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EVALUATION OF ANTIULCER ACTIVITY IN *CANNA INDICA RHIZOMES*

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ABSTRACT

With the rapid progress and advancement in various fields of human activities, the field of medicine and allied sciences has also made rapid strides. The synthesis of many chemicals and their introduction into therapeutics as drugs has certainly revolutionized the treatment of diseases. Peptic ulcer disease is a serious gastrointestinal disorder that requires a well targeted therapeutic strategy. A number of drugs including proton pump inhibitors and H2 receptor antagonists are available for the treatment of peptic ulcer, but clinical evaluation of these drugs has shown incidence of relapses, side effects and drug interactions. In an attempt to search a potent and safe medication for peptic ulcer, *Canna indica* rhizomes is being screened for its anti ulcer activity. *Canna indica rhizomes* were collected in Toopranpet village of Nalgonda district. Methanolic extraction method was used for extracting the active chemical constituents from plant materials. Acute toxicity study was carried out in male Swiss albino mice. MECI are considered to be safe up to the dose levels of 1000 mg/kg (b.w). By Asprin induced ulcer method, the standard drug of ranitidine showed 48.32% of ulcer inhibition. The % inhibition of 100 mg/kg, 200 mg/kg, and 400 mg/kg values are 19.35, 23.61, and 43.89 respectively. By Pyloric ligation induced ulcer method, the standard drug of ranitidine showed 79.23% of ulcer inhibition. The % inhibition of 100 mg/kg, 200 mg/kg, and 400 mg/kg values are 28.3, 53.46 and 65.45 respectively.

KEYWORDS: Canna indica, Indian shot, Rhizomes, Peptic ulcer and Herbal drugs.

INTRODUCTION

Over the past decade, herbal medicine has become a topic of global importance, making an impact on both world health and international trade. Medicinal plants continue to play a central role in the healthcare system of large proportions of the world's population.[1] With the rapid progress and advancement in various fields of human activities, the field of medicine and allied sciences has also made rapid strides. The synthesis of many chemicals and their introduction into therapeutics as drugs has certainly revolutionized the treatment of diseases.[2] Peptic ulcer disease is a serious gastrointestinal disorder that requires a well targeted therapeutic strategy. A number of drugs including proton pump inhibitors and H2 receptor antagonists are available for the treatment of peptic ulcer, but clinical evaluation of these drugs has shown incidence of relapses, side effects and drug interactions.[3] In Ayurveda, peptic ulcer mostly refers to *Amlapitta* or *Parinamasula. Amlapitta* is a disease of the gastrointestinal tract, especially of the stomach. *Amlapitta* literally means, pitta leading to sour taste.[4] In an attempt to search a potent and safe medication for peptic ulcer, *Canna indica* rhizomes is being screened for its anti ulcer activity.

MATERIALS AND METHOD

Plant Material

Canna indica L. (known as Saka siri, Indian shot, Canna, Bandera, Chancle, Coyol or Platanillo and Kardal in Marathi) is a species of Canna genus, belonging to the family Cannaceae, a native of the Carribean and tropical Americas that is also widely cultivated as a garden plant. It is a perennial growing from 0.5m to 2.5m, depending on the variety. It is hardy to zone 10 and is frost tender. The flowers are hermaphrodite. The seeds are small, globular, black pellets, hard and heavy enough to sink in water. They resemble shotgun pellets giving rise to the plants common name of Indian shot.[5]

Plant Collection

Canna indica rhizomes were collected in Toopranpet village of Nalgonda district and authenticated by Prof. P Suresh, Department of Botany, Government degree college Ibrahimpatnam, Rangareddy district. The rhizomes of the plant were stored in herbarium at the college for further reference.

CLASSIFICATION

Kingdom	Plantae – Plants
Subkingdom	Tracheobionta – Vascular plants
Super division	Spermatophyta – Seed plants
Division	Magnoliophyta – Flowering plants
Class	Liliopsida – Monocotyledons
Subclass	Zingiberidae
Order	Zingiberales
Family	Cannaceae – Canna family
Genus	*Canna* L. – canna
Species	*Canna indica* L. – Indian shot

Figure 1: *Canna indica* plant.

Figure 2: *Canna indica* rhizomes.

Extraction and Isolation

The rhizomes of *Canna indica* (100 gm) was extracted by methanol (60-80^{o}C) for 6 hrs in Soxhlet extractor. The methanol extract was evaporated in vacuum until a constant weight was achieved. MECI means methanol extract of *Canna indica*. It gave 2.44% of the residue.[6]

Chemical Constituents

Rhizomes yield fat, traces of an alkaloid, gum and starch. Phytochemical screening yielded phenols, sterols, flavonoids and saponins.

Study of red flowers yielded four anthocyanin pigments apart from quercetin and lycopene: Cyanidin – 3 – O - (6"-O-α-rhamnopyranosyl) - β-glucopyranoside, Cyanidin – 3 – O - (6"-O-α- hamnopyranosyl) - β-galactopyranoside, Cyanidin-3 – O – β - glucopyranoside, and Cyanidin – O – β – galactopyranoside.[7]

Animals

Albino rats (150-200 gm) of either sex were used for the experiment. They were kept in the animal house in a controlled room temperature at 25 ± 2^{o}C, relative humidity 44 - 56%, light and dark cycles of 10 and 14 hrs, respectively for 1 week before the experiment. The animals were grouped and housed in polyacrylic cages for further experiment.

Drugs and Chemicals

Extract: The MECI was dissolved in 1% Tween 80 as a vehicle and administered P.O in a dose of 100 mg/kg, 200 mg/kg and 400 mg/kg.

Standard drug: The ranitidine was dissolved in 1% Tween 80 and administered i.p in a dose of 27 mg/kg.

Acute Toxicity studies

The Acute Toxicity studies were performed in order to establish the therapeutic index of a test drug. The experiment was conducted according to the OECD, 423 guidelines.[8] It was administered as 5,100, 1000 and 2000 mg/kg.

Experimental design:

Rats were divided in to 5 groups. Each group contains 6 rats and treated with the following drug for five successive days and 6th day aspirin was administered and to evaluate the antiulcer activity.

Group 1: Control - Normal saline (1ml/kg)
Group 2: Ranitidine – 27 mg/kg (standard control)
Group 3: MECI - 100 mg/kg
Group 4: MECI – 200 mg/kg
Group 5: MECI – 400 mg/kg.

Aspirin Induced Ulcer Method

Aspirin at a dose of 200 mg/kg (20 mg/ml suspension in 1% CMC (Carboxy methyl cellulose) was administered orally to 18 hr fasted animals. After 1hr the test drug was administered on 6th day. The ulcers were scored after 4 hrs. The stomach was taken out and cut open along the greater curvature and ulcers were scored by a person in the glandular portion of the stomach. The ulcer index was calculated by adding the total number of ulcers per stomach and the total severity of ulcer per stomach.[9]

Pylorus Ligation Induced Ulcer Method

Rats were divided in to 5 groups. Each group contains 6 rats. Each weighing about 150-200 gm and fasted for 4 hrs with free access to water. Pylorus ligation induced ulcer method was performed under diethyl ether anesthesia to each animal. Animals were given to MECI 100 mg/kg, 200 mg/kg and 400 mg/kg b.w. ranitidine was prepared in 1% Tween 80 suspension as a vehicle orally immediately after pylorus ligation.[10,11,12,13]

Animals were sacrificed 6 hrs later the stomach was carefully removed and gastric contents were collected.

The gastric juice was centrifuged at 3000 rpm for 30 min. and then volume of gastric juice was measured. Acidity in the supernatant was determined by titration with 0.01N NaOH and expressed as m.eq/l. The stomach was cut open along the greater curvature and pinned on a soft board for evaluating gastric ulcers and ulcer index is calculated using formula:

Ulcer index = 10/x

Where x = Total mucosal area / Total ulcerated area.

RESULTS AND DISCUSSION

The etiology of peptic ulcer is unknown in most of the cases, yet it is generally accepted that it results from an imbalance between aggressive factors and the maintenance of mucosal integrity through the endogenous defense mechanisms. To regain the balance, different therapeutic agents including plant extracts may be used.

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.

Asprin – Induced Gastric Ulcer Method

Table 1: Asprin induced ulcer method of Methanol extracts of *Canna indica* rhizomes.

Groups	ASPIRIN (mg/kg)	Ulcer Index	Ulcer Inhibition(%)
Ulcer Control 0.9% saline	-	3.981± 0.5631	-
Ranitidine (27 mg/kg)	0.2	1.16± 0.1667 **	48.32
MECI (100 mg/kg)	0.2	2.213±0.987**	19.35
MECI (200 mg/kg)	0.2	2.85± 0.1763**	23.61
MECI (400 mg/kg)	0.2	3.652± 0.8456***	43.89

Values are expressed in Mean ± SEM, (n=6), when compared with control,

P<0.05, P<0.01, P<0.001 *, **, *** respectively, Oneway ANOVA followed by Dunnet's t – Test.

NSAIDs like indomethacin and aspirin induces gastric lesions by inhibiting cyclo-oxygenase (COX) resulting in less formation of prostacyclin, the predominant prostanoid produced in the gastric mucosa.

The general ulcer inducing methods are aspirin induced ulcer, pyrolic ligation method, cold restraint stress induced ulcers, ethanol induced ulcers, cold water immersion method, swimming stress ulcer method. These models represent some of the most common causes of gastric ulcer in humans.

Ulcer is defined as the erosion in the lining of the stomach or duodenum and is caused by the disruptions of the gastric mucosal defense and repair systems. Ulcer in the stomach is called gastric ulcer and in the duodenum is called duodenal ulcer, together peptic ulcer.

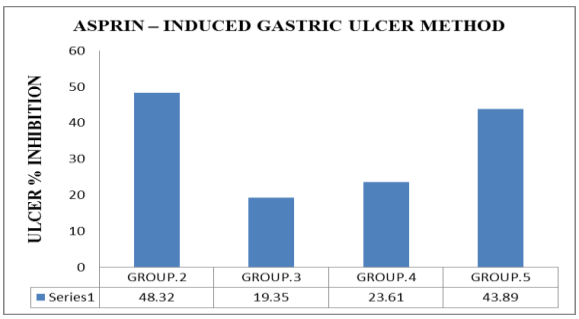

Figure 3: Asprin induced ulcer method of Methanol extracts of *Canna indica* rhizomes.

Group 2: Ranitidine – 27 mg/kg (standard control)
Group 3: Methanol extracts of *Canna indica rhizomes* - 100 mg/kg
Group 4: Methanol extracts of *Canna indica rhizomes* – 200 mg/kg
Group 5: Methanol extracts of *Canna indica rhizomes* – 400 mg/kg.

The ulcer inhibition percentage is shown in Table 1. The standard drug of ranitidine showed 48.32% of ulcer inhibition. The % inhibition of (Figure 3.) 100 mg/kg, 200 mg/kg, and 400 mg/kg values are 19.35, 23.61, and 43.89 respectively. If the concentration of MECI increases ulcer percentage inhibition also increased.

Pylorus Ligated Induced Ulcer Method

The causes of gastric ulcer pyloric ligation are believed to be due to stress induced increase in gastric hydrochloric acid secretion and/or stasis of acid and the volume of secretion is also an important factor in the formation of ulcer due to exposure of the unprotected lumen of the stomach to the accumulating acid. The anti ulcer activity of the plant of Methanol extract of *Canna indica* rhizomes was evaluated by employing pyloric ligation induced ulcer method & aspirin induced ulcer methods. Ulcers results from extrinsic factors like Helicobacter pylori, Non steroidal anti-inflammatory drugs (NSAIDs), Tobacco smoking, Alcohol, Stress and Intrinsic factors like Acid & Pepsin, Acid Reflux. These factors can be used to induce ulcer in animal models.

Table 2: Gastric volumes in Pyloric ligation induced ulcer method.

Groups	Dose (mg/kg)	Gastricvolume(ml)	P^H	Free Acidity
Ulcer Control	0.9 % saline	2.84±0.5978	2.85±0.0916	56.83±0.833
Ranitidine	(27 mg/kg)	3.91±0.1128 **	4.53±0.0954 **	35.16±1.014 **
MECI	(100 mg/kg)	2.127± 0.784**	2.513±0.8087**	4.85±0.894*
MECI	(200 mg/kg)	2.997±0.482**	3.68±0.8061 **	41.5±0.738 **
MECI	(400 mg/kg)	3.590±0.436***	3.75±0.2565 **	37.16±0.303 **

Values are expressed in Mean ± SEM, (n=6), when compared with control, P<0.05, P<0.01, P<0.001, *, **, *** respectively, Oneway ANOVA followed by Dunnet's t – Test.

Gastric volumes were significant to tested groups. Ranitidine showed 3. 91, methanolic extracts of *Canna indic* rhizomes 100 mg/kg, 200 mg/kg and 400 mg/kg, had 2.127, 2.997, 3.59 respectively as shown in Table 2. The ulcer inhibition percentage is shown in Table 3, Figure 4. The standard drug of ranitidine showed 79.23% of ulcer inhibition. The % inhibition of 100 mg/kg, 200 mg/kg, and 400 mg/kg values are 28.3, 53.46, and 65.45 respectively. If the concentration of MECI increases ulcer percentage inhibition also increased.

Table 3: Pyloric ligation induced ulcer method.

Groups	Dose (mg/kg)	Ulcer Index	Ulcer Inhibition (%)
Ulcer Control	0.9% saline	5.58± 0.2126	-
Ranitidine	(27 mg/kg)	1.937±0.1675**	79.23
MECI	(100 mg/kg)	2.013±0.987**	28.3
MECI	(200 mg/kg)	2.95± 0.4641**	53.46
MECI	(400 mg/kg)	3.58±0.1257**	65.45

Values are expressed in Mean ± SEM, (n=6), when compared with control,P<0.05, P<0.01, P<0.001 *, **, *** respectively, Oneway ANOVA followed by Dunnet's t – Test.

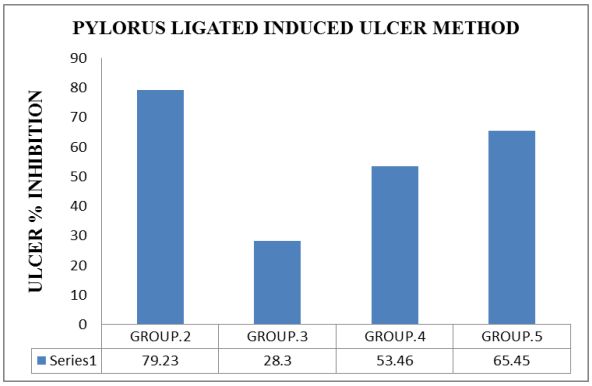

Figure 4: Pylorus ligated induced ulcer method of Methanol extracts of *Canna indica* rhizomes.

Group 2: Ranitidine – 27 mg/kg (standard control)
Group 3: Methanol extracts of *Canna indica rhizomes* - 100 mg/kg
Group 4: Methanol extracts of *Canna indica rhizomes* – 200 mg/kg
Group 5: Methanol extracts of *Canna indica rhizomes* – 400 mg/kg.

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SUMMARY AND CONCLUSION

In the present study, methanolic extract of *Canna indica* rhizomes showed a promising antiulcer effect on peptic ulcer models in pyloric ligation and aspirin induced methods in rats. Hence oral administration of the methanolic extract of *Canna indica* rhizomes have the potential to reduce the formation of peptic ulcers. This property of methanolic extract of *Canna indica* rhizomes action would be highly beneficial for treatment of various types of peptic ulcers in human beings and reduce the cost burden of the society.

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