Latin American Journal of Pharmacy
(formerly *Acta Farmacéutica Bonaerense*)

Lat. Am. J. Pharm. **42** (5): (2023)

Antiulcer Activity of the Ethanolic Extract of the Aerial Part of *Ipomoea* carnea Jacq. in Rats

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Abstract:
Background: The goal of the current study was to examine the anti-ulcer potential of an ethanolic extract of the aerial part of the convolvulaceae plant Ipomoea carnea Jacq. in rats.
Methods: Thirty six animals were used in the investigation, which were divided into six groups of six rats each for the purpose of evaluating antiulcer activity. For 24 hours, all of the rats were starved. Following the fasting period, oral indomethacin (40 mg/kg) was administered. All samples of the plant extract were given 60 min prior to Indomethacin as follows: Group I animals received distilled water (0.5 mL/kg b.w.; orally) and served as control. Group II animals received distilled water (0.5 mL/kg b.w.; orally) and served as ulcer control. Group III rats received Omeprazole (30 mg/kg b.w.; orally), and served as the reference drug group for comparison. Groups IV, V and VI received EIC orally at 100, 200, and 400 mg/kg b.w., respectively. To evaluate a number of parameters, gastric juice was collected. Gastric volume, ulcer index, pH, free acidity and total acidity in the gastric juice of Indomethacin-induced (InI) rats were used to measure the antiulcer activity. Additionally, the markers of oxidative stress were measured, including lipid peroxidation (LPO), superoxide dismutase (SOD), reduced glutathione (GSH), and catalase (CAT).
Results: A significant ($p<0.05$) decrease in gastric volume, ulcer index, free acidity and total acidity in the gastric juice of InI rats served as evidence that the ethanolic extract (EE) of aerial part of Ipomoea carnea Jacq. (AIC) had antiulcer activity on InI ulcer in rats in a dose-dependent manner. Additionally, the elevated LPO and SOD levels were dramatically reduced by the pre-treatment with EE of AIC. Also, in a dose-dependent way, the lowered GSH and CAT levels were elevated in InI ulcerated rats.
Conclusion: The current investigation showed that InI rats exposed to the EE of AIC had strong dose-dependent antiulcer activity.

Keywords: Ipomoea carnea, Antiulcer, Ethanolic, Indomethacin

Introduction

The prevalence of peptic ulcers has increased over the past few decades, according to research [1]. An imbalance between the mucosal defence system and acid production in the stomach lumen has been associated to gastric ulcers [2–3]. Prostaglandins, healing factors, and the mucous layer of mucin-bicarbonate secretion reflect the defensive factors, whereas pepsin and acid represent the aggressive factors [4]. In the duodenum, lower oesophagus, and inner lining of the stomach, peptic ulcers cause sores to appear [4-5]. Antacids, proton pump inhibitors, and histamine (H2) receptor antagonists are the mainstays of conventional treatment for individuals with peptic ulcers [3,6]. Additionally, antibiotics and potassium competitive acid blockers have gained widespread acceptance as possible antiulcer treatments [7]. Antiulcer medications, however, have been shown to have a variety of adverse side effects, which has resulted in their withdrawal from clinical use [8]. Since ancient times, individuals who have been diagnosed with deadly diseases have been treated with herbal medicines and their extracts [9-10]. As a result, during the past few decades, the usage of herbal drug items has been increasingly important. In order to develop a new treatment for stomach ulcers, efforts are routinely made

to isolate active components from natural sources. *Ipomoea carnea* Jacq, commonly known as Bush morning glory, is a plant belonging to the convolvulaceae family [11]. This plant is widely distributed throughout the world, especially in the American tropics, Argentina, Brazil, Bolivia, Pakistan and Sri Lanka [12]. It is widely spread throughout India, but is most common in Madhya Pradesh, Uttarakhand, and Chhattisgarh [13]. The species is used as a home cure in the traditional medical systems of Ayurveda, Siddha, and Unani [12-14]. *Ipomoea carnea* has been reported to have substantial antioxidant activities in its methanolic extract [15], while the plant's aqueous extract is known to have anti-diabetic characteristics [16]. Additionally, the fact that mature, green *Ipomoea carnea* leaves had superior anti-inflammatory capabilities in comparison to the outcomes attained by etoricoxib [17] was indicative of the ability of the leaves' aqueous extracts to reduce inflammation. *Ipomoea carnea* extract also exhibits substantial antibacterial and anticancer effects, with a dose-dependent effect, according to studies [18-19]. *Ipomoea carnea* leaves have powerful wound-healing properties due to the presence of flavonoids and other compounds with a free radical scavenging mechanism [20]. Furthermore, *Ipomoea carnea* plant parts constitute a significant source of secondary metabolites, particularly phenolic compounds, as is widely acknowledged [21]. Various metabolites, including flavonoids, tannins, glycosides, alkaloids, carbohydrates, and phenolic compounds, are said to be present in the plant's aerial parts, including the stem, leaves, flowers, and seeds [19]. Swainsonine and the calystegines B1, B2, B3, and C1 were also found in the aqueous ethanolic extract of the plant's aerial section [12]. Additionally, the plant's aerial extract contains substances including hexadecanoic acid, stearic acid, n-octadecanol, octacosane, hexatriacontane and tetracontane [22]. To know whether the herb has strong antiulcer capabilities, however, appropriate research has not been done. The current study's goal was to evaluate the antiulcer activity of AIC against InI ulcers in rats because there hasn't been enough research in this area.

Materials And Methods

2.1 Animals

The experiment employed six groups, each made up of six Wistar albino rats (180-200 g), which were randomly chosen from the institutional animal house. Animals were housed in polypropylene cages with bedding made of husk, standard pellet diet, and unrestricted access to water. The animals were kept in a 12 h light/dark cycle at a temperature of 25±2 °C. The research protocol was approved by the Institutional Animal Ethical Committee (GDGU/IAEC/2022/26) and guidelines were strictly adhered to before performing animal studies.

2.2 Plant Material

Fresh vegetative and floral parts of *Ipomoea carnea* Jacq. were collected from Haridwar, Uttarakhand from August to October 2021. The plant was authenticated by Dr. Sandeep Kumar, Assistant Professor, Department of Botany and Microbiology, Gurukul Kangari, (Deemed University), Haridwar. The vegetative and floral part of Ipomoea carnea Jacq were submitted to the herbarium ref no. Bot and Micro/PIC/102 Department of Botany and Microbiology, Gurukul Kangari, (Deemed University), Haridwar.

2.3 Preparation of Ethanolic Extract

The plants' aerial parts were cleaned of external dirt and undesirable elements immediately after collection. The aerial parts of plant were cleaned by washing two times in tap water followed by once washing in distilled water. For 72 hours, the plant parts were shade-dried, from which the petioles, midribs, and twigs were removed after drying in the shade. After that, the dried plant parts were manually ground into a coarse powder. This 100 g of powdered material underwent a 95% ethanol Soxhlet extraction. Soxhlet extract dried at 60°C on water bath produced a yield of 14-18% of ethanol extract was found to be 14-18%. The ethanolic extract was suspended in distilled water before giving to rats since the extract was only sporadically soluble in water.

2.4. Experimental Protocol

The experimental protocol was divided into six groups, each containing six animals. The groups were divided as under:

Group I: Normal Control - the rats were given distilled water (0.5 mL/kg b.w.; orally)
Group II: Ulcer Control - the rats were given distilled water (0.5 mL/kg b.w.; orally)
Group III: Standard Drug Group - the rats were given Omeprazole (30 mg/kg b.w.; orally)
Group IV: Test Group - the rats received EE of AIC (100 mg/kg b.w.; orally)
Group V: Test Group - the rats received EE of AIC (200 mg/kg b.w.; orally)
Group VI: Test Group - the rats received EE of AIC (400 mg/kg b.w.; orally)

2.5 Antiulcer Activity Evaluation of EE of AIC

The method described by Aguwa and Mittal [23] was followed with minor modifications for the experiment. Thirty albino rats were taken. They were divided into five groups of six rats each. All the rats were starved for 24 h. After the fasting period, Indomethacin (40 mg/kg, p.o.) was given. All samples of the plant extract were given 60 min prior to indomethacin as follows: Group I animals received distilled water (0.5 mL/kg b.w.; orally) and served as control. Group II animals received distilled water (0.5 mL/kg b.w.; orally) and served as ulcer control. Group III rats received Omeprazole (30 mg/kg b.w.; orally), and served as the reference drug group for comparison. Groups IV, V and VI received EIC orally at 100, 200, and 400 mg/kg b.w., respectively. The animals were sacrificed by cervical dislocation five hours after the treatment, and the stomach was rapidly removed. The stomach was cut along its greater curvature in order to extract the gastric juice and place it in sterile centrifuge tubes. After centrifuging the juice, the amount of supernatant was measured. Using a pH metre, the juice's pH was immediately determined, and then it underwent biochemical examination. The free acidity and total acidity were assessed as described by Hawk, 1947 [24], and indicated as meq/L/100 g tissue.

2.6 Determination of Ulcer index

The stomachs' greater curvature was sliced open, and any gastric contents or blood clots were removed by cleaning with saline, and then examined under a 5x magnification lens to check for ulceration. The incidence and severity of lesions were evaluated using the following arbitrary grading system [25] as, 0.0 = Normal, 0.5 = Red coloration, 1.0 = Spot ulcers, 1.5 = Haemorrhagic streaks, 2 = Ulcers and 3 = Perforations. Mean ulcer score for each animal is expressed as Ulcer Index. The percentage of ulcer protection was determined by
Percentage inhibition of ulceration was calculated by using following formula [26], as below:
% Inhibition of Ulceration= (Ulcer index Control-Ulcer index Test) × 100/Ulcer index Control

2.7 Assessment of Oxidative Stress Parameters

Various oxidative stress parameters were conducted in order to assess the extent of oxidative damage. The method of Ohkawa et al. (1979) was used to measure lipid peroxidation (LPO) [27]. According to Marklund and Marklund (1974) [28], Superoxide dismutase (SOD) activity was determined. The Ellman, 1959 [29] approach was used to evaluate the activity of reduced glutathione (GSH), and by using the Sinha (1972) method, the activity of catalase (CAT) was calculated [30].

2.8 Statistical analysis

One-way analysis of variance (ANOVA) was performed on the data. To assess the significance of mean differences between distinct treatment groups, Tukey's multiple comparison test was used. The values were expressed as mean ± SEM and p value<0.05 was considered significant.

Results

3.1 Effect of EE-AIC on Gastric Volume, pH, Free and Total acidity

When compared to the normal control group, the ulcer control group (Group II) had significantly higher gastric volume, free acidity, and total acidity despite having lower gastric pH. When compared to the ulcer control (group II), pretreatment with omeprazole (group III) considerably improved the aforementioned parameters as shown by a decrease in gastric volume, free acidity, and total acidity as well as a rise in gastric pH. A dose-dependent reduction in the levels of all the aforementioned parameters in the gastric juice was observed in groups IV, V, and VI following pretreatment with EE of AIC prior to InI (Table 1).

3.2 Effect of EE-AIC on Antiulcer Activity

Rats pretreated with the EE of AIC following InI experienced a dose-dependent reduction in stomach ulcers. InI rats received 85.20% ulcer prevention from the conventional medication, i.e Omeprazole. At dosages of 100 mg/Kg, 200 mg/Kg, and 400 mg/Kg, Moreveor, EE of AIC demonstrated 54.44, 62.27, and 68.68 percent ulcer prevention in InI rats, respectively (Table 2).

3.3 Effect of EE-AIC on LPO and SOD

When compared to the normal control group (Group I), InI dramatically elevated LPO and SOD levels in the ulcer control group (Group II). When compared to ulcer control (group II), pretreatment with the standard drug omeprazole (group III) dramatically reduced LPO and SOD levels in InI rats. In groups IV, V, and VI of InI rats, pre-treatment with EE of AIC resulted in a dose-dependent reduction in LPO and SOD levels. (Table 3).

3.4 Effect of EE-AIC on GSH and CAT

When compared to the normal control group (Group I), InI caused a significant drop in GSH and CAT levels in the ulcer control group (Group II). When compared to ulcer control (group II), pre-treatment with the common

medicine omeprazole (group III) significantly raised the GSH and CAT levels in InI rats. Similar, dose-dependent increases in GSH and CAT activity were also seen in rats pre-treated with EE of AIC (groups IV, V, and VI) (Table 3).

Parameters	Group I	Group II	Group III	Group IV	Group V	Group VI
Gastric Volume (mL)	3.2 ± 0.07	4.95 ± 0.11	3.05 ± 0.09 m***	4.88 ± 0.12 m***, n**	4.02 ± 0.14 m***, n**	4.37 ± 0.1 m***, n**
pH	2.3 ± 0.01	1.95 ± 0.04	5.24 ± 0.13 m***	3.12 ± 0.12 m***, n**	3.88 ± 0.14 m***, n**	4.46 ± 0.11 m***, n**
Free acidity (mEq/L)	40.34 ± 2.14	62.36 ± 1.97	32.48 ± 1.98 m***	54.24 ± 2.04 m***, n**	53.33 ± 1.45 m***, n**	48.27 ± 1.96 m***, n**
Total acidity (mEq/L)	50.78 ± 1.58	74.23 ± 2.38	42.26 ± 1.84 m***	66.36 ± 2.03 m***, n**	58.32 ± 1.78 m***, n**	57.78 ± 2.12 m***, n**

Table 1. Effect of EE-AIC on secretory parameters in Indomethacin-induced rats.

The results are expressed as mean ± SEM. m represents comparison of group II with groups III-VI; n represents comparison of group III with groups IV-VI. **p < 0.01; ***p < 0.001

Parameters	Group I	Group II	Group III	Group IV	Group V	Group VI
Ulcer Index	0.00±0.00	5.62±0.14	0.82±0.03 m***	2.56±0.02 a***, n**	2.12±0.01 m***, n**	1.76±0.02 m***, n**
% Ulcer Protection	__	__	85.40	54.44	62.27	68.68

Table 2. Effect of EE-AIC on antiulcer activity in Indomethacin-induced rats.

The results are expressed as mean ± SEM. m represents comparison of group II with groups III-VI; n represents comparison of group III with groups IV-VI. **p < 0.01; ***p < 0.001

Parameters	Group I	Group II	Group III	Group IV	Group V	Group VI
TBARS (nM of MDA formed/min/mg protein	0.38 ± 0.005	0.66 ± 0.013	0.45 ± 0.008 m***	0.55 ± 0.01 m***, n**	0.56 ± 0.01 m***, n**	0.51 ± 0.011 m***, n**
SOD (units/mg protein)	0.92 ± 0.015	1.77 ± 0.02	1.02 ± 0.014 m***	1.68 ± 0.018 m*** , n**	1.55 ± 0.014 m***, n**	1.34 ± 0.021 m***, n**
GSH (u/mg protein)	6.12 ± 0.11	1.88 ± 0.08	5.84 ± 0.16 m***	3.66 ± 0.01 m*** , n**	4.98 ± 0.12 m*** , n**	4.84 ± 0.11 m*** , n**

Catalase (µM of H2O2 utilised/min/ mg protein)	7.35 ± 0.17	2.32 ± 0.09	6.71 ± 0.22 m***	3.29 ± 0.12 m***, n**	4.58 ± 0.14 m***, n**	5.23 ± 0.15 m***, n**

Table 3. Effect of EE-AIC on LPO, SOD, GSH and CAT in Indomethacin-induced rats.

The results are expressed as mean ± SEM. m represents comparison of group II with groups III-VI; n represents comparison of group III with groups IV-VI. **p < 0.01; ***p < 0.001

Discussion

The imbalance of preventive and aggressive factors that is related to peptic ulcers is mostly caused by inflammation [3,31]. Increased pepsin activity and acid secretion, as well as decreased mucus and bicarbonate production and decreased stomach mucosal blood flow, are regarded to be the main contributors to gastric ulceration [32-33]. Peptic ulcers can be brought on by a variety of techniques, but the most common method is the indomethacin-induced model [34]. Some reports claim that indomethacin induction activates pepsin and increases stomach acid, which results in the formation of ulcers [35]. It is well accepted that the causes of InI ulcers are gastric mucosa autodigestion and a breakdown of the stomach mucosal barrier [35–36]. The results of the current investigation demonstrated that pre-treating InI rats with omeprazole and EE of AIC at doses of 100, 200, and 400 mg/Kg (groups IV–VI) provided a comparable antiulcer effect, as shown by a decrease in stomach volume, free acidity, and total acidity with a corresponding rise in gastric pH (Table 1). Additionally, EE of AIC demonstrated antiulcer action in rats with InI ulcers as evidenced by a considerable reduction in ulcer index (Table 2). This antiulcer action may be connected to the plant extract's strengthening of the mucosal defence system, as demonstrated by a decrease in gastric secretion, free acidity, total acidity, and ulcer index with a corresponding rise in gastric pH.

It is widely known that secondary metabolites, especially phenolic chemicals, are abundant in *Ipomoea carnea* plant sections [37]. According to reports, the plant's aerial parts, including the stem, leaves, flowers, and seeds, contain a variety of metabolites, including flavonoids, tannins, glycosides, alkaloids, carbohydrates, and phenolic chemicals. [11-12]. Swainsonine and the calystegines B1, B2, B3, and C1 were also found in the aqueous ethanolic extract of the plant's aerial section. Additionally, the plant's aerial extract contains substances including hexadecanoic acid, stearic acid, n-octadecanol, octacosane, hexatriacontane, tetracontane, and 3-diethylamino-1-propanol [22,37]. The phytoconstituents obtained from medicinal plants have a variety of actions that have antiulcerogenic effect. Phenolic compounds and flavonoids have an antiulcer effect because of their cytoprotective, anti-inflammatory, antioxidant, anti-H. pylori, and anti-secretory activities [38]. Phenolic chemicals and flavonoids improve the production of prostaglandins, stress resistance, the production of antioxidant enzymes, and wound healing capabilities [39]. Additionally, flavonoids increase capillary resistance and microcirculation. Tannins directly protect the top layer of the mucosa and modify its structure to increase its resistance to toxins and physical injury [40]. The EE of AIC may have a significant antiulcer and antioxidant impact because of the existence of active secondary metabolites like phenolic compounds, tannins, flavonoids, saponins, and polyterpenes.

Oxidative stress, which is brought on by an unbalance between free radicals and antioxidants, damages cells and tissues. Numerous studies have shown that oxidative stress both develops and aggravates peptic ulcers [41-42]. Superoxide anion, hydrogen peroxide, and hydroxyl radicals are only a few examples of the oxygen-derived free radicals that play a significant role in the pathophysiology of damage to the gastrointestinal mucosa [43]. Significant reactive oxygen species (ROS) created by oxygen, such as free radicals, have been linked to the peroxidation of lipids. It is possible that the production of the aforementioned ROS is responsible to cause the enhanced lipid peroxidation in the gastric juice of the InI rats [44]. Furthermore, it is known that SOD scavenges the superoxide radicals responsible for lipid peroxidation. The amount of hydrogen peroxide free radical produced also rises as a result of this interaction, increasing the risk of oxidative damage [45]. Furthermore, oxidative stress decreases CAT and GSH levels while increasing LPO and SOD levels [41-42]. A buildup of free radicals, which can initiate the process of lipid peroxidation and induce membrane damage, may also result from the loss of stomach mucosal GSH. This claim is backed by the current study's findings, which showed that the EE of AIC dramatically reduced LPO and SOD levels. Additionally, the pretreatment of InI rats with EE of AIC led to an increase in the levels of CAT and GSH (Table 3). The ability of the stomach mucosa to maintain a healthy balance between free radicals and the enzymes that scavenge them, SOD and CAT, is related to the findings of the current study. The EE of AIC may have demonstrated antiulcer activity by lowering lipid peroxidation and reducing free radicals in the gastric mucosa of rats treated with InI. It has been shown that a

variety of plant extracts may inhibit the rise in LPO and SOD along with an increase in GSH and CAT in several models of ulcer induction in rats. Their ability to act as antioxidants and neutralise free radicals led to their antiulcer capabilities [46]. Our most recent research supports these reports. Omeprazole and EE of AIC pretreatment resulted in effective protection in the status of all acid secretory parameters, ulcer index, LPO, SOD, GSH, and CAT in the gastric juice of InI rats (Tables 1-3). In order to elucidate the precise mechanism of ulcer prevention offered by EE of AIC, further research is undergoing in our laboratory[47, 48].

Conclusion

In conclusion, the present study showed that, in a dose-dependent manner, EE of AIC had antiulcer activity that was comparable to that of the reference medication, omeprazole. The antiulcer efficacy of EE of AIC may be due to the decrease in gastric acid secretion, protection of the mucosal barrier, and restoration of mucosal secretions. Additionally, the antioxidant or free radical scavenging properties of the plant extract may be the cause of the antiulcer action that it demonstrated. Due to its antiulcer action and favourable safety profile, *Ipomoea carnea* Jacq.'s aerial extract may one day be used to treat patients presented with peptic ulcers..

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