International Journal of Research
Available at https://edupediapublications.org/journals
e-ISSN: 2348-6848
p-ISSN: 2348-795X
Volume 04 Issue 10
September 2017

Assessment Of The Anti-Ulcer Potential Of Some Indian Medicinal Plants Extract In Rats

Lakshmi Priya.G & Dr. Mary Josephine Rani.A
[1]Deptof Zoology, Auxilium college, Vellore, Tamil Nadu, India.
Email: lakshmiak22@gmail. & comlakshmiarun22@gmail.com,

ABSTRACT

The antiulcer activity of the poly herbal formulation (composed of the leaf extracts from Lantana camara, Annona muricata, Kalanchoe pinnata) was evaluated in pylorus ligated ulcer model in rats. The extract at dose of 1000mg/kg produced significant inhibition of gastric lesion induced by above mentioned method. The extract reduced ulcerative lesion, gastric volume, free and total acidity and pH of gastric juice in the model. The result obtained suggesting that extract possesses significant anti-ulcer activity.

Keywords: Antiulcer, gastric lesion, Lantana camara, Annona muricata, Kalanchoe pinnata, free acidity, total acidity, ulcer index, gastric juice.

INTRODUCTION

Peptic ulcers are a common disorder of the entire gastrointestinal tract. Of nearly 8 to 10% of the global population affected by peptic ulcers, approximately 5% of them suffer from gastric ulcers[5]. The ulcers that affect the gastrointestinal system are usually aggravated by a disproportion between destructive and defensive factors in the stomach. Although considered as multifactorial disease.

Gastric ulcer is one of the major gastrointestinal disorders that affect considerable number of people around the world, while growing in occurrence and prevalence globally [6]. Some authors refer to gastric ulcers as the new "plague" of the 21st century [22]. It has been projected that 14.5 million of the worldwide population are affected by gastric ulcers with a mortality rate of 4.08 million [15]. The pathophysiology of gastric ulcer is associated with the imbalance between aggressive and protective factors in the stomach. Gastric mucosal damage occurs when noxious factors "overwhelm" an intact mucosal defense, or weakening of the mucosal defensive mechanisms [14]. The noxious factors in this context include alcohol ingestion, acid and pepsin secretion, poor diet, stress, reactive oxygen species (ROS), the use of non-steroidal anti-inflammatory drugs (NSAIDs) and Helicobacter pylori infection [25,35]. On the other hand, the key defense factors and mechanisms that afford mucosal defense include sufficient mucus secretion and mucosal blood flow, bicarbonate secretion, intact mucus barrier, prostaglandins, surface active phospholipids, increased levels of antioxidants, activity of anti-inflammatory compounds and adequate levels of nitricoxide (NO) [35,18,3].

Medicinal plants are part and parcel of human society to combat diseases, from the dawn of civilization [10]. There exists a plethora of knowledge, information and benefits of herbal drugs in our ancient literature of Ayurvedic (Traditional Indian Medicine), Siddha, Unani and Chinese medicine. According to the World Health Organization, 2003 about 80% of the population of developing countries being unable to afford pharmaceutical drugs rely on traditional medicines, mainly plant based, to sustain their primary health care needs [12].

A retrospection of healing power of plants, a return to natural remedies is absolute need of our time. Medicine of plant origin is based upon the premise that plants contain natural substances that can promote health and alleviate illness [1]. Stomach ulcer is among the major disease of GI, for which a large number of traditional and modern medicines are being utilized. Among these, the medicines of plant origin are more popular because of their less adverse effect [23].

The ligation of the pyloric end of the stomach causes accumulation of gastric acid in the stomach. This increase in the gastric acid secretion causes ulcers in the stomach. The lesions produced by this method are located in the lumen region of the stomach [9]. Pyloric ligation enhances mucosal damage because it interferes with gastric mucosal resistance and modulates the level of cytoprotective PGs, cytokines, membrane lipid peroxidation (TBARS) and endogenous glutathione [31].

Medicinal plants represent an important source of medically important compounds. Since ancient time, medicinal plants are used to cure several types of health problems. Systemic analysis of these plants provides a variety of bioactive molecules for the development of newer pharmaceutical products. Recently, there is a growing interest in the pharmacological evaluation of various plants used in different traditional system of medicine. In last few decades, many of traditionally known plants have been extensively studied by advanced scientific techniques and reported for various medicinal properties viz, anticancer activity, anti-inflammatory activity, antidiabetic activity, anthelmintic, antibacterial activity, antifungal activity, hepatoprotective activity, antioxidant activity, larvicidal activity etc[24,13,27]. *Lantana camara* Linn.is a flowering ornamental plant belonging to family Verbenaceae.*L. camara* is also known as Lantana, Wild Sage, Surinam Tea Plant, Spanish flag and West Indian lantana. *L. camara* is a well-known medicinal plant in traditional medicinal system and recent scientific studies have emphasized the possible use of *L. camara* in modern medicine.

Lantana camara introduced in India as an ornamental plant but entirely naturalized and found throughout India. However, it is listed as one of the significant medicinal plants of the world [26].The plant Lantana camara (Verbanaceae), generally known as wild or red sage is the most widespread species of this genus and it is a woody straggling plant with various flower colors, red, pink, white, yellow and violet. It is an ever green strong smelling shrub, with stout recurred prickles, leaves opposite, ovate, acute or sub- acute, crenate -serrate, scab rid on both side [33].

Scientific classification

Kingdom: Plantae

Order : Lamiales

Family : Verbenacea

Genus : *Lantana*

Species : *camara*

L. camara is a low erect or subscandent vigorous shrub withtetrangular stem, stout recurved pickles and a strong odourof black currents. Plant grows up to 1 to 3 meters and it canspread to 2.5 meter in width. Leaves are ovate or ovateoblong, acute or

sub acute crenate serrate, rugoseabove,scabrid on both sides. The leaves are 3-8 cm long by 3-6 cmwide and green in colour. Leaves and stem are covered withrough hairs. Small flower held in clusters (called umbels).Colour usually orange, sometime varying from white to redin various shades and the flower usually change colours asthey ages. Flowers are having a yellow throat, in axillaryhead almost throughout the year. The calyx is small, corollatube slender, the limb spreading 6 to 7 mm wide anddivided in to unequal lobes. Stemen four in two pairs,included and ovary two celled, two ovuled. Inflorescencesare produced in pairs in the axils of opposite leaves. Inflorescences are compact, dome shaped 2-3 cm across and contain 20-40 sessile flowers. Root system is very strong and it gives out new fresh shoots even after repeated cuttings [28].

Annona muricata L. belongs to the family of Annonaceae has a widespread pantropical distribution and has been pridely known as corossol. It is a widespread small tree and has its native in Central America [2]. Intensive chemical investigations of the leaves and seeds of this species have resulted in the isolation of a great number of acetogenins. The isolated compounds display some of the interesting biological or the pharmacological activities, such as antitumoral, cytotoxicity, antiparasitic and pesticidal properties. Roots of these species are used in traditional medicine due to their antiparasitical and pesticidal properties [7].

Scientific classification

Kingdom: Plantae-Plants

Class: Magnoliopsida

Order: Magnoliales

Family: Annonaceae

Genus: Annona

Species: muricata

The genus name ‘Annona’ is from the Latin word ‘anon’, meaning ‘yearly produce’, referring to the fruit production habits of the various species in this genus. Annona muricata is a slender, evergreen tree, 5-10 m in height and 15 cm in diameter; trunk straight; bark smooth, dull grey or grey-brown, rough and fissured with age; inner bark pinkish and tasteless; branches at first ascending with the crown forming an inverted cone, later spreading; crown at maturity spherical due to lack of apical dominance; twigs brown or grey, bearing minute raised dots (lenticels); root system extensive and superficial, spreading beyond the diameter of the crown although shallow rooted; juvenile plants have a taproot that is eventually lost. Leaves alternate, 7.6-15.2 cm long, 2.5-7.6 cm wide, leathery, obovate to elliptic, glossy on top, glabrous on underside, simple; stipules absent; blade oblanceolate, green on top, paler and dull on under side with fine lateral nerves; a strong, pungent odour; petioles short, 3-10 mm long [4].

The knowledge of traditional medicine and medicinal plants and their study of scientific chemical principles may lead to the discovery of newer and cheaper drugs. Kalanchoe pinnata (Lam., syn. Bryophyllumpinnatum, B. calycinum; Local name: Pathorkuchi, Coughpatha;English name: Air plant; Family: Crassulaceae) is an herbfound ubiquitously in Bangladesh. It has tall hollow stems,fleshy dark green leaves that are distinctly scallopedand trimmed in red, and bell-like pendulous flowers [8].

Kalanchoe pinnata (K. pinnata) has become naturalizedin temperate regions of Asia, Australia, New Zealand, WestIndies, Macaronesia, Mascarenes, Galapagos, Melanesia,Polynesia, and Hawaii. It is also widely distributed in thePhilippines, where it is known as katakatakaorkatakatakawhich means astonishing or remarkable [8]. The leaves of K. pinnata have a variety of uses in the traditional system of medicine in Bangladesh. They are eaten fordiabetes, diuresis, dissolving kinney stones, respiratorytract infections, as well as applied to wounds, boils, andinsect bites [8]. It is useful for preventing alcoholic, viral andtoxic liver damages. The aqueous extract of this plant haveshown anti-inflammatory, anti-diabetic, anti-tumorandcutaneousleishmanicidal activities [19,30,32,34].

Scientific classification

Kingdom: Plantae-Plants
Class: Magnoliopsida
Order: Saxifragales
Family: Crassulaceae stonecrop family
Genus: Kalanchoe
Species: pinnata

Kalanchoe pinnata (Family: Crassulaceae) is an important plant which has many traditional medicinal uses. *Kalanchoe pinnata* (Family: Crassulaceae) is an erect, succulent, perennial shrub that grows about 1.5 m tall and reproduces through seeds and also vegetatively from leaf bubils. It has a tall hollow stems, freshly dark green leaves that are distinctively scalloped and trimmed in red and dark bell-like pendulous flowers. This plant can easily be propagated through stems or leaf cutting. It is an introduced ornamental plant that is now growing as a weed around plantation crop. *K. pinnata* is used in ethnomedicine for the treatment of earache, burns, abscesses, ulcers, insect bites, whitlow, diarrhoea and cithiasis[21]. In traditional medicine, *Kalanchoe* species have been used to treat ailments such as infections, rheumatism, and inflammation [20] and have immunosuppressive effect as well [17].

MATERIALS AND METHODS

Collection And Extraction Of The Plant

The leaves of L.camara, A.muricata and K.pinnatum were collected around Vellore district. After washing the plant with running water, the leaves were separated and dried in shade for 20 days at room temperature. After shade drying, the leaves were grinded through blender and converted into coarse of powder. The powder was extracted by continuous hot extraction using the Soxhlet apparatus. The extracts were collected and preserved in a desiccator until used for further studies.

Test animal

Adult healthy wistar rats weighting 150 g were used and kept in the animal house. The animals were kept in plastic cages (34 × 47 × 18 cm3) at animal house, in an air conditioned environment with four rats in each cage and maintained at room temperature of (25 ± 2) _C with relative humidity (60% ± 10%) under 12 h night and light cycle. The animals used for the experiment were approved by animal ethics committee.

Preparation and Dose of the Test Drug

The dose of the test drug was calculated by the method of Miller and Tainter (1944), found to be 1000mg/kg the dose of the extract was calculated with

reference, the aqueous extract of the drug was used in the dose of 150mg/kg. Standard drug, Rabeprazole (Manufactured in India by Cipla Laboratories Ltd.) was used in the dose of 20mg/kg.

Phytochemical analysis

The preliminary phytochemical analysis of *L.camara*, *A.muricata*, *K.pinnata*leaves aqueous extract was carried out for carbohydrate, saponins, flavonoids, triterpenoids, tanins and alkaloids.

Acute Toxicity Study

The oral acute toxicity study of aqueous extract of L.camara, A.muricata, K.pinnatum
Were evaluated according to Organization for Economic Cooperation and Development (OECD) guideline 420 on wistar rats, where the limit test dose of 1000 mg/kg was used. All the animals were kept at overnight fasting before to every experiment with free excess to water. The test drug was administered and observed for 14 days to determine urea, creatinine, SGOT, SGPT level.

EXPERIMENTAL DESIGN

The rats were randomly divided into 6 groups, of 4 rats each as follows:

Group-I: Control group animals received no treatment.

Group-II: animals were pylorus ligated (Negative control).

Group-III: animals received 1000 mg/kg body weight of freshly prepared L.camara.

Group-IV: animals received 1000 mg/kg bodyweight of freshly prepared A.muricata.

Group-V: animals received 1000 mg/kg body weight of freshly prepared K.pinnatum.

Group-VI: animals received 20mg/kg body weight of Rabeprazole.

All treatments were administered orally for 11 days. Score of mucosal damage were microscopically observed.

Histological observation

In the 11th day, after 24 h fasting the animals were sacrificed and stomach of each animal was opened along the greater curvature. Specimens of the gastric tissue were fixed in 10% buffered formalin and were processed in the paraffin tissue-processing machine. Sections of the stomach were sectioned at 5µm and stained with hematoxylin and eosin for histological evaluation [11]. Paraffin sections were stained with toluidine blue. The effect of drugs was evaluated through assessment of inflammatory and necrotic changes in the mucosal tissue.

Pyloric ligated Gastric Ulceration and Its Protection Studies

Before ulcer induction animals of both control and experimental groups kept separately in standard controlled conditions were fasted for 24 h with free access to water. The rats were anesthetize prior to ligation of the pylorus. A long incision was made in the abdomen just below the sternum on the anesthetized rats. The stomach was exposed, and a thread was passed around the pyloric sphincter and tied in a tight knot. Care was taken while tying the knot to avoid involving blood vessels in the knot. The abdomen was sutured, and the skin was cleaned of any blood spots or bleeding. The animals were sacrificed 4 h after ligation by cervical dislocation [29]. *L.camara, A.muricata, K.pinnata* leaves aqueous

extract was administered orally 30 min prior to ethanol treatment to see the gastroprotective effect. Rabeprazole were administered orally at a dose of 20 mg/ kg body weight respectively.

Assessment of gross mucosal damage

The lesion in the glandular portion was examined under a 10 x magnifying glass and length was measured using a divider and scale and gastric lesion was scored as follows:

0 - Normal colored stomach,
0.5 - Red coloration,
1- Spot ulceration,
1.5 - Hemorrhagic streak,
2 - ulcers
3- Perforations

Ulcer index of each animal was calculated by adding the values and their mean values were determined and percentage inhibition was calculated [16].

% Protection = (Ulcer index Control - Ulcer index Test) × 100

Ulcer index Control

Determination of *pH* and volume of gastric juice

Gastric juice (1 mL) was diluted with 1 mL distilled water and was measured using a pH meter and the volume of gastric juice also measured by measuring tubes.

Free and Total Acidity

1ml of supernatant liquid is pipetted and diluted it to 10ml with distilled water. The solution was titrated against 0.01N NaOH using Topfer's reagent (Dimethyl-amino-azobenzene with phenolphthalein) as indicator. The end point was noted when the solution turns to orange color; this corresponds to the free acidity. Titration was continued further till the solution regained pink color to evaluate total acidity.

Acidity was calculated by using the formula:

$$\text{Acidity} = \frac{\text{Volume of NaOH} \times \text{Normality of NaOH}}{1.\ 1\ \text{N}} \times 100$$

RESULTS

Preliminary phytochemical screening

The phytochemical screening of the plant extract revealed the presence of various bioactive costituents like alkaloids, flavonoids, saponins and tanins.

Acute Toxicity Study

The oral acute toxicity study of aqueous extract of *L.camara, A.muricata, K.pinnatum*
Were evaluated according to Organization for Economic Cooperation and Development (OECD) guideline 420 on wistar rats, where the limit test dose of 1000 mg/kg was used.
No mortality observed for 14days.

Ethanol Induced Ulcers in Rats

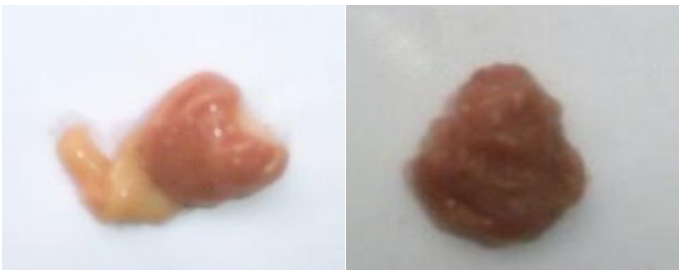
In the present study the anti-ulcer activity of leaves of *L.camara, A.muricata, K.pinnatum*. Revealed that the minimum ulcer index was observed with Rabeprazole.

Table:1 Effect of *L.camara, A.muricata, K.pinnatum* leaves aqueous extract gastric juice volume, pH, total acidity, free acidity, total ulcer index and ulcer protection.

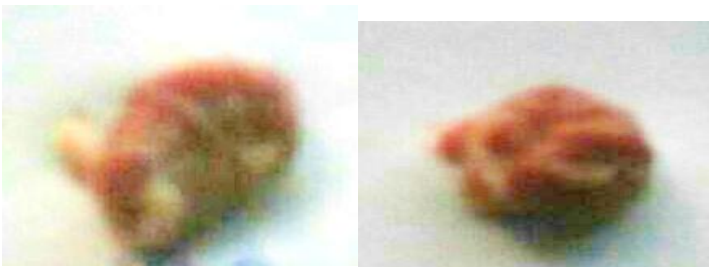
Group	Gastricjuice volume in ml	Gastricjuice pH	Free acidity (mEq/dl)	Total acidity (mEq/dl)	TotalUlcer index	Ulcer protection(%)
Control	2.97±0.20	3.1±0.30	49.6±0.10	35.2±0.30	0.01±0.00	99.7
Disease control	7.45± 0.07	1.35±0.07	98.02±0.93	114.55±0.83	3.55±0.16	11.5
L.camara 150mg/kg	1.62± 0.07	1.82±0.05	39.05±0.53	34.6±0.27	2.29±0.08	43.4
A.muricata 150mg/kg	2.37± 0.05	2.27±0.07	35.01±0.37	32.62±0.12	1.32±0.05	67.25
K.pinnata 150mg/kg	1.86±0.06	2.57±0.09	37.97±0.16	33.55±0.26	1.82±0.25	54.75
Rabeprazole 20mg/kg	2.57±0.09	2.82±0.05	33.25±0.38	31.3±0.36	0.55±0.26	86.5

Values are expressed as mean ± SEM. *P* >0.05 when compared to normal control group by Statistical analysis by One-way ANOVA followed by Dunnett's method.

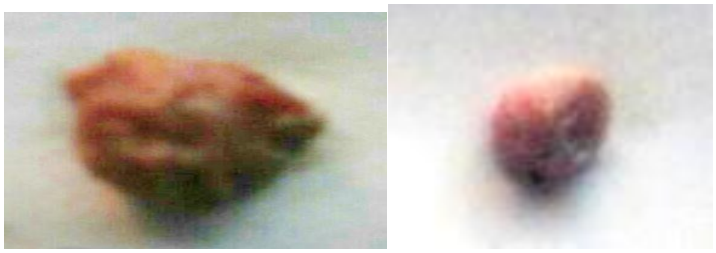
Fig: 1 Morphological Features of Stomach in Ethanol Induced Ulcer



a. Normal control **b. Experimental Control**



c. L.camara 150mg/kg **d. A.muricata 150mg/kg**

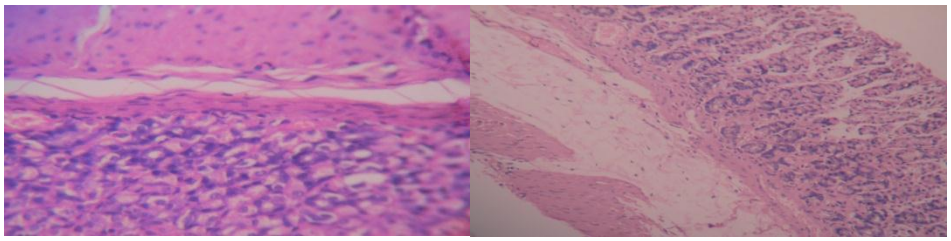


e. K.pinnata 150mg/kg **f. Rabeprazole 20mg/kg**

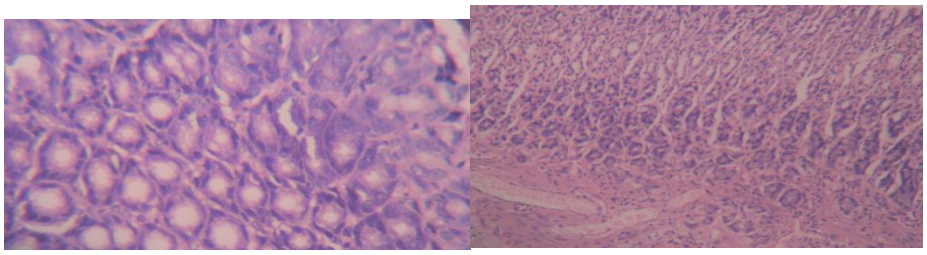
Morphological study of stomach

In normal group stomach integrity was maintained and appeared normal. In control group severe bleeding, perforation, spot ulcer were observed but, in standard group and extract treated groups, animal showed less ulceration and stomach integrity was maintained.

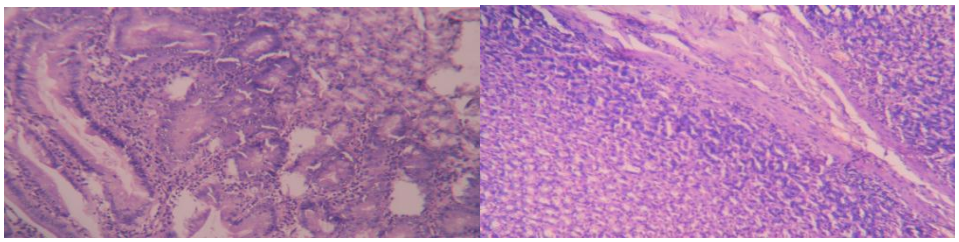
Fig: 2 Histology of Stomach in Indomethacin induced Ulcer



a. Normal control **b. Experimental Control**



c. L.camara 150mg/kg **d. A.muricata 150mg/kg**



e. K.pinnata 150mg/kg **f. Rabeprazole 20mg/kg**

Histopathological study

Histopathological examination of gastric mucosa in the normal control group showed intact gastric mucosa and continuous epithelial surface. Experimental control revealed mucosal ulceration. In *L.camara* (150mg/kg) group, superficial erosions and few ulcers accompanied with mild inflammatory was observed. In *A.muricata* (150mg/kg) group, slight ulcer with inflammatory infiltrate and congestion in few areas was observed. In *K.pinnata* (150mg/kg) group, section revealed intact mucosa with no inflammation. In Rabeprazole (20mg/kg) group, showed intact gastric mucosa without any inflammatory.

DISCUSSION

Peptic ulcer is the most common gastrointestinary disorder in clinical practice. Considering the several side effects (arrhythmia's, impotence, funaecomastia and haematopoeitic changes) of modern medicine [1], indigenous drugs possessing fewer side effects should be looked for as a better alternative for the treatment of peptic ulcer.

Pylorus ligation induced ulcers are due to auto digestion of the gastric mucosa and breakdown of the gastric mucosal barrier. These factors are associated with the development of upper gastrointestinal damage including lesions, ulcers and life threatening perforation and hemorrhage. It is also showed development of gastric ulcers in pyloric ligation model. Volume of gastric secretion is an important factor in the production of ulcer due to exposure of unprotected lumen of the stomach to the accumulating acid.

Flavonoids are among the cytoprotective materials for which antiulcerogenic efficacy has been extensively confirmed. It is suggested that, these active compounds would be able to stimulate mucus, bicarbonate and the prostaglandin secretion and counteract with the deteriorating effects of reactive oxidants in gastrointestinal lumen. The antiulcer activity of the extracts could be correlated to their proanthocyanidine (flavonoid) content. Flavonoids are proven antioxidants and are also demonstrated to have antiulcer activity [18].

The anti-ulcer activity of the leaves aqueous extract of *L.camara, A.muricata, K.pinnatum* was evaluated against gastric lesions induced by pyloric ligation.

Treatment with *L.camara, A.muricata, K.pinnatum* protected the gastric mucosa from damage by increasing the mucin content significantly. Apparently, the free radicals scavenging property of *L.camara, A.muricata, K.pinnatum* might contribute in protecting the oxidative damage to gastric mucosa. Based on the results that we obtained the *A.muricata* shows high level of gastro protection than the *L.camara, K.pinnata* and also its closer with rabeprazole.

CONCLUSION

Herbal products are well thought-out to be symbols of safeguard in comparison to the synthetic product that are regarded as unsafe to human life and environment. While herbs had been priced for their medicinal significance. The three plants extracts and anti- ulcer drug that RABI compared. Among these, the anti-ulcer drug Rabeprazole and*A.muricata*were more effective than the *L.camara, K.pinnatum* in pylorus ligation model.

REFFERENCE

[1] Akhtar AH, Ahmad KU. (1995). Anti-ulcerogenic evaluation of the methanolic extracts of some indigenous medicinal plants of Pakistan in aspirinulcerated rats. J. Ethnopharmacol. 46: 1-6.

[2] AlassaneWele, Yanjun Zhang, ChristelleCaux, Jean-Paul Brouard,Jean-Louis Pousset, Bernard Bodo, Annomuricatin C., (2004). "A novel cyclohexapeptide from the seeds of Annona muricata", C R Chimie, 7: 981–988.

[3] Amaral GP, de Carvalho NR, Barcelos RP, Dobrachinski F, PortellaRde L, da Silva MH, et al., (2013). Protective action of ethanolic extract of Rosmarinusofficinalis L. in gastric ulcer prevention induced by ethanol in rats. Food and Chemical Toxicology. 55:48–55.

[4] Anon., (1986). " The useful plants of India", Publications & Information Directorate, CSIR, New Delhi, India.

[5] Calam J, Baron JH.,(2001). Pathophysiology of duodenal and gastric ulcer and gastric cancer. Brit Med J.323:980–3.

[6] Chen H, Liao H, Liu Y, Zheng Y, Wu X, Su Z, et al., (2015). Protective effects of pogostone from PogostemonisHerba against ethanol-induced gastric ulcer in rats. Fitoterapia. 100:110–7.

[7] Christophe Gleye, Alain Laurens,ReynaldHocquemiller, Olivier Laprevote, Laurent Serani and Andre Cave, Cohibins A and B., (1997). "Acetogenins from roots of Annona muricata", Phytochemistry. 44(8): pg1541 -1545.

[8] Ghani A. (203). "Monographs of the recorded medicinal plants", Medicinal Plants of Bangladesh. 2nd ed. Asiatic Society of Bangladesh., p. 271-272.

[9] Goulart YC, Sela VR, Obici S, Vanessa J, Martins C, Otobone F *et al.*, (2005). Evaluation of gastric anti-ulcer activity in a hydroethanolic extract from *Kielmeyeracoriacea*. Braz Arch BiolTechn. 48(1):211-16.

[10] Grieve M, (2005). www.botanical.com/botanical/mgmh /h/henna- 24.html in April11.

[11] Hajrezaie M, Golbabapour S, Hassandarvish P, Gwaram NS, Hadi AH, Ali HM, et al., (2012). Acute toxicity and gastroprotection studies of a new Schiff base derived copper(II) complex against ethanol induced acute gastric lesions in rats. *PLosOne*doi: 10.1371/journal.pone.0051537.

[12] Kirtikar KR and Basu BD., (1956). Indian Medicinal Plant, 2nd ed., volume 3, India press publisher, Allahabad. 314-315.

[13] Kumar SV, Sankar P and Varatharajan R., (2009). Anti-inflammatory activity of roots of *Achyranthesaspera*. PharmaceuticalBiology. 47 (10); 973-975.

[14] Laine L, Takeuchi K, Tarnawski A., (2008). Gastric mucosal defense and cytoprotection: bench to bedside. Gastroenterology. 135(1):41–60.

[15] Laloo D, Prasad SK, Krishnamurthy S, Hemalatha S., (2013). Gastroprotectiveactivity of ethanolic root extract of Potentillafulgens Wall. ex Hook. J Ethnopharmacol.146(2):505–14.

[16] Malairajan . P Gopalakrishnan. G Narasimhan. S Veni. K.J Kavimani. S ., (2007). *J. Ethnopharmacol.*110, 348-351.

[17] McKenzie RA, DunsterPJ., (1986). "Hearts and flowers: Bryophyllum poisoning of cattle", Aust. Vet. J. 63: 222.

[18] Mota KS, Dias GE, Pinto ME, Luiz-Ferreira A, Souza-Brito AR, Hiruma-Lima CA, et al., (2009) Flavonoids with gastroprotective activity. Molecules. 14(3):979–1012.

[19] Muzitano MF, Falcão CAB, Cruz EA, Bergonzi MC, Bilia AR, Vincieri FF, et al., (2009). "Oral metabolism and efficacy of Kalanchoepinnata flavonoids in a murine model of cutaneous leishmaniasis", Planta Med.75: 307-11.

[20] Nayak BS, Marshall JR, Isitor G., (2010). "Wound healing potential of ethanolic extract of *Kalanchoe pinnata* Lam. Leaf-A preliminary study", Indian J. Experim. Biol, 2010; 48: 572-576.

[21] Okwu DE, Nnamdi FU., (2011). "Two novel flavonoids from *Bryophyllumpinnatum*and their antimicrobial Activity", J. Chem. Pharm. Res.3(2):1-10.

[22] O'Malley P. (2003). Gastric ulcers and GERD: the new "plagues" of the 21st century update for the clinical nurse specialist. Clinical Nurse Specialist CNS. 17(6):286–9.

[23] Rajkapoor B, Anandan R, Jayakas B., (2002). Anti-ulcer effect of *Nigella saliva* Linn. against gastric ulcers in rats. Current Science. 82 (2):177-179.

[24] Rajkumar V et al., (2009). Evaluation of cytotoxic potential of *Acoruscalamus*rhizome. Ethnobotanical Leaflets. 13 (6); 832-839.

[25] Rang HP, Dale MM, Ritter JM, Flower RJ GH., (2012). Rang and Dale's Pharmacology. 7th ed. Edinburgh: Elsevier Churchill Livingstone.

[26] Ross IA., (1999). "Medicinal plants of the world. Chemical constituents, traditional and modern medical uses", New Jersey, Humana Press.

[27] Sabu MC and Kuttan R., (2002).Anti-diabetic activity of medicinal plants and its relationship with their antioxidant property. Journal ofEthnopharmacology. 81 (2); 155-160.

[28] Sastri BN., (1962). "The wealth of India", CSIR New Delhi, India.

[29] Shay H, Komarov SA, Fels SS, Meranze D, Gruenstein M, Siplet H., (1945). A simplemethod for the uniform production of gastric ulceration in the rat.Gastroenterol.5:43–61.

[30] Sidhartha PA, ChandhuriKW., (1999). "Anti-inflammatory action of Bryophyllumpinnatumleaf extract", Fitoterapia.41: 527-533.

[31] Singh S, Khajuria A, Taneja SC, Khajuria RK, Singh J, Johri RK, *et al*., (2008). The gastric ulcer protective effect of boswellic acids, a leukotriene inhibitor from Boswelliaserrata in rats. Phytomedicine.15:408-15.

[32] Supratman UT, Fujita K, Akiyama H, Hayashi A, Murakami H, Sakai K, et al., (2000). "Anti-tumor Promoting Activity of Bufadienolides from Kalanchoe pinnata andK. daigremontianabutiflora",BiosciBiotechnol Biochem.165: 947-949.

[33] Thamotharan G, Sekar G, Ganesh T, Saikatsen, Raja Chakraborty, Senthil.kumar N., (2010) "Antiulcerogenic effect of *Lantana camara* Leaves on in vivo test models in Rats", Asian. Jour. Pharm.Clinical. Res. 3: 57-60.

[34] Torres-Santos ECS, Da Silva AG, Costa APP, Santos APA, Rossi- Bergmann B., (2003). "Toxicological analysis and effectiveness of oral Kalanchoe pinnata on a human case of cutaneous leishmaniasis", Phytother Res. 17: 801-803.

[35] Zheng YF, Xie JH, Xu YF, Liang YZ, Mo ZZ, Jiang WW, et al., (2014). Gastroprotective effect and mechanism of patchouli alcohol against ethanol, indomethacin and stress-induced ulcer in rats. ChemBiol Interact. 222C:27–36.