ORIGINAL ARTICLE

INTERNATIONAL JOURNAL OF RESEARCH IN PHARMACEUTICAL SCIENCES

Published by JK Welfare & Pharmascope Foundation Journal Home Page: www.ijrps.com

Gastroprotective effect of leaves of *Breyniavitis-Idaea*

Poojitha M*[1], Saravanakumar A[2], Satyanarayana S V[3]

[1]Department of Pharmaceutical Sciences, Jawaharlal Nehru Technological University Anantapur, Ananthapuramu, Andhra Pradesh, India
[2]Department of Pharmacology, Sri Venkateswara College of Pharmacy, RVS Nagar, Chittoor, Andhra Pradesh, India
[3]Department of Chemical Engineering, Jawaharlal Nehru Technological University Anantapur, Ananthapuramu, Andhra Pradesh, India

Article History:

Received on: 27 Feb 2020
Revised on: 21 Mar 2020
Accepted on: 14 Apr 2020

Keywords:

Breyniavitis-idaea,
Ethanol induced,
Indomethacin induced,
Pylorus ligation,
Cold resistant stress,
Dose Dependent

ABSTRACT

Due to the lure backs of synthetic drugs that are being used medical field has turned over to the traditional medicine which are devoid of side effects and major adverse effects. So that Herbal drugs were seen as probable replacements for the handling of PUD without showing side effects and equaling the treatment efficacy. The literature review on investigations of antiulcer activity of various plant drug, the present investigation was carried out to investigate the antiulcer potential, chemical constituents present in the methanol extract of traditional plant Breyniavitis-idaea. Gastric ulcers in experimental animals were brought by four different models like Ethanol(Alcohol) induced, NSIDS (Indomethacin) induced, Pylorus ligation method and Cold resistant stress induced method by comparing with the standard drug namely omeprazole (20mg/kg) which exhibited the dose dependent capacity of the extract (125mg/kg,250mg/kg, 500mg/kg) and also the biochemical parameters like ALP, GSH, pH and Gastric volume contents were estimated in all the selected groups (Design of Experiment). The results obtained from the study has helped to identify that 500mg/kg of plant extract has gastro protective effect in all the chosen models in comparison to the omeprazole (20mg/kg) standard drug. Owing to the prevalence of different phytoconstituents like poly phenols and flavonoids shown the dose dependent potent gastroprotective activity.

*Corresponding Author

Name: Poojitha M
Phone: 8332063418
Email: poojithamallapu91@gmail.com

ISSN: 0975-7538

DOI: https://doi.org/10.26452/ijrps.v11i2.2247

Production and Hosted by

IJRPS | www.ijrps.com

INTRODUCTION

PUD (Peptic Ulcer Disease) distresses most of the people in the world and disabling their daily activities. It is noted as one the commonest and stubborn diseases that occur in people and affect their lives (Antonio *et al.*, 2004).

There are various factors involved to cause the disease such as oxidative stress, chronic and excessive smoking, malnutrition and due to chronic use drugs like NSAID's and steroids. The imbalances in the offensive and defensive factors like HCl, enzymes, H. Pylori and Mucin, prostaglandins NO2 and carbonates and bicarbonates act as common factors in causing the PUD (Baggio *et al.*, 2003; Chiang *et al.*, 2005; Cho and Ogle, 1979; Cho *et al.*, 1976).

One of the major setbacks of the PUD treatment is the incidence and development of drug tolerance and others being relapse of disease, noting of side

Table 1: Gastroprotective Effect of *MEBV* in experimental animals

Gastroprotective Effect of MEBV in experimental animals							
Cold-Restraint	(% I)	NA	No inhibition	49.51	59.00	73.73	79.32
	UI	No ulcerous lesions	11.27 + 1.52	5.69+ 0.33*	4.62+ 0.37*	2.96 + 0.41**	2.33 + 0.39**
Pylorus ligation	(% I)	NA	No inhibition	33.85	58.96	73.60	77.74
	UI	No ulcerous lesions	18.64 + 0.52	12.33 + 0.41*	7.65 + 0.47**	4.92 + 0.19**	4.15 + 0.28**
Indomethacin	(% I)	NA	No inhibition	48.732	59.923	70.481	75.900
	UI	No ulcerous lesions	7.76 ± 0.720	4.90 ± 0.352*	4.01 ± 0.35**	3.04 ±0.58**	2.48 ± 0.421**
Ethanol model	(% I)	NA	No inhibition	42.420	58.32	70.044	75.280
	UI	No ulcerous lesions	18.69 ± 1.420	10.35 ± 0.391*	8.04 ± 0.460**	4.57 ±0.844**	4.62 ±0.491**
Group		I	II	III	IV	V	VI

(% I= Percentage of inhibition, UI= Ulcer index)
Data be situated epitomized as mean ± S.E.M, ANOVA shadowed by Dunnett's multiple comparison test. *P < 0.01 and **P< 0.001 as equated to control (n = 6 in each group)

Table 2: Effect of MEBV on GSH (μg/mg protein)

Group	Alcohol persuaded gastric ulcer model	NSAIDS persuaded gastric ulcer model	Pylorus ligation Persuaded ulcer model	Cold-restraint stress persuaded Gastric ulcer model
I	2.87± 0.330	3.05± 0.221	2.75± 0.222	2.94± 0.285
II	0.97± 0.270	0.92± 0.272	0.81± 0.26	0.94± 0.352
III	1.31± 0.321*	1.35± 0.171*	1.35± 0.22*	1.54± 0.172*
IV	1.37± 0.220**	1.54± 0.122**	1.52± 0.37**	1.65± 0.371**
V	1.65± 0.890**	1.69± 0.220**	1.74± 0.33**	1.82± 0.330**
VI	1.77± 0.331**	1.76± 0.240**	1.78± 0.24**	1.87± 0.220**

All the numbers set were expressed as mean ± SEM.*P< 0.01 when compared with control group.P< 0.01 when compared with normal group

effects on clinical observation after treatment.

These draw backs of synthetic drugs make the efficacy of drugs quite arguable. This triggered the scope for search and development of newer drugs that treat PUD. Herbal drugs were seen as potential alternatives for the treatment of PUD without showing side effects and equaling the treatment efficacy (Danielsson *et al.*, 2003; Fellenius *et al.*, 1981).

Following the literature review on investigations of antiulcer activity of various plant drug, the current study was used to explore the antiulcer potential, chemical elements present in the methanol extract of leaves of Breynia vitis-idaea., (Family: Poaceae) and the same is being reported here (Flemstrom *et al.*, 1982).

MATERIALS AND METHODS

Collection and Authentication of the plant material

The plant part of Breyniavitis-idaea (Family: Phyllanthaceae) leaves were obtained from Chittoor District, validated by Dr. Madhava Chetty, Asst Profes-

Table 3: Effect of MEBV on ALP (IU/L) of gastric ulcer persuaded models

Group	Alcohol persuaded gastric ulcer model	Indomethacin persuaded gastric ulcer model	Pylorus ligation persuaded ulcer model	Cold-restraint stress persuaded Gastric ulcer model
I	68.22± 2.54	59.24± 2.21	70.29± 2.32	76.47± 2.46
II	179.54± 2.33	188.19± 3.42	195.67± 3.38	204.22± 3.52
III	123.64± 2.43*	120.14± 3.52*	130.41± 3.22*	130.19± 2.76*
IV	113.35± 2.58**	115.22± 2.32**	116.52± 2.41**	120.49± 2.33**
V	82.45± 1.48**	86.33± 1.24**	85.22± 1.57**	98.27± 1.67**
VI	79.54± 1.12**	83.21± 1.54**	82.12± 1.33**	89.37± 1.19**

All values in the statistics set were expressed as mean ± S.E.M.*P< 0.01 when equated with control group. P< 0.01 when compared with normal set

Table 4: Effect of MEBV on Gastric volume (ml/100g)

Group	Alcohol made gastric ulcer model	NSAIDS made gastric ulcer model	Pylorus ligation made ulcer model	Cold-restraint stress made Gastric ulcer model
I	0.38 ±0.03	0.36 ±0.02	0.45 ±0.02	0.57 ±0.02
II	2.66 ±0.05	2.39 ±0.01	2.47 ±0.03	2.57 ±0.05
III	1.12 ±0.84*	1.02 ±0.03*	1.17 ±0.02*	1.22 ±0.03*
IV	0.93 ± 0.87**	0.91 ±0.05**	0.99±0.05**	0.92±0.05**
V	0.68 ± 0.91**	0.64 ±0.05**	0.69 ±0.03**	0.69±0.02**
VI	0.54 ±0.05**	0.54±0.03**	0.57 ±0.05**	0.58 ±0.05**

All values in the data set were articulated as mean ± S.E.M.*P< 0.01 when equated with control group. P< 0.01 when equated with normal group

Table 5: Effect of MEBV on pH of gastric contents

Group	Alcohol persuaded gastric ulcer model	Indomethacin persuaded gastric ulcer model	Pylorus ligation persuaded ulcer model	Cold-restraint stress persuaded Gastric ulcer model
I	5.11 ±0.19	5.60 ±0.33	5.61 ±0.41	5.67 ±0.22
II	1.49 ±0.33	1.52 ±0.21	1.62 ±0.22	1.58 ±0.12
III	3.74±0.12*	3.90 ±0.17*	3.58 ±0.33*	3.69 ±0.17*
IV	4.46 ± 0.59**	4.50 ±0.14**	4.48 ±0.37**	4.45 ±0.52**
V	4.84 ± 0.31**	4.87 ±0.22**	4.95 ±0.19**	4.79 ±0.37**
VI	5.22 ±0.29**	5.17 ±0.41**	5.22 ±0.33**	5.33 ±0.22**

All values in the data set were voiced as mean ± S.E.M.*P< 0.01 when equated with control group. P< 0.01 when equated with normal group

sor, Department of Botany, Sri Venkateswara university, Tirupati 517502, Andhra Pradesh, India.

Animals Used

Albino rats of either sex weighing 150–200g were kept in a 12 h light or dark cycle at a constant moderate thermal condition at 25°C with free access to libitum.

Acute toxicity study

Acute toxic dose of methanol extract of leaves of Breynia vitis-idaea., (Family: Poaceae) were determined following OECD guideline no. 423 (Acute Toxic Class Method). Found that the test extracts weren't deadly or toxic to the experimental animals was smooth at 2000mg/kg dose.

Ethical clearance was approved by IAEC (Institutional Animal Ethical Clearance) Reg No: SVCOP/IAEC/007/2016-17.

Design of Treatment

Group I- control (1%W/V CMC, 10 ml/kg b.w) p.o

Group II- Negative control (1%W/V CMC, 10 ml/kg b.w) p.o

Group III- MEBV (125mg/kg b.w) p.o

Group IV- MEBV (250mg/kg b.w) p.o

Group V- MEBV (500mg/kg b.w) p.o

Group VI- Std.Omeprazole (20mg/kg b.w) p.o

Ulcer inducing models

Ethanol Induced Gastric Ulcer

8ml/kg of alcohol was administered to all the assemblies of rats excluding the assembly 1 for which is well thought-out as normal healthy group (Grijalva and Novin, 1990; Gupta *et al.*, 1985). The ulcer catalog for to each rat was taken as the mean ulcer score (Hase and Moss, 1973).

NSAIDS (Indomethacin) Induced Gastric Ulcer

Ulcers lesions in the stomachs of experimental animals were induced with the help of indomethacin (40 mg/kg p.o) administered to all groups after fasting for 24h (Hoogerwerf *et al.*, 2001).

Pyloric Ligation Induced Gastric Ulcer

This procedure was not performed on normal healthy group (group 1). After 4h from surgery, animals were forfeited through cervical dislodgment and score of ulcers was noted on the dissevered stomachs (Kahraman *et al.*, 2003).

Cold-Restraint Stress-Induced Ulcers

Followed as per (Manonmani *et al.*, 1995).

Measurement of ulcer index

Ulcer index (UI), and percentage of inhibition of ulcer lesions (%I) were calculated as described in (Pillai and Santhakumari, 1984).

$$\%I = \frac{(USc - USt)}{USc} \times 100$$

Statistical analysis

All the numbers were articulated as mean $\pm$ standard error mean (SEM). Implication of variances among the group was calculated by using ANOVA.

RESULTS AND DISCUSSION

The methanol extracts of leaves of Breynia vitis-idaea showed a certainly defensive effects contrary to ulcers persuaded by alcohol, NSAIDS (indomethacin), Pylorus ligation and cold restraint models. The release of free radicles is the mechanism seen in ethanol induced ulcers which can be further supported by its improved activity in pylorus ligated method (Sasajima *et al.*, 1978).

The extract valor has also had an asset to rise prostaglandins thereby constructing a mucosal layer for shielding the ulcer from any direct exposure to the acid which is apparent from indomethacin induced gastric ulceration model (Shah *et al.*, 1997).

The NSAID drug is a COX inhibitor which disrupts the membrane integrity and causing rupture in the flow of blood. The extract might have helped in production of endogenous prostaglandins for protecting the ulcers (Shay *et al.*, 1945; Singh and Majumdar, 1999; Szabo *et al.*, 1985). Gastric ulceration made by cold restraint stress is undoubtedly facilitated by the upsurge in gastric motility, degranulation of mast cells, decreased gastric mucosal blood, lowering in the prostaglandin synthesis and excretion of glycoproteins in the mucus (Taira *et al.*, 2005; Valle *et al.*, 2005; Warrier *et al.*, 1995; Weiner, 1996).

Any of the above factors could have played an important role in the formation of ulcers. Finally, the extract was proven to have antioxidant activity and it is proven successful in thwarting the ulcers produced due to the physical strain or stress which produces reactive oxygen species detrimental to the stomach lining (Yamamoto *et al.*, 1992).

CONCLUSIONS

MEBV has exhibited dose reliant inhibition in ethanol induced stomach ulcer lesions and stimulate the secretion of prostaglandins or possess prostaglandins like-substances reveals that the as a potent inhibitor of stomach mucosal abrasions caused by ethanol, indomethacin, pylorus ligation and cold-restraint stress in rats. Further, our results support the ethnopharmacological claims of Breynia vitis-idaea as potent anti-ulcer agent. Etiologies of ulcers produced in different ulcer models are different. The study concluded that MEBV and its dynamic constituents may emerge as more effective healing agent to counter gastric ulcer.

Conflict of interest

Authors affirm that No interest of conflicts.

REFERENCES

Antonio, J. M., Gracioso, J. S., Toma, W., Lopez, L. C., Oliveira, F., Brito, A. R. M. S. 2004. Antiulcerogenic activity of ethanol extract of Solanum variabile (false "jurubeba"). *Journal of Ethnopharmacology*, 93(1):83–88.

Baggio, C. H., Freitas, C. S., Rieck, L., Marques, M. C. A. 2003. Gastroprotective effects of a crude extract of Baccharis illinita DC in rats. *Pharmacological*

Research, 47(1):93–98.

Chiang, Y. M., Chang, J. Y., Kuo, C. C., Chang, C. Y., Kuo, Y. H. 2005. Cytotoxic triterpenes from the aerial roots of Ficus microcarpa. *Phytochemistry*, 66(4):495–501.

Cho, C. H., Ogle, C. W. 1979. Cholinergic-mediated gastric mast cell degranulation with subsequent histamine H1- and H2-receptor activation in stress ulceration in rats. *European Journal of Pharmacology*, 55(1):23–33.

Cho, C. H., Ogle, C. W., Dai, S. 1976. Acute gastric ulcer formation in response to electrical vagal stimulation in rats. *European Journal of Pharmacology*, 35(1):215–219.

Danielsson, G., Norgren, L., Truedsson, L., Andreasson, A., Danielsson, P., Nilsson, A., Swartbol, P. 2003. Flavonoid treatment in patients with healed venous ulcer: flow cytometry analysis suggests increased CD11b expression on neutrophil granulocytes in the circulation. *Vascular Medicine*, 8(2):83–88.

Fellenius, E., Berglindh, T., Sachs, G., Olbe, L., Elander, B., Sjöstrand, S.-E., Wallmark, B. 1981. Substituted benzimidazoles inhibit gastric acid secretion by blocking (H+ + K+) ATPase. *Nature*, 290(5802):159–161.

Flemstrom, G., Garner, A., Nylander, O., Hurst, B. C., Heylings, J. R. 1982. Surface epithelial HCO3(-) transport by mammalian duodenum in vivo. *American Journal of Physiology-Gastrointestinal and Liver Physiology*, 243(5):G348–G358.

Grijalva, C. V., Novin, D. 1990. The Role of the Hypothalamus and Dorsal Vagal Complex in Gastrointestinal Function and Pathophysiology. *Annals of the New York Academy of Sciences*, 597(1 Neurobiology):207–222.

Gupta, M. B., Nath, R., Gupta, G. P., Bhargava, K. P. 1985. A study of the anti-ulcer activity of diazepam and other tranquillosedatives in albino rats. *Clinical and Experimental Pharmacology and Physiology*, 12(1):61–66.

Hase, T., Moss, B. J. 1973. Microvascular Changes of Gastric Mucosa in the Development of Stress Ulcer in Rats. *Gastroenterology*, 65(2):224–234.

Hoogerwerf, W. A., Pasricha, P. J., Hardman, J. G., Limbird, L. E., Gilaman, A. G. 2001. Agents used for control of gastric acidity and treatment of peptic ulcers and gastroesophageal reflux disease. pages 1005–1019. Mc Graw-Hill.

Kahraman, A., Erkasap, N., Köken, T., Serteser, M., Aktepe, F., Erkasap, S. 2003. The antioxidative and antihistaminic properties of quercetin in ethanol-induced gastric lesions. *Toxicology*, 183(1-3):133–142.

Manonmani, S., Vishwanathan, V. P., Subramanian, S., Govindasamy, S. 1995. Biochemical studies on the antiulcerogenic activity of Cauvery 100, an ayurvedic formulation in experimental ulcers. *Indian Journal of Pharmacology*, 27:101–105.

Pillai, N., Santhakumari, G. 1984. Effects of Nimbidin on Acute and Chronic Gastroduodenal Ulcer Models in Experimental Animals. *Planta Medica*, 50(02):143–146.

Sasajima, M., Nakane, S., Saziki, R., Saotome, H., Hatayama, K., Kyogoku, K., Tanaka, I. 1978. Studies on the anti-ulcer effects of isoprenyl flavonoids (1). The anti-ulcer effects of isoprenyl chalcone extracted from Sophora subprostrata (author's transl). Nihon yakurigaku zasshi. *Folia pharmacologica Japonica*, 74(8):897–905.

Shah, A. H., Khan, Z. A., Baig, M. Z. A., Qureshi, S., Bekairi, A. M. 1997. Gastroprotective effects of pretreatment with Zizyphus sativa fruits against toxic damage in rats. *Fitoterapia*, 3:226–234.

Shay, H., Kamorow, S. A., Fele, S. S., Meranz, D., Gruensteinh, Siplet, H. 1945. A simple method for the uniform production of gastric ulceration in the rat. *Gastroenterology*, 5:43–61.

Singh, S., Majumdar, D. K. 1999. Evaluation of the gastric antiulcer activity of fixed oil of Ocimum sanctum (Holy Basil). *Journal of Ethnopharmacology*, 65(1):13–19.

Szabo, S., Trier, J. S., Brown, A., Schnoor, J. 1985. Early Vascular Injury and Increased Vascular Permeability in Gastric Mucosal Injury Caused by Ethanol in the Rat. *Gastroenterology*, 88(1):228–236.

Taira, T., Ohdomari, A., Nakama, N., Shimoji, M., Ishihara, M. 2005. Characterization and Antifungal Activity of Gazyumaru (Ficus microcarpa) Latex Chitinases: Both the Chitin-Binding and the Antifungal Activities of Class I Chitinase Are Reinforced with Increasing Ionic Strength. *Bioscience, Biotechnology, and Biochemistry*, 69(4):811–818.

Valle, D. L., Braunwald, E., Fauci, A. S., Kasper, D. L., Hauser, S. L., Longo, D. L., Jameson, J. L. 2005. Peptic ulcer diseases and related disorders. volume 16, pages 1746–1762.

Warrier, P. K., Nambiar, V. P. K., Ramankutty, C. 1995. Indian medicinal plants a compendium of 500 species. *Department for Environment, Food and Rural Affairs*, 3:6–7.

Weiner, H. 1996. Use of Animal Models in Peptic Ulcer Disease. *Psychosomatic Medicine*, 58(6):524–545.

Yamamoto, K., Kakegawa, H., Ueda, H., Mutsumoto, H., Sudo, T., Miki, T., Satoh, T. 1992. Gastric Cytoprotective Anti-Ulcerogenic Actions of Hydroxychalcones in Rats. *Planta Medica*, 58(05):389–393.