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Mukesh B Chawda
Shree Dhoothapapeshwar
Ayurvedic Research Foundation
(SDARF), Navi Mumbai,
Maharashtra-410206.

Nitin A Mundhe
Shree Dhoothapapeshwar
Ayurvedic Research Foundation
(SDARF), Navi Mumbai,
Maharashtra-410206.

Venu Gopal Jonnalagadda
Shree Dhoothapapeshwar
Ayurvedic Research Foundation
(SDARF), Navi Mumbai,
Maharashtra-410206.

Kapil S Thakur
Shree Dhoothapapeshwar
Ayurvedic Research Foundation
(SDARF), Navi Mumbai,
Maharashtra-410206.

MK Vahalia
Shree Dhoothapapeshwar
Ayurvedic Research Foundation
(SDARF), Navi Mumbai,
Maharashtra-410206.

Shekhar S Shitut
Shree Dhoothapapeshwar
Ayurvedic Research Foundation
(SDARF), Navi Mumbai,
Maharashtra-410206.

Correspondence:
Nitin A Mundhe
In-charge of Biomedical Services,
Shree Dhoothapapeshwar
Ayurvedic Research Foundation
(SDARF), Navi Mumbai,
Maharashtra-410206.

Anti-Ulcer activity of Plantacid® suspension in Wistar rats: A pilot study

Mukesh B Chawda, Nitin A Mundhe, Venu Gopal Jonnalagadda, Kapil S Thakur, MK Vahalia, Shekhar S Shitut

Abstract

Background: The main intent of this study is to evaluate the antiulcer activity of Plantacid® suspension on non-steroidal anti-inflammatory drugs (NSAID's) -induced ulcers in the rat model.

Methods: 24 Wistar Rats weighing around 180-200g were fasted for 12 hours before the study and arbitrarily divided into 4 groups of 6 animals each. The 4 groups were: Vehicle (1 ml/kg, p.o), indomethacin (100 mg/kg, p.o), Plantacid® suspension (2.7 ml/kg, p.o), and Ranitidine (100 mg/kg, p.o) groups respectively. The treatment was given 60 minutes before the administration of indomethacin. Effect of Plantacid® suspension was studied by calculating the ulcer score, total number of ulcers, ulcer index and percentage inhibition. The results showing *p* values <0.05 were considered significant and all values are expressed as mean ± S.E.M.

Results: Significant decrease in ulcer score (*p*<0.05), total number of ulcers (*p*<0.0001), ulcer index (*p*<0.001), and % inhibition of ulcer was reduced by 82.06%, and 90.04 % in Plantacid® suspension and Ranitidine treated groups respectively, as compared to the indomethacin group.

Conclusion: The results indicate that Plantacid® suspension has showed antiulcer activity in experimental animals and corroborates Ayurvedic use of Plantacid® suspension in gastric ulcers.

Keywords: Plantacid®, Suspension, antiulcer, indomethacin, ranitidine etc.

1. Introduction

Peptic ulcer embraces both gastric and duodenal ulcers and has been a major threat to the world's population until the last decade of the 21st century. The epidemiological data and its complications have shown striking geographical variations in incidence and prevalence [1]. Current research has shown that approximately 10 % population of the world has been affected by gastrointestinal disorders [2]. However, about 19 out of 20 peptic ulcers are duodenal. An estimated 15000 deaths occur each year as a consequence of peptic ulcer. Annual incidence estimates of peptic ulcer hemorrhage and perforation were 19.4–57 and 3.8–14 per 100,000 individuals, respectively [3, 4].

The gastric mucosal damage is a common pathological condition occurred on gastrointestinal track. The multicomplex mechanisms revealed that it has multifactorial pathogenesis of peptic ulcer. Generally it depends on the imbalance between aggressive and defensive factors of gastric mucosa [5, 6]. However, gastric acid, pepsin, H. Pylori, and bile salts have come under the category of aggressive factors and making secretion, cellular mucus, bicarbonate secretion, mucosal blood flow and cell turnover may belong to defensive factors [7]. The ulcer located in the stomach is known as gastric ulcer, and that located in the duodenum is called a duodenal ulcer. Therefore, both are grouped together, and termed as peptic ulcer. Gastric and duodenal ulcers are common pathologies that may occur due to wide numbers of factors like stress, smoking noxious drug containing medicines, including nonsteroidal anti-inflammatory drugs (NSAIDs) [8]. NSAIDs is worldwide used for treatment for the treatment of pain, rheumatic and cardiovascular diseases, and more recently for the prevention of colon cancer [9]. During the course of medication of NSAIDs inhibits Cyclo-oxygenase enzyme (COX) and suppress prostaglandin (PG)-mediated effects on mucosal protection [10]. Despite great advances in the understanding of the peptic ulcer illness, its etiology has not been completely elucidated.

Ayurveda is renowned for Holistic Health, speaks to every prospect, element and facet of liveliness [11]. It is a simple, practical scientific discipline of life, existing since more than 5000 years. Basically, it originates in India and having a great function in the worldwide for the health guardianship system [12]. Its concepts about health and disease, promote the use of herbal tea compounds, special diets, and other unique health practices. However, sufficient scientific data with esteem to preventative and efficaciousness of Ayurvedic provision is

lacking due to a large turn of constituents in their formulation and mechanism of actions being unclear. Drug discovery with a single compound may not be useful in all diseases. And hence rationally designed Ayurvedic formulation could also be considered as a viable option. Plantacid® is an herbal-mineral preparations in suspension descriptor, marketed by Solumiks Herbaceuticals Limited. It contains Yashtimadhu (*Glycyrrhiza glabra*)^[13], Amalaki (*emblica officinalis*)^[14], Neer Brahmi (*Bacopa monnieri*)^[15], Bhrungaraja (*Eclipta alba*)^[12], Mukta Shukti Bhasma^[14, 16]. Mukta Shukti is obtained from sea water) as active ingredients, which have been investigated for antiulcer activity in various animal models.

Currently wide numbers of drugs are marketed for treatment of ulcers such as H₂-receptor blockers, proton pump inhibitors, antacids, and antibiotics. Many of these drugs pose adverse effects like dizziness, drowsiness, gas accumulation, headache, nausea, vomiting, inflammation of the nose, etc.^[17] Despite the availability of a large number of medicines, still management of the ulceration is one of the challenging problems because currently available therapy for limited efficacy and unwanted side effect.

2. Materials and Methods

2.1 Animals:

A total of 24 healthy Wistar rats (180-200 g, 6-8 weeks) were procured from the In-House Animal Facility of Shree Dhootapapeshwar Ayurvedic Research Foundation (SDARF). Animals were provided with standard diet and water ad libitum. Animals were housed in plastic cages below Standard conditions, temperature 20 ± 2°C and humidity 50-60%, with 12 h dark/light cycle. The Animals were acclimatized for a minimum period of 1 week prior to the start of the study. The experimental protocol was approved by the Institutional Animal Ethics Committee of SDARF. The An experiment was conducted according to the guidelines of the Committee for the Purpose of Control and Supervision of Experiments on Animals.

2.2 Chemicals

Plantacid® suspension was procured from Solumiks Herbaceuticals Limited (Mumbai). All other drugs and analytical grade chemicals were purchased locally.

2.3 Experimental Design

All the animals were randomly divided into five groups i.e., Group I : (normal control): 0.1% carboxy methyl cellulose (CMC) solution.

Group II : 0.1% CMC solution + indomethacin (100 mg/kg p.o.).

Group III : Ranitidine (100 mg/kg) + indomethacin (100 mg/kg).

Group IV : Plantacid® suspension ((2.7 ml/kg, p.o)) + indomethacin (100 mg/kg).

Plantacid® suspension dose in rats was selected from the human therapeutic dose (HTD) (15 ml/day) by using the formula, rat dose (200 g) = HTD × 0.018.

2.4 NSAID'S-induced ulcers

After 12 h fasting, Group I and II were administered to 0.1% CMC solution and Group III with ranitidine (100 mg/kg), and

IV was administered with Plantacid® suspension at 2.7 ml/kg, before 1 h of indomethacin in 0.1% CMC solution (100 mg/kg, p.o). All the test compounds were administered orally. Four hours after indomethacin administration, the animals were sacrificed by using the CO₂ chamber. The stomach was removed and opened along the greater curvature. The stomachs were gently rinsed with water to remove the gastric contents and blood clots. The inner surface of free stomach was examined for gastric lesions¹⁸. The number of ulcers was counted. Ulcer scoring was carried out according to the method by as given below. The scores were: 0 = no ulcer, 1 = superficial ulcer, 2 = deep ulcer, 3 = perforations.

2.5 Ulcer scores

Ulcer index was measured by using the following formula

$$UI = UN + US + UP \times 10 - 1.$$

UI is the ulcer index; UN is the average number of ulcers as per animal; US is the average number of severity score and UP is the percentage of animals with ulcers.

2.6 Percentage inhibition of ulceration:

Percentage inhibition of ulceration was calculated as follows:

$$\text{Percentage inhibition of ulceration} = \frac{(\text{U I control}) - (\text{U I Test}) \times 100}{(\text{U I control})}$$

3. Statistical analysis

Data expressed as mean ± SD ($n = 6$) and analyzed by one way analysis of variance was used to compare multiple groups in the study and Kruskal-Wallis test was used for ulcer index. A ($P < 0.05$) was considered significant.

4. Result

In the present study, antiulcer activity of Plantacid® suspension was studied in NSAID's induced ulcers in the stomach in Wistar rats. The rats treated with indomethacin alone significantly ($P < 0.001$) produced ulcers in the stomach compared with the normal control group (Fig IA & IB). However, treatment with Plantacid® suspension and Ranitidine showed ($p < 0.05$) significant reduction in ulcer as compared to positive control animals (Fig IC). Likewise, treatment with Plantacid® suspension and Ranitidine showed a significant ($p < 0.001$) decrease in ulcer index and also significant ($p < 0.001$) increases in the percentage of inhibition were observed in Plantacid® suspension and Ranitidine treated rats with compared to positive control rats.

Table 1: Effect of Plantacid® suspension on Total no. of ulcers, Ulcer Index and % inhibition of ulcer. All values were expressed as mean ± SEM ($n=6$). Where, *** $p < 0.001$. a vs normal control and b vs indomethacene control.

Groups	Total number of Ulcers	Ulcer Index	% Inhibition
Group I	0	0	100
Group II	10.83±1.25***a	23.33±1.2***a	0
Group III	0.50±0.22***b	3.6±1.65***b	84.56***b
Group IV	0.33±0.21	1.76±1.12	92.45

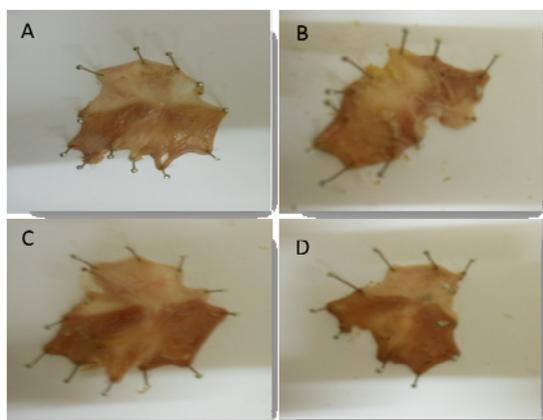


Fig 1: Effect of Plantacid® suspension on non-steroidal anti-inflammatory drugs induced ulcers in rats (A) Normal control (B) Indomethacene treated (c) Plantacid® suspension treated (D) Ranitidine treated

5. Discussion

In the present study, gastric ulcers were induced by indomethacine, and the ulcers engendered were studied for identification of the gastroprotective effect of Plantacid® in rats. Gastric ulceration was judged by microscopically as well as macroscopically. Administration of indomethacin caused multiple ulcerations with hemorrhage by gross examination along with significant increases in gastric ulcer index as compared to normal control animals. More after these results were substantiated by the histological evaluation of gastric mucosa. However, injuries like necrosis of mucosa, congestion of blood vessels were found with indomethacin treated rats. The ulceration induced by indomethacine is attributed due to various processes, like generation of reactive oxygen species, decreasing the levels of antioxidant parameters, initiation of lipid peroxidation, infiltration of leukocytes, and inhibition of prostaglandins [19].

The ulcers engendered were studied for identification of the gastroprotective effect of Plantacid®. The oral administration of indomethacin (100 mg/kg P O) induced gastric damage in all positive control rats. While Ranitidine reduced damage to 92.45 % as compared to positive control animals. However, Plantacid® suspension was found to be significantly inhibited indomethacine induced ulcers by 84.56 % as compared to positive control animals. Likewise, treatment with Plantacid® suspension and Ranitidine significantly reduced the generation gastric lesions as compared to positive control animals.

In the present study, indomethacin, a non-selective COX inhibitor, caused significant gastric ulcers by inhibiting the COX enzyme and thereby, reducing the synthesis of PGs. Inhibition of PGs synthesis can exert injurious actions on the gastric and duodenal mucosa as it abrogates a number of prostaglandin dependent defense mechanisms [20]. However, In the stomach, prostaglandins play a pivotal role in the maintenance of mucosal integrity of surface epithelial cells by engenderment of mucus or forbearance of gastric acid secretion and withal by stimulating the bicarbonate secretion [7]. So, extensive utilization of indomethacin or NSAID's may cause the inhibition of Cyclo-oxygenase which further decreases mucus and bicarbonate supply, reduce mucosal

blood flow and causes vascular injury, leukocyte accumulation and decreases cell turnover [21, 23]. Also, many of studied showed that inhibition of cyclo-oxygenase is directly involved in the generation of Reactive oxygen species, increased expressions of interleukins and induction of apoptosis [24]. It was observed that Plantacid® suspension showed significant reduction in the total number of ulcers in the indomethacin-induced ulcers in rats. These results suggest that the gastroprotective effect of Plantacid® suspension might be due to involvement of prostaglandins through mucus secretion in the stomach.

In conclusion, Plantacid® suspension produces significant antiulcer activity in indomethacine induced ulcers in rats. According to the present findings, the gastroprotective effect of Plantacid® suspension in the prevention of ulcers might be due to the production of prostaglandins in the stomach. Results suggest that Plantacid® suspension having a significant gastroprotective effect in rats

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Conflict of Interest: All authors declare that, we don't have any interest.

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