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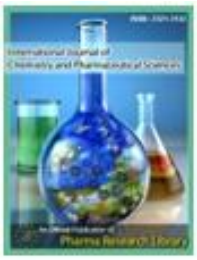

R E S E A E C H A R T I C L E

Evaluation of Methanolic Extract of Seed of Macuna Pruriens for Antiulcer Activity

N. Kalpana Devi[1]*, Chandrika Dontha[2], D.S.S.N. Neelima[3]

[1,2]*Teegala Krishna Reddy College of Pharmacy, Hyderabad, Telangana State.*
[3]*Vikas Institute of Pharmaceutical Sciences, Rajahmundary.*

A B S T R A C T

Ulcer is a major global problem affecting day to day life in humans and the causative factors being unavoidable such as stress, use of non steroidal antiinflammatory drugs (NSAID's) etc. Evaluation of Methanolic Extract of Seed of Macuna Pruriens for Antiulcer Activity. In this study we observed that, methanol and extract of macuna provides significant antiulcer effect against gastric ulcers in rats. The antiulcer activity of extracts may be a arrtributed to their flavanoids content and antioxidant property. The extract of the plants macuna produced significant reduction in the ulcer index, ulcer score, when compared to control. The preliminary phytochemical analysis of macuna pruriens extract showed the presence of flavanoids, saponins and alkaloids.

Key Words: Macuna, Anti-ulcer, flavanoids.

A R T I C L E I N F O

CORRESPONDING AUTHOR
N. Kalpana Devi
Teegala Krishna Reddy College of pharmacy,
Hyderabad, Telangana state, India.
MS-ID: IJCPS3666

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C O N T E N T S

1. Introduction

Man has used plants as medicines for thousands of years. Traditionally peptic ulcers have been described as an imbalance between the luminal acid peptic attack versus the mucosal defense. The treatment of peptic ulcers with plant products used in folk medicine and the protection of induced gastric ulcer in laboratory animals using medicinal plants were reported. Generally plant seeds have been found to be effective against ulcer in experimental animals and exhibit several biological effects. The present study has, therefore, been conducted to evaluate the antiulcer activity of methanolic extract of Mucuna pruriens seeds using ulcer models in rats since this extract has potent anti parkinsonism activity as previously reported. Mucuna pruriens (Fabaceae) is tropical legume commercially known as velvet bean or konch, which is climbing shrub grows widely throughout the tropical Africa, India and the Caribbean. The konch plant is used in combination for Herbal remedies. The seeds of Mucuna pruriens are used in high demand for various

illnesses such as Parkinson disease, used to increase libido in both men and women due to its dopamine inducing property. In History mainly it is used as aphrodisiac. A number of major components have been identified in the konch plant are high concentration of levodopa, 5-htp, nicotine, N,N-DMT, bufotenine, dimethyl tryptamine, carboline. The Mucuna pruriens seed has been claimed to have antiulcer activity, but no detailed scientific investigations have been carried out to define the antiulcer activities of Mucuna pruriens. Thus the present investigation sets out to study the antiulcer activity of Mucuna pruriens seed extract. The effect produced was compared with that of ranitidine, a standard drug.

Clinical Symptoms

Symptoms of a peptic ulcer can be:

Abdominal pain, classically epigastria with severity relating to mealtimes, after around 3 hours of taking a meal (duodenal ulcers are classically relieved by food, while gastric ulcers are exacerbated by it); Bloating and abdominal fullness, Waterbrash (rush of saliva after an episode of regurgitation to dilute the acid in esophagus). Nausea, and lots of vomiting, Loss of appetite and weight loss, Hematemesis (vomiting of blood); this can occur due to bleeding directly from a gastric ulcer, or from damage to the esophagus from severe/continuing vomiting. Melena (tarry, foul-smelling feces due to oxidized iron from hemoglobin). Rarely, an ulcer can lead to a gastric or duodenal perforation. This is extremely painful and requires immediate surgery.

Epidemiology

Disability-adjusted life year for peptic ulcer disease per 100,000 inhabitants in 2004[22]. The lifetime risk for developing a peptic ulcer is approximately 10%[23]. In Western countries the prevalence of Helicobacter pylori infections roughly matches age (i.e., 20% at age 20, 30% at age 30, 80% at age 80 etc.). Prevalence is higher in third world countries. Transmission is by food, contaminated groundwater, and through human saliva (such as from kissing or sharing food utensils [24]. Peptic ulcer disease had a tremendous effect on morbidity and mortality until the last decades of the 20th century, when epidemiological trends started to point to an impressive fall in its incidence[25].The reason why the rates of peptic ulcer disease decreased is thought to be the development of new effective medication and acid suppressants and the discovery of the cause of the condition, H. pylori. In the United States about 4 million people have active peptic ulcers and about 350,000 new cases are diagnosed each year. Four times as many duodenal ulcers as gastric ulcers are diagnosed. Approximately 3,000 deaths per year in the United States are due to duodenal ulcer and 3,000 to gastric ulcer [26].

Types of Ulcers

Most Common Types of Ulcers

Peptic Ulcer:

Any ulcer that is exposed to pepsin is referred to as peptic ulcers. Peptic ulcers are found in the lining of stomach or duodenum. Pepsin is normally present along with hydrochloric acid in the stomach lining. There are many symptoms of peptic ulcers that are worth checking out.

Gastric Ulcer:

When a peptic ulcer is in stomach, it is called a gastric ulcer. The symptoms of gastric ulcers are more specific than peptic ulcer symptoms.

Duodenal Ulcer:

When a peptic ulcer is in duodenum, it is called a duodenal ulcer. This type of peptic ulcer develops in the first part of the small intestine. Some of the symptoms of a duodenal ulcer are interestingly quite opposite to those of gastric ulcers. Duodenal ulcers are the most common ulcers found in the Western world.

Stress Ulcer:

Stress ulcers are a group of lesions (or lacerations) found in the esophagus, stomach or duodenum. These are normally only found in critically ill or severely stressed patients

Mechanism of action

Peptic ulcer occur in that part of gastrointestinal tract which is exposed to gastric acid and pepsin i,e the stomach and duodenum It results probably due to imbalance between the aggressive(acid, pepsin, bile and H.pyroli) and the defensive(gastric mucus and bicarbonate secretion, prostaglandins, nitric oxide, innate resistance of the mucosal cells) factors. A variety of psychosomatic humoral and vascular derangements have been implicated and the importance of helicobacter pyroli infection as a contributor to ulcer formation. In gastric ulcer,generally acid secretion is normal or low.In duodenal ulcer,acid secretion is high in half of the patients but normal in the rest. Notwithstanding whether production of acid is normal or high, it does contribute to ulceration as an aggressive factor,reduction of which is the main approach to ulcer treatment.

Secretion of gastric acid, mucus and bicarbonate:

The control of the gastrointestinal tract is through nervous and humoral mechanism.

- Acid secretion from gastric parietal cells by a proton pump. Three endogeneous secretagogues for acid are histamine, acetyl choline and gastrin
- Prostaglandins E2 and I2 inhibit acid, stimulate mucus and bicarbonate secretion, and dilate mucosal blood vessels.

The genesis of peptic ulcer involves:

- Infection of gastric mucosa with helicobacter pyroli. An imbalance between the mucosal damaging (acid, pepsin) and the mucosal protecting agents (mucus, bicarbonate, prostaglandins E2 and I2, nitric oxide).
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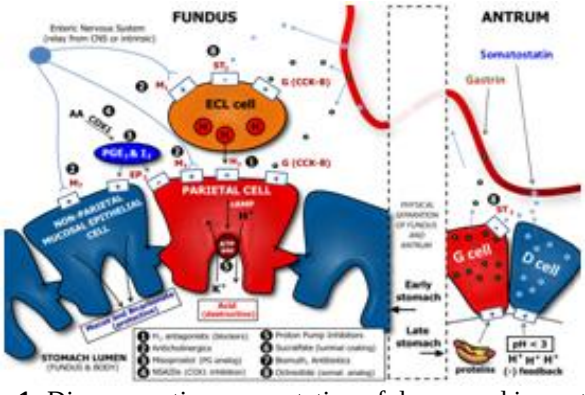

Fig 1: Diagrammatic representation of drugs used in peptic ulcer

Antacids:
They are simplest of all the therapies for treating the symptoms of excessive gastric acid secretion. They directly neutralize acid, thus raising the gastric pH this also has the effect of inhibiting the activity of peptic enzymes, which practically ceases at pH 5.

Prostaglandins:
It synthesized in the gastric mucosa mainly by cyclo oxygenase-1 stimulate mucus and bicarbonate secretions, decrease acid secretion and cause vasodilation.

Histamine H_2 receptor antagonist:
Histamine H_2 receptor antagonists competitively inhibit histamine actions at all H_2 receptors, but their main clinical use is as inhibitors of gastric acid secretion. Proton pump inhibitors are the agents which irreversibly inhibits the H+/K+ ATPase (the proton pump) the terminal step in the secretory pathway.

Management

Dietary changes that may be helpful:
People with ulcers have been reported to eat more sugar than people without ulcers, though this link may only occur in those with a genetic susceptibility toward ulcer formation. Sugar has also been reported to increase stomach acidity, which could aggravate ulcer symptoms. Salt is a stomach and intestinal irritant. Higher intakes of salt have been linked to higher risk of stomach (though not duodenal) ulcer. As a result of these reports, some doctors suggest that people with ulcers should restrict the use of both sugar and salt, although the benefit of such dietary changes remains unknown. Many years ago, researchers reported that cabbage juice accelerated healing of peptic ulcers. Drinking a quart of cabbage juice per day was necessary for symptom relief in some reports. Although only preliminary modern research supports this approach, many doctors claim considerable success using one quart per day for 10 to 14 days, with ulcer symptoms frequently decreasing in only a few days.

Carrot juice may be added to improve the flavor. Fiber slows the movement of food and acidic fluid from the stomach to the intestines, which should help those with duodenal, though not stomach, ulcers. When people with recently healed duodenal ulcers were put on a long-term (six-month), high-fiber diet, threat of ulcer recurrence was dramatically reduced in one controlled study, though short term (four-week) use of fiber in people with active duodenal ulcers led to only negligible improvement. The relationship between food allergies and peptic ulcers has been reported at least as far back as the 1930s.Exposing the lining of the stomach to foods to which a person is allergic has been reported to cause bleeding in the stomach. Although additional research is needed, avoiding food allergens may be helpful for people with peptic ulcers. Consult with a doctor to determine food sensitivities.

Surgical Care:
Surgical intervention is required in a small percentage of infants and in children with complications of peptic ulcer disease that include perforation, obstruction, intractable pain, and bleeding unresponsive to medical or endoscopic therapy.

- A bleeding ulcer can be treated with a simple plication or over sewing of the bleeding source. A more definitive procedure, such as vagotomy and pyloroplasty, may be required.
- In patients with stress ulcers related to brain injury or burns, the procedure of choice may be pyloroplasty and antrectomy.
- Total gastrectomy is rarely performed to treat multiple gastric ulcers in pediatric patients.
- For perforation, repair is performed by using a simple closure or oversewing.
- Gastric-outlet obstruction is surgically relieved with vagotomy and pyloroplasty or gastroenterostomy.

Indigenous plants
A large number of drugs have been used for the purpose of ulcer treatment are Garcina cambogia, Jatropha curcas, Kielmeyera coriacea, Mimosa pudica, Leucas lavandulifolia, Morinda citrifolia linn, Terminaalia chebula, Zapoteca portoricensis, Piper cubeba linn, Cantella asiatica, Aspilla africana, Bryophyllum pinnatum.

Plant profile:

Fig 2: Macuna Pruriens Plant

Fig 3: Macuna Pruriens Seed

Botanical name: Mucuna pruriens
Family: Fabaceae.
Local names: Cowitch, cowage, velvet bean, cow-itch, buffalo bean.
Sanskrit: Atmagupta
Bengal: Alkushi
Hindi: konch
Marati: khaajkuiri
Habitat: grow all over India and Andaman and Nicobas islands.
Chemical constituent: 40mg/gm of L-Dopa, alkaloids Leaves: 0.5% L-DOPA, 0.006% dimethyltryptamine (DMT), 0.0025% 5-MeO-DMT and 0.003% DMT n-oxide.

Seeds: levserotonin (5-HT), 5-HTP, nicotine, N,N-DMT (DMT), bufotenine, and 5-MeO-DMT

Uses: Parkinson disease, astringent, laxative, aphrodisiac, tonic, anti helminthic.

Earlier work done:

- Alcoholic extract of seeds of Mucuna pruriens has an Antiperoxidation property.(Ratheesh et al.2010).
- Mucuna pruriens extract,l-dopa research,supplement uses for Parkinson diseases, fertility and sexual enhancement.(Ray Sahelian et al..2007).
- Invitro studies with alcoholic extract of Mucuna pruriens showed no change on rate of aerial oxidation of GSH content but it significantly inhibited FeSo4 induced lipid peroxidation.(Phytotherapy research 2002).

2. Materials and Methods

Plant material collection:

The Medicinal plant extracts was collected locally at Tirupathi. The botanical identity was confirmed by Dr. Madhavashetty, Department of Botany. Sri Venkateswara University, Tirupathi.

Preparation and Extraction:

Shade dried powdered plant material was kept for maceration with alcohol for 48hrs, and distillation was carried out to extract the drug.The plant extract was concentrated, and the extract was administred per orally to the animals by mixing with adequate quantity of water.

Qualitative chemical tests:

The phytochemical screening of extracts of plants was carried out to detect Flavonoids,Tannins,Saponins,Alkaloids and Steroids.

Test for Flavonoids: Alkaline reagent test.

Test for Saponins: Aqueous test.

Test for Alkaloids: Mayer's test, Dragendroff's reagent.

Test for Steroids: Libermann-Burchard test.

Pharmacological studies

Experimental animals:

A female albino rat of wistar strain weighing 150-200gm was used.The animals were fed with commercial rat feed pellets (gold mohur) and were given water and ad libitum.They were kept in polypropylene cages in well ventilated room under hygienic conditions.

Acute Toxicity Studies

Acute oral toxicity studies of the methanolic extract of Macuna pruriens was carried out as per the OECD guide lines and the non-toxic dose was found. One –tenth and the one –twentieth of the non-toxic upper bound dose of the extract from the limit test was considered for the experimental procedure.

Pylorus Ligation Model

Gastric ulcers were induced by pylorus ligation model Animals were divided in six groups (n= 8). Group I receives no treatment, serves as normal animals. Group II received vehicle (distilled water 2 ml/animal) that serves as vehicle control. Group III received standard drug ranitidine (38 mg/kg b weight, per oral) one hour prior to pylorus ligation. Group IV, V and VI received PDP (2.5 ml/animal, per oral), PH (1ml/ animal, per oral) and PDP+PH (2.5 ml and 1ml/animal, per oral) respectively for 30 days. At the end of the treatment schedule, the animals of all groups were starved for 48 h with free access to drinking water. Under light ether anesthesia, the pylorus of rat was ligated, 19 h later the ligated rats were sacrificed by decapitation. The abdomen was opened, stomach was removed after ligating the cardiac end and opened along the greater curvature. The contents were drained into a centrifuge tube and centrifuged at 2000 rpm, 3 min (REMI R8C Laboratory Centrifuge) for assessing parameters like acid volume, gastric pH, total acidity, free acidity, ulcer index.

The stomach was thoroughly washed under running tap water and pinned onto a cork plate. The no of ulcers and severity was scored as per Rao et. al, 1990.The stomach were removed also from Group I as mentioned earlier and antioxidant parameters like lipid peroxidation, reduced glutathione, catalase and nitrite were assessed in all the groups.

The parameters monitored in pylorus ligation model are:

a) Gastric pH

b) Acid volume

c) Total acidity

A known amount of gastric residue was titrated with 0.1 N NaOH. The total acidity however was determined by titration using phenolphthalein (1% alcoholic) as indicator.

Reading was taken (ml NaOH) for total acidity

Y = ml of 0.1 N NaOH x 10

Where,

Y = Total acidity (mEq/L).

d) Free acidity

A known amount of gastric residue was titrated with 0.1 N NaOH. Add two drops of Methyl orange reagent which changes to a salmon color when all the free hydrochloric acid was neutralized.

Reading was taken (ml NaOH) for free acidity

Y = ml of 0.1 N NaOH x 10

Where,

Y = Free acidity (mEq/L).

e) MUN - Mean of number of ulcers per animal.

f) MUS – Mean of severity score per animal.

Statistical Analysis

Stastiscal analysis was carried out using Graphpad prism software. All data were expressed as Mean + Standard Mean Error. Groups of data were compared with one way analysis of variance followed by Dunnett 't' test. Values were considered statistically significant at $p<0.05$.

Indomethacin induced model:

Group I: No treatment serve as normal.

Group II: Received standard drug

Group III:

Test drug was administrated as high and low dose orally in 0.1% Tween 80 solution, 10 min prior to oral indomethacin in a dose of 40 mg/kg(8mg /ml dissolved in 0.1%Tween solution). 6 hours later, the rats were sacrificed in anaesthetic ether and their stomach was removed. Stomach were washed under tap water and examined under a 3 fold magnifier. The mean count of ulcers and ulcer score for each group being calculated.

3. Results and Discussion

Ulcer is a major global problem affecting day to day life in humans and the causative factors being unavoidable such as stress, use of non steroidal antiinflammatory drugs (NSAID's) etc. The rat being omnivorous resembles man nutritionally. It is advisable to use adult rats of either sex for the antiulcer studies[3]. Pylorus ligation model is considered as a potential tool to evaluate efficacy of new drugs against gastric ulcers. Pylorus ligation–induced ulcers are produced due to autodigestion of the gastric mucosa by gastric acid and breakdown of the gastric mucosal barrier.

.The preliminary phytochemical analysis of macuna pruriens extract showed the presence of flavanoids, saponins and alkaloids. It is also reported that, the flavanoids like flavone glycosides and isoflavonoids have been isolated. Flavanoids are among the cytoprotective materials for which antiulcerogenic efficacy has been extensively confirmed. It is suggested that, these active constituents would be able to stimulate mucus,bicarbonate and prostaglandin secretion and counteract with the deteriorating effects of reactive oxidants in g.i lumen. So, the antiulcer activity of Mucuna may be arrtibuted to its flavanoids content.

In this study we observed that,methanolic extract of macuna provide significant antiulcer effect against gastric ulcer in rats. Both the extract of the plants Macuna produced significant reduction in the ulcer index, ulcer score, when compared to control. It is suggested that, these active constituents would be able to stimulate mucus, bicarbonate and prostaglandin secretion and counteract with the deteriorating effects of reactive oxidants in g.i lumen. So, the antiulcer activity of Mucuna may be arrtibuted to its flavanoids content. In this study we observed that, methanolic extract of macuna provide significant antiulcer effect against gastric ulcer in rats. Both the extract of the plants Macuna produced significant reduction in the ulcer index, ulcer score, when compared to control.

The plant showed significant effect on healing of ulcers induced by ethanol, indomethacin, cysteamine hydrochloride, pyloric ligation models. Ethanol induced gastric lesions formation may be due to stasis in gastric flow which contribute to the development of the haemorrhage and necrotic aspects of tissue injury. Alcohols rapidly penetrates the gastric mucosa apparently causing cell and plasma membrane damage leading to increased intracellular membrane permeability to sodium and water. Indomethacin is known to be related with the inhibition of cyclooxygenase that prevent prostaglandins biosynthesis, which inturn inhibits the release of mucus, a defensive factors against g.i.t damage. Cysteamine hydrochloride inhibits the alkaline mucus secretion from the brunner's glands in the proximal duodenum and stimulates the rate of gastric acid secretion. Gastric emptying is also delayed and serum gastrin concentration is increased.

Pharmacological activity of Macuna pruriens (Pylorus Ligation Model)

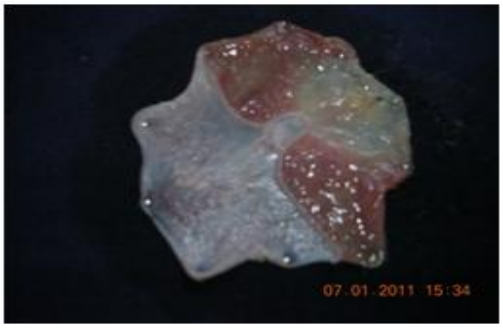

Fig 4: Normal stomach

Fig 5: Normal control

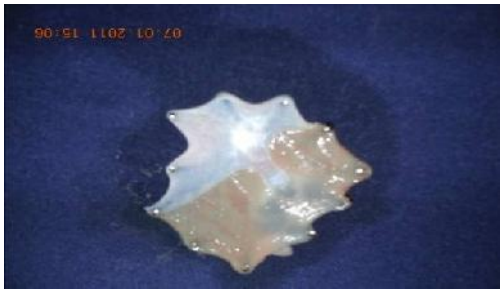

Fig 6: Standard control

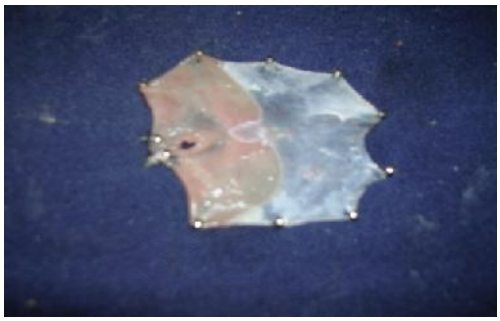

Fig 7: 200mg/kg peroral

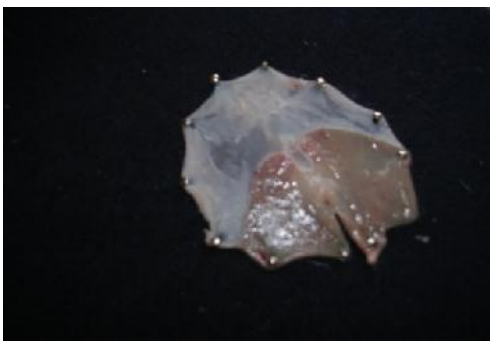

Fig 8: 200mg/kg peroral

Table 1: Effects of methanolic seed extract of Mucuna pruriens on pyrolic induced in rats

S.No	Volume of HCl	pH	Total acidit (meq/lit)
Normal control	2.85 ±0.24	1 ±00	55.26 ±1.08
Standard control	A 0.91± 0.17	a 6.34 ±0.21	A 15.26± 1.11
Test 1	B 1.45± 0.11	a 6.983 ±0.04	B 37.46 ±2.06
Test 2	B 1.32 ±0.11	a 7.65± 0.022	A 29.13± 2.6

a=p<0.0001, b=p<0.055

Table 2: Effects of methanolic seed extract of Mucuna pruriens on pyrolic induced in rats

cc	MUN	MUS	MUI
Normal control	5.23± 0.244	3.5± 0.18	18.61± 1.33
Standard control	A 1.85+0.31	b 1.71± 0.22	A 4.29± 0.39
Test 1	B 2.85± 0.60	b 2.54± 0.34	B 7.11 ±1.63
Test 2	A 2.01± 0.25	b 1.96± 0.26	B 6.95± 1.48

a=p<0.001, b=p<0.05

Table 3: Effect of methanolic extract of roots of Macuna pruriens on Indomethacin induced gastric ulcer in rats

S.No	Ulcer Index	Ulcer protection
Normal control	17.61± 1.13	0
Standard control	A 2.11 ±0.23	88.12
Test 1	A 6.98± 0.34	58.45
Test 2	A 3.9 ±0.30	75.30

a=p<0.0001

4. Conclusion

In this study we observed that, methanol and extract of macuna provides significant antiulcer effect against gastric ulcers in rats. The antiulcer activity of extracts may be a arrtributed to their flavanoids content and antioxidant property. The extract of the plants macuna produced significant reduction in the ulcer index, ulcer score, when compared to control.

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