Available online at www.pharmaresearchlibrary.com

Pharma Research Library

International Journal of Current Trends in Pharmaceutical Research

2013, Vol. 1(1): 7-11

Research Article

Pharma Research Library

Antiulcer activity of *Terminalia Chebula* in Pyloric Ligature induced Gastric Ulcers

Dimak Chand Sahu*[1], Anil Kumar Rai[1], Sanjay J. Ingle[2], Girendra Kumar Gautam[2], Ravi Prakash[2]

[1]Department of Pharmacology SIRT, Bhopal, Madhya Pradesh, India
[2]Malhotra College of Pharmacy, Bhopal, Madhya Pradesh, India
**E-mail: dc.sahu0010@gmail.com*, gk100781@gmail.com

ABSTRACT

Various factors that have been implicated in the pathogenesis of gastric ulcers are an increase in gastric acid secretion, pepsin activity and oxidative stress in the gastric mucosa, and a decrease in mucous and bicarbonate secretion. The poly herbal formulation of the many plants like *Withania somnifera* and *Ocimum sanctum* have been shown to exhibit anti-ulcer properties and are regular constituents in Ayurvedic Rasayana for the treatment of the same. *Terminelia chebula* is also known for its properties contributing to overall gastric care. So, all the individual constituents are well known for their anti-ulcer properties, on the basis of their different phytochemical constituents.

Key words: Antiulcers activity, *Terminalia chebula*, Ayurvedic Rasayana, leukotrienes, endothelins

INTRODUCTION

Gastric ulcer is one of the most common gastrointestinal diseases. The exact Causes of Gastric ulcer disease is not known but it may be result from an imbalance between acid-pepsin Secretion and mucosal defences factors. Gastric ulcer disease occurs mainly due to consumption of NSAIDs, infection by H. pylori, stress or due to pathological condition such as zollinger-Ellison Syndrome.[1-5]

Gastric ulcer, one of the most widespread, is believed to be due to an imbalance between aggressive and protective factors. The gastric mucosa is continuously exposed to potentially injurious agents such as acid, pepsin, bile acids, food ingredients, bacterial products (Helicobacter pylori) and drugs[6-7].

These agents have been implicated in the pathogenesis of gastric ulcer, including enhanced gastric acid and pepsin secretion, inhibition of prostaglandin synthesis and cell proliferation growth, diminished gastric blood flow and gastric motility[8].

Drug treatment of Gastric ulcers is targeted at either counteracting aggressive factors (acid, pepsin, active oxidants, platelet taggravating factor "PAF", leukotrienes, endothelins, bile or exogenous factors including NSAIDs) or stimulating the mucosal defences (mucus, bicarbonate, normal blood flow, prostaglandins, nitric oxide). The goals of treating Gastric ulcer disease are to relieve pain, heal the ulcer and prevent ulcer recurrence. Currently there is no cost-effective treatment that meets all these goals. Hence, efforts are on to find a suitable treatment from natural product sources[9-13].

METHOD & MATERIAL

Extract Preparation:

The Leaves of *Terminalia chebula* were shade dried and reduced to coarse powder in a mechanical grinder. The powdered material obtained was then subjected to successive extraction by Hot Percolation Method using petroleum ether, chloroform, and methanol solvents in a soxhelet extractor. The different extracts obtained were evaporated at 48°C to get a semisolid mass. The extracts thus obtained were subjected to phytochemical analysis. The percentage yield of Alcoholic extract was found to be 42.50%w/w and it was used for further studies[14].

Animals:

Either sex Male Albino rats weighing 150-180 g Age- 4-5 month were procured from the institutional animal house and were housed in groups of 3. The animals were acclimatized for a duration of 7 days at 25 ± 1C and 12:12 h light-dark cycle with free access to food and water. The animals were deprived of food 24 h before the study and transfer to metabolic cages.

Experimental protocol:

An Antiulcer study was carried out using the test drug with 6 groups of animal (Each groups had 6 animals) by Pyloric Ligature Induced Gastric Ulcers in Rats.A minimum effective anti-ulcer dose was calculated. This was taken as the lowest dose and the efficacy of the test drug was further evaluated in doses of 250, 400 and 500 mg/kg body weight. The anti-ulcer efficacy of *Terminelia chebula* was compared against standard drugs viz., ranitidine (20 mg/kg body weight) and omeprazole (25 mg/kg body weight).The dose for ranitidine and omeprazole was calculated from their corresponding ulcer healing doses used in man. The test drug and the standard drugs were suspended in 1 per cent gum acacia and were administered in a dose of 2ml/kg body weight per orally[15].

Pyloric Ligature Induced Gastric Ulcers

One day before the induction of ulcers, animals were divided into groups (n=6) and drugs/vehicle was administered as follows. Group I received drugs/vehicle was administered as mentioned under pyloric ligature induced gastric ulcers, group II received omeprazole (25 mg/kg body weight), group II received ranitidine (20 mg/kg body weight), groups IV, V and VI received *Terminelia chebula* in doses of 250, 400 and 500 mg/kg body weight respectively, per orally. The animals were then fasted (with free access to water) for a period of 24 h so as to ensure complete gastric emptying and a steady state gastric acid secretion. The 24 h fasted animals were again administered with the drugs/vehicle on the morning of the experiment.

Sixty minutes after administration of the drugs/vehicle, the animals were anaesthetized using anaesthetic ether and a midline incision was made just below the xiphoid process. The stomach was lifted out and ligated at the level of the pylorus following which it was replaced and the abdomen wall was closed by interrupted sutures. The animals were then housed separately and food and water was withheld for duration of 4 h following which they were sacrificed by an overdose of anaesthetic ether. The stomach was then dissected out, gastric contents were collected and the boundary and ulcerated area was traced as mentioned above[16].

Statistical Analysis

Comparison of means was done by One-way ANOVA followed by Dunnett's multiple comparison. $P<0.05$ was considered to be significant[17].

Determination of Ulcer Index:

The ratio of total surface area and the total ulcerated area was determined and scoring of the ulcer index was done according to the method described by Ganguly. Percentage protection was calculated in the drug treated groups against control using the formula:

% protection = (1-ulcer index in test/ulcer index in control) x 100

RESULT & DISCUSSION

The extent of gastric ulceration in the control group was more severe in the pyloric ligature model (Table I) as compared to the aspirin induced gastric ulcer model. *Terminelia chebula* produced a dose dependent and significant (P<0.01) reduction in the ulcer index. Here also, maximum protection was seen in the omeprazole treated group.

Higher doses of *Terminelia chebula* (250, 400 and 500 mg/kg body weight) were more efficacious than ranitidine in reducing ulcer index in the treated animals. *Terminelia chebula* showed a dose dependent and significant (P<0.01) reduction in lipid peroxidation products in the stomach tissue compared to control. Even though omeprazole produced maximum protection from ulcers, *Terminelia chebula* (500 mg/kg body weight) produced maximum reduction in lipid peroxidation products. The volume of gastric secretion and total acidity was significantly (P<0.01) reduced in all drug treated groups as compared to control.

Table I. Efficacy of EETC in pyloric ligature induced gastric ulcers in rats

Group	Treatment	Ulcer index (% protection)	MDA (nM/g tissue)	Gastric volume (ml/100g body weight)	Gastric *p*H	Total acidity	Adherent gastric mucus(mg/g tissue)
I	Positive Control	0.83 ± .04	147.0± 0.39	5.36 ± 0.19	2.02 ± 0.09	119.54± 3.76	197.23± 4.17
II	Ranitidine (20mg/kg)	0.45±0.07** (45.78)	2501.± 0.22**	3.52± 0.08**	4.16 ± 0.13**	71.25± 2.34**	223.500 ± 3.96**
III	Omeprazole(25 mg/kg)	0.25 ± 0.04** (72.08)	68.45 ± 0.44**	4.19 ± 0.10**	5.11 ± 0.19**	36.82± 2.19**	216.67 ± 2.72**
IV	EETC (250 mg/kg)	0.52 ± 0.02** (37.34)	99.87 ± 0.24**	3.96 ± 0.14**	3.12 ± 0.15**	84.13± 3.05**	403.56 ± 4.500
V	EETC (400 mg/kg)	0.35 ± 0.03** (57.83)	72.54 ± 0.36**	3.58 ± 0.09**	3.97 ± 0.13**	65.67± 4.06**	215.67 ± 2.58*
VI	EETC (500 mg/kg)	0.30 ± 0.05** (64.06)	61.75 ± 0.24**	3.12 ± 0.15**	4.13 ± 0.13**	51.34± 2.79**	228.34 ± 3.19**

EETC = Ethanolic Extract of *Terminelia chebula*

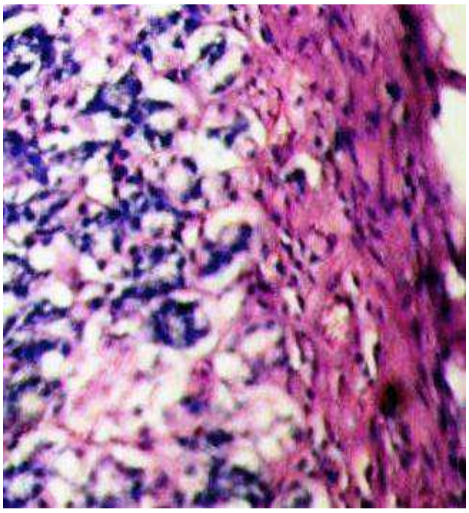
Data expressed as mean ± SE (n=6). Statistical analysis by One-way ANOVA followed by Dunnett's Multiple Comparison*P**<0.05, **<0.01 compared to control.

CONCLUSION

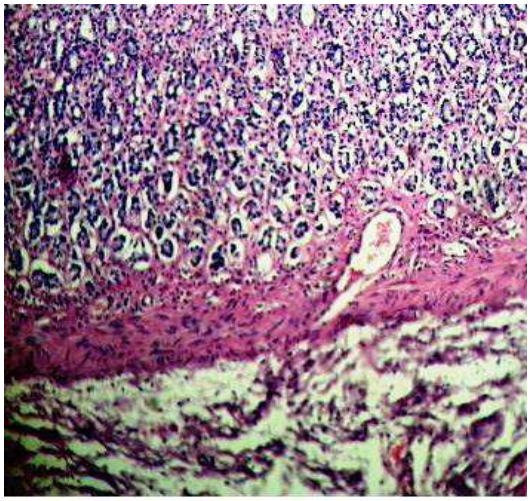
Terminelia chebula produced a dose dependent reduction of gastric juice volume and total acidity. *Terminelia chebula* was superior to both ranitidine and omeprazole in reducing the gastric volume, and was superior to ranitidine in reducing total acidity. Gastric pH was also found to be significantly (P<0.01) increased in all drug treated groups as compared to control with maximum increase being produced by omeprazole.

Adherent gastric mucus content was also found to be significantly increased in all the standard drugs treated groups. Even though *Terminelia chebula* produced a dose dependent increase in the adherent mucus content, it was statistically significant result in the three doses (250, 400 and 500 mg/kg). At the highest dose (500 mg/kg), *Terminelia chebula* was superior to both omeprazole and ranitidine in increasing the adherent gastric mucus content.

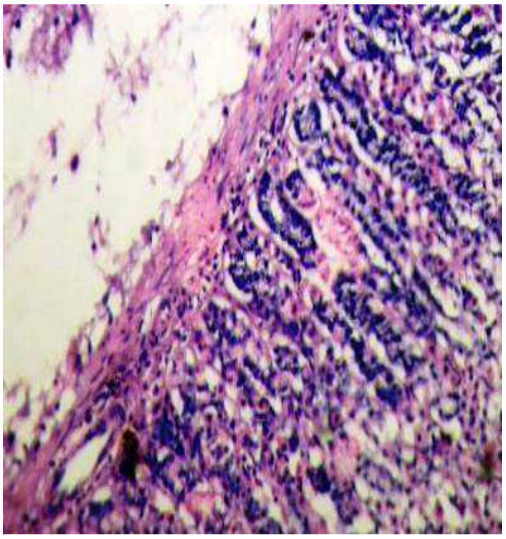
Histopathology of pyloric ligation induced ulcer model



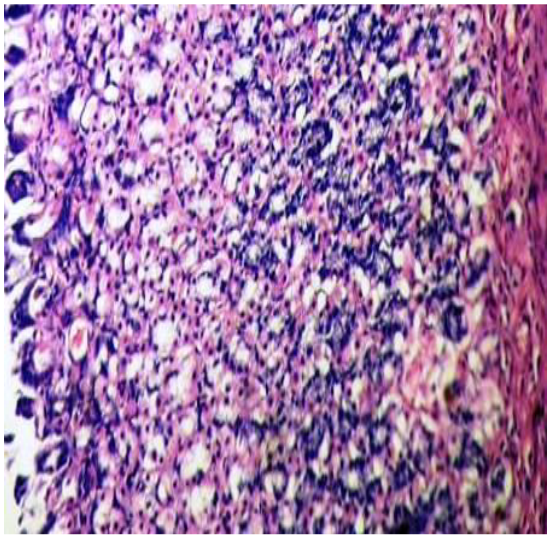
Control
Shows normal appearance Control



Pylorus ligation
Shows ulceration and inflammation



EETC (250mg/kg)
Shows approx normal appearance



EETC (500mg/kg)
Shows normal appearance

REFERENCES

1. Toma W., Hiruma-Lima CA., Guerrer RO., Souza AR., Preliminary studies of *Mammea Americana* L (Guttiferae) bark/latex extract point to an effective antiulcer effect on gastric ulcer models in mice,*Phytomedicine*, 4005, 12, 345-50.
2. Borelli F., Izzo AA., The plant kingdom as a source of anti-ulcer remedies, *PhytotherRes* 4000, 14, 581-91.
3. Kokate C.K, Purohit A.P. and Gokhale S.B. (4008). Pharmacognosy, Thirty ninth, Edition, NiraliPrakashan, 260 – 261.
4. Anand K. K., Singh B., Saxena A. K., Chandan B. K., Gupta V. N. and Bhardwaj V. (1997). The Hepatoprotective principle in the fruits of *Terminaliabelerica*-bioassay guided activity, 36,315-321.
5. Khan Arif-Ullah and GilaniAnwarul Hassan (40008). Pharmacodynamic Evaluation of Terminaliabelerica for its antihypertensive effect. 16, 6-14.
6. BiradarYogesh S., JagatapSheetal, Khandelwal K. R. and SinghaniaSmita S. (4008). Exploring of antimicrobial act ivity of triphalamashi an ayurvedic formulation, 107-113.
7. Afzalakhtar M, Rabber-Bhatti MH, Aslam M (1997). Antibacterial activity of plant Diffusate against *Xanthomonascompestrispv*. citri. Int. J. Pest Manage. 43(2):149-153.
8. Ahmad I, Mehmood Z, Mohammad F (1998). Screening of some Indian medicinal plants for their antimicrobial properties. J. Ethnopharmacol. 62(2):183-193.
9. Bag A, Bhattacharyya SK, Bharati P, Pal NK, Chattopadhyay RR (4009). Evaluation of antibacterial properties of Chebulicmyrobalan (fruit of *Terminaliachebula*Retz.) extracts against methicillin resistant *Staphylococcus aureus*and trimethoprim sulphamethoxazoleresistant uropathogenic*Escherichia coli*. Afr. J. Plant Sci.3(2):025-029.
10. Bauer AW, Kirby WMM, Sherris JC, Turk M (1966). Antibiotic susceptibility testing by a standardized single disk method. Am. J. Clin. Pathol. 45:493-496.
11. GandhipuramPeriyasamySenthil Kumar, PalanisamyArulselvan, DuraiarajSathish Kumar and SorimuthuPillai Subramanian. Anti-Diabetic activity of fruits of *Terninaliachebula*on Streptozotocin induced Diabetic rats, Journal of Health Science. 4006; 52(3): 283-291.
12. Grover IS and Bala S. Anti-mutagenic activity of *Terminaliachebula*(myroblan) in *Salmonella typhimurium*, Indian Journal. of Experimental Biology. 1992; 500(4): 339-341.
13. Hazra B, Sarkar R, Biswas S and N Mandal. Comparative study of the antioxidant and reactive oxygen species scavenging properties in the extracts of the fruits of *Terminaliachebula, Terminaliabelerica and Emblicaofficinalis*, BMC Complement Altern Med. 2010; 10: 20.
14. HogadeMaheshwar G*, Deshpande S.V and Pramod H.J. Anticonsultant activity of *Terminaliachebula*retz. againstmes and ptz induced seizures in rats, Journal of Herbal Medicine and Toxicology. 2010; 4(2): 123-126.
15. Hongbo Ma, YunpengDiao, Danyu Zhao, Kun Li and Tingguo Kang. A new alternative to treat swine influenza A virus infection: extracts from *Terminaliachebula*Retz, African Journal of Microbiology Research. 2010; 4(6): 497- 499.
16. Jagetia GC, Baliga MS, Malagi KJ and SethukumarKamath M. The evaluation of the radioprotective effect of Triphala (an ayurvedic rejuvenating drug) in the mice exposed to g-radiation, Phytomedicin. 4002; 9: 99–108.
17. Jagtap AG and Karkera SG. Potential of the aqueous extract of *Terminaliachebula*as an anticaries agent, Journal of Ethnopharmacology.1999; 68: 299–306.