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EVALUATION OF ANTIULCER ACTIVITY OF CASTOR OIL IN RATS

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ABSTRACT
To study the antiulcer activity of oil of Ricinus communis seed using different models of gastric ulceration in rats. Antiulcer activity of castor oil was studied in rats by administration of ethanol or aspirin or by pyloric ligation. Castor oil was administered in the dose of 500 mg/kg and 1000 mg/kg orally 30 min prior to ulcer induction. The antiulcer activity was assessed by determining and comparing the ulcer index in the test drug group with that of the ulcerated control group. Gastric total acid output and pepsin activity were estimated in the pylorus ligated rats. Ranitidine and Sucralfate were used as a reference drug. The ulcer index in the castor oil treated animals was found to be significantly less in all the models compared to ulcerated control animals. This antiulcer property was more prominent in animals in whom ulcers were induced by ethanol, aspirin and pyloric ligation. Ranitidine (30 mg/kg) produced a significant gastric ulcer protection when compared with the control group. The anti-ulcer activity of castor oil was however, less than that of ranitidine. Our results suggest that castor oil possesses significant antiulcer property which could be either due to cytoprotective action of the drug or by strengthening of gastric mucosa and thus enhancing mucosal defence.

Key words: Cytoprotection, Mucosal defence, Ulcer protection, Ricinus communis.

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INTRODUCTION

Gastric hyperacidity and ulcer are very common causing human suffering today. It is an imbalance between damaging factors within the lumen and protective mechanisms within the gastro duodenal mucosa. Although prolonged anxiety, emotional stress, hemorrhagic surgical shock, burns and trauma are known to cause severe gastric irritation, the mechanism is still very poorly understood.

Eranda has been freely used all over India since centuries. In day to day life, it is commonly used as a purgative. Ayurvedic Samhitas have praised it as an asset in treating rheumatic disorders. The botanical name of eranda is *Ricinus communis* and it belongs to family Euphorbiaceae. The seeds contain 45% of fixed oil, which consists glycerides of ricinoleic, isoricinoleic, stearic and dihydroxystearic acids. The seeds have lipases and a crystalline alkaloid, ricinine. It also contains phenolic compounds.[1] The leaves and the stem also contain ricinine. Detection of palmitic (1.2), stearic (0.7), arachidic (0.3), hexadecenoic (0.2), oleic (3.2), linoleic (3.4), linolenic (0.2), ricinoleic (89.4%) and dihydroxy stearic acids as esters in castor oil by GLC.[2]

The seeds, seed oil, leave and the roots of eranda have great medicinal value. The plant is equally useful, both internally as well as externally. Externally, eranda is effectively used in the diseases of vata associated with pain and swellings. Internally, eranda is used as a potent drug in treating diseases of vata viz. arthritis, sciatica, facial palsy, paralysis, bodyache, tremors, headache etc.[3] In the Indian system of medicine, the leaf, root and seed oil of this plant have been used for the treatment of inflammation and liver disorders[4]as they have been found to be hepatoprotective[5],laxative[6] and diuretic[7]. The antifertility activity of 50% ethanolic extract of R. communis has also been reported.[8] Roots and aerial parts are useful in the treatment of diabetes.[9] Fifty percent of ethanolic extract of the root, stem and leaves of this plant showed hypoglycemic activity.[10, 11]

MATERIALS AND METHODS

Experimental animals: The study was conducted on Albino rats (Wistar) of 200-250 g and maintained under standard conditions (room temperature 24- 27^{o}C and humidity 60-65%) with 12 h light and dark cycle. The food in the form of dry pellets (Amrut Lab., Pune) and

water were available ad libitum. The animal experiments were approved by the ethics committee of the institute.

Chemicals and drugs: Castor oil, Ethanol (Yash chem., Pune), aspirin (Research lab, Mumbai), ranitidine(cipla, Mumbai), Sucralfate (Dr.Reddys lab, Mumbai), carboxy methyl cellulose (CMC), trichloroacetic acid (Research lab, Mumbai), phenol reagent (Research lab, Pune), bovine albumin serum (Research lab. fine chem. industries, Mumbai),std. phenol solution (Research lab, Pune), conc. HCL (Research lab. fine chem. industries, Mumbai), NAOH (Research lab. fine chem. industries, Mumbai) were used in the study.

EXPERIMENT DESIGN

Acute Toxicity Studies

The acute toxicity study was done as per the OECD guidelines (423). The compounds were administered orally in different doses, where 24h toxicity was recorded to identify the toxic dose. No mortality and no signs of toxicity were found at the dose of 5000 mg/kg body weight of castor oil. Therefore, it meight be considered that castor oil have an LD50 value above 5000 mg/kg. Two doses 500 mg/kg and 1000 mg/kg were selected for present study.[12]

Gastric cytoprotection method

Albino rats (Wistar) of 200-250 g are maintained under standard conditions (room temperature 24- 27oC and humidity 60-65%) with 12 h light and dark cycle. The food in the form of dry pellets (Amrut Lab., Pune) and water were available ad libitum. Rats of either sex, were randomly divided in to 5 groups of 6 animals in each group.

Group-I: Normal control (Normal saline)
Group-II: Ulcerated control (1 ml ethanol, p.o.).
Group-III: Sucralfate (400 mg/kg, p.o.).
Group-IV: Castor oil (500 mg/kg, p.o.).
Group-V: Castor oil (1000 mg/kg, p.o.).

Thirty minutes after the test or reference drug or the control vehicle treatment, 1 ml of ethanol was orally administered to each rat. After 1 h the rats were euthenised with excess of anesthetic ether and stomach was cut open along the greater curvature, cleared of residual matter with saline and the inner surface was examined for ulceration. Ulcer index and % ulcer protection were calculated.[13,14]

Aspirin-induced gastric mucosal damage

Albino rats (Wistar) of 200-250 g were selected, fasted for 36 h. Rats of either sex, were randomly divided in to 5 groups of 6 animals in each group.

Group-I: Normal control (Normal saline)
Group-II: Ulcerated control (500 mg/kg, p.o.).
Group-III: Ranitidine (50 mg/kg,i.p.).
Group-IV: Castor oil (500 mg/kg, p.o.).
Group-V: Castor oil (1000 mg/kg, p.o.).

After 30 min., aspirin suspended in 1% CMC in water (20 mg/ml) at a dose of 500 mg/kg was administered orally to all the animals and 4 h later, the animals were sacrificed. The stomach was removed and opens along the greater curvature. The number of ulcer spots in the glandular portion of the stomach were counted in both control and drug treated animals and the ulcer index was calculated.[15,16]

Pyloric ligation method

In this method, albino rats were fasted in individual cages for 24 h. Care was being taken to avoid coprophagy. Rats of either sex were randomly divided in to 5 groups of 6 animals in each group.

Group-I: Normal control (Normal saline)
Group-II: Ulcerated control (1% CMC, 5 ml/kg, p.o.).
Group-III: Ranitidine (30 mg/kg, i.p.).
Group-IV: Castor oil (500 mg/kg, p.o.).
Group-V: Castor oil (1000 mg/kg, p.o.).

Castor oil or reference drug or control vehicle was administered 30 min prior to pyloric ligation. Under light ether anesthesia, the abdomen was opened and the pylorus was ligated. The abdomen was then sutured. At the end of 4 h after ligation, the animals were sacrificed with excess of anesthetic ether, and the stomach was dissected out. Gastric juice was collected and its volume was measured. The glandular portion was then exposed and examined for ulceration. Ulcer index was determined.[16,17]

Statistical analysis

The Statistical analysis was performed by using One Way ANOVA followed by Dunnet's comparision test. The values are expressed as mean ± SEM and the *P<0.05 was taken as significant.

RESULTS

Effect of Castor oil in pylorus ligated rats

Pylorus ligation in ulcerated control group had produced ulcer in all animals and the mean ulcer index was 4.70±0.29 indicating the ulcerogenic effect.Another ulcerogenic effect as compared to normal control was measured as follows; mean gastric content volume as 6.28±0.15, pH as 1.87±0.07, free acidity as 37.33 ± 1.80, total acidity as 74.13 ± 1.70, pepsin content as 5.56 ± 0.69, indicating the ulcer production in animals.

Pylorus ligation also produced ulcers in all the castor oil pretreated animals.However, the ulcer index showed significant dose dependent reduction in the animal pretreated with castor oil 500 mg/kg (UI; 3.21 ± 0.15) and 1000 mg/kg (UI; 2.35 ± 0.15).It indicated 31.70% gastroprotection at 500 mg/kg and 50% gastroprotection at 1000 mg/kg as compared with ulcerated control. The results indicate that the higher dose of castor oil i.e. 1000

mg/kg was effective in protecting ulcers in pylorus ligated rats.

Pylorus ligation had produce ulcers in all animals pretreated with Ranitidine 30 mg/kg. However, ulcer index (1.88 ± 0.11) showed significant reduction as compared with ulcerated control and showed 60 % gastroprotection.

Effect of Castor oil in Aspirin induced gastric ulcer

Aspirin induced ulcerated control group had produced ulcer in all animals and the mean ulcer index was 2.25 ± 0.21 indicating the ulcerogenic effect. Aspirin also produced ulcers in all the castor oil pretreated animals. However, the ulcer index showed significant dose dependent reduction in the animal pretreated with castor oil 500 mg/kg (UI; 1.25 ± 0.07) and 1000 mg/kg (UI; 0.95 ± 0.15).It indicated 44.44% gastroprotection at 500 mg/kg and 57.77% gastroprotection at 1000 mg/kg as compared with ulcerated control. The results indicate that the higher dose of castor oil i.e. 1000 mg/kg was effective in protecting ulcers in aspirin treated rats.

Aspirin had produce ulcers in all animals pretreated with Ranitidine 30 mg/kg. However, ulcer index (0.45 ± 0.11) showed significant reduction as compared with ulcerated control and showed 80 % gastroprotection.

Effect of Castor oil in ethanol induced gastric ulcer

Ethanol induced ulcerated control group had produced ulcer in all animals and the mean ulcer index was 4.72 ± 0.07 indicating the ulcerogenic effect. Ethanol also produced ulcers in all the castor oil pretreated animals. However, the ulcer index showed significant dose dependent reduction in the animal pretreated with castor oil 500 mg/kg (UI; 2.58 ± 0.21) and 1000 mg/kg (UI; 2.30 ± 0.11).It indicated 45.33% gastroprotection at 500 mg/kg and 51.27% gastroprotection at 1000 mg/kg as compared with ulcerated control. The results indicate that the higher dose of castor oil i.e. 1000 mg/kg was effective in protecting ulcers in ethanol treated rats.

Ethanol had produce ulcers in all animals pretreated with Sucralfate 400 mg/kg. However, ulcer index (1.2 ± 0.29) showed significant reduction as compared with ulcerated control and showed 74.57 % gastroprotection.

DISCUSSION

The preliminary phytochemical evaluation performed in the present study demostrated that the castor oil contains fatty oils (40-45%), proteins (20-25%), lectins (0.1-0.7%), ricin (3000 ppm).It also contains alpha tocopherol (9 ppm), linoleic acid, niacin (13 ppm), gamma tocopherol (459 ppm), quercitrin, etc.

The finding of the present study demonstrated that castor oil possess antiulcer activity against the ulceration caused by pylorus ligation, aspirin and ethanol.

In pylorus ligated rats, gastric acid is associated with sever ulceration of the rat gastric mucosa .The activation of vagus –vagal-reflux by stimulation of pressure receptors in the antral gastric mucosa is believed to increase gastric acid secretion. The digestive site of accumulated gastric juice and interference of gastric blood circulation responsible for ulceration.

It is evident from the present result that castor oil has potent ulcer protective activity at a dose 500 mg/kg and 1000 mg/kg, but at the dose 1000 mg/kg was more potent. The ulcer index of castor oil treated rat was comparable to those of ulcerated control rats. There was significant decrease in ulcer index in castor oil treated rats and ranitidine treated rats.

There was significant decrease in the volume of gastric content, free acidity, total acidity, peptic activity and increase in Ph in castor oil treated rats in dose dependent manner as compared with ulcerated control rats. The activity of castor oil was less than ranitidine (30 mg/kg).

Several non-steroidal anti-inflammatory drugs like; aspirin are known to induce gastric damage by suppression of prostaglandins. In the stomach, prostaglandins play a vital protective role , stimulating the secretion of bicarbonate and mucus maintaining mucosal blood flow and regulating mucosal cell turn over and repair. Oxy radicals may play important role in the aspirin induced erosive gastritis. After an initial hydrophobic intermolecular interaction, the free carboxyl group present in all NSAIDs forms a strong electrostatic bond with the positively charged head group of zwitterionic phospholipids of mucus layer and, in doing so, increase the phospholipids solubility, neutralize its surface activity. Thus, NSAIDs topically act on tissue to disrupt the hydrophobic protective lining of the mucus gel layer.[18]

It is evident from the present result that castor oil has potent ulcer protective activity at a dose 500 mg/kg and 1000 mg/kg, but at the dose 1000 mg/kg was more potent. The ulcer index of castor oil treated rat was comparable to those of ulcerated control rats. There was significant decrease in ulcer index in castor oil treated rats and ranitidine treated rats.

Ethanol produces necrotic lesions in the gastric mucosa by its direct toxic effect reducing the secretion of bicarbonate and production of mucus, increase vascular permeability and decreases non-protein sulf-hydryl groups (NP-SH) of gastric mucosa. Also, increase xanthine oxidase activity and malonyl-dialdehyde level. The ethanol also depresses tissue level of DNA, RNA and proteins, leading to flow stasis and injured area.[19]

In the present study, castor oil has potent ulcer protective activity at a dose 500 mg/kg and 1000 mg/kg, but at the

dose 1000 mg/kg was more potent. The ulcer index of castor oil treated rat was comparable to those of ulcerated control rats. There was significant decrease in ulcer index in castor oil treated rats and ranitidine treated rats.

CONCLUSION

In conclusion, it appears that castor oil possess anti-ulcerogenic principles like flavanoids, tannins and saponins. These phytoconstituents provides protection against gastric mucosal damage induced by pylorus ligation, aspirin and ethanol, through inhibition of gastric acid, pepsin, histamine and free radical and stimulation of mucus secretion.

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Table 1: Effect of castor oil on volume and pH of gastric content in pylorus ligated rats

Sr. No.	Treatment (mg/kg)	Volume of gastric juice (ml)	pH of gastric juice
1	Normal control	1.16±0.05	3.87±0.05
2	Ulcerated control	6.28±0.15	1.87±0.07
3	Ranitidine (30)	2.92±0.11	3.60±0.06
4	Castor oil (500 mg/kg)	4.04±0.07*	2.11±0.07*
5	Castor oil (1000 mg/kg)	3.32±0.06**	3.24±0.10**

Values are expressed as mean ± S.E.M., n=6, Ranitidine 30 mg/kg, Castor oil 500,1000 mg/kg, *p<0.05, **p<0.01, as compared with ulcerated control using one way ANNOVA followed by Dunnet test.

Table 2: Effect of castor oil on free acidity and total acidity in pylorus ligated rats

Sr. No.	Treatment (mg/kg)	Free acidity (meq/L/100gm)	Total acidity (meq/L/100gm)
1	Normal control	9.74 ± 0.60	26.4 ± 0.68
2	Ulcerated control	37.33 ± 1.80	74.13 ± 1.70
3	Ranitidine (30 mg/kg)	14.40 ± 0.36	32.4 ± 0.76
4	Castor oil (500 mg/kg)	34.66 ± 0.66	71.06 ± 0.60
5	Castor oil (1000 mg/kg)	21.6 ± 0.93**	44.8 ± 1.21**

Values are expressed as mean ± S.E.M., n=6, Ranitidine 30 mg/kg, Castor oil 500,1000 mg/kg, *p<0.05, **p<0.01, as compared with ulcerated control using one way ANNOVA followed by Dunnet test.

Table 3: Effect of castor oil on pepsin content in pylorus ligated rats

Sr. No.	Treatment (mg/kg)	Pepsin content (mcg/ml)
1	Normal control	0.89 ± 0.01
2	Ulcerated control	5.56 ± 0.69
3	Ranitidine (30 mg/kg)	2.39 ± 0.63
4	Castor oil (500 mg/kg)	4.47 ± 0.09
5	Castor oil (1000 mg/kg)	3.07 ± 0.14**

Values are expressed as mean ± S.E.M., n=6, Ranitidine 30 mg/kg, Castor oil 500,1000 mg/kg, *p<0.05, **p<0.01, as compared with ulcerated control using one way ANNOVA followed by Dunnet test.

Table 4: Effect of castor oil on ulcer index and % gastro protection in pylorus ligated rats

Sr. No.	Treatment (mg/kg)	Ulcer index (Mean± SEM)	% Gastro protection
1	Normal control	-	100
2	Ulcerated control	4.7 ± 0.29	-
3	Ranitidine (30 mg/kg)	1.88 ± 0.11	60
4	Castor oil (500 mg/kg)	3.21 ± 0.15*	31.70*
5	Castor oil (1000 mg/kg)	2.35 ± 0.15**	50**

Values are expressed as mean ± S.E.M., n=6, Ranitidine 30 mg/kg, Castor oil 500,1000 mg/kg, *p<0.05, **p<0.01, as compared with ulcerated control using one way ANNOVA followed by Dunnet test

Table 5: Effect of castor oil on ulcer index and % gastro protection in aspirin induced gastric lesion in rats.

Sr. No.	**Treatment (mg/kg)**	**Ulcer index (Mean± SEM)**	**% Gastro protection**
1	Normal control	-	100
2	Ulcerated control	2.25 ± 0.21	-
3	Ranitidine (30)	0.45 ± 0.11	80
4	Castor oil (500 mg/kg)	1.25 ± 0.07*	44.44*
5	Castor oil (1000 mg/kg)	0.95 ± 0.15**	57.77**

Values are expressed as mean ± S.E.M., n=6, Aspirin 500 mg/kg, Ranitidine 30 mg/kg, Castor oil 500,1000 mg/kg, *p<0.05, **p<0.01, as compared with ulcerated control using one way ANNOVA followed by Dunnet test.

Table 6: Effect of castor oil on ulcer index and % gastro protection in ethanol induced gastric ulcer in rats.

Sr. No.	**Treatment (mg/kg)**	**Ulcer index (Mean± SEM)**	**% Gastro protection**
1	Normal control	-	100
2	Ulcerated control	4.72 ± 0.07	-
3	Sucralfate (400 mg/kg)	1.2 ± 0.29	74.57
4	Castor oil (500 mg/kg)	2.58 ± 0.21*	45.33*
5	Castor oil (1000 mg/kg)	2.30 ± 0.11**	51.27**

Values are expressed as mean ± S.E.M., n=6, Sucralfate 400 mg/kg, Castor oil 500,1000 mg/kg, *p<0.05, **p<0.01, as compared with ulcerated control using one way ANNOVA followed by Dunnet test.

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