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Original Article

Protective Role of Oxitard in Drug Induced Ulcers In Rats

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ABSTRACT

This study was performed to determine the effects of oxitard on indomethacin induced ulcers in rats. Albino rats (Wister strain) of either sex weighing between 150-200gms were randomly allotted into three groups with eight animals each. Rats housed in individual cages and fasted for 24 hours; Indomethacin was administered orally in the dose of 20mg/kg body weight and kept fasting for 4 hours. Oxitard was mixed with Carboxy Methyl Cellulose powder and diluted with distilled water. The solution was administered orally through the gavages in the dose of 200mg /kg/day. Omeprazole (20mg/kg) was administered intra peritoneally as a standard drug for present study. At the end of study, rats were sacrificed, stomachs were dissected out and stored in 5% formalin solution, ulcer index and histological changes were observed. It was found that, Oxitard showed statistically significant anti ulcer activity comparable to standard drug omeprazole. The mean ulcer indexes of two drugs are formed to be statistically significant. (P value is 0.001). Therefore, the results were suggestive of anti ulcerogenic activity of oxitard.

1. Introduction

Peptic ulcer is a chronic disease which impairs the quality of life and is associated with increased morbidity and mortality [1]. Imbalance between the “aggressive” and “defensive” factors and presence of acid-pepsin play an important role in aetiopathogenesis [2].

Peptic ulcer disease is a worldwide problem. Statistics from all sources indicate 10% or more of adult population are affected within their life time and 50% of healthy individuals complain of dyspepsia [3]. Peptic ulcer affects individuals from 20-60 years of age with males being predominantly affected. The incidence of duodenal ulcer is more frequent than gastric ulcer (Ratio 4:1). According to recent estimates 2% males and 1.5% females have peptic ulcer [4]. Although the incidence of peptic ulcer disease is markedly reduced after the introduction of newer groups of drugs but perforation, bleeding recurrent and refractory ulcers often due to Helicobacter pylori infection still remain as major problems [5].

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Recent epidemiological studies show annual deaths due to disease is about 3000 and is mainly due to perforation, and in more than two thirds of patients relapse occurs and one third of patients develop bledding [6]. 60% of healed peptic ulcer recurs in one year and 80-90% recurs in two years [7]. Considering the present status, the antacids provide symptomatic relief without inhibiting the gastric secretion nor efficiently promoting healing. The H2 receptor blockers and proton pump inhibitors although decrease the acid secretion and promote healing of ulcer, but have not proved their worth in preventing relapse and recurrence [8]. Also “acid rebound” after cessation of therapy and long term adverse effects limit their utility [9]. The anticholinergics, prostaglandin analogs and ulcer protective agents are not very effective antiulcer agents. Ulcer healing drugs like Carbenoxolone is associated with increased mineralocorticoid activity[10].

Oxitard is a phytopharmaceutical formulation; it inhibits oxidation reactions, thereby preventing the damage caused by free radicals. Thus, protects the vital organs and keeps the person healthy. Oxitard has antioxidant, adaptogenic, gastro protective, cardio protective and immunomodulatory actions. Its combined therapeutic activity also helps in prevention of photo damage and oxidation related tissue damage [11].

2.Materials and Methods:

2.1.Selection, care and preparation of animal:

Albino rats (Wister strain) of either sex weighing between 150-200gms were used for the study. Animals are obtained from Raghavendra enterprises, Bangalore .They were maintained on synthetic pelleted feed supplied by Pranav Agro Industries Ltd. Sangli, Maharashtra and water *ad libitum* in the Central Animal House of the FIMS Institution. Animals are housed in a temperature 35 2 C and 12/12 hour light- dark cycle environment, in cages (4 per cage) with mesh bottom to prevent coprophagy. They were randomly, allocated to different experimental groups and placed individually in cages prior to the experimentation animals were fasted for 24 hours, allowing free access to drinking water.

2.2.Indomethacin induced gastric ulcer [12]:

Albino rats housed in individual cages and fasted for 24 hours. Indomethacin was administered orally in the dose of 20 mg/kg body weight and kept fasting for 4 hours animals were sacrificed and stomachs were isolated out, external surface was studied for hemorrhage, congestion and perforation. The stomach were cut along the lesser curvature and studied for gastric lesions using magnifying lens by an individual who was unaware of the drug and control animals.

2.3.Oxitard

Composition: Each gram of Oxitard contains Mangifera indica Linn. (Anacardiaceae; bark, 340 mg), Glycyrrhiza glabra Linn. (Papilionaceae; rhizome, 100 mg), Syzygium aromaticum Linn. Merr. and L.M. Perry (Myrtaceae; flower bud, 100 mg), Vitis vinifera Linn. (Vitaceae; fruit, 21 mg), Emblica officinalis Linn. (Euphorbiaceae; fruit, 200 mg) and Daucus carota Linn. D. Vulgaris (Umbelliferae; root, 200 mg) [13].

The constituent plants of the formulation were procured from authentic sources from The Himalaya Drug Co R & D Centre Makali, Bangalore, India. Drug given by oral route by using Carboxy methyl cellulose as a vehicle.

Omeprazole: It was the standard drug for present study. Propylene glycol is served as vehicle for omeprazole. Omeprazole (20mg/kg) was administered intra peritoneally [14].

2.4.Pretreatment studies:

Three groups of eight albino rats were selected for the present study. First group is taken as control group that is indomethacin induced gastric ulcer group. In this group rats were fasted 12 hours and then indomethacin is administrated orally through the gastric gavages (20 mg/kg b.w). The rats were sacrificed 6 hours after indomethacin administration by the stunning method. The stomachs were opened along the lesser curvature, stomach were isolated and washed in normal saline. Then the stomachs were observed with the help of magnifying lens, studied its external and internal surface and observed hemorrhage, dilation of blood vessels, ulceration, perforation, size and number of ulcers and ulcer index was evaluated according to the severity of ulcers [15]. The stomach was stored in the formalin.

Second group is taken as a test (Oxitard) group. Oxitard powder was mixed with Carboxy methyl cellulose administrated orally (200mg/kg b.w). The treatment schedule was once a day and it is continued five days. After completing the five days rats was kept 24 hours fasting and then indomethacin is given orally after 4 hours rats was sacrificed stomachs were opened and washed with normal saline and fixed in 5% formalin.

Third group is taken as a standard (omeprazole) group rats were kept 24 hours fasting and then omeprazole is given intraperitonially injection (5mg) this treatment was continued six days in the last day rats were kept fasting and after the administration of omeprazole indomethacin is administered orally after 4 hours of omeprazole administration and rats was killed after 6 hours stomachs was opened and washed with normal saline and stored in 5% formalin solution.

Ulcer indexing [16]:

The dissected out stomachs were cut open along the greater curvature and the inner surface was examined for ulceration. The open stomachs were fixed on to a board with the help of pins and studied by individuals who were blinded for test drugs and control animals.

Ulcer number: Total numbers of ulcers in each stomach were noted and peticheal hemorrhage congestion etc. was also noted.

Ulcer size: with the help of magnifying lens the size of each ulcer measured along the length any lesion with in 1 mm was taken as pin point.

Indomethcin induced gastric ulcer [16, 17]: Ulcer indexing was done according to the modified scoring system of adami et al as follows;

0= No lesions, 1= hemorrhagic suffusions, 2= from 1-5 small ulcers up to 3 mm size. 3= many small ulcers more than 5 or 1 ulcer of more than 3 mm, 4= many ulcers of more than 3 mm, 5=perforated ulcers. The mean scores for each group were then calculated and the results were analyzed using unpaired student-'t' test.

2.5.Histological studies:

A portion of the ulcer region in the stomach was dissected out and fixed in 5% buffered neutral formalin solution for histological observations. Afrter fixations, tissues were embedded in paraffin , solid sections were cut at 5 µm and stained with hematoxylin and eosin (18). The sections were examined with the help of a pathologist under light microscope and photomicrographs were taken.

3.Results:

The control group presented with features of ulceration. On gross examination serosal surface of stomach showed marked induration, dilated blood vessels, ecchymosis and hemorrhagic sites. Mucosal surface presented with features of severe degree of

hyperemia, congestion and large number of pin point ulcers of varying sizes with central clots, features of perforation in the stomach. The ulcer index was (UI: 50 ± 3.5). Microscopic features were suggestive of acute gastric ulceration with de-epithelialization.

Animal pre treated with Oxitard showed few signs of mucosal injury, but the percentage of damage was less compared to control group. Serosal surface revealed very few dilated blood vessels and peticheal hemorrhages. Mucosal surface revealed few ulcers of varying sizes. Correspondingly the ulcer index also was reduced (U.I 20 ± 1.79). These features were suggestive of anti ulcer activity of oxitard.

Animals treated with omeprazole maintained near normal pattern. Serosal surface looked amber colored with few signs of dilated blood vessels and hemorrhagic suffusions. Mucosal surface retained the normal rughae pattern with minimal signs of mucosal injury. The ulcer index was markedly reduced (U.I 10 ± 1.7). Thus animals treated with standard drug omeprazole showed antiulcer activity.

The present study showed that oxitard has anti ulcer effect in drug induced peptic ulcers in rats. The results were parallel to animal treated with standard drug omeprazole.

Table1: Ulcer index and injury percentage

Group	Mean Ulcer Index ± SEM	%Injury
Control	50± 3.5	100%
Oxitard	2±1.79*	30%
Omeprazole	10±1.96*	10%

SEM = Standard error of mean, *Probability = P<0.001 in all groups.

Fig1: Indomethacin induced ulcers

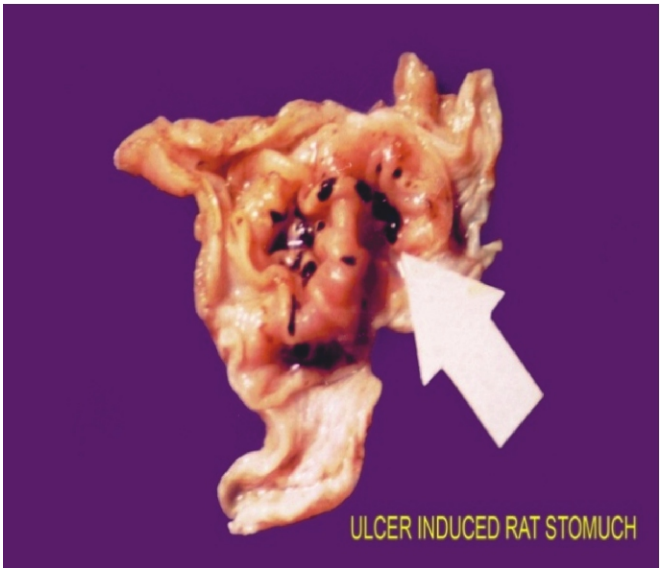


Fig 2: Treated with Oxitard

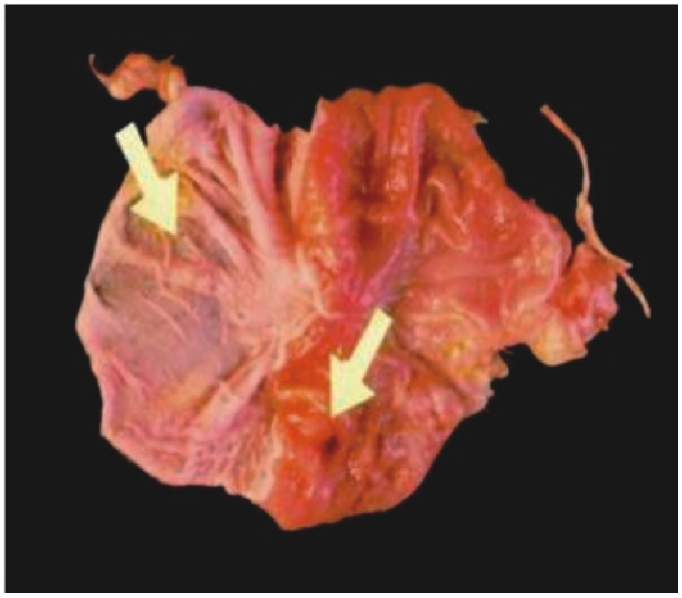


Fig 3: Histology of ulcer induced rat stomach (40X)

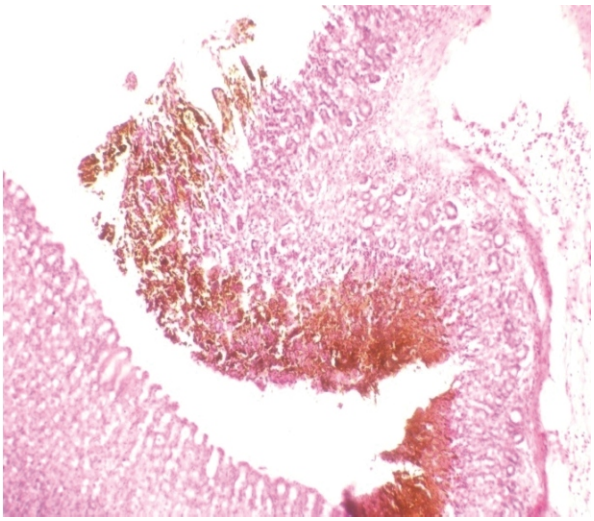
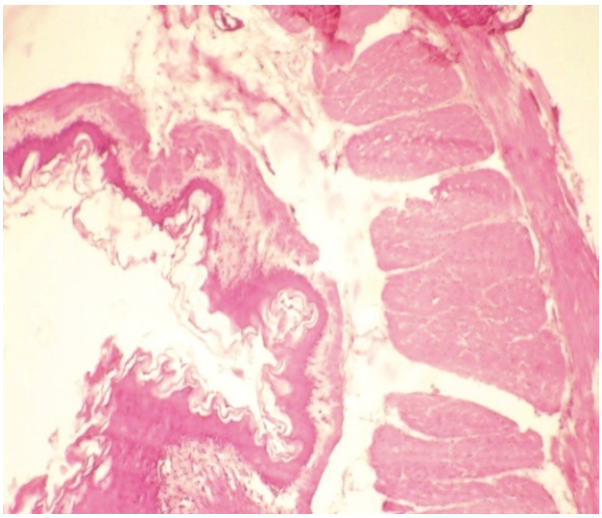


Fig 4: Histology of Oxitard treated stomach (10X)



4.Summary and Conclusion:

In the present study the anti ulcer effect of Oxitard is evaluated in comparison with standard drug omeprazole. Histopathological studies revealed features of acute gastric ulceration, with deepithelialization and sites of oedema and hemorrhage.

Five days administration of Oxitard protected animals from ulcerogenic effects of indomethacin. On gross examination there were occasional ulcers and areas of hemorrhage, but in comparison to control group, the percentage of mucosal damage was markedly reduced. The ulcer index was correspondingly reduced in the group. Analysis of data revealed the percentage of ulcer protection by both the test and standard drug were almost same.

Oxitard showed statistically significant anti ulcer activity comparable to standard drug omeprazole. The mean ulcer indexes of two drugs are formed to be statistically significant. (P value is 0.001). Therefore, the results were suggestive of anti ulcerogenic activity of oxitard.

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