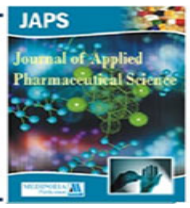
Journal of Applied Pharmaceutical Science
Available online at www.japsonline.com



ISSN: 2231-3354
Received on: 28-02-2012
Revised on: 09-03-2012
Accepted on: 26-03-2012

Herbal Drugs With Anti Ulcer Activity

Dilpreet Kaur, A. C. Rana, Nidhi Sharma and Sunil Kumar

Dilpreet Kaur, A. C. Rana, Nidhi Sharma and Sunil Kumar
Rayat Institute of Pharmacy, Railmajra, S. B. S. Nagar, Punjab, India.

For Correspondence
Mr. Sunil Kumar
Assistant Professor
Department of Pharmacology
Rayat Institute of Pharmacy
Railmajra, S. B. S Nagar.
Pin Code-144514
Contact No. +91-9815520843
Fax- 188125001

ABSTRACT

A peptic ulcer is an erosion in a segment of the gastro intestinal mucosa, typically in the stomach (gastric ulcer) or first few centimeters of duodenum (duodenal ulcer) that penetrates through the muscularis mucosae. Contrary to popular belief, ulcer is not caused by spicy food but instead is most commonly due to either an infection or long term use of medications. Standard treatment is a combination of drugs including antibiotics and a proton pump inhibitors. Literature suggests that number of synthetic drugs are used in the management of peptic ulcers but elicit several adverse effects. Therefore Indian herbal plants stand out as being exceptional for its ethnic, ethobotanical and ethno-pharmaceutical use. In this review attempts have been made to know about some plants which may be used in treatment or prevention of peptic ulcers. Various plants like *Cynodon dactylon, Ocimum sanctum, Glycyrrhiza glabra, Ficus religiosa* proved active in antiulcer therapy.

Keywords: Peptic ulcer, medicinal plants, antiulcer activity.

INTRODUCTION

Peptic ulcer is defined as a break off in the continuity of the mucosa of stomach or duodenum as a consequence of some medications like non-steroidal anti-inflammatory drugs (NSAIDS), gastric acids and pepsin finally causes lesions in intestinal mucosa (Verma *et al.*, 2010). Basically, word “peptic” is derived from Greek term “peptikos” whose meaning is related to digestion .Various reports indicates that old age group patients are more prone to gastric ulcer. Younger individuals have higher risk of duodenal ulcers (Richardson, 1990, Lunevicius and Morkevicius, 2005, Pahwa *et al.*, 2011). The pathogenesis of peptic ulcer disease includes a complex imbalance between gastric offensive factors like acid, pepsin secretion, *Helicobacter pylori (H.pylori)*, bile salts, ethanol, some medications like NSAIDS, lipid peroxidation, nitric oxide (NO) and defensive mucosal factors like prostaglandins (PG’s), gastric mucus, cellular renovation, blood flow, mucosal cell shedding, glycoproteins, mucin secretion, proliferation and antioxidant enzymes like catalase (CAT), superoxide dismutase (SOD) and glutathione levels (Marietta and John, 2010). Peptic ulcer can be categorized on the basis of location and on the severity of disease. Numerous other factors are also responsible for progression of peptic ulcers like tumor necrosis factor-α (TNF α), reactive oxygen species (ROS), release of histamine, incidence of apoptosis and bile acids secretion (Singha *et al.*, 2008; Fatemeh *et al.*, 2011).

Evidences indicate that NSAIDS-induced ulcers are very common (Griffin, 1991). NSAIDS helps in progression of ulcer by conquering the expression of enzyme cyclo-oxygenase (COX) which has been documented to inhibit the conversion of arachidonic acid (AA) to PG's (Vane and Botting, 1995) that impairs the mucosal barrier and results in corrosive action with pepsin that together are responsible for progression of peptic ulcers. There is pronounced evidence that oxygen derived free radicals plays a crucial role in the pathogenesis of the injury of various tissues, including the digestive system (Vaananenn *et al.,* 1991). The role of TNF-α in the pathogenesis of gastric ulcer is well established. TNF-α is a cytokine which initiates the inflammatory process through stimulation of migration of leukocytes into inflammatory sites therefore plays a significant role in formation of gastric ulcers (Lychkova *et al.,* 2010). Besides TNF-α also activates extrinsic apoptotic pathway through caspase-3 initiation which leads to gastric injury (Hwang *et al.,* 2008). Increased TNF-α activate caspase-3, which is one of the major effector caspases involved in apoptotic cell death. Finally, caspases leads to neutrophil activation through various chemoattracts thus a vicious cycle exists which leads to gastric damage (Abuzarova *et al.,* 2008). Moreover *H.pylori* is too implicated in peptic ulcer progression. *H.pylori* is a gram negative bacillus, motile, microaerophilic, flagellated, spiral shaped bacterium, which secretes the distinct enzyme urease that converts urea to ammonia, which further reduces the acidity of stomach, making it sanatorium for *H. pylori* (Pandey *et al.,* 2010). Type I strains of *H.Pylori* possess a pathogenic activity, that encodes the effector protein cytotoxin-associated gene A (cagA). After translocation into the host cell, cagA effects cell shape, increases cell motility, disturbs cell junctional activity and thus responsible for gastric carcinomas and gastric ulcers (Buti *et al.,* 2011).

There are enormous chemical agents available for the treatment of peptic ulcers but proclaim serious side effects like H_2 antagonists is the precipitating cause of impotence, headache, skin rash, arrhythmias where as the use of proton pump inhibitors is a unforeseeable cause for hypergastrinemia and atrophic gastritis. The use of antacids leads to stomach distention, belching, constipation and there is risk of ulcer perforation and other drugs like anticholinergics induce constipation, dry mouth, urinary retention, blurred vision, xerostomia and precipitation of glaucoma (Reilly, 1999, Franco and Richter, 1998). Ulcer protectives causes constipation, triggers diarrhoea, dizziness, edema and hypophosphatemia where as abdominal cramps, uterine bleeding and abortion is the probable cause of prostaglandin analogues (Akthar *et al.,* 1992). So herbal drugs have preserved their importance due to relatively less toxic, better cultural acceptability, better compatibility with human body, lesser adverse effects, economical, effective and easy availability (Pandey *et al.,* 2008). This paper outlines the properties of some medicinal plants that exhibit antiulcer activity. Although extensive research has been conducted in this area, recent studies with significant findings involving *Cynodon dactylon, Ocimum sanctum, Glycyrrhiza glabra, Ficus religiosa,*are emphasized here.

Cynodon dactylon

Cynodon dactylon (L.) pers. is a creeping grass found in warm climates all over the world (Singh *et al.,* 2009). It belongs to the family Poaceae. It is also known as Durva grass, Bermuda grass, Dog's Tooth grass, Bahama grass, Devil's grass, Couch grass, Indian Doab, Scutch grass, Dhub, Doob and Durba in different regions (Oudhia, 2003). It is the most sacred plant of India next to tulsi. The plant contains crude proteins, carbohydrates, mineral constituents, oxides of magnesium, phosphorous, calcium, sodium, potassium, vitamin-c, carotene, hydroquinone, levoglucosenone, furfural, hexadecanoic acid, ethyl ester, linolenic acid, ethyl ester and d-mannose (Shabi *et al.,* 2010). The plant has been long used in the traditional medicines to treat various ailments such as cancer, convulsions, cough, cramps, diarrhea, dropsy, dysentery, epilepsy, headache, hemorrhage, hypertension, hysteria, measles, rubella, snake bite, sores, stones, tumors, urogenital disorders, warts and wounds (Chopra *et al.,* 1999, Pal, 2009). Advanced studies on this plant have been reported that it possess antiulcer, antidiabetic, antidiarrheal, diuretic, antimicrobial, immunomodulatory, antiepileptic, anti-inflammatory, anti arrhythmic , antibacterial , chemoprotective and hepatoprotective activities (Parekh *et al.,* 2005, Patil *et al.,* 2005, Parekh *et al.,* 2005, Singh *et al.,* 2007, Najifi *et al.,* 2008, Surendra *et al.,* 2008, Kumar *et al.,* 2004, Ravindra *et al.,* 2009, Baskar and Ignacimuthu, 2010, Kumar *et al.,* 2010, Santhi and annapoorani, 2010, Garg and paliwal, 2011). Alcoholic extract of *C. dactylon* was screened for antiulcer activity in albino rats at dose level of 200,400 and 600 mg kg^{-1} b.wt (Patil *et al.,* 2005). The extract at 400 mg kg^{-1} and 600 mg kg^{-1} showed significant (>0.001) antiulcer activity as compared to the standard drug ranitidine. The alcoholic extract inhibited ulceration by inhibiting output volume and total acidity. The ulcer healing activity of the plant extract may be due to antisecretory property associated with an enhancement of the local healing process. Aerial parts of Bermuda grass herb are reported to contain flavonoids (Nair, 1995). The preliminary phytochemical investigation of the alcoholic extract of bermuda grass showed the presence of flavanoids, which may be responsible for antiulcer property. It is hoped that *C. dactylon* would serve as a useful tool for the researchers for proper evaluation of the plant and for the development of new, safer, potent and cost effective drugs in future.

Ocimum sanctum

Ocimum sanctum, commonly known as *Tulsi* is the most popular member of the genus *ocimum* and is considered as a sacred plant by the Hindus in India (Singh *et al.,* 2011). The name tulsi is derived from 'Sanskrit' which means "matchless one" (Bansod and Rai, 2008). The plant grows wild in India but it is widely cultivated in home and temple gardens. There are about 160 species in this genus broadely dispersed over the warm region of the globe *ocimum sanctum, ocimum gratissimum* (Ramtulsi), *ocimum* (Dulaltulsi),*ocimum basilicum* (bantulsi), *kilimandscharicum, ocimumum americanum, ocimum camphora, ocimum miranthum* are examples of known important species of genus *ocimum* which

grows in different parts of world and has been used extensively used in traditional medicine for a wide range of ailments (Shahedur *et al.,* 2011, Vinod *et al*., 2011). The whole parts of plant such as leaves, flowers, stem, root, seeds etc are known to possess a wide range of pharmacological properties and have been used by traditional medical practitioners as a expectorant, analgesic, anticancer, antiasthmatic, antiemetic, diaphoretic, antidiabetic, antifertility, hepatoprotective, hypotensive, hypolipidmic antistress agents (Heinrich, 2009). The chemical composition of *O. sanctum* is highly complex, containing many nutrients and other biologically active chemically compounds but eugenol is the principle constituent of tulsi, has been found to be largely responsible for the management of various types of diseases (Lalit *et al*., 2011). Tulsi has specific aromatic odour because of presence of essential or volatie oil, mainly concentrated in the leaf. The leaf contains eugenol, euginal (also called as eugenic acid), urosolic acid, carvacrol, linalool, limatrol, caryophyllene, methyl carvicol (also called as estragol) while the seed volatile oil have fatty acids and sitosterol, in addition seed mucilage contains small amounts of sugars and the anthocyans are present in green leaves (Yanpallewar *et al*., 2004). *Ocimum* is known as general vitalizer and increases physical endurance but it does not contains caffeine or other stimulants. The stem and leaves contains number of constituents including saponins, flavonoids, triterpenoids and tannins (Shishoda *et al*., 2003). In addition it contains phenolic compounds which exhibit antioxidant and anti-inflammatory activities (Dhar *et al.,* 1968). It also contains two water soluble flavanoids orientin and vicenin shows protection against radiation induced chromosomal damage in human blood lymphocytes (Uma *et al*., 2000). Advanced studies on this plant have been reported that it possess antiulcer activity, insecticidal activity, antiemetic activity, antistress activity, analgesic activity, antioxidant activity, heart tonic activity, antidiabetic activity, antitubercular activity, immunomodulator activity and antifertility effect (Rajeswari, 1952, Sen, 1993, Singh, 1995, Hussain *et al.,* 2001, Prakash and Gupta, 2005, Glolade and lockwood, 2008, Shankar *et al.,* 2009, Khan *et al*., 2010, Tabassum *et al.,* 2010, Vinod *et al.,* 2011). A team of scientist evaluated the antiulcerogenic activity in Aspirin (ASP), Alcohol (AI), cold restraint (CRU), pyloric ligation (PL) induced gastric ulcer models in rats, histamine-induced (HST) duodenal ulcer in *guinea pigs* and ulcer healing activity in acetic-acid induced (AC) chronic-ulcer model (Dharmani *et al.,* 2004). *O. sanctum* significantly reduces acid secretion and enhances mucus secretion (Madal *et al.,* 1993). It has been reported that fixed oil of *O.sanctum* possess significant antiulcer activity against Aspirin, Indomethacin, alcohol (ethanol 50%), histamine, reserpine, serotonin or stress-induced ulcers in rats (Singh *et al.,* 2007). The fixed oil shows antiulcer activity due to its lipoxygenase inhibitory, histamine antagonistic and anti-secretory effects (Singh and Majumdar *et al.,* 1999). Research must be attempted towards purifications of *tulsi* components and their characterization in terms of chemical nature and bio-pharmacological activities. Probably such natural components might prove to be potentially beneficial but comparatively less toxic. So plants belonging to *Ocimum* genus could contribute a lot towards economy and healthy problem.

Glycyrrhiza glabra

Glycyrrhiza glabra is most commonly used herb in western and eastern herbal medicine and has been used in the management of various diseases for more than 4000 years. The name *glycyrrhiza* is derived from the ancient greek term "*glykos*" meaning sweet, and "*rhiza*" meaning root (Lakshmi *et al.,* 2011). It is commonly known as licorice root, reglisse (French), lacrosse (German), sweet wood. It is from the *leguminosae* family which belongs to the genus containing fourteen species. Liquorice also contains amino acids, asparagin, bitters, essential oil, fat, female hormone estrogen, glycosides, gums, mucilage, protein resin, saponins, starches, steroids, sterols, tannin, volatile oil, flavonoids include liquiritin, isoliquirtin, liquiritigenin and rhamnoliquirilin and other present flavonoids are glucoliquiritin, apioside, prenyllicoflavone A, shin flavanone and shinptero carpen glycosides, female hormone estrogen, protein resin, saponins, sterols, yellow colouring matter- the yellow colour is due to the presence of anthoxathin glycoside known as isoliquiritin (Isbrucker RA and Burdock GA, 2006). The root of *G. glabra* contains the chief constituent known as glycyrrhizin which is 60 times sweeter than sugar. In traditional siddha system of medicine, liquorice is used as a demulcent, expectorant, antitussive, laxative and sweetener. It is also used in the treatment of acute respiratory problems, gastric ulcers, gastritis, inflammatory conditions in general and adrenal exhaustion (Fukai *et al*., 2002) Components of licorice root have both estrogenic and anti-estrogenic activity. So it is therefore an important herb in the management of hormone related female disorders. *G. glabra* exhibit wide spectrum of activities antiulcer-activity, antioxidant-activity, immunostimulatory effects, antihyperglycemic, anticonvulsant, antiinflammatory, antimicrobial, anticarcinogenic effects (Segal *et al.,* 1985, Demizu *et al*., 1988, Chopra and Simon, 2000, Ambawade et al ., 2002, Taro *et al.,* 2002, Krausse *et al*., 2004, Shirazi *et al.,* 2007, Panneerselvam *et al.,* 2009). Bafna PA were studied pepticare, which is a herbomineral formulation of the ayurveda medicine consisting of the herbal drugs *glycyrrhiza glabra linn, Emblica officinalis* and *tinospora cordifolia* at various doses (125, 250,500,1000m/kg, P.O) of pepticare on gastric on gastric secretion and gastric ulcers in pylorus-ligation and on ethanol-induced ulcers (Bafna and Balaraman, 2005). Bennett demonstrated deglycyrrhizinated licorice using a rat model of Aspirin-induced gastric mucosal damage (Bennett *et al.,* 1980). He suggested that several components exist in the extract which promote gastric healing, although in consistencies are apparent between these studies. *Glabra* reduces stomach secretion produces thick protective mucus which covers the lining of stomach and therefore protects from peptic ulcers and other inflammatory diseases. Further it has been reported to raising the local concentration of prostaglandins which promotes mucous secretion and cell proliferation in the stomach (Khare, 2004). Presence of such a wide range of chemical compounds indicates that the plant

could serve as a "lead" for the development of novel agents having good efficacy in various disorders in the coming years.

Ficus religiosa

Ficus religiosa, commonly known as "peepal tree" is one of the foremost plants utilized from antiquity till to date (Ghani, 1998). It is also known by various other names as bo tree, bodhi tree, Buddha tree, sacred tree etc. It belongs to family moraceae (Hamed, 2011). The bark of *F. religiosa* is reputed to have a number of chemical constituents. It contains tannins, saponins, flavonoids, steroids, terpenoids and cardiac glycosides (Ruby *et al.*, 2000). The bark has also been reported to contain bergapton, bergaptol, lanosterol, β- sitosrerol, stigmasterol, lupen-3-one, β-sitosterol-α-glucoside (phytosterolin), vitamin K1, lupeol, lupeol acetate, α-amyrin acetate (Joseph and Justin, 2010). *Ficus religiosa* has been extensively used in traditional medicine for the management of various types of diseases like diarrhoea, asthma, cough, toothache, migraine, in gastric problems, haematuria, diabetes, diarrhoea, leucorrhoea, anxiety, cardiac tonic, vomiting (Pandit *et al.*, 2010, Khan *et al.*, 2011). *F. religiosa* possess a wide range of pharmacological activities anti-ulcer activity, anti-convulsant activity, anti-inflammatory activity, anti-microbial activity, anti-anthelmentic activity , anti-asthmatic and anti-amnesic (Malhotra *et al.*, 1960, Viswanathan *et al.*, 1990, Hemaiswarya *et al.*, 2009, Kaur *et al.*, 2010, Khan *et al.*, 2011, Patil *et al.*, 2011, Sawarkar *et al.*, 2011). The alcoholic extract of *F. religiosa* was screened for antiulcer activity in swiss albino rats against pylorus ligation induced ulcers, ethanol induced ulcers and asprin-induced ulcers at dose level of 250 mg\kg and 560 mg\kg. The alcoholic extract of *F. religiosa* inhibited ulceration by significantly decreasing the gastric volume, total acidity, free acidity and ulcer index (Saha and Goswami, 2010). The ethanolic extract of stem bark of *F. religiosa* also exhibited potential antiulcer activity exhibited potential antiulcer activity. The antiulcer activity of *F. religiosa* was evaluated in vivo against cold restrained stress and indomethacin-induced gastric ulcers and pylorus ligation assay. The extract (100, 200 and 400 mg\kg) significantly reduced the ulcer index in all assay used (Khan *et al.*, 2011). Since *F. religiosa* is a non toxic, highly promising natural crude drug having a wide spectrum of biological functions. It is expected that it may find application as a novel drug in the near future to control various diseases.

ACKNOWLEDGEMENT

We are highly thankful to Management and Chairman of our college S. Gurwinder Bahra and S. Nirmal Singh Rayat for their co-operation and providing us scientific facilities.

REFERENCES

Abuzarova ER., Gorshkov OV., Chernova OA., Chernov VM., Akberova NI., Abdulkhakov RA. Ulcer disease and their associations with persistence of Mycoplasma hyorhinis and Helicobacter pylori genotypes. Eksp klin Gastroentrol. 2008: 27-31.

Akthar MS., Akthar AH., Khan MA. Antiulcerogenic effects of *Ocimum basilicum* extracts, volatile oils and flavanoids glycosides in albino rats. International J of Pharmacognosy. 1992; 30: 97–104.

Ambawade V., Kasture VS., Kasture SB. Anticonvulsant Activity of roots and rhizomes of *Glycyrrhiza glabra Linn.* Indian J Pharmacology. 2002; 34: 251-255.

Buti et al. Helico bacter Pylori cytotoxin-associated gene A(cag A)subverts the apoptosis-stimating protein of $p^{53}(ASPP_2)$ tumor suppressor pathway of the host. 2011; 1-6.

Baskar AA., Ignacimuthu S. Chemopreventive effect of *Cynodon dactylon* (L.) Pers. extract against DMH-induced colon carcinogenesis in experimental animals. Exp Toxicol Pathol. 2010; 62(4): 423-431.

Bansod S and Rai M. Antifungal Activity of Essential Oils from Indian Medicinal Plants against Human Pathogenic *Aspergillus fumigatus* and *A. niger*. World Journal of Medical Sciences. 2008; 3(2): 81-88.

Bafna PA and Balaraman R. Anti-ulcer and anti-oxidant activity of pepticare, a herbomineral formulation. J Phytomedicine. 2005; 12(4): 264-70.

Bennett A., Clark-Wibberley T., Stamford IF., Wright JE. Aspirin-induced gastric mucosal damage in rats: cimetidine and deglycyrrhizinated liquorice together give greater protection than low doses of either drug alone. J Pharmacy and Pharmacology.1980; 32: 151.

Chopra., R.N., Nayar S.L., Chopara I.C. Council of scientific and Industrial research (CSIR), 1st Edn council of Scientific and Industrial research (CSIR), New Delhi. 1999; 88.

Chopra D and Simon D. The Chopra Centre Herbal Handbook: Forty Natural Prescriptions for Perfect Health. Three Rivers Press, New York, 2000.

Dhar M L., Dhar M M., Dhawan BN., Mehrotra BN., Roy C. Screening of Indian plants for biological activity, Part I. Indian Journal of Experimental Biology. 1968; 6232–247.

Dharmani P., Kuchibhotla V. K., Maurya R., Srivastava S., Sharma S., Patil G. Evaluation of anti-ucerogenic and ulcer-healing properties of *ocimum sanction* Linn. J. Ethnophamacol. 2004; 93:197-206.

Demizu S., Kajiyama K., Takahashi K., Hiraga Y., Yamamoto S., Tamura Y., Okada K., Kinoshita T. Antioxidant and antimicrobial constituents of licorice: isolation and structure elucidation of new benzofuran derivative. Chem. Pharm. Bull. 1988; 36: 3474-3479.

Fatemeh N., Ali M. A., Soheila A., Masoumeh G., Hamid M., Mohammad K. African Journal of Pharmacy and pharmacology. 2011; 5(2): 155-159.

Franko TG, Richter JE. Proton-pump inhibitors for gastric acidrelated disease. Cleve. Clin. J. Med. 1998; 65: 27-34.

Fukai T., Ali M., Kaitou K., Kanda T., Terada S., Nomura T. Anti-Helicobacter pylori flavonoids from licorice extract. Life Sci. 2002; 71: 1449-1463.

Griffin MR., Piper JM., Daugherty JR., Snowden M., Ray WA. Non steroidal anti-inflammatory drug use and increased risk for peptic ulcerdisease in elderly persons. Ann Intern Med. 1991; 114(4): 257-263.

Garg VK., Paliwal SK. Anti-inflammatory activity of aqueous extract of *Cynodon dactylon*. Int J Pharmacol. 2011; 1-6.

Glolade A.A., Lockwood G.B. Toxicity of *Ocimum Sanctum* L. Essential oil to Aedes aegyptilarvae & its chemical composition: jeobp. 2008; 11(2): 148-153.

Ghani A. Medicinal plants of Bangladesh with chemical constituents and uses Asiatic Society of Bangladesh Dhaka. 1998; 236.

Hwang HJ., kim P., kim C.J., Lee HJ., Shim I., Yin CS., Yang Y., Hahm DH. Antinociceptive effect of amygdalin isolated from prunus armeniaca on formalin- induced pain on rats. Pharm. Bull. 2008; 31(8): 1559-156.

Heinrich M. Plantas medicinalis Iberoamericanas. Journal of ethnopharmacology. 2009; 124(3): 656-657.

Hussain EHMA., Jamil K., Rao M. Hypoglycemic, hypolipidemic and antioxidant properties of Tulsi (*Ocimum sanctum*) on streptozotocin induced diabetes in rats. Indian J of Clin Biochemistry. 2001; 16(2): 190-194.

Hemaiswarya S., Poonkothai M., Raja R., Anbazhagan C. Comparative study on the antimicrobial activities of three Indian medicinal plants. Egypt J Biol. 2009; 1: 52-57.

Hamed M.A. Beneficial effect of *Ficus religiosa* Linn. on high fat induced hypercholesterolemia in rats. Food Chem. 2011; 129: 162-170.

Isbrucker RA and Burdock GA. Regulatory Toxicology and Pharmacology. 2006; 46: 167-192.

Joseph B and Justin SR. Phytopharmacological and Phytochemical Properties of three *Ficus* species: An overview. International journal of pharma and Bio sciences. 2010; 1(4).

Kumar SS., Rai PK., Mehta S, Kumar RS., Watal G. Assessment of Antidiabetic potential of cynodon dactylon extract in streptozocin diabetic rats. Indian Journal of clinical Biochemistry. 2004; 24(4).

Kumar R, Bheemachari, Patel M, Bansal R, Singh L. Evaluation of antiepileptic activity of leaf extract of *Cynodon dactylon* in validated animal models. Int J Pharm Res. 2010; 1(2): 65-73.

Khan., M.R.I., M.A. Islam., M.S. Hossain., M. Asadujjaman., M. I. I. Wahed et al. Antidiabetic effects of the different fractions of ethanolic extracts of Ocimum sanctum in normal and alloxon induced diabetic rats. J.Sci. Res. 2010; 2: 158-168.

Krausse R., Bielenberg J., Blaschek W., Ullmannu. In vitro anti-*Helicobacter Pylori* activity of extractum liquiritiae glycyrrhizin and its metabolites. J Antimicrob Chemother. 2004; 54(1): 243-246.

Khare CP. Encyclopedia of Indian Medicinal Plants. New York: Springer-Verlag. 2004; 233-5.

Khan M. S. A., Hussain S. A., Jais A. M. M., Zakaria Z. A., Khan M. Anti-ulcer activity of *Ficus religiosa* stem bark ethanolic extract in rats. J Med Plants Res. 2011; 5(3): 354-359.

Kaur H., Singh D., Singh B., Goel R. K. Anti-amnesic effect of *Ficus religiosa* in scopolamine-induced anterograde and retrograde amnesia. Pharm Biol. 2010; 48(2): 234-40.

Lunevicius R., Morkevicius M. Management strategies early results, benefits and risk factors of laparoscopic repair of perforated peptic ulcer. World J surg. 2005; 29: 1299-1310.

Lychkova AE., Tsaregorodtseva TM., Serova TI. Cytokine profile during experimental gastric and duodenal ulcers: The serotonin role. Eksp. Klin.Gastro entrol. 2010; 2: 37-39.

Lalit M., Amberkar MV., Meena Kumari. *Ocimum Sanctum* Linn (Tulsi)- An overview international Journal of pharmaceutical sciences review and research. 2011; 7(1): 51-53.

Lakshmi T, Geetha R.V. Glycyrrhiza Glabra Linn commonly known as licorice: A therapeutic Review. International Journal of pharmacy and pharmaceutical sciences. 2011; 3(4): 20-25. Marietta J. O. E Bertleff., John F. Lange. Perforated peptic ulcer disease: A review of history and treatment. Dig Surg. 2010; 27: 161-169.

Mandal S., D.N.Das., K.De. Ocimum sanctum linn a study on gastric ulceration and gastric secretion in rats. Ind. J. Physiol. Pharmacol., 1993,37:91-92.

Malhotra C. L., Das P. K., Dhalla N. S. Parasympatholytic activity of *Ficus religiosa* Linn. Indian J Med Res. 1960; 48: 734-742.11; 3: 152-153.

Najafi M., Nazemiyeh H., Ghavimi H., Gharakhani A., Garjani A. Effects of hydroalcoholic extract of *Cynodon dactylon* (L.) Pers. on ischemia/reperfusion-induced arrhythmias. DARU 2008; 16 (4): 233-238.

Nair G.A. Seminar on Research in Ayurveda and Siddha. J. Ethnopharmacol. 1995; 57: 20-22.

Oudhia, P., 2003. Traditional medicinal knowledge about herb Doobi (cynodon dactylon) in Chhatisgarh, India. http://www. Botanical . com \ column_poudhia/III_doobi.html.

Pahwa R., Neeta., Vipin K., Kohli K. Clinical manifestations, causes and management strategies of Peptic Ulcer Disease. International Journal of pharma sciences and drug research. 2010; 2(2): 99-10.

Pandey R., Misra V., Misra S.P., Dwivedi M., Kumar A., Tiwari B.K. *Helicobacter pylori* and gastric cancer. Asian Pac J cancer Prev. 2010; 11(3): 583-588.

Pandey M.M., S. Rastogi., A.K. Rawat. The internet journal of alternative medicine. 2008; 6(1): 1-10.

Patil M., Jalalpure SS., Prakash NS., Kokate C.K. Antiulcer properties of *cynodon dactylon* extracts in rats. Acta Horticultural. 2005; 680-115.

Pal DK. Determination of brain biogenic amines in *cynodon dactylon* pers. and *cyperus rotundus* treated mice. Int J pharm Sci. 2009; 1(1): 190-197.

Parekh J., Jadeja D., Chanda S. Efficacy of aqueous and methanol extracts of some medicinal plants for potential antibacterial activity. Turk J Biol. 2005; 29: 203-210.

Prakash P and Gupta Nellu. Therapeutic uses of *Ocimum sanctum* Linn. With a note on eugenol & its pharmacological actions, a short review. Indian J. Physiol. Pharmacol. 2005; 49(2): 125-131.

Panneerselvam K., Kuppuswamy K., Kodukkur VP. Hypolipidemic activity of 18β-glycyrrhetinic acid on streptozotocin-induced diabetic rats. Eur J Pharmacology. 2009; 612(1-3): 93-97.

Pandit R., Phadke A., Jagtap A. Antidiabetic effect of *Ficus religiosa* extract in streptozotocin-induced diabetic rats. J Ethnopharmacol. 2010; 128: 462-466.

Patil M. S., Patil C. R., Patil S. W., Jadhav R. B. Anticonvulsant activity of aqueous root extract of *Ficus religiosa*. J Ethanopharmacol. 2011; 133: 92-96.

Richardson CT. Role of Aggressive Factors in the pathogenesis of Peptic Ulcer Disease. Scand J Gastroenterol. 1990; 25(1): 37-43.

Reilly JP. Safety profile of the proton-pump inhibitors. Am. J.Health Syst. Pharm. 1999; 56(23): S11-S17.

Ravindra Babu DS, Neeharika V, Pallavi V, Reddy MB. Antidiarrheal activity of *Cynodondactylon*. Pers. Pharmacogn Mag. 2009; 5: 23-27.

Ruby J., Nathan PT., Balasingh J., Kunz TH. Chemical composition of fruits and leaves eaten by short- nosed fruitbat, Cynopterus sphinx. J Chem Ecol. 2000; 26: 2825-41.

Rajeshwari S. Ocimum Sanctum. The Indian home remedy. Cipla Ltd, Bombay, (1992).

Singha S., Khajuriaa A., Tanejab SC., Khajuriab RK., Singha S., Qazia GN. The gastric ulcer protective effect of boswellic acids, aleukotriene inhibitor from Boswellia serrata, in rats. Phytomed 2008; 15(6-7): 408-415.

Singh V., Birendra V.K., Vishal S. A review on ethnomedical uses of *ocimum sanctum* (Tulsi). International research Journal of pharmacy. 2011; 2(10): 1-3.

Shahedur Rahman., Rezuanul Islam., Kamruzzaman., Khasrul Alam., Abu Heena Mastofa Jamal. *Ocimum sanctum* L: A Review of photochemical and pharmacological Profile. American Journal of drug discovery and development. 2011; 1-15.

Shishodia S, Majumdar S, Banerjee S, Aggarwal BB. Urosolic acid inhibits nuclear factor-kappa B 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 2003; 63:4375-83.

Sen P. Therapeutic potentials of tulsi: From experience to facts. Drugs news and views. 1993; 1(2): 15-21.

Shankar M., Bijay R., Mirdha., Mahapatra S.C. The science behind sacredness of tulsi (*ocimum sanctum* Linn.) Indian J physiol pharmacol. 2009; 53(4): 291-306.

Singh S., Taneja M., Majumdar DK. Biological activities of *Ocimum sanctum* L. fixed oil- An overview. Indian J Exp Biol. 2007; 45: 403-412.

Singh S., Majumdar DK. Evaluation of the gastric antiulcer activitry of fixed oil- *Ocimum sanctum* (Holy basil). J Ethnopharmacol. 1999; 65: 6513-19.

Singh S.K., P.K.Rai., S.Mehta., R.K Gupta., G.Watal. Curative effect of *cynodon dactylon* against STZ induced hepatic injury in diabetic rats. Ind J.clin. Biochem. 2009; 24:4010-413.

Shabi MM., Gayathri K., Venkalakshmi R., Sasikala C. Chemical constituents of hydro alcoholic extract and phenolic fraction of *Cynodon dactylon* . Int J chem. Tech res. 2010; 2(1): 149-154. Surendra V., Prakash T., Sharma UR., Goli D., Fadadu SD., Kotresha D. Hepatoprotective activity of aerial parts of *Cynodon dactylon* against CCl_4 induced hepatotoxicity in rats. Pharmacogn Mag. 2008; 4: 195-201.

Singh S.K., A.N. Kesari., R.K Gupta., D.Jaiswal., G. watal. Assessment of antidiabetic potencial of *cynodon dactylon* extract in streptozotocin diabetic rats. J. Ethnopharmacol. 2007; 114: 174-179.

Santhi R, Annapoorani S. Efficacy of *Cynodon dactylon* for immunomodulatory activity. Drug Invention Today. 2010; 2 (2): 112-114.

Segal R., Pisanty S., Wormser R., Azaz E., Sela MN. Anticariogenic activity of licorice and glycyrrhizine I: Inhibition of in vitro plaque formation by Streptococcus mutans. J Pharmaceutical Sciences. 1985; 74: 79–81.

Shirazi MH., Ranjbar R., Eshraghi S., Sadeghi G., Jonaidi N., Bazzaz N., Izadi M., Sadeghifard N. An Evaluation of Antibacterial Activity of *Glycyrrhiza glabra Linn* Extract on the Growth of Salmonella, Shigella and ETEC E. coli. *J Biological Sciences*. 2007; 7(5): 827-829.

Saha S and Goswami G. Study of anti ulcer activity of *Ficus religiosa* L. on experimentally induced gastric ulcers in rats. Asian Pacific Journal of Tropical Medicine. 2010; 791-793. Sawarkar H. A., Singh M. K., Pandey A. K., Biswas D. In vitroanthelmintic activity of *Ficus bengalhensis, Ficus caria* & *Ficus religiosa*: a comparative anthelmintic activity. International J PharmTech Research. 2011; 3: 152-153.

Tabassum I., Siddiqui Z N., Rizvi S J. Effects of *Ocimum sanctum and Camellia sinensis* on stress-induced anxiety and depression in male albino *Rattus norvegicus*. Indian J pharmacol. 2010; 42(5): 283-288.

Taro N., Toshio F., Toshiyuki A. Chemistry of phenolic compounds of licorice (Glycyrrhiza species) and their estrogenic and cytotoxic activities. J Pure Appl. Chem. 2002; 74(7): 1199-1206.

Uma Devi P., Ganasoundari A., Vrinda B., Srinivasan KK., Unnikrishnan MK. Radiation protection by the *Ocimum* flavonoids orientin and vicenin: Mechanisms of action. Radiat Res. 2000; 154: 455-60.

Verma M. A Review on Peptic ulcer: A global threat. J Pharm Res. 2010; 3(9): 2088-2091.

Vaananenn PM., Medding JB., Wallace JI. Role of oxygen-derived free radicals in indomethacin induced gastric injury. Am J Physiol. 1991; 261: G470–G475.

Vane JR and Botting RM. Mechanism of action of non steroidal anti inflammatory drugs. Am J Med. 1998: 104; 2S-8S.

Vinod K., Chandra H., Andola., Hema lohani., Nirpendra chauhan. Pharmacological review on *ocimum sanctum* Linnaeus: A queen of herbs. Journal of pharmacy research. Journal of pharmacy research. 2011; 4(2), 366-368.

Vinod K., Andola H. C., Lohani H., Chauhan N. Pharcological review on *ocimum sanctum* Linnaeus: A queen of herbs. Journal of pharmacy research. 2011; 4(2): 366-368

Viswanathan S., Thirugnanasambantham P., Reddy M. K., Narasimhan S., Subramaniam G. A. Anti-inflammatory and mast cell protective effect of *Ficus religiosa.* Ancient Sci Life. 1990; 10: 122-125.

Yanpallewar SU., Rai S., Kumar M., Acharya SB. Evaluation of antioxidant and neuroprotective effect of *Ocimum sanctum* on transient cerebral ischemia and long term cerebral hypoperfusion. Pharmacol Biochem Behav. 2004; 71(9): 155-164.