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ANTI-ULCER ACTIVITY OF AQUEOUS EXTRACT OF ANNONA SQUAMOSA LEAVES ON RATS

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Abstract:

The anti-ulcer activity of aqueous extract of Annona squamosa leaves was investigated on a indomethacin induced ulcer models in wistar rats. In model the common parameter determined was ulcer-index. aqueous extract of dosage 175, 350 mg/kg p.o produced significant inhibition of gastric lesions induced by indomethacin induced ulcers. The extract 175mg/kg & 350mg/kg showed significant ($p<0.01$) reduction in gastric volume, free acidity and ulcer index as compared to control. This present study indicate that Annona squamosa leaves extract have potential anti ulcer activity. This results may further suggests that aqueous extract was found to posses antiulcerogenic as well as ulcer healing property,which might be anti secretory activity.

Key words: *anti-ulcer,annona squamosa, antisecretory ,indomethacin*

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INTRODUCTION:

Herbal plants cheaper accessibility and with fewer or no side effects) herb defined as any part of a plant which can be used for medicine, cooking, cosmetic uses and as a scent or dye. Herb plants produce and contain a variety of chemical substances that act upon the body.This plant are used to prevent, relieve, and treat illness. From a "scientific" perspective, many herbal treatments are considered experimental. The reality is, however, that herbal medicine has a long and respected history. The current worldwide trend towards utilization of plant- derived remedies has, therefore, created adire needed accurate and upto date information on the properties and uses, efficacy, safety and quality of medicinal products. Many plant components are now synthesized in large laboratories for use in pharmaceutical preparations. For example, vincristine (an antitumor), digitalis (a heart regulator), and ephedrine (a bronchodilator used to decrease respiratory congestion) were all originally discovered through research on plants. (Kokate C.K., 1995). There is a worldwide 'green revolution, (Mukherjee, P.K., 2002) which is reflected in the belief that herbal remedies are safer and less damaging to the human body than synthetic drugs. Furthermore, underlying this upsurge of interest in plants is the fact that many important drugs in use today were derived from plants or from starting molecules of plant origin.

The plant *Annona squamosa Linn.* Belongs to Annonaceae family. It is small, semi-deciduous tree, found throughout India. It is traditionally used in anti-tumor, anti- diabetic and anti-lipidaemic activity. The bark can be used stop diarrhoea in children and adults. Fruit is used to make a hair tonic. The plant is reported to contain 1-tritriacontanol (1) (17),(+)-o-methyl armepavine (2) (15), N-methyl corydaldine(3) (18), lanuginosone (4) (19,20), (+) anomuricine (5)(21),isocorydine (6) (22), N-methy1-6,7-dimethoxy isoquinolone (7)(23), 6,7-dimethoxy-2-methyl iosqninolinium (8) (24,25), 13-sitosterol (9) and 3-sitosterol-3-043-D-glucopyranoside (10) (26), 1-(443-D-glucopyranosylixypheny1)-2-(3-D- glucopyranosyloxy)-ethane (11)(26) and Rutin(Dinesh.K and Yadav,2011).

Gastric hyperacidity and ulcer are very common cause of human sufferings today. Although prolonged axity, emotional stress, hemorrhagic surgical shock, burns and trauma are known to cause severe gastric irritation,the mechanism is still poorly understood(Rao et al.,2004). The present work attempts to evaluate the antiulcer potential of *Annona squamosaLinn.*

MATERIALS AND METHODS:

This study was conducted in the pharmacology laboratory, Department Of Pharmacology,
Sri Indu Institute Of Pharmacy, Sheriguda, Hyderabad, R.R Dist, A.P, India.

Collection and extraction:

The fresh leaves of *Annona Squamosa* L were collected from local area at Ibrahimpatnam, Hyderbad. The material was taxonomically identified, confirmed and authenticated by Botanical Department,JNTUH..

The collected leaves were shade dried at 21°c over polythene cover and the dried material was crushed to coarse powder with mechanical grinder. The powder was stored in airtight container which was used for extraction. About 70 gm of air dried powdered material was soaked in 1000ml distilled water and heat till solvent separation of extract. Separated filtrate extract is filtered by using muslin cloth .and the liquid is centrifuge at 10000 rpm by separating sediment. At the end of the extraction process the marc was taken out and it was dried. After drying, the powdered marc was weighed & again packed. The yield obtained is 14 gms

Preliminary phytochemical screening of extracts:

Qualitative chemical tests were conducted for aqueous extracts to identify the various phytoconstituents employing standard screening tests(Kokate,2002). aqueous extract gave positive test for steroids, saponins, tannins, phenolic compounds and flavonoids.

Animals:

Healthy adult wister albino rats of weighing 150-200gms were used for the study. The animals were obtained from animal house and were housed in polypropylene cages. The animals were maintained under standard laboratory conditions (25^{O} C±2^{O}C;12hr light and dark cycle). The animals were fed with standard diet and water *adlibitum.* Ethical clearance was obtained from the Institutional Animal Ethical Committee before performing the study on animals was taken for conducting antiulcer activities.

Acute oral toxicity studies:

Acute oral toxicity study for aqueous extract *of Annona squamosa* leaves was carried out as per OECD guideline 425.

indomethacin induced ulcer:

Male albino-Wistar rats were divided in to four groups as mentioned above of six animals per group and animals were fasted for 24 hrs prior to the experiment in perforated steel cages to avoid coprophagy.

Group I - control.(20 mg/kg,b.wt of indomethacin)
Group II - received 20mg/kg, p.o omeprazole as standard.

Group III - received 175mg/kg, p.o aqueous extract of *Annona squamosa* leaves.
Group IV - received 350mg/kg, p.o aqueous extract of *Annona squamosa* leaves.

Group was kept as control without any treatment. One hour after the drug treatment, the animals were treated with indomethacin 20mg/kg by p.o, to induce ulcers. The animals were sacrificed after 4hrs and stomach was opened and percentage inhibition of ulcer was determined. **(Kannappan *et al.*, 2008, Panda *et al.*, 1993, Parmar NS *et al.*, 1991, Pati K.S. *et al.*, 2008).**

Animals in all the groups were fasted for 36 h after the respective assigned treatment and were anaesthetized with anesthetic ether. The abdomen was opened by a small midline incision below the xiphoid process. Precaution was taken to avoid traction to the blood supply. The stomach was sutured with interrupted sutures. Animals were allowed to recover and stabilize in individual cages and were deprived of water during post-operative period. Four hours after , the animals were sacrificed by an excess dose of ether. The stomach was carefully removed and the gastric contents were collected. The gastric juice was centrifuged at 1000rpm and gastric volume was measured. Free and total acidities of the supernatant were determined by titration with 0.01 N NaOH by using phenopthalein as indicator and expressed as mEq/ L /100 gms. The stomach was cut open along the greater curvature and pinned onto a soft board for evaluating the Gastric ulcers and to calculate ulcer index. Ulcer scoring is done according to the scale mentioned below. (Vogel *et al.*, 2002).

ULCER INDEX (UI)
0 — Normal colored stomach
0.5 — Red coloration
1 — Spot ulceration
1.5 — Haemorrhagic streak
2 — Ulcers>3mm
3 — ulcers>5mm(perforation)

Percentage inhibition:
Percentage inhibition was calculated using the following formula. (Malairajan et al., 2007) Percentage protection = Control(M) — Test (UI) x 100 control (UI)

Statistical studies:
The data obtained by the various parameters was statistically evaluated by one way analysis of variance (ANOVA) followed by Dunnet's 't' test using Graph Pad Prism software. (Trail version) The mean values ± SEM were calculated for each parameter.

RESULTS:

Phytochemical screening:
The preliminary Phytochemical screening of the extract of *Annona squamosaleaves* showed the presence of carbohydrates, alkaloids, sterols, flavonoids, saponins, tannins and phenolic compounds, Protein and amino acids. The various phytoconstituents present in the extract.

Acute toxicity studies ($1D_{50}$):
There was no change in normal behavioural pattern of extract treated animals and no sign and symptoms of toxicity were observed during the observations which was done continuously for the first two hours and then observed upto 24 hours for mortality. The extract was safe upto maximum dose of 2000mg/kg body Extract at 175 and 350mg/kg are taken as lower dose and higher dose.

Indomethacin induced ulcer:
Omeprazole at both doses of Significant ($p<0.001$) decrease in ulcer score was produced by Omeprazole, extract 175 and 350mg/kg when compare to control. Extract 350mg/kg produced in ulcer index % inhibition comparable ($p<0.01$) to that of Omeprazole. The percentage protection against ulcer by Omeprazole, extract at 175mg/kg and 350mg/kg body weight were found to be

Table No 1: Effect of *Annona squamosa* Leaf extracton indomethacin induced ulcers

Treatment	Dose (mg/kg.b.wt)	Ulcer index	% inhibition	Gastric acid output	%inhibition	Vol of gastric juice
Contol	20	29.6±1.5	-	98.67±24.5	-	4.48±0.117
Standard	20	11.6±0.8	60%	35.83±15.3	64%	2.68±0.18
Test dose	175	17.88±1.538	39%	68.39±8.75	22%	4.28±0.093
Test dose	350	9.16±3.1	69%	48.67±14.7	51%	3.05±0.163

All values represent Mean ± SEM, n=6 in each group. ***P<0.001, **P<0.01, Control group is compared with standard and extract doses

DISCUSSION:

Most of the studies demonstrate the importance of natural products in drug discovery. In these study antiulcer activity of aqueous extract of *Annona squamosa* has been studied. The antiulcer study was evaluated using indomethacin induced in rats.

Most of the studies demonstrate the importance of natural products in drug discovery. The use of phytoconstituents as drug therapy to treat major ailments has proved to be clinically effective and less relatively toxic than the existing drugs. The acute oral toxicity study result showed that the plant leaf is safe.

Peptic ulcer describes a condition in which there is a discontinuity in the entire thickness of the gastric and duodenal mucosa that persists as a result of acid and pepsin in gastric juice. Peptic ulcer disease (PUD) is a serious gastrointestinal disorder that requires a well targeted therapeutic strategy. It includes number of drugs such as proton pump inhibitors and H2 receptor antagonists are available for the treatment of peptic ulcer, Peptic ulcer occurs due to an imbalance between aggressive (acid, pepsin) and defensive (gastric mucosal barrier) factors of gastric mucosa. indomethacin induced model shows significant percentage inhibition when compared with standard.. The ulcer index parameter was used for the evaluation of ulcer activity. Moreover the disturbance of defensive factor like mucus secretion, bicarbonate secretion and mucosal blood flow has been reported to cause ulcer.

CONCLUSION:

It was found that antiulcer activity exhibited was due to mucosal defensive factor. Hence it can be used for management of peptic ulcer.

Chemical substances derived from plant have got a very long history in treatment of human diseases. Nearly 50% of new chemical entities introduced during the past two decades were from natural products.

Further research is required to isolate the active phytoconstituents present in the extract and experimentation on the healing action of drug on chronic ulcer as well as on the possible side effects. The investigation on mode of action may pave way for establishment of new anti-ulcer therapy regimen.

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