioxidants to relieve oxidative stress in gastric ulcers. Polyphenols, tannins, essential oils, flavonoids, notably quercetin, carotenoids, vitamin C, vitamin A, and minerals are among the molecules of immense interest in bioassays due to their significant antioxidant effects. In the present review, several natural anti-ulcer medicinal plants along with their antioxidative mechanism have been reported. Electronic databases including PubMed, Google Scholar and Scopus were explored to identify the antioxidant and gastroprotective potential of all the plants.

Keywords: Botanicals; Antioxidants; Ulcer; Gastroprotective; Natural products

Resumen: El estrés oxidativo es una causa clave de trastornos gastrointestinales, principalmente úlceras estomacales. Múltiples mecanismos intrínsecos y extrínsecos hacen que el cuerpo produzca especies reactivas de oxígeno (ROS). El sistema de defensa antioxidante del cuerpo protege contra estas especies reactivas. Cuando el grado de producción de ROS excede el rango normal, el sistema de defensa natural del cuerpo no logra neutralizar estos peligrosos radicales libres, lo que requiere de una fuente exógena de antioxidantes naturales. Los remedios herbales naturales se han empleado ampliamente como antioxidantes para aliviar el estrés oxidativo en las úlceras gástricas. Los polifenoles, los taninos, los aceites esenciales, los flavonoides, en particular la quercetina, los carotenoides, la vitamina C, la vitamina A y los minerales se encuentran entre las moléculas de mayor interés en los bioensayos debido a sus importantes efectos antioxidantes. En la presente revisión se han reportado varias plantas medicinales naturales antiulcerosas junto con su mecanismo antioxidante. Se exploraron bases de datos electrónicas como PubMed, Google Scholar y Scopus para identificar el potencial antioxidante y gastroprotector de todas las plantas.

Palabras clave: Botánicos; Antioxidantes; Úlcera; Gastroprotector; Productos naturales

INTRODUCTION

Reactive oxygen species (ROS) are byproducts of the normal biological metabolic reactions. The formation of a limited amount of ROS has beneficial impacts on several physiological functions like pathogen clearance, wound healing, and cell regeneration. ROS are key signaling molecules. Yet, excessive generation of ROS disrupts the body's homeostasis, resulting in oxidative damage to tissues (Checa & Aran, 2020). ROS are produced as a result of alcohol consumption, ultraviolet (UV) radiation, cigarette smoking, nonsteroidal anti-inflammatory drugs (NSAIDs), and a range of other environmental variables (Bhattacharyya *et al.*, 2014). Infections and cardiac injury can also increase ROS levels. The primary source of ROS generation is the gastrointestinal (GI) system. Consumption of materials and pathogens may result in the production of cytokines and other inflammatory mediators, resulting in oxidative stress. Oxidative stress can cause peptic ulcers and other GI pathogenic diseases (Suzuki *et al.*, 2012). ROS can be generated by a number of intracellular compartments, including mitochondria, peroxisomes, the endoplasmic reticulum, the cytosol, plasma membranes, nuclei, and extracellular spaces (Balaban *et al.*, 2005; Forrester *et al.*, 2018). The electron transport chain of mitochondria is the primary location for ROS generation in mammalian cells (Zhao *et al.*, 2019). Enzymes involved in catalysis of ROS-producing chemical reactions are peroxidases, NADPH oxidase, xanthine oxidase (XO), glucose oxidase, lipoxygenases (LOXs), cyclooxygenases (COXs), nitric oxide synthase and myeloperoxidase (MPO) (Bhattacharyya *et al.*, 2014). The equations for these enzymes' operations that produce free radicals are depicted in Figure No. 1.

Numerous environmental factors are contributing of oxidative stress. Pollutants in the air, radiations such as x-rays or neutrons, cigarette smoke, medicines, foods, and xenobiotics can all cause oxidative stress (Mena *et al.*, 2009; Poljšak & Fink, 2014). In addition, chemical agents including quinones, organic solvents; heavy metals and pesticides are common exogenous sources of ROS (Chung *et al.*, 2006; Phaniendra *et al.*, 2015). Figure No. 2 illustrates a variety of endogenous and exogenous sources, with an emphasis on the references most relevant to the GI tract.

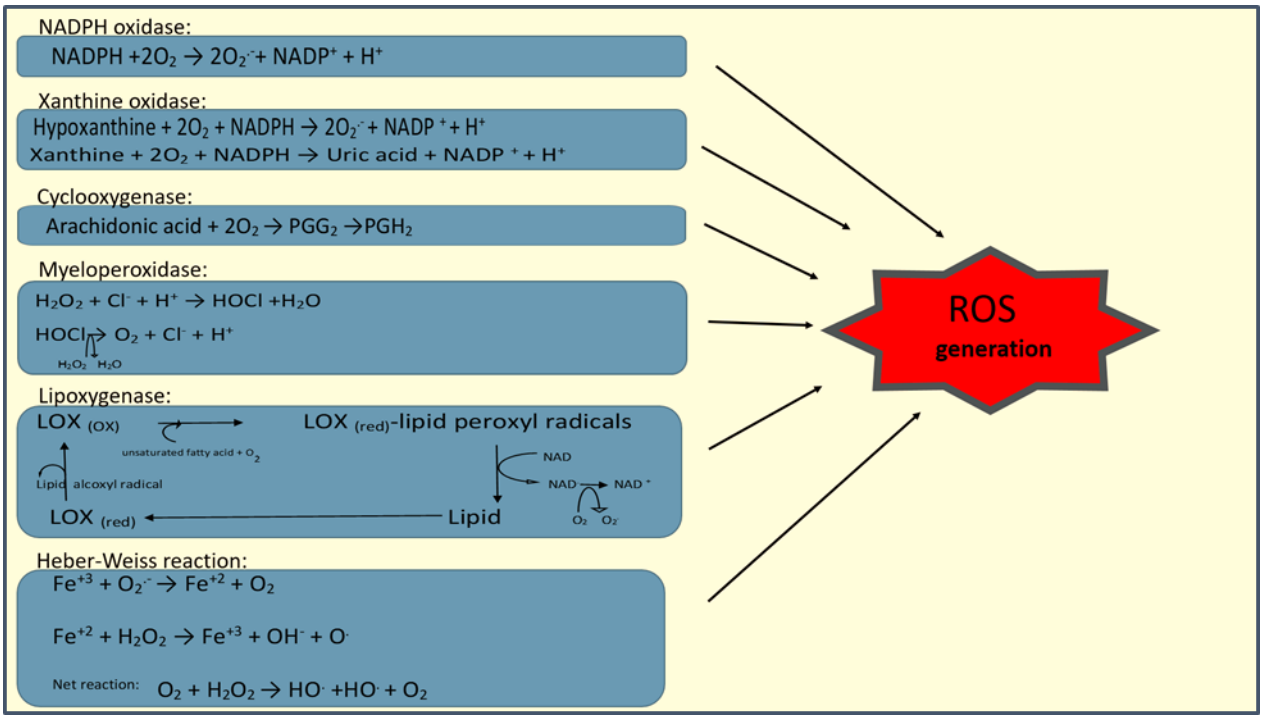

Figure No. 1
The equations of the enzymes involved in catalysis of ROS-generating chemical reactions

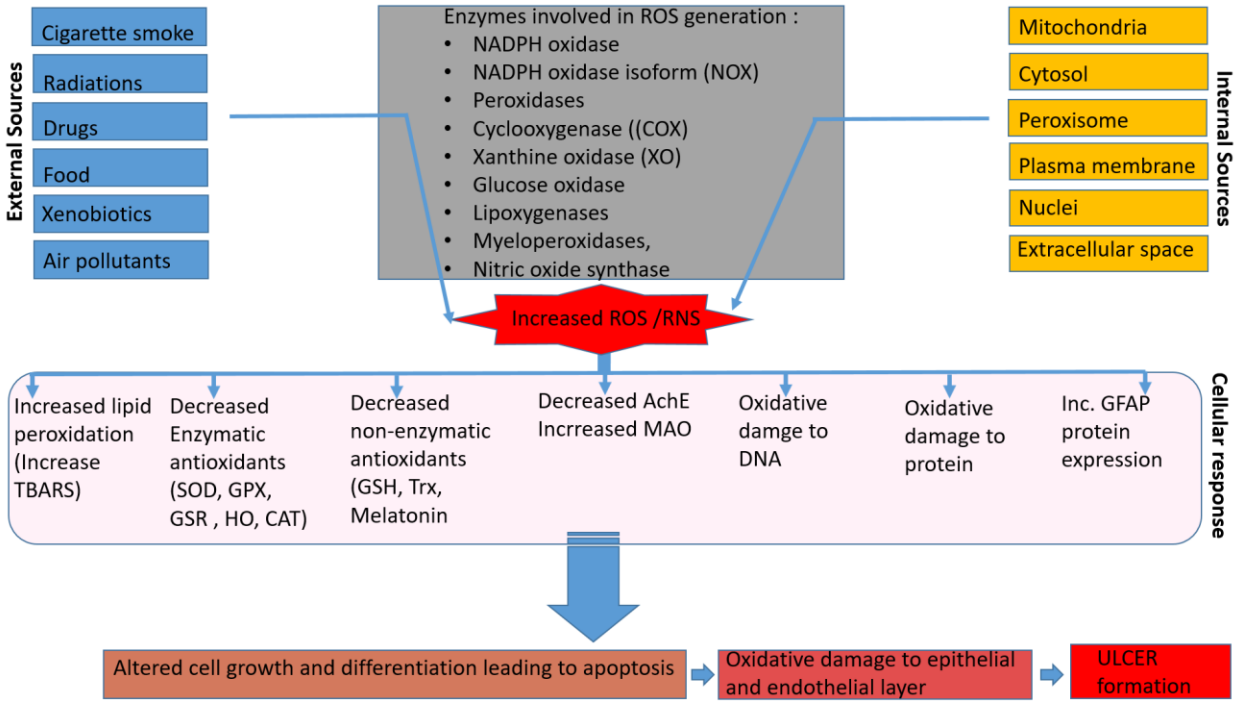

Figure No. 2
Sources of ROS and enzymes involved in oxidative stress and cellular oxidative damage

Defensive system against Reactive Oxygen Species

The ability of human and other living organismic cells to carry out oxidation reactions during metabolic activities is critical. Several ROS are generated during the oxidation processes, which are then inactivated by antioxidants to keep their levels within a certain range in the body. The excessive generation of ROS is extremely harmful to biological molecules (Di Meo & Venditti, 2020; Yang & Lian, 2020). Because antioxidants guard against the detrimental effects of ROS and restore the redox antioxidant balance, the live body can only withstand a limited amount of oxidative stress (Abdel-Saeed & Salem, 2019; Abdoon *et al*., 2020; Elghobashy *et al*., 2020; Hussain *et al*., 2021a; Liu *et al*., 2021; Mushtaq *et al*., 2021; Sayyar *et al*., 2021).

The antioxidative defense system, which comprises both enzymatic and non-enzymatic antioxidants, is made up of several defensive antioxidants molecules. However, this antioxidative defense mechanism has a low capabilities to eliminate ROS. If the ROS level surpasses an unacceptable threshold, the antioxidative defence system will be unable to eliminate all ROS, resulting in oxidative stress and oxidative deterioration of important biological components in cells such as DNA, proteins, and lipids presented in Figure No. 2 (Surai *et al*., 2019). External antioxidant substances can also aid in the removal of free radicals from the body. Natural medicinal plants contain antioxidant properties such as vitamin A, vitamin E, flavonoids, carotenoids, phenols, and tannins (Lobo *et al*., 2010).

Endogenous antioxidants

These antioxidants are of two forms enzymatic and non-enzymatic antioxidants.

Enzymatic antioxidants

These include glutathione peroxidase, superoxide reductase, catalase, glutathione-reductase, and superoxide dismutase. Among these antioxidants superoxide dismutase, glutathione peroxidase (GPX) and catalase (CAT) are considered as first-line antioxidants against ROS (Ighodaro & Akinloye, 2018).

***Superoxide dismutase* (SOD)**

SOD are enzymes requiring metal ion cofactor. Human body is composed of three isoforms of SOD: manganese-requiring mitochondrial enzyme (Mn-SOD), copper and zinc-containing enzyme (Cu-Zn-SOD) and Cu-Zn containing SOD (EC-SOD)

(Younus, 2018; Feng *et al.,* 2021).

***Catalase* (CAT)**
Catalase enzymes are mainly located in peroxisome and catalyze the dismutation of hydrogen peroxide to water and oxygen. In humans, the enzyme is found in a greater amount in erythrocytes, liver and kidney however, the catalase enzyme expressed in all organs of the body (Nandi *et al.,* 2019).

***Glutathione peroxidase* (GPX)**
The enzyme oxidizes glutathione (GSH) into glutathione (also called glutathione disulfide, GSSG) and simultaneously reduces H_2O_2 to H_2O and lipid hydroperoxides (ROOH) to respective alcohols. The GPX reaction is coupled to glutathione reductase (GSSG-R), which maintains reduced glutathione (GSH) levels (De Oliveira-Silva *et al*., 2019).

***Glutathione reductase* (GSR or GR)**
This enzyme is responsible for the reversible oxidation of glutathione disulfide (GSSG) to glutathione (GSH). GR protects haemoglobin and cellular membranes from oxidative stress by generating GSH (Couto *et al*., 2016).

***Heme oxygenase* (HO)**
Heme oxygenase (HO) enzyme is involved in the breakdown of heme and generates biliverdin, carbon monoxide and iron. There are two isoforms, HO-1 and HO-2. HO-2 is constitutively expressed, and HO-1 is inducible (Chen *et al*., 2019). HO-1 does not involve directly in antioxidant enzymatic function, against oxidative stress (Vanella *et al.,* 2012).

Non-enzymatic antioxidants
***Glutathione* (GSH)**
It is mainly found in reduced form. In gastric mucosa, it performs the function of antioxidant barrier. The level of GSH is much higher in the gastric tissues providing additional protection against effects of gastric acid (Kwon *et al.,* 2019). The *H. pylori* infection-induced inflammation further enhance the production of ROS. However, mucosal damage by free radicals is prevented by local glutathione (Matthews & Butler, 2005).

Melatonin
Melatonin is a hormone that is secreted by the pineal gland but is also found in lymphocytes, bone marrow, the GI system, and the retina (Tordjman *et al.,* 2017). It can also be present in yeast, oats, and other plants. It deactivates the hydroxyl and peroxyl radicals. This hormone has been irreversibly oxidised and cannot be returned to its original state. As a result, it is known as a deadly or suicide antioxidant (Moniruzzaman *et al*., 2018; Tan *et al*., 2000). Melatonin's anti-inflammatory benefits in animal research and limited human studies show that supplementary melatonin may be beneficial in colitis (Terry *et al*., 2009; Zhao *et al.,* 2021).

***Thioredoxin* (Trx)**
The thioredoxin complex system is composed of thioredoxin (Trx) and thioredoxin reductases (TrxR). Trx is an oxidoreductase containing disulphide group and is involved in regulating redox-sensitive transcription factors activity. Thioredoxin binding protein-2 (TBP-2) is also considered as a regulator of Trxand involved in the negative regulation of Trx. The TBP-2 also performs regulatory functions in cellular redox reactions (Ghareeb & Metanis, 2020).

Exogenous antioxidants
***Vitamin* C**
Vitamin C or ascorbic acid is obtained from fresh vegetables and fruits. Vitamin C prevents the oxidation by donating electrons to free radicals and several species are reduced by it including ROS, HOCl, sulfur radicals, O_3, RNS (Kaźmierczak-Barańska *et al.,* 2020; Namratha *et al*., 2021).

Carotenoids
Food-derived vitamin A is known as provitamin A or carotenoid. Fruits and vegetables with green leaves are potential sources of carotenoids (Larsson *et al.,* 2007). Beta-carotene has been found in mouse studies to reduce lipid peroxidation (Hosseini *et al.,* 2010; Toti *et al.,* 2018).

***Vitamin* E**
It is an ubiquitous and vital antioxidant that prevents lipid peroxidation and so protects cell membranes (Ni & Eng, 2012). Alpha tocopherol is the most physiologically active form of vitamin E (Huang *et al.,* 2002). Vitamin E inhibits lipid peroxidase activity by destroying lipid peroxyl radicals (LOO) (Ni & Eng, 2012). As a pro-oxidant, vitamin E is also implicated in the reduction of Fe or Cu (Floridi *et al*., 2009).

Minerals
Manganese (Mn), iron (Fe), copper (Cu), selenium (Se) and Zinc (Zn) are essential components of

antioxidant enzymes and are known to be antioxidant micronutrients. Among these minerals Mn, Cu and Zn are essentially considered as ionic cofactors of superoxide dismutase (Cu/Zn-SOD) (Wolonciej *et al.*, 2016).

Antioxidants medicinal plants

In recent years, medicinal plants have gained special attention of scientific community in treating various diseases and disorders of both humans and animals (Al-Sarraj, 2021; Ashraf *et al*., 2021; Hussain *et al*., 2021b; Majeed *et al*., 2021; Moryani *et al*., 2021; Murtaza *et al*., 2021; Rafay *et al*., 2021; Rehman *et al*., 2021; Wajiha & Qureshi, 2021; Aidy *et al*., 2022; Doudach *et al*., 2022; Naseer *et al*., 2022; Saif *et al*., 2022). The extracts of medicinal plants comprising of standardized contents of flavonoids, tannins, polyphenols, vitamins and minerals have been investigated for their total antioxidant activity and these medicinal plants have also been reported for the treatment of gastric ulcer by ameliorating the oxidative stress in the body (Table No. 1). The potential therapeutic candidates have also been described below along with their antioxidant mechanism of action against peptic ulcer.

Mimosa pudica

Mimosa pudica belongs to the family, Fabaceae. The English name of this plant is 'touch me not'. It belongs to tropical countries and several subtropical regions. The phytochemical constituents of *M. pudica* are quercitin, saponins, flavonoids, tannins, mucilage, naringin. For the treatment of intestinal ulcers, the decoction of the seeds and leaves is consumed. The fresh leaves of *M. pudica* have been indicated to have gastroprotective, anti-ulcer and antioxidant activity of extracts of the leaf may assist in treating the ulcer. Alkaloid mimosine is considered as the active constituent of the plant (Vinothapooshan & Sundar, 2010). In another research study, the antioxidant activity of aqueous extract and ethanolic extract of *M. pudica* leaves was evaluated in ethanol-induced and pylorus ligation induced gastric ulcers. The results indicate that ethanolic extract significantly increased gastrointestinal pH and antioxidant enzymes such as CAT, SOD and decrease the lipid peroxidation indicated by reduced content of MDA with respect to control (Momin *et al*., 2011).

Zingiber officinalis and Zingiber zerumbet

Zingiber officinalis and *Zingiber zerumbet* belong to the family, Zingiberaceae and the English name is Ginger. The main pungent compound is 6-gingerol, which shows various pharmacological activities. The extract of *Z. officinalis* also contains gingerols which inhibit prostaglandin E2 (Banerjee *et al.*, 2011). The active phenolic compounds, including zingerone and gingerol, inhibiting parietal cell H^+, K^+-ATPase, play an important role in proton pump inhibition and decrease gastric acid secretion. *Z. officinalis* plays a protective role against *Helicobacter pylori* induced ulcers (Siddaraju & Dharmesh, 2007).

It also acts as a natural antioxidant against gastric ulcers (Jiang *et al.*, 2008). Moreover, extract also recovered the 2.6 fold increased level of thiobutyric acid reactive substance (TBARS) levels indicating the decrease in lipid peroxidation or damage to ulcerous tissue (Dharmesh *et al*., 2011)

Moreover, Sidahmed *et al.* (2015), indicated that *Z. zerumbet* played an important role as a gastroprotective agent in an ethanol-induced gastric ulcer rat model. It was demonstrated that prophylactic treatment with omeprazole or zerum bone in rats decreased ulcer area significantly in comparison to the ulcer control group.

Camellia sinensis

Camellia sinensis belongs to the family, Theaceae and the English name is Tea plant. *Camellia sinensis* is the most common beverage used. Among several green tea constituents, epigallocatechin gallate and polyphenol suppress the expression of tumor necrosis factor-alpha gene (Fujiki *et al.*, 2002). An investigation on *Camellia sinensis* extract indicated that the extract assists in treating *H. pylori*-related peptic ulcers by inhibiting the urease enzyme of the bacterium, hence inhibiting bacterial colonization (Matsubara *et al.*, 2003). Several other *in-vivo* studies inferred the inhibiting effect of plant extract on ulcer formation by enhancing cell vacuolation by vacuolating cytotoxin A and urea conduction in *H. pylori* infection and prevent gastric ulcer (Ruggiero *et al.*, 2007).

Rao *et al.* (2008), demonstrated the protective activity against gastric ulcers of *Ficus glomerata* fruit in gastric ulcer rat models. The fruit was given per mouth at a dose of 50, 100, and 200 mg/kg body weight, twice daily for five days for prevention against ulcer formation by alcohol and cold stress. The study reported a dose-dependent reduction of ulcer and prevention from the oxidative damage of gastric mucosa as antioxidant agent. The study results indicated that *F. glomerate* has gastroprotective potential contributed by gastric defense factors (Rao

et al., 2008).

In another study, hydroalcoholic extract of green tea (*Camellia sinensis* L.) was observed on chronic gastric ulcers of rats. It was found that extract prevented the reduction of the level of glutathione (GSH) and reduced the content of lipid hydroperoxide (LOOH). Moreover, the extract administration restored the SOD activity as compared to control group (Borato *et al.*, 2016).

Aloe barbadensis

Abarbadensis belongs to the family, Liliaceae and its English name is "aloe vera". The constituents of the plant are isobarbaloin, aloin and emodin whereas the active chemical constituents include isobarbalin, sponins and barbalin. The aloe gel extracted from the leaves was used to treat ulcerative colitis in rats. The aloe vera gel treated the acetic acid-induced ulcerative colitis in rat models and produce anti-inflammatory, antioxidant and wound healing effects. Moreover, the gel also boosts the immune system of animals (Subramanian *et al.*, 2007).

Aloe vera was compared to omeprazole and cimetidine, to determine the most potent therapeutic drug. The anti-ulcer effect was observed by administering the drugs to ulcerative model in rats and it was inferred that aloe vera showed greater healing potential than cimetidine and omeprazole as no traces of ulcer were noticed in the stomach of animals after 7 days of treatment (Sai *et al.*, 2011). The antiulcer and antioxidant activity of *Aloe vera* juice was determined in ethanol-induced ulcerated rat models. The administration of plant gel decreased ulcer index and acid secretion and increased activity of oxidative enzymes including reduced glutathione and superoxide dismutase. In addition, Plant also reduced the activity of alkaline phosphatase and lipid peroxidase enzyme treatment. The results of the study showed that the gel has good efficiency to treat gastric ulcer (Subramanian *et al.*, 2007).

Curcuma longa

Curcuma longa belongs to the family, Zingiberaceae with English name turmeric. The plant possesses anti-inflammatory and antioxidant potential and is involved in down regulation of proteins encoding genes, which play an important role in acute inflammation. The phytochemical constituents are involved in reducing gastric acid secretion and inhibiting the pro-inflammatory cytokines like tumor necrotic factor-alpha (TNF-a) (Salehi *et al.*, 2017). Mahattanadul *et al*. (2006), reported in their study that *C. longa* rhizome protected the formation of acid reflux esophagitis.

On the other hand, when used in combination with dimethyl sulfoxide, it reduced the esophagitis ulcer index to almost that of lansoprazole drug (Mahattanadul *et al.*, 2006). Herbal drugs can be useful for suppressing and preventing *H. pylori*-related ulcerative infection. Therefore, *C. longa* plant products have revealed as strong antioxidants bearing potential to treat gastric diseases (Langmead & Rampton, 2001; Amalraj *et al*., 2017).

Asparagus racemosus

Asparagus racemosus belongs to the family, Asparagaceae and the English or common name is 'curer of hundred diseases'. The habitat of *A. racemosus* is tropical and subtropical dry and deciduous forests. Significant parts of the plant used for the extraction of chemical constituents are tuberous roots and shoots. The major phytochemical constituents having healing potential are steroidal saponins like Shatavarin (Alok *et al.*, 2013).

The roots of the plant contain four types of shatavarin, including Shatavarin I–IV. Additionally, quercitin-3-glucorinide, rutin, stigmasterol, sitosterol and several unidentified saponins are also present (Goyal & Sairam, 2021). The plant's tubers are used as an aphrodisiac, cooling agents, diuretic, tonic and demulcent and are applied for the synthesis of various medicated oils. The mixture of fresh juice of the plant roots with honey is also given to treat gastrointestinal disorders. The powder of roots is employed to enhance the strength and vigour and as an antiulcerogenic agent (Mazumder *et al.*, 2008). The antioxidant effect of the plant was evaluated in swim (restraint) stress and indomethacin (NSAID) induced ulcerous model of rats. The administration of plant improved the antioxidant defense system by increasing the level of catalase, superoxide dismutase and ascorbic acid and by decreasing lipid peroxidation (Bhatnagar *et al.*, 2005; Sabiu *et al.*, 2016).

Annona squamosa

Annona squamosa belongs to the family, Annonaceae and the English name is sugar apple tree. *A. squamosa* is a deciduous tree growing at an altitude of 5-10 m**.** It is located throughout the Philippines and Americas. The tree is commonly growing in secondary forests at low and medium altitudes. The barks of the tree hold a large quantity of tannic acid. The pulp of the fruit contains extractive matters, gum,

ash and sugar. Bark also contains a principle constituent similar to 'cathartin'. The parts mostly used for the pharmacological purpose are seeds, bark, fruit and leaves. The bark powder is used to treat mouth ulcers. The juice of bark is added to coconut milk and is given to boot out colicky pains. These barks are also brushed to strengthen the teeth. Leaves are used for treating headache gastric pain and gastric ulcer. The stem-bark extract is applied for an antidiarrheal purpose with cathartin (Suleiman *et al.*, 2008).

The aqueous extracts of *A. squamosa* were investigated for antiulcer activity in aspirin 7801 plus pyloric ligation induced gastric ulcer models of rats. The antioxidant activity of plant extracts was determined by *in vitro* assays such as nitric oxide scavenging activity and lipid peroxidase inhibiting assay. The extract showed the potential to significantly scavenge nitric oxide and inhibited the lipid peroxidation (Dos Santos & Sant'na, 2001)

Azadirachta indica

Azadirachta indica belongs to the family Meliaceae with English name neem. It is an evergreen medicinal plant and grown throughout India and in several countries of Africa. It is typically grown in tropical and semi-tropical regions of the world. It is a native tree of India and is studied to be part of India's genetic biodiversity. Nowadays, the tree is also cultivated in the western hemisphere's tropical areas and several countries of Asia. The tree exhibits furrowed, short, dark brown to grey bark and pinnate leaves. The main chemical constituent of neem with pharmacological properties is 'azadirachtin'. It is used to prepare a neem-based pesticide that is natural, biodegradable, environment friendly and safe at the farmer's level. Many other chemical compounds found in the neem tree, including nimbin, nimbidol, nimbidin, quercetin and sodium nimbinate. However, nimbin provides antioxidant, antihistamine, antipyretic, antifungal and anti-inflammatory properties. Neem seed oil is composed of a large percentage of active compounds combined with several fatty acids including stearic acid, palmitic acid, oleic acid, linoleic acid and so on. Whereas, less amount is also present in bark and leaves of neem tree. Nimbidin contains anti-ulcer, antifungal, analgesic, antibacterial and antiarrhythmic properties. Nimbidol shows antipyretic, antitubercular and antiprotozoal properties. Sodium nimbinate exhibits spermicidal, antiarthritic and diuretic properties. At the same time, quercetin contains antioxidant, antiprotozoal, antibacterial and anti-inflammatory properties (Nathan *et al.*, 2005; Veitch *et al.*, 2007; Alzohairy, 2016). The plant protects against oxidative damage of gastric mucosa by inhibiting lipid peroxidation and by removing the endogenous hydroxyl radical, a major factor for causing ulcer. Moreover, the *in-vitro* study indicated that bark extract of the plant also protected the gastric mucosal DNA from harmful effect of hydroxyl radical (Bandyopadhyay *et al*., 2002).

***Alstonia* spp.**

Alstonia spp. belongs to the family Apocynaceae and the English name is devil tree. *Alstonia* spp. comprises 40-60 species and grows mostly in the Malaysian region native to the tropical and subtropical areas. The trees can grow quite long, as *A. pneumatophore* may grow to 60 m in height. *Alstonia longifolia* species is mostly located in Central America. The active constituents include coumarins, phlobotannins, reducing sugars, alkaloids, simple phenolic, steroids, flavonoids, and saponins. The percentage of lipids and saponins are more significant than other agents. Several compounds are found in *A. scholaris* which may make the plant pharmacologically valuable for the cure of various diseases. It was reported that the antioxidant potential of *A. scholaris* was because of the presence of phenolic compounds. Flavonoids are polyphenolic compounds that are involved in scavenging of free-radical, hydrolytic enzyme inhibition and anti-inflammatory activity. The plants' flavonoids and saponins are used in treating peptic ulcers and dysentery (Antony *et al.*, 2011). The antioxidant activity of the plant was evaluated by determining lipid peroxidation. The extract of *A. scholaris* leaves in ethanol, showed significant antioxidant activity by reducing lipid peroxidation (Vanita & Deepali, 2019).

Moringa oleifera

Moringa oleifera belongs to the family Moringaceae and the English name is horseradish tree. The plant grows naturally in the Western and sub-Himalayan regions and countries like Pakistan, Arabia, Africa, Asia Minor and India. The plant's principal chemical constituents are saponins, tannins, kaempferol, flavonoids, alkaloids, zeatin, quercetin, and terpenoids (Subitha *et al.*, 2011). The principal constituents of the plant are beta carotene, beta sitosterol and quercetin. In folklore medicine, this plant has high pharmacological importance. The leaves of *M. oleifera* are consumed to treat peptic

ulcers, especially by Indian people. Flower buds of the plant are extensively used in Pakistan and indicated to prevent peptic ulcer formation (Subitha *et al.*, 2011).

The antioxidant activity of *M. oleifera* was determined. It was found that oxidative stress markers (MDA) increased significantly and the antioxidant biomarkers (GST, SOD and GPX) decreased significantly as compared to control group. It was inferred that *M. oliefera* leaves extract has good antioxidant and antiulcer activities and the extract has the potential to scavenge free radicals and protect against gastric ulceration (Almuzafar, 2018).

Myrtus communis

Myrtus communis belongs to the family Myrtaceae and the English or common name is Myrtle. It is cultivated in tropical, subtropical, mediterranian and temperate regions of the world. The plant's chemical constituents are present in ripe berries composed of Myrtle's oil (essential oil), citric acid, resin, tannin, sugar and malic acid. Powdered leaves are useful to cure ulcers and wounds. The fruit, Myrtle berry, is considered as carminative and administered for treatment of internal ulceration (Sisay & Gashaw, 2009). A topical dosage form of *M. communis* was applied for wound healing activity in rat excision wounds (Rezaie *et al.*, 2012). *M. communis* fruits were used to prevent peptic ulcers associated to indomethacin, ethanol and pylorus ligation in rat model via suppression of gastric acid and other secretions. The main active constituent considered for antiulcer activity is oil of Myrtle (Sumbul *et al.*, 2010).

In vitro study indicated that myrtle berry seed extract was rich in total polyphenols and anthocyanins hence, showing antioxidant activity. *In vivo* study on the plant showed antioxidant activity by increasing hydrogen peroxide (H_2O_2) and free iron levels. Moreover, myrtle berry seed extract also regulates other intracellular mediators (Sebai *et al.*, 2014).

Psidium guajava

Psidium gujava belongs to the family Myrtaceae and the English name is Guava. This tree is grown throughout India and Bengal. It's tree is native to central America and is present in tropical and subtropical regions throughout the world. The chemical constituents present in the plant are crystals of calcium oxalate, resin and tannins. Leaves are composed of fat, resin, tannin, volatile oil, mineral salts, chlorophyll and cellulose. The active constituents of *P. guajava* include guaijaverin, galactose-specific lecithins, quercetin and flavonoids. The decoction of the leaves of the plant is employed to treat ulcers and is an effective gargle for mouth ulcers and swollen gums. Methanol leaf extract was administered orally to rats for 10 days to treat ethanol-related peptic ulcers. The extract significantly reduced ulcer symptoms when compared to the control group (Uduak *et al.*, 2012).

The free radical scavenging potential of extract of *P. guajava* in ethanol was investigated by 2, 2-diphenyl-1-picrylhydrazyl (DPPH) and nitric oxide radical inhibition assays. It was concluded from results that the plant has significant free radical scavenging property because of the presence of flavonoids. As the bioflavonoid mostly show the potential of the gastric protection through inhibition of free radicals (Jayakumari *et al.*, 2012).

Sesbania grandiflora

Sesbania grandiflora belongs to family Fabaceae. *It* is a decorative plant and is grown at Western Himalayas plains and Sri Lanka. The chemical constituents of the plant include tannins, saponins and triterpenes. Active constituents include saponins and tannins. The leaves of the plant are employed to prepare soup and taken orally in several countries especially in India for healing peptic ulcer. The decoction of leaves is administered orally as vermifuge. The leaves are taken and boiled in the milk of cow and then administered orally in Kikuku village of Tanzania, for healing gastric ulcers. Moreover, the leaves are first boiled in water and then administered by mouth to cure ulcer by Paliyar tribals of India (Alahakoon & Ganegoda, 2019).

An ethanol extract of *S. grandiflora* leaves was given orally to rats to cure aspirin, ethanol, and indomethacin-related peptic ulcers (400 mg per kilogramme body weight). The extract stopped gastric mucosal layer damage and dramatically lowered stomach acid output (Bhalke *et al.*, 2010).

Antioxidant effect of the hydroalcoholic extract of the plant was evaluated against the acetic acid induced ulcerative colitis mice. The extract containing polyphenols and flavonoids showed potent antioxidant activity by restoring the normal levels of MDA GSH, SOD, MPO, and NO. Hence the plant showed a potent protective effect against ulcerative colitis (Gupta *et al.*, 2018).

Shorea robusta

Shorea robusta belongs to the family Dipterocarpaceae and the English name is Sal tree. It is commonly grown at sub-Himalayan sections and the Western Bengal forests. The chemical constituents of the plant include trihydroxy ursenoic acid and tetrahydroxy ursenoic acid, alpha amyrin, asiatic acid, beta amyrin, ursolic acid, mangiferonic acid and uvaol. The active constituents of *S. robusta* are amyrin and ursolic acid. The ointment of a mixture of *S. robusta*, cinnabar, calamus draco, ghee and mastiche employed for foetid ulcers (Singh & Kumar, 2018). In a study, *S. robusta* extract was administered orally to pylorus ligation induced and the ethanol-induced ulcerative rats. It was found that the extract provided significant protection against gastric ulcer (Santhoshkumar *et al.*, 2012).

S. robusta includes natural resins that are efficient therapeutic components for ulcer therapy. The gastroprotective activity of *S. robusta* resin was tested in two doses on rats suffering pyloric ligation and ethanol-induced gastric ulcers.The results indicated that pretreatment with the resin of the plant prevented gastric mucosal damage and normalize the antioxidant markers (catalase (CAT), glutathione peroxidase (GPx), glutathione-S-transferase (GST), lipid peroxidation (LPO) and superoxide dismutase (SOD) in ethanol-induced model (Santhoshkumar *et al*., 2012).

Solanum nigrum

Solanum nigrum belongs to the family Solanaceae and the English name is black nightshade berries. The plant is found all over India. The principal active constituents are saponins, phytosterol, flavonoids, and alkaloids. The fresh leaves are used for the cure of intestinal ulcer by Paliyar tribals of the Indian region (Mayilsamy & Rajendran, 2013). *S. nigrum* leaf extract in water was given to rats to protect them from pylorus ligation, which causes peptic ulcers (Shree *et al.*, 2012).

In another study, the *S. nigrum* extracts were evaluated for determining gastro-protective and anti-oxidant activity in indomethacin-induced and pylorus ligated induced gastric ulcerative models of rats. *S. nigrum* pretreatments significantly elevate SOD activity and GSH as well as NO contents as compared to gastric ulcerative control group. Moreover, the extract significantly reduce MDA content as compared to gastric ulcerative control group. Hence, it was inferred from results that *S. nigrum* protected against gastric-ulceration (Zaghlool *et al.*, 2019).

Tamarindus indica

Tamarindus indica belongs to the family *Caesalpiniaceae* and the English name is Tamarind tree. It is an evergreen tree, native to South India and is grown in Burma, Pakistan and India. The plant is composed of malic acid, tartaric acid, acetic acid and citric acid, invert sugar, pectin and gum. Seeds are composed of fat, albuminoids, fibre whereas, the fruit contains traces of oxalic acid and tannins. The tannins in the plant are considered to be active constituents in this plant. The decoction of the plant leaves is consumed as a wash against indolent ulcers and enhances the ulcer healing activity. In a study, the extract of seed in methanol considerably decreases the secretion of gastric juice in the ulcer model of rats compared to control (Kalra *et al.*, 2011). A study examined at the antioxidant capabilities of plant extracts derived from the stem, bark, androots. Plant extracts were examined for phosphor molybdenum (PM), hydrogen peroxide, and PPH radical scavenging to determine their antioxidant activity. According to the findings, the antioxidant potential of both plant extracts was similar. As a result, both extracts exhibited high antioxidant activity (Borquaye *et al.*, 2020).

Terminalia chebula

Terminalia chebula, sometimes known as myrobalan, is a combretaceae plant. It grows in the Northern Indian and Bengal woods. The chemical components of the plant include lucilage, a colourant (brownish yellow), tannic acid, gallic acid, and chebulinic acid. Chebulinic acid, tannins, sorbitol, and gallic acid are among the bioactive ingredients of *T. chebula. Triphala* ash is applied in powder form on syphilitic ulcers to remove the ulcer exudates. Fine powder is mixed with dry *T. chebula* catechu and myrobalans, and then rubbed into a thick paste with blending oil or ghee to make ointment for wounds with chronic wounds and ulcers (Jantrapirom *et al.*, 2021). *T. chebula* methanolic solution was given orally to patients with gastric ulcers at dose rates of 250 and 500 mg per kilogramme body weight, and it cured and reduced the ulcer's symptoms (Raju *et al.*, 2009). *T. chebula* fruit extract had substantial in vitro ferric-reducing antioxidant activity, and an in vivo examination of the extract revealed that administration with the plant's extract reduced oxidative stress indicators such as glutathione disulfide level and lipid peroxidation. As a result,

plants have a high potential for preventing oxidative damage (Saha & Verma, 2016).

Table No. 1
Potent antioxidant rich medicinal plants for the treatment of peptic ulcer

Botanical name	Extract/ part used	Active constituent	Animal model	Antioxidative mechanism	References
Alliaceae					
Allium sativum	Fresh juice and dried powder of garlic bulbs	Allicin, diallyl disulfide, Diallyl trisulfide	Indomethacin -induced gastric ulcer in rats	Elevated SOD and CAT activity, lowered MDA conc.	Azamthulla *et al*., 2009 Tope *et al*., 2014 Martins *et al*., 2016
Anacardiaceae					
Mangifera indica	Ethanolic extract of seed and kernel powder	Anthocyanins and flavonoids	Acid alcohol-induced ulcer in rats	Reduced LPO activity, increased GSH and SOD activity	Prabhu & Rajan, 2015
Asteraceae					
Artemisia campestris	Aqueous extract	Limonene, myrcene, β-phellandrene, α-pinene	Aspirin induced gastric ulcer in rats	Increase SOD, CAT and GPX activity and decrease H_2O_2 and free iron levels	Sebai *et al*., 2014
Matricaria chamomilla	hydroalcoholic extract	α-Bisabolol chamazulene	ethanol-induced gastric mucosal injury	Significantly decreased the content of MDA, and increased GSH, Serum β-carotene and retinol levels at 200 mg/kg dose of extract	Cemek *et al*., 2010 Singh *et al*., 2011
Apiaceae					
Foeniculum vulgare	Aqueous extract	anethole and d-fenchone	Ulcer induced in rats	significantly reduce MDA concentartion, and β-carotene, nitrate, retinol, GSH, and ascorbic acid, levels increased.	Birdane *et al.*, 2007
Basellaceae					
Basella alba	ethyl acetate extract of leaves	Kaempferol	Ulcerated rats	Reduce antioxidant enzymes level such as lipid peroxidase and SOD, whereas increase CAT and GPX level	Jaiswal & Rao, 2016
Brassicaceae					
Brassica oleracea	Broccoli extract	sulforaphane	acetylsalicylic acid– induced gastric ulcer in rats	increased SOD activity, GSH-PX activity, total antioxidant status, total thiolnitric oxide levels, endothelial nitric oxide synthase,	Zeren *et al*., 2016

				dimethylargininedimethylaminohydrolases, nuclear factor erythroid 2–related factor 2, and HO-1 expressions	
Burseraceae					
Protium heptaphyllum	Burseraceae	α-pinene, terpinolene, α-phellandrene, limonene, sesquiterpenes	ethanol, nonsteroidal anti-inflammatory drugs and acetic acid induced ulcer in male wistar rats	increase the GSH and GR levels and maintained the same levels of SOD and GPX	Araujo *et al.,* 2011
Caricaceae					
Carica papaya	Alcoholic extract of dried fruits	Vit. C, vit, B, flavonoids, folate, pantothenic acids	Pylorus-ligated and aspirin-induced ulcer in rats	Antioxidant activity by decreasing MDA levels and increasing the activity of GSH, SOD and CAT	Rajkapoor *et al.,* 2003 Sadek, 2012
Euphorbiaceae					
Croton macrostachyus	Methanol extract	Flavonoids phenolic compounds	Induced ulcer in odents	antioxidant, anti-inflammatory activity	Mekonnen *et al.,* 2020
Fabaceae					
Libidibia ferrea	Dry extract of pods	Galloylquinic acid	acetic acid-induced chronic ulcer model.	reduce the DPPH radical and eliminate 2,2-Azino-bis (3-ethylbenzothiazoline-6-sulfonate) (ABTS) radical	Prazeres *et al.,* 2019
Lamiaceae					
Mentha piperita Mentha haplocalyx	menthol	Menthol	ethanol-induced gastric ulcers in rats.	Decrease the activity of myeloperoxidase MPO and SOD, and increase the protein levels of GSH, GSH-PX and GSR. It also decreases the levels of TNF-α and IL-6	Rozza *et al., 2*014
Mimosaceae					
Acacia catechu	Aqueous or 95% ethanolic extracts of heartwood and roots	Flavonoids (catechin) and tannins	Aspirin + pylorus-ligated model, absolute alcohol-induced models in rats	Antioxidant activity by H^+ donation, superoxide scavenging and acting as reducing agent	Alambayan *et al.,* 2015 Kumar *et al.*,2017

Malvaceae					
Althaea officinalis	Aqueous extract of flowers	flavonoids and mucilage	pyloric-ligation and indomethacin-induced gastric-ulcer model in rats	Antioxidant activity, pretreatment expressed a significant increase in GSH, and NO levels and SOD activity reduce pro-inflammatory cytokines formation like TNF-α and IL-1β	Zaghlool *et al.*, 2019
Abelmoschus esculentus	Aerial parts	Flavonoids (quercetin) and carotenoids	Ethanol-induced gastric ulcer in Wistar rats	scavenging activity toward hydroxyl and peroxyl radicals and superoxide anions	Abourehab *et al.*, 2015 Ortaç *et al.*, 2018
Abutilon indicum	Leaves	Quercetin, alkaloids, saponins and tannins, starch, glycosides and flavonoids	Pylorus ligated and ethanol induced ulcer	NO inhibition and superoxide scavenging	Chakraborthy, 2009 Ardalani *et al.*,2019
Myrtaceae					
Corymbia citriodora	Ellagitannin rich fraction obtained from dry leaves	ellagitannin	ethanol-induced gastric ulceration in rats.	increase GSH and SOD levels in a dose-dependent manner	Al-Sayed & El-Naga, 2015
Phyllanthaceae					
Phyllanthus emblica	butanol extract of fruit	polyphenols (ellagic acid, chebulinic acid, gallic acid, quercetin)	Indomethacin induced model of ulcerous rat	SOD level remained unaltered while significantly decrease MDA content	Bandyopadhy *et al.*, 2000
Piperaceae					
Piper betel	Ethanolic extract	allylpyrocatechol	Indomethacin induced ulcer in male Sprague-Dawley rats	Antioxidant activity (Decreases ROS, as well as inhibits ROS/NF-κB dependent pathway within gastric tissue)	Bhattacharya *et al.*, 2007
Plumbaginaceae					
Plumbago auriculata	Ethanol extract	Flavonoids	Ulcerative model of animal	*In vitro* antioxidant activity assays including DPPH assay, Lipid peroxidase inhibition assay indicated positive results.	Ittiyavirah & Paul, 2016

Polygonaceae					
Rumex patientia	Aqueous extract	Rutin Kaempferol	Ethanol induced ulcer in rat model	Antioxidant action reduce ethanol-induced ulcer zone	Süleyman *et al.*, 2002
Puniaceae					
Punica granatum	Ethanol extract of dried peel	punicalagins and ellagitannin	Ulcer model of rats	Decrease free radicals lipid peroxidation (LPO and nitric oxide NO) and antioxidant enzymes SOD whereas, increase CAT and GSH	Chauhan *et al*., 2017
Rutaceae					
Citrus decumana	ethyl acetate extract	Naringin Naringenin	Ulcerative model in rats	Reduce TBARS and ulcer index and increase GSH, SOD and CAT in the blood and tissue samples	Sood *et al.*, 2010
Aegle marmelos	methanolic extract of unripe fruit	mucilage and marmelosin	Helicobacter pylori-Lipopolysaccharide (HP-LPS) induced gastric ulcer in Sprague Dawley (SD) rats	Antioxidant action prevented the reduction of antioxidant enzymes (SOD, CAT GSH-PX, GSR and glutathione transferase (GST)) and non-enzymatic antioxidants (reduced glutathione, vitamin C and vitamin E)	Ramakrishna *et al*., 2015
Vitaceae					
Cissus quadrangularis	Methanol extract of dried stem	Amino acids, carbohydrates, steroids, glycosides, saponins, phytosterols, tannins, polyphenols,triterpenoids	Aspirin-induced gastric ulcer in rats	Antioxidant activity by lowering TNF-α, IL-1β, reduced activity of NOS-2. Increased activity of SOD, CAT and GSH, lowered activity of LPO in mitochondria	Jainu & Devi, 2006 Srinivas *et al.*, 2013

CONCLUSION

A wide variety of medicinal plants have been reported for possessing antioxidant activity to the treat peptic ulcer. In this review, the scientific evidences proving the therapeutic potential of natural plants were explored from electronic databases. The specific plants have their effectiveness against peptic ulcer through antioxidant mechanism of action including enhancement of antioxidant enzymes (SOD, GSH, CAT etc) level and reduction of MDA level and inhibition of ROS/NF-κB dependent pathway. Studies on the antiulcer activity of the

investigated plants revealed that their extract possess significant antioxidant activity by scavenging free radicals and by restoring and maintaining the oxidative balance of the body.

REFERENCES

Abdel-Saeed H, Salem NY, 2019. Evaluation of total antioxidant capacity, malondialdehyde, catalase, proteins, zinc, copper and IgE response in ovine verminous pneumonia. **Int J Vet Sci** 8: 255 - 258.

Abdoon ASS, Attia MZ, El-Toukhey NE, Kandil OM, Sabra HA, Soliman SS. 2020. Effect of reproductive status and season on blood biochemical, hormonal and antioxidant changes in Egyptian buffaloes. **Int J Vet Sci** 9: 131 - 135.

Abourehab MAS, Khaled KA, Sarhan HAA, Ahmed OAA. 2015. Evaluation of combined famotidine with quercetin for the treatment of peptic ulcer: *In vivo* animal study. **Drug Des Devel Ther** 9: 2159 - 2169. **http://doi.org/10.2147/DDDT.S81109**

Aidy A, Bahmani M, Pirhadi M, Kaviar V, Karimi E, Abbasi N. 2022. Phytochemical analysis and antimicrobial effect of essential oil and extract of *Loranthus europaeus* Jacq. on *Acinetobacter baumannii*, *Staphylococcus aureus*, and *Pseudomonas aeruginosa*. **Kafkas Univ Vet Fak Derg** 28: 161 - 167. **http://doi.org/10.9775/kvfd.2021.26626**

Alahakoon C, Ganegoda GSS. 2019. Sesbania grandiflora the anti-ulcer effect: A review. **J Pharmacogn Phytochem** 8: 879 - 882. **https://doi.org/10.52711/0975-4385.2021.00029**

Alambayan J, Vats M, Sardana S, Sehrawat R. 2015. Evaluation of antiulcer activity of roots of *Acacia catechu* Willd. (Mimosoideae). **J Pharmacogn Phytochem** 79: 79 - 84. **https://doi.org/10.18203/2394-6040.ijcmph20214551**

Al-Sarraj FMB. 2021. A Review on the impacts of *Azadirachta indica* on multi-drug resistant extended spectrum beta lactamase positive of *Escherichia coli* and *Klebsiella pneumonia*. **Adv Life Sci** 8: 228 - 232.

Almuzafar HM. 2018. Effect of *Moringa oleifera* leaves extract on the oxidative stress and gastric mucosal ulcer induced by indomethacin in rats. **Afr J Biotechnol** 17: 51 - 56. **https://doi.org/10.5897/AJB2017.16272**

Alok S, Jain SK, Verma A, Kumar M, Mahor A, Sabharwal M. 2013. Plant profile, phytochemistry and pharmacology of *Asparagus racemosus* (Shatavari): A review. **Asian Pac J Trop Dis** 3: 242 - 251. **https://doi.org/10.1016%2FS2222-1808(13)60049-3**

Al-Sayed E, El-Naga RN. 2015. Protective role of ellagitannins from *Eucalyptus citriodora* against ethanol-induced gastric ulcer in rats: Impact on oxidative stress, inflammation and calcitonin-gene related peptide. **Phytomedicine** 22: 5 - 15. **https://doi.org/10.1016/j.phymed.2014.10.002**

Alzohairy MA. 2016. Therapeutics role of *Azadirachta indica* (Neem) and their active constituents in diseases prevention and treatment. **Evid Based Complement Alternat Med** 2016: 7382506. **https://doi.org/10.1155/2016/7382506**

Amalraj A, Pius A, Gopi S, Gopi S. 2017. Biological activities of curcuminoids, other biomolecules from turmeric and their derivatives: A review. **J Tradit Complement Med** 7: 205 - 233. **https://doi.org/10.1016/j.jtcme.2016.05.005**

Antony M, Menon DB, James J, Dev L, Veetil AKT, Thankamani V. 2011. Phytochemical analysis and antioxidant activity of *Alstonia scholaris*. **Pharmacogn J** 3: 13 - 18. **https://doi.org/10.5681%2Fapb.2013.061**

Araujo D, Takayama C, De-Faria FM, Socca EAR, Dunder RJ, Manzo LP, Luiz-Ferreira A, Souza-Brito ARM. 2011. Gastroprotective effects of essential oil from *Protium heptaphyllum* on experimental gastric ulcer models in rats. **Rev Bras Farmacogn** 21: 721 - 729. **https://doi.org/10.1590/S0102-695X2011005000117**

Ardalani H, Hadipanah A, Sahebkar A. 2019. Medicinal plants in the treatment of peptic ulcer disease: A review. **Mini Red Ved Med** 20: 662 - 702. **https://doi.org/10.2174/1389557520666191227151939**

Ashraf F, Sajid A, Khan B, Rahman HU, Khan S, Ullah S, Ullah Q, Rafiullah, Anwar M, 2021. Antiviral activity of *Withania somnifera* and *Curcuma longa* against foot and mouth disease virus. **Continental Vet J** 1: 25 - 31.

Balaban RS, Nemoto S, Finkel T. 2005. Mitochondria, oxidants, and aging. **Cell** 120: 483 - 495. **https://doi.org/10.1016/j.cell.2005.02.001**

Bandyopadhyay U, Biswas K, Chatterjee R, Bandyopadhyay D, Chattopadhyay I, Ganguly CK, Chakraborty T, Bhattacharya K, Banerjee RK. 2002. Gastroprotective effect of Neem (*Azadirachta indica*) bark extract: Possible involvement of H+-K+-ATPase inhibition and scavenging of hydroxyl radical**. Life Sci** 71: 2845 -

2865. **https://doi.org/10.1016/S0024-3205(02)02143-4**

Banerjee S, Mullick HI, Banerjee J, Ghosh A. 2011. *Zingiber officinale*:'a natural gold. **Int J Pharma Bio Sci** 2: 283 - 294. **https://doi.org/10.1016/j.ultsonch.2022.106048**

Bhalke RD, Giri MA, Anarthe SJ, Pal SC. 2010. Antiulcer activity of the ethanol extract of leaves of *Sesbania grandiflora* (Linn.). **Int J Pharm** 2: 206 - 208. **https://doi.org/10.52711/2231-5713.2022.00004**

Bhatnagar M, Sisodia SS, Bhatnagar R. 2005. Antiulcer and antioxidant activity of *Asparagus racemosus* Willd and *Withania somnifera* Dunal in rats. **Ann New York Acad Sci** 1056: 261 - 278. **https://doi.org/10.1196/annals.1352.027**

Bhattacharya S, Banerjee D, Bauri AK, Chattopadhyay S, Bandyopadhyay SK. 2007. Healing property of the *Piper betel* phenol, allylpyrocatechol against indomethacin-induced stomach ulceration and mechanism of action. **World J Gastroenterol** 13: 3705 - 3715. **https://doi.org/10.3748%2Fwjg.v13.i27.3705**

Bhattacharyya A, Chattopadhyay R, Mitra S, Crowe S. 2014. Oxidative stress: An essential factor in the pathogenesis of gastrointestinal mucosa diseases. **Physiol Rev** 94: 329 - 354. **https://doi.org/10.1152/physrev.00040.2012**

Birdane FM, Cemek M, Birdane YO, Gülçin I, Büyükokuroğlu E. 2007. Beneficial effects of *Foeniculum vulgare* on ethanol-induced acute gastric mucosal injury in rats. **World J Gastroenterol** 13: 607 - 611. **https://doi.org/10.3748%2Fwjg.v13.i4.607**

Borato DG, Scoparo CT, Maria-Ferreira D, Da Silva LM, De Souza LM, Iacomini M, Werner MFDP, Baggio CH. 2016. Healing mechanisms of the hydroalcoholic extract and ethyl acetate fraction of green tea (*Camellia sinensis* (L.) Kuntze) on chronic gastric ulcers**. Naunyn Schmiedebergs Arch Pharmacol** 389: 259 - 268. **https://doi.org/10.1007/s00210-015-1200-8**

Borquaye LS, Doetse MS, Baah SO, Mensah JA. 2020. Anti-inflammatory and anti-oxidant activities of ethanolic extracts of *Tamarindus indica* L. (Fabaceae). **Cogent Chem** 6: 174 - 182**.** **https://doi.org/10.1080/23312009.2020.1743403**

Cemek M, Yilmaz E, Büyükokuroğlu ME. 2010. Protective effect of *Matricaria chamomilla* on ethanol-induced acute gastric mucosal injury in rats. **Pharm Biol** 48: 757 - 763. **https://doi.org/10.3109/13880200903296147**

Chakraborthy GS. 2009. Antioxidant activity of *Abutilon indicum* leaves. **Int J Pharmatech Res** 1: 1314 - 1316**.**

Chauhan I, Sharma A, Gangwar M, Gautam MK, Singh A, Goel RK. 2017. Gastric antiulcer and ulcer healing effects of *Punica granatum* Peel extract in rats: role of offensive and defensive mucosal factors and oxidative stress. **Int J Pharm Sci** 9: 6 - 15. **https://doi.org/10.22159/ijpps.2017v9i5.9851**

Checa J, Aran JM. 2020. Reactive oxygen species: drivers of physiological and pathological processes. **J Inflamm Res** 13:1057-1061. **https://doi.org/10.2147%2FJIR.S275595**

Chen SD, Wang XY, Nisar MF, Lin M, Zhong JL. 2019. Heme oxygenases: Cellular multifunctional and protective molecules against UV-induced oxidative stress. **Oxid Med Cell Longev** 1: 1 - 17. **https://doi.org/10.1155/2019/5416728**

Chung MY, Lazaro RA, Lim D, Jackson J, Lyon J, Rendulic D, Hasson AS. 2006. Aerosol-borne quinones and reactive oxygen species generation by particulate matter extracts. **Environ Sci Technol** 40: 4880 - 4886. **https://doi.org/10.1021/es0515957**

Couto N, Wood J, Barber J. 2016. The role of glutathione reductase and related enzymes on cellular redox homoeostasis network**. Free Radic Biol Med** 95: 27 - 42. **https://doi.org/10.1016/j.freeradbiomed.2016.02.028**

De Oliveira-Silva JA, Pinto-Yamamoto JU, de Oliveira RB, Monteiro VCL, Frangipani BJ, Kyosen SO, Martins AM, D'almeida V. 2019. Oxidative stress assessment by glutathione peroxidase activity and glutathione levels in response to selenium supplementation in patients with mucopolysaccharidosis I, II and VI. **Genet Mol Biol** 42: 1 - 8. **https://doi.org/10.1590%2F1678-4685-GMB-2017-0334**

Dharmesh SM, Nanjundaiah SM, Annaiah HNM. 2011. Gastroprotective effect of ginger rhizome (*Zingiber officinale*) extract: Role of gallic acid and cinnamic acid in H+, K+-ATPase/H. pylori inhibition and anti-oxidative mechanism. **Evid Based Complement Alternat Med** 1: 1 - 13. **https://doi.org/10.1093/ecam/nep060**

Doudach L, Al-mijalli SH, Abdallah EM, Mrabti HN, Chibani F, El Abbes FM. 2022. Antibacterial evaluation of the roots of moroccan *Aristolochia longa* against referenced Gram-positive and Gram-negative bacteria.

Adv Life Sci 9: 116 - 121.
Di Meo S, Venditti P. 2020. Evolution of the knowledge of free radicals and other oxidants. **Oxid Med Cell Longev** 1: 1 - 32. **https://doi.org/10.1155/2020/9829176**
Dos Santos AF, Sant'Ana AEG. 2001. Molluscicidal properties of some species of Annona. **Phytomedicine** 8: 115 - 120. **https://doi.org/10.1078/0944-7113-00008**
Elghobashy KA, Eldanasoury MM, Elhadary AA, Farid M. 2020. Phytochemical constituent, HPLC profiling and antioxidant activity of *Passiflora incarnata* and *Arctium lappa* leaves extracts. **Int J Vet Sci** 9: 42 - 49.
Feng L, Yuxia C, Zichen W, Zipeng L, Ahmad MJ, Ming L, Tengyun G, Shenhe L. 2021. The effect of exogenous melatonin on milk somatic cell count in Buffalo. **Pak Vet J** 41: 152 - 155. **https://doi.org/10.29261/pakvetj/2020.074**
Floridi A, Piroddi M, Pilolli F, Matsumoto Y, Aritomi M, Galli F. 2009. Analysis method and characterization of the antioxidant capacity of vitamin E-interactive polysulfone hemodialyzers. **Acta Biomater** 5: 2974 - 2982. **https://doi.org/10.1016/j.actbio.2009.04.011**
Forrester SJ, Kikuchi DS, Hernandes MS, Xu Q, Griendling KK. 2018. Reactive oxygen species in metabolic and inflammatory signaling. **Circ Res** 122: 877 - 902. **https://doi.org/10.1161/circresaha.117.311401**
Fujiki H, Suganuma M, Okabe S, Kurusu M, Imai K, Nakachi K. 2002. Involvement of TNF-α changes in human cancer development, prevention and palliative care. **Mech Ageing Dev** 123: 1655 - 1663. **https://doi.org/10.1016/S0047-6374(02)00101-X**
Ghareeb H, Metanis N. 2020. The thioredoxin system: a promising target for cancer drug development. **Eur J Chem** 12: 10175 - 10184. **https://doi.org/10.1002/chem.201905792**
Goyal RK, Sairam K. 2021. Anti-ulcer drugs from indigenous sources with emphasis on *Musa sapientum*, *Tamra bhasma*, *Asparagus racemosus* and *Zingiber officinale*. **Indian J Pharmacol** 34: 1 - 100. **https://doi.org/10.1016/S0047-6374(02)00101-x**
Gupta RA, Motiwala MN, Mahajan UN, Sabre SG. 2018. Protective effect of *Sesbania grandiflora* on acetic acid induced ulcerative colitis in mice by inhibition of TNF-α and IL-6. **J Ethnopharmacol** 219: 222 - 232. **https://doi.org/10.1016/j.jep.2018.02.043**
Hosseini F, Naseri MKG, Badavi M, Ghaffari MA, Shahbazian H, Rashidi I. 2010. Effect of beta carotene on lipid peroxidation and antioxidant status following renal ischemia/reperfusion injury in rat. **Scand J Clin Lab Inv** 70: 259 - 263. **https://doi.org/10.3109/00365511003777810**
Huang HY, Appel LJ, Croft KD, Miller ER, Mori TA, Puddey IB. 2002. Effects of vitamin C and vitamin E on *in vivo* lipid peroxidation: Results of a randomized controlled trial. **Am J Clin Nutr** 76: 549 - 555. **https://doi.org/10.1093/ajcn/76.3.549**
Hussain Z, Khan JA, Arshad MI, Muhammad F, Abbas RZ. 2021a. Protective effects of cinnamon, cinnamaldehyde and kaempferol against acetaminophen-induced acute liver injury and apoptosis in mouse model. **Pak Vet J** 41: 25 - 32. **https://doi.org/10.29261/pakvetj/2020.090**
Hussain S, Javed M, Abid MA, Khan MA, Syed KS, Faizan M, Feroz F. 2021b. *Prunus avium* L.; Phytochemistry, nutritional and pharmacological review. **Adv Life Sci** 8: 307 - 314.
Ighodaro OM, Akinloye OA. 2018. First line defence antioxidants-superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GPX): Their fundamental role in the entire antioxidant defence grid. **Alexandria J Med** 54: 287 - 293. **https://doi.org/10.1016/j.ajme.2017.09.001**
Ittiyavirah SP, Paul AS. 2016. Gastroprotective effect of plumbagin and ethanolic extract of plumbaginales in experimentally-induced ulcer. **J Herb Med Pharmacol** 5: 92 - 98. **https://doi.org/10.4196%2Fkjpp.2021.25.5.403**
Jainu M, Devi CSS. 2006. Gastroprotective action of *Cissus quadrangularis* extract against NSAID induced gastric ulcer: Role of proinflammatory cytokines and oxidative damage. **Chem Biol Interact** 161: 262 - 270. **https://doi.org/10.1016/j.cbi.2006.04.011**
Jaiswal S, Rao CV. 2016. Evaluation of standardized fractions of *Basella alba* leaves as gastroprotective activity on ulcerated rats. **Orient Pharm Exp Med** 16: 5 - 11. **https://doi.org/10.1007/s13596-016-0244-8**
Jantrapirom S, Hirunsatitpron P, Potikanond S, Nimlamool W, Hanprasertpong N. 2021. Pharmacological benefits of Triphala: a perspective for allergic rhinitis. **Front Pharmacol** 12: 700 - 706. **https://doi.org/10.3389/fphar.2021.628198**
Jayakumari S, Anbu J, Ravichandiran V, Anjana A, Siva Kumar GM, Singh M. 2012. Antiulcerogenic and free

radical scavenging activity of flavonoid fraction of *Psidium guajava* Linn leaves. **Int J Pharm Pharm Sci** 4: 170 - 174. **https://doi.org/10.1016/j.sjbs.2020.10.026**

Jiang SZ, Wang NS, Mi SQ. 2008. Plasma pharmacokinetics and tissue distribution of [6]-gingerol in rats. **Biopharm Drug Dispos** 29: 529 - 537. **https://doi.org/10.1002/bdd.638**

Kalra P, Sharma S, Suman SK. 2011. Antiulcer effect of the methanolic extract of *Tamarindus indica* seeds in different experimental models. **J Pharm Bioallied Sci** 3: 236 - 241. **https://doi.org/10.4103/0975-7406.80778**

Kaźmierczak-Barańska J, Boguszewska K, Adamus-Grabicka A, Karwowski BT. 2020. Two faces of vitamin C-antioxidative and pro-oxidative agent. **Nutrients** 12: 1 - 19. **https://doi.org/10.3390/nu12051501**

Kumar R, Arora R, Mahajan J, Mahey S, Arora S. 2017. Polyphenols from Cutch tree (*Acacia catechu* Willd.): Normalize *in vitro* oxidative stress and exerts antiproliferative activity. **Braz Arch Biol Technol** 60: 1 - 18. **https://doi.org/10.1590/1678-4324-2017160728**

Kwon DH, Cha HJ, Lee H, Hong SH, Park C, Park SH, Kim GY, Kim S, Kim HS, Hwang HJ, Choi YH. 2019. Protective effect of glutathione against oxidative stress-induced cytotoxicity in RAW 264.7 macrophages through activating the nuclear factor erythroid 2-related factor-2/heme oxygenase-1 pathway. **Antioxidants** 8: 82. **https://doi.org/10.3390/antiox8040082**

Langmead L, Rampton DS. 2001. Review article: Herbal treatment in gastrointestinal and liver disease benefits and dangers. **Aliment Pharmacol Ther** 9: 1239 - 1252. **https://doi.org/10.1046/j.1365-2036.2001.01053.x**

Larsson SC, Bergkvist L, Näslund I, Rutegård J, Wolk A. 2007. Vitamin A, retinol, and carotenoids and the risk of gastric cancer: a prospective cohort study. **Am J Clin Nutr** 85: 497 - 503. **https://doi.org/10.1093/ajcn/85.2.497**

Liu B, Li Y, Mehmood K, Nabi F, Ahmed S, Tauseef-ur-Rehman, Faheem M, Ashraf M, Tang Z, Zhang H. 2021. Role of oxidative stress and antioxidants in thiram-induced tibial dyschondroplasia**. Pak Vet J** 41: 1 - 6. **https://doi.org/10.29261/pakvetj/2020.094**

Lobo V, Patil A, Phatak A, Chandra N. 2010. Free radicals, antioxidants and functional foods: Impact on human health. **Pharmacogn Rev** 8: 118 - 126. **https://doi.org/10.4103%2F0973-7847.70902**

Mahattanadul S, Radenahmad N, Phadoongsombut N, Chuchom T, Panichayupakaranant P, Yano S, Reanmongkol W. 2006. Effects of curcumin on reflux esophagitis in rats. **J Nat Med** 60: 198 - 205. **https://doi.org/10.3390%2Fijms20061477**

Majeed Y, Shaukat MB, Abbasi KY, Ahmad MA, 2021. Indigenous plants of Pakistan for the treatment of diabetes: A review. **Agrobiol Rec** 4: 44 - 63. **https://doi.org/10.47278/journal.abr/2020.028**

Martins N, Petropoulos S, Ferreira ICFR. 2016. Chemical composition and bioactive compounds of garlic (*Allium sativum* L.) as affected by pre- and post-harvest conditions: A review. **Food Chem** 211: 41 - 50. **https://doi.org/10.1016/j.foodchem.2016.05.029**

Matsubara S, Shibata H, Ishikawa F, Yokokura T, Takahashi M, Sugimura T, Wakabayashi K. 2003. Suppression of Helicobacter pylori-induced gastritis by green tea extract in Mongolian gerbils. **Biochem Biophys Res Commun** 310: 715 - 719. **https://doi.org/10.1016/j.bbrc.2003.09.066**

Matthews GM, Butler RN. 2005. Cellular mucosal defense during Helicobocter pylori infection: A review of the role of glutathione and the oxidative pentose pathway. **Helicobacter** 4: 298 - 306. **https://doi.org/10.1111/j.1523-5378.2005.00327.x**

Mayilsamy M, Rajendran A. 2013. Ethnomedicinal plants used by paliyar tribals in Dindigul district of Tamil Nadu, India. **Int J Innov** 3: 146 - 152.

Mazumder P, Farswan M, Parcha V, Singh V. 2008. Hypoglycemic and antioxidant activity of an isolated compound from *Ficus arnottiana* bark. **Pharmacologyonline** 3: 509 - 519. **https://doi.org/10.1016/S2221-6189(13)60130-4**

Mekonnen AN, Atnafie SA, Mohammedbirhan AWA. 2020. Evaluation of antiulcer activity of 80% methanol extract and solvent fractions of the root of *Croton macrostachyus* Hocsht: Ex Del. (Euphorbiaceae) in rodents. **Evid Based Complementary Altern Med** 2020: Article 2809270. **https://doi.org/10.1155/2020/2809270**

Mena S, Ortega A, Estrela JM. 2009. Oxidative stress in environmental-induced carcinogenesis. Mutation research/genetic toxicology and environmental mutagenesis. **Mutat Res** 674: 36 - 44. **https://doi.org/10.1016/j.mrgentox.2008.09.017**

Momin FN, Kalai BR, Godse VS, Patole NS, Shikalgar T, Naikwade NS. 2011. Gastroprotective effect of *Mimosa pudica* leaves extract on *in-vivo* test models in rats: **J Biol Act Prod Nat** 1: 160 - 167. **https://doi.org/10.1080/22311866.2011.10719083**

Moniruzzaman M, Ghosal I, Das D, Chakraborty SB. 2018. Melatonin ameliorates H2O2-induced oxidative stress through modulation of Erk/Akt/NFkB pathway. **Biol Res** 51: 1 - 7. **https://doi.org/10.1186/s40659-018-0168-5**

Moryani AA, Rajput N, Naeem M, Shah AH, Jahejo AR. 2021. Screening of the herbs and evaluation of their combined effects on the health and immunity of coccidiosis challenged broiler chickens. **Pak Vet J** 41: 228 - 234. **https://doi.org/10.29261/pakvetj/2021.005**

Mushtaq A, Aslam B, Muhammad F, Khan JA. 2021. Hepatoprotective activity of *Nigella sativa* and *Piper nigrum* against concanavalin A-induced acute liver injury in mouse model. **Pak Vet J** 41: 78 - 84. **https://doi.org/10.29261/pakvetj/2020.076**

Murtaza S, Khan JA, Aslam B, Faisal MN. 2021. Pomegranate peel extract and quercetin possess antioxidant and hepatoprotective activity against concanavalin A-induced liver injury in mice**. Pak Vet J** 41: 197 - 202. **https://doi.org/10.29261/pakvetj/2020.097**

Nandi A, Yan LJ, Jana CK, Das N. 2019. Role of catalase in oxidative stress- and age-associated degenerative diseases. **Oxid Med Cell Longev** 1: 1 - 19. **https://doi.org/10.1155/2019/9613090**

Namratha ML, M Lakshman, M Jeevanalatha, Kumar BA. 2021. Assessment of vitamin c protective activity in glyphosate-induced hepatotoxicity in rats. **Pak Vet J** 41: 439 - 445. **https://doi.org/10.29261/pakvetj/2021.021**

Naseer O, Khan JA, Shahid M, Rabbani AH, Ahmad AS, Sohail ML, Naseer J, Bilal M, Waqas A, Saleem MU, Khan YR, Ali A, Hussain K. 2022. Growth, hematological and histopathological responses to Guar (*Cyamopsis tetragonoloba*) and salinomycin sodium for ameliorating deleterious effects of coccidiosis in broiler chicken. **Kafkas Univ Vet Fak Derg** 28: 19 - 26. **http://doi.org/10.9775/kvfd.2021.26216**

Nathan SS, Kalaivani K, Murugan K, Chung PG. 2005. The toxicity and physiological effect of neem limonoids on *Cnaphalocrocis medinalis* (Guenée) the rice leaffolder. **Pestic Biochem Phys** 81: 113 - 122. **https://doi.org/10.1016/j.pestbp.2004.10.004**

Ni Y, Eng C. 2012. Vitamin E protects against lipid peroxidation and rescues tumorigenic phenotypes in cowden/cowden-like patient-derived lymphoblast cells with germline SDHx variants. **Clin Cancer Res** 18: 4954 - 4961. **https://doi.org/10.1158/1078-0432.CCR-12-1055**

Ortaç D, Cemek M, Karaca T, Büyükokuroğlu ME, Özdemir Z, Kocaman AT, Güoneş S. 2018. *In vivo* anti-ulcerogenic effect of okra (*Abelmoschus esculentus*) on ethanol-induced acute gastric mucosal lesions. **Pharm Biol** 56: 165 - 175. **https://doi.org/10.1080/13880209.2018.1442481**

Phaniendra A, Jestadi DB, Periyasamy L. 2015. Free radicals: properties, sources, targets, and their implication in various diseases. **Indian J Clin Biochem** 30: 11 - 26**. https://doi.org/10.1007/s12291-014-0446-0**

Poljšak B, Fink R. 2014. The protective role of antioxidants in the defence against ROS/RNS-mediated environmental pollution. **Oxid Med Cell Longev** 2014: 671539. **https://doi.org/10.1155/2014/671539**

Prabhu K, Rajan S. 2015. Assessment of antiulcer activity of ethanolic extract of *Mangifera indica* seed kernel using acid ethanol induced ulcer model **Int J Curr Microbiol Appl Sci** 4: 854 - 860. **https://doi.org/10.7860%2FJCDR%2F2016%2F20384.8470**

Prazeres LDKT, Aragão TP, Brito SA, Almeida CLF, Silva AD, De Paula MMF, Farias JS, Vieira LD, Damasceno BPGL, Rolim LA, Veras BO, Rocha IG, Silva Neto JC, Bittencourt MLF, Gonçalves Rde CR, Kitagawa RR, Wanderley AG. 2019. Antioxidant and antiulcerogenic activity of the dry extract of pods of *Libidibia ferrea* Mart. ex Tul. (Fabaceae). **Oxid Med Cell Longev** 2019: 1983137. **https://doi.org/10.1155/2019/1983137**

Rafay M, Ghaffar MU, Abid M, Malik Z, Madnee M. 2021. Phytochemicals analysis and antimicrobial activities of *Echinops echinatus* from Cholistan desert, Pakistan. **Agrobiol Rec** 5: 21 - 27. **https://doi.org/10.47278/journal.abr/2021.001**

Rajkapoor B, Jayakar B, An R, Murugesh N. 2003. Antiulcer effect of dried fruits of *Carica papaya* Linn in rats. **Indian J Pharm Sci** 65: 638 - 642. **https://doi.org/10.1155%2F2014%2F519590**

Raju D, Ilango K, Chitra V, Ashish K. 2009. Evaluation of anti-ulcer activity of methanolic extract of *Terminalia chebula* fruits in experimental rats. **J Pharm Sci Res** 1: 101. **https://doi.org/10.2147%2FJEP.S125383**

Ramakrishna YG, Savithri K, Kist M, Devaraj SN. 2015. Aegle marmelos fruit extract attenuates Helicobacter pylori lipopolysaccharide induced oxidative stress in Sprague Dawley rats. **BMC Complement Altern Med** 15: 375 - 389. **https://.doi.org/10.1016/s0016-5085(99)70496-8**

Rao C V, Verma AR, Vijayakumar M, Rastogi S. 2008. Gastroprotective effect of standardized extract of *Ficus glomerata* fruit on experimental gastric ulcers in rats. **J Ethnopharmacol** 115: 323 - 326. **https://doi.org/10.1016/j.jep.2007.09.019**

Rehman K, Hamayun M, Khan SS, Ahmad, Wali S. 2021. Efficiency of Virgin's mantle (*Fagonia cretica* L.) as an antibacterial and antifungal agent. **Adv Life Sci** 8: 233 - 237.

Rezaie A, Mohajeri D, Khamene B, Nazeri M, Shishehgar R, Zakhireh S. 2012. Effect of *Myrtus communis* on healing of the experimental skin wounds on rats and its comparison with zinc oxide. **Curr Res J Biol Sci** 4: 176 - 185. **https://doi.org/10.2174/157016381766620071216395 6**

Rozza AL, Meira de Faria F, Souza Brito AR, Pellizzon CH. 2014. The gastroprotective effect of menthol: Involvement of anti-apoptotic, antioxidant and anti-inflammatory activities. **Plos One** 9: 1 - 6. **https://doi.org/10.1158/1078-0432.ccr-12-1055**

Ruggiero P, Rossi G, Tombola F, Pancotto L, Lauretti L, Del Giudice G, Zoratti M. 2007. Red wine and green tea reduce *H pylori*- or VacA-induced gastritis in a mouse model. **World J Gastroenterol** 13: 349 - 354. **https://doi.org/10.1158/1078-0432.ccr-12-1055**

Sabiu S, Garuba T, Sunmonu TO, Sulyman AO, Ismail NO. 2016. Indomethacin-induced gastric ulceration in rats: Ameliorative roles of *Spondias mombin* and *Ficus exasperata*. **Pharmaceut Biol** 2: 180 - 186. **https://doi.org/10.1158/1078-0432.ccr-12-1055**

Sadek KM. 2012. Antioxidant and immunostimulant effect of *Carica papaya* Linn. aqueous extract in acrylamide intoxicated rats. **Acta Inform Med** 20: 180 - 185. **https://doi.org/10.5455/aim.2012.20.180-185**

Sai KB, Radha KL, Gowrinath RM. 2011. Anti-ulcer effect of *Aloe vera* in non-steroidal anti-inflammatory druginduced peptic ulcers in rats. **Afr J Pharm Pharmacol** 5: 1867 - 1871. **https://doi.org/10.5897/AJPP11.306**

Saif R, Ashfaq K, Ali G, Iftekhar A, Saeeda Z, Yousaf MZ. 2022. Computational prediction of *Cassia angustifolia* compounds as a potential drug agents against main protease of SARS-nCov2. **Adv Life Sci** 9: 36 - 40.

Salehi M, Karegar-Borzi H, Karimi M, Rahimi R. 2017. Medicinal plants for management of gastroesophageal reflux disease: A review of animal and human studies. **J Alt Complement Med** 23: 82 - 95. **https://doi.org/10.1089/acm.2016.0233**

Santhoshkumar M, Anusuya N, Bhuvaneswari P. 2012. Antiulcerogenic effect of resin from *Shorea robusta* Gaertn. on experimentally induced ulcer models. **Int J Pharm Pharm Sci** 5: 269 - 272. **https://doi.org/10.3390/plants10071348**

Sayyar HT, Afroz S, Assad T. 2021. Evaluation of phytochemical screening, antimicrobial and antioxidant activities of ethanol extracts of *Cucumis flexouses* and *Cucumis reticulatus* seeds. **Pak Vet J** 41: 142 - 146. **https://doi.org/10.29261/pakvetj/2020.089**

Sebai H, Jabri MA, Souli A, Hosni K, Selmi S, Tounsi H, Tebourbi O, Boubaker S, El-Benna J, Sakly M. 2014. Protective effect of *Artemisia campestris* extract against aspirin-induced gastric lesions and oxidative stress in rat. **RSC Advances** 4: 49831 - 49841. **https://doi.org/10.1039/C4RA08564G**

Shree GGK, Parvathi S, Ramkumar PSS, Priya SS. 2012. Pharmacological and phytochemical evaluation of anti-ulcerogenic potential of *Solanum nigrum*. **Int J Pharm Sci Res** 3: 2837 - 2840. **https://doi.org/10.13040/IJPSR.0975-8232.3(8).2837-40**

Sidahmed HMA, Hashim NM, Abdulla MA, Ali HM, Mohan S, Abdelwahab SI, Taha MME, Fai LM, Vadivelu J. 2015. Antisecretory, gastroprotective, antioxidant and anti-helicobcter pylori activity of zerumbone from *Zingiber zerumbet* (L.) smith. **Plos One** 10: 1 - 21. **https://doi.org/10.1371%2Fjournal.pone.0121060**

Siddaraju MN, Dharmesh SM. 2007. Inhibition of gastric H+,K+-ATPase and Helicobacter pylori growth by phenolic antioxidants of *Zingiber officinale*. **Mol Nutr Food Res** 51: 324 - 332. **https://doi.org/10.1158/1078-0432.ccr-12-1055**

Singh O, Khanam Z, Misra N, Srivastava MK. 2011. Chamomile (*Matricaria chamomilla* L.): An overview. **Pharmacogn Rev** 9: 82 - –95. **https://doi.org/10.4103/0973-7847.79103**

Sisay M, Gashaw T. 2009. Ethnobotanical, ethnopharmacological and phytochemical studies of *Myrtus communis* Linn: A popular herb in Unani System of Medicine. **J Evid Based Integr Med** 22: 1035 - 1043.

https://doi.org/10.1177/2156587217718958

Sood S, Muthuraman A, Arora B, Bansal S, Bali M, Sharma P. 2010. Potential effect of *Citrus decumana* extract on stress induced peptic ulcer in rat. **Lat Am J Pharm** 29: 52 - 56

Srinivas TL, Lakshmi SM, Shama SN, Reddy GK. 2013. Medicinal plants as anti-ulcer agents. **J Pharmacogn Phytochem** 2: 91 - 97.

Subitha K, Ayyanar TM, Sekar T. 2011. Ethnomedicinal plants used by Kani tribals in Pechiparai forests of Southern western Ghats, Tamil Nadu, India. **Int Res J Plant Sci** 2: 349 - 354.

Subramanian S, Sathish Kumar D, Arulselvan P, Senthilkumar GP, Mahadeva Rao US. 2007. Evaluation of anti-ulcerogenic potential of *Aloe vera* leaf gel extract studied in experimental rats. **J Pharmacol Toxicol** 2: 85 - 97.

Suleiman MM, Dzenda T, Sani CA. 2008. Antidiarrhoeal activity of the methanol stem-bark extract of *Annona senegalensis* Pers. (Annonaceae). **J Ethnopharmacol** 116: 125 - 130. **https://doi.org/10.1016/j.jep.2007.11.007**

Süleyman HI, Demirezer LO, Kuruüzüm-Uz A, Akçay FI. 2002. Gastroprotective and antiulcerogenic effects of *Rumex patientia* extract. **Pharmazie** 57: 204 - 205.

Sumbul S, Mohd Aftab Ahmad, Asif M, Saud I, Akhtar M. 2010. Evaluation of *Myrtus communis* Linn. berries (common myrtle) in experimental ulcer models in rats**. Hum Exp Toxicol** 29: 935 - 944. **https://doi.org/10.1177/0960327110364154**

Surai PF, Kochish II, Fisinin VI, Kidd MT. 2019. Antioxidant defence systems and oxidative stress in poultry biology: An update. **Antioxidants** 8: 235 - 242. **https://doi.org/10.3390/antiox8070235**

Suzuki H, Nishizawa T, Tsugawa H, Mogami S, Hibi T. 2012. Roles of oxidative stress in stomach disorders**. J Clin Biochem Nutr** 50: 35 - 39. **https://doi.org/10.3164/jcbn.11-115SR**

Tan DX, Manchester LC, Reiter RJ, Qi WB, Karbownik M, Calvoa JR. 2000. Significance of melatonin in antioxidative defense system: Reactions and products. **Biol Signals Recept** 9: 137 - 159. **https://doi.org/10.1159/000014635**

Terry PD, Villinger F, Bubenik GA, Sitaraman SV. 2009. Melatonin and ulcerative colitis: Evidence, biological mechanisms, and future research. **Inflamm Bowel Dis** 15: 134 - 140. **https://doi.org/10.1002/ibd.20527**

Tope S, Sunday O, Gabriel A. 2014. Mechanisms of antiulcerogenic effect of garlic (*Allium sativum*) in albino rats. **Eur J Med Plants** 8: 571 - 578. **https://doi.org/10.9734/EJMP/20148140**

Tordjman S, Chokron S, Delorme R, Charrier A, Bellissant E, Jaafari N, Fougerou C. 2017. Melatonin: Pharmacology, functions and therapeutic benefits. **Curr Neuropharmacol** 15: 434 - 443. **https://doi.org/10.2174/1570159X14666161228122**

Toti E, Chen CY, Palmery M, Villaño Valencia D, Peluso I. Non-provitamin A. provitamin A. 2018. Carotenoids as immunomodulators: recommended dietary allowance, therapeutic index, or personalized nutrition?. **Oxid Med Cell Longev** 2018: 4637861. **https://doi.org/10.1155/2018/4637861**

Uduak EU, Timbuak JA, Musa SA, Ikyembe DT, Abdurrashid S, Hamman WO. 2012. Ulceroprotective effect of methanol extract of *Psidium guajava* leaves on ethanol induced gastric ulcer in adult wistar rats. **Asian J Med Sci** 4: 75 - 78.

Vanella L, Sanford C, Kim DH, Abraham NG, Ebraheim N. 2012. Oxidative stress and heme oxygenase-1 regulated human mesenchymal stem cells differentiation. **Int J Hypertens** 2012: Article ID 890671. **https://doi.org/10.1155/2012/890671**

Vanita, K. Deepali M. 2019. Evaluation of antipyretic and antiulcer activity of ethanolic extract of leaves of *Alstonia scholaris* L. in albino wistar rats. **Asian J Pharm Clin Res** 12: 203 - 208. **https://doi.org/10.22159/ajpcr.2019.v12i12.35630**

Veitch GE, Beckmann E, Burke BJ, Boyer A, Maslen SL, Ley SV. 2007. Synthesis of azadirachtin: A long but successful journey. **Angew Chem Int Ed** 46: 7629 - 7632. **https://doi.org/10.1002/anie.200703027**

Vinothapooshan G, Sundar K. 2010. Anti-ulcer activity of Mimosa pudica leaves against gastric ulcer in rats. **Res J Pharm Biol Chem Sci** 1: 606 - 614

Wajiha, Qureshi NA, 2021. *In vitro* anticoccidial, antioxidant activities and biochemical screening of methanolic and aqueous leaves extracts of selected plants. **Pak Vet J** 41: 57 - 63. **https://doi.org/10.29261/pakvetj/2020.071**

Wolonciej M, Milewska E, Roszkowska-Jakimiec W. 2016. Trace elements as an activator of antioxidant enzymes.

Postepy Higieny Medycyny Doswiadczalnej 70: 1483 - 1498.

Yang S, Lian G. 2020. ROS and diseases: role in metabolism and energy supply. **Mol Cell Biochem** 467: 1 - 12. **https://doi.org/10.1007/s11010-019-03667-9**

Younus H. 2018. Therapeutic potentials of superoxide dismutase. **Int J Health Sci** 12: 88 - 93.

Zaghlool SS, Abo-Seif AA, Rabeh MA, Abdelmohsen UR, Messiha BAS. 2019. Gastro-protective and anti-oxidant potential of *Althaea officinalis* and *Solanum nigrum* on pyloric ligation/indomethacin-induced ulceration in rats. **Antioxidants** 8: 512. **https://doi.org/10.3390/antiox8110512**

Zeren S, Bayhan Z, Kocak FE, Kocak C, Akcilar R, Bayat Z, Simsek H, Duzgun SA. 2016. Gastroprotective effects of sulforaphane and thymoquinone against acetylsalicylic acid--induced gastric ulcer in rats. **J Surg Res** 203: 348 - 359. **https://doi.org/10.1016/j.jss.2016.03.027**

Zhao RZ, Jiang S, Zhang L, Yu ZB. 2019. Mitochondrial electron transport chain, ROS generation and uncoupling. **Int J Mol Med** 44: 3 - 15. **https://doi.org/10.3892/ijmm.2019.4188**

Zhao ZX, Yuan X, Cui YY, Liu J, Shen J, Jin BY, Feng BC, Zhai YJ, Zheng MQ, Kou GJ, Zhou RC. 2021. Melatonin mitigates oxazolone-induced colitis in microbiota-dependent manner. **Front Immunol** 12: 2 - 7. **https://doi.org/10.3389/fimmu.2021.783806**