GASTROPROTECTIVE ACTIVITY OF CUCUMIS SATIVUS L

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ABSTRACT
The objective was to investigate antiulcer activity of Ethanol Extract of Cucumis sativus (EECS) on indomethacine induced experimental ulcer models. The anti-ulcer effect of EECS at 150 mg/kg were evaluated in indomethacine induced ulcer models using Albino rats compared with Ranitidine used as a standard drug. In the conditions of inhibition of release of gastric juice, hydrochloric acid and neutralization activity. The anti ulcer activity was noted after drug administration. All data were analyzed by one-way ANOVA followed by Dunnet test. A maximum anti ulcer activity was found at 150 mg/kg of EECS, which was near equivalent to that of standard drug Ranitidine. Histopathological study of the stomach also exhibited almost normal architecture, when compared to Indomethacine treated group ingredients.

KEY WORDS: Cucumis sativus L, Indomethacine, PUD and Ranitidine.

INTRODUCTION
In the very last few decades, there is a tremendous growth in the region of herbal medicine. It is coming popularized in both developing and in the developed countries due to its natural origin because of its lesser side effects. Herbal remedies provide a lot of drugs for the treatment of internal diseases which are considered to be stubborn and incurable by other system of medicines.
It aims both to prevention and cures the diseases.\textsuperscript{[2]} In an ancient system the traditional medicines like Siddha, Chinese, Ayurveda and Japanese have been approved for the prevention diagnosis and treatment for liver disorders. This effort is to prove scientific insight behind the traditional adoption. Better therapeutic effect, less toxicity, good patient compliance and cost efficiency are important reasons for choosing drug from natural sources.\textsuperscript{[3]} Ayurvedic and herbal medicinal products contain a combination of a number of chemical compounds that may give the predictable activity in amalgamation.\textsuperscript{[4]}

*\textit{C. sativus*} L (\textit{F. Cucurbitaceae}) is a well known plant also has a deep history in the treatment of gastric disease with emollient effect. These \textit{Cucurbitaceae} plants are richly composing of flavonoids, phenolic acids, carotenoids and triterpinoids. These have an important role in alternative systems of medicine like Ayurveda and Siddha due to its various pharmacological activities like hepatoprotective, antidiabetic, cytotoxic, anti inflammatory and larvicidal effects.\textsuperscript{[5,6]}

Peptic ulcer disease (PUD) is a serious gastrointestinal disorder that requires a well targeted therapeutic strategy. The formation of PUD depends on the presence of acids and peptic activity of gastric juice and the breakdown of mucosal defenses. A number of drugs, including proton pump inhibitors and H2 receptor antagonists are available for the treatment of peptic ulcer, on the same side the clinical evaluation of these drugs has shown a number of relapses, side effects. Stomach ulcer is among the major disease of GIT, for which a large number of traditional and modern medicines are being utilized. So that, the medicines of plant origin are more accepted due to their less adverse effect.\textsuperscript{[7]}

This has been the important for the development of new antiulcer drugs and the search for novel molecules has been extended to herbal drugs that offer improved protection and reduced side effect. Drugs of plant origin are approaching popularity and are being investigated for a number of disorders.

The present study was used to evaluate the gastric protective effect of EECS in which peptic ulcer was induced by Indomethacine treatment.\textsuperscript{[1]}
MATERIAL AND METHODS

1. Drugs and Chemicals
All reagents procured were analytical grade.
Ranitidine (Ranbaxy Pharmaceuticals Ltd) purchased from the local drug store.

2. Plant collection
Fresh leaves of *C. sativus* L., was collected from field of Komarapalayam and authenticated by Dr. P. Satyanarayana, Scientist D & Head office in charge, Southern Regional Centre, TNAU campus, Coimbatore. Voucher specimen (No: JKKNCP/0102/13) has been deposited in the Department of Pharmacognosy, JKK Nataraja College of Pharmacy, Komarapalayam, Tamilnadu, India

Preparation of Plant Extracts
The dried leaves of *C. sativus* L. was extracted with Pet.Ether and then ethanol was subjected to solvent extraction.

**Ethanol extract of Cucumis sativus Linn. (EECS)**
Fine powdered Leaves of *C. sativus* L. were extracted with ethanol (60-80°C) using soxhlet apparatus. The extract was filtered and evaporated to separate solvent and residue. The semisolid residue which obtained was stored in desiccator until further use.

**Animals**
Albino rats either sex weighing between 175 ± 25gm was used in this evaluation. These rats aged between 2 -2.5 months were procured from animal house located in JKK Nataraja College of Pharmacy, Komarapalayam. They were housed in well ventilated stainless-steel cages at room temperature (24±2°C) in hygienic condition under natural light and dark schedule and were fed on a standard laboratory diet. Food and water were given ad libitum.

**Experimental protocol**
**Acute oral toxicity study**
The acute oral toxicity study was followed by using OECD GUIDELINES - 423 (Organization of Economic Co-operation and Development) - Fixed dose procedure (FDP).

Acute toxicity study was performed for EECS according to the acute toxic classic method as per OECD (423) guidelines[^5^], Albino rats were used for acute toxicity study. The animals were kept in fasting condition for overnight providing only water, then the extract was
administered orally at the doses of 5, 50, 300, and 2000 mg/kg and observed for 16 days. If death was observed in 2 out of 3 animals, then the dose administered was concluded as toxic dose. Animals aren't showing signs of toxicity including mortality; nature, severity, and duration of effects up to the dose level of 2000 mg/kg for the extract.[8-10]

**Antiulcer activity**

*Group 1-* Normal control rats, which received distilled, water (1 ml/kg) orally.
*Group 2-* Receives Indomethacine (25 mg/kg) as a single dose for 3 days
*Group 3-* Receives Rantidine (100 mg/kg) as a standard reference drug (Std).
*Group 4-* Receives EECS (150 mg/kg) once daily.

*Group 2 and Group 4* receives Indomethacine (25 mg/kg) as a single dose for 3 days as an ulcerative agent 1 hour before the ulcerogenic procedures.

The animals were sacrificed 6 hr. after the administration of necrotizing agent. The stomachs were removed and opened along with the greater curvature of the stomach; the ulcer index was evaluated according to severity and scored microscopically with the help of a hand lens (10x) as follows.[11, 12, 13]

**Scoring of ulcer**[15]

0 = Normal colored stomach,
0.5 = Red coloration,
1 = Spot ulcers,
1.5 = Haemorrhagic streaks,
2 = Ulcer > 3 mm but < 5 mm,
3 = Ulcers > 5 mm

**Calculation of ulcer Index:**[16]

\[
UI = UN + US + UP \times 10 - 1
\]

UI = Ulcer Index
UN = Average of number of ulcer per animal
US = Average of severity score
UP = Percentage of animal with ulcer
Determination of Acidity

\[
\text{Acidity} = \frac{\text{Volume of NaOH} \times \text{Normality of NaOH}}{0.1} \times 100 \text{mEq/L}
\]

Determination of Percentage Protection:

\[
\% \text{ Protection} = \frac{\text{Control mean ulcer index} - \text{Test mean ulcer index}}{\text{Control mean ulcer index}} \times 100
\]

In the present study, evaluated for EECS anti-ulcer activity against Indomethacin induced gastric ulcer model.\cite{14,17} The results of study are tabulated in Table-I.

**Histopathological studies**

The stomach from all groups were removed quickly, opened along the greater curvature, and thoroughly rinsed with ice-cold saline. After recording the ulcers produced in the stomach, a section of the gastric tissue was taken from the anterior part of the stomach and kept in a 10% formalin solution. After 24 h of fixation the tissues are embedded in a paraffin block, it was cut into sections of 5 microns onto a glass slide and stained with hematoxylin-eosin for histological assessment of the gastric mucosa.

**RESULT AND DISCUSSION**

The use of nonsteroidal anti-inflammatory drugs (NSAIDs) is known to be the major risk factor in gastric ulcers. The mechanisms optional for the gastric damage produced by NSAIDs are hang-up of prostaglandin synthesis and inhibition of epithelial cell modification in the ulcer margin, which is critical for the re epithelization of the ulcer cave.\cite{18} There has been a more important in finding natural antioxidants from plant materials to restore synthetic ones for effective management of therapeutic drug toxicity such as peptic ulcer.\cite{19,20}

In the present study, indomethacin, one of NSAIDs family, caused a remarkably significant increase in ulcer index, gastric juice free and total acidity and PH. Oral administration of RAN significantly reduced the ulcer index, gastric juice free and total acidity and PH. EECS provided a marked effect in gastro protective activity.
### Table 1: Effect of EECS and Ranitidine on Indomethacin-induced gastric lesions

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Body wt. gms</th>
<th>Treatment group</th>
<th>Vol. of Gastric Juice (ml)</th>
<th>Free Acidity (Eq/I) 100gm</th>
<th>Total Acidity (Eq/I) 100gm</th>
<th>Ph</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>175±25</td>
<td>control</td>
<td>1.2±0.71</td>
<td>33.66±3.14</td>
<td>42.33±3.14</td>
<td>7.33±0.33</td>
</tr>
<tr>
<td>2.</td>
<td>175±25</td>
<td>Ulcer Control Indomethacine 25mg/kg</td>
<td>10.1±2.39**</td>
<td>83.16±6.16**</td>
<td>104±6.16**</td>
<td>2.55±0.32**</td>
</tr>
<tr>
<td>3.</td>
<td>175±25</td>
<td>Ranitidine 100mg/kg</td>
<td>2.28±0.64†</td>
<td>36±7.63†</td>
<td>45±2.60†</td>
<td>7.4±0.36†</td>
</tr>
<tr>
<td>4.</td>
<td>175±25</td>
<td>EECS 150mg/kg</td>
<td>4.25±0.34†</td>
<td>49±5.79†</td>
<td>60.5±8.87†</td>
<td>4.75±0.77†</td>
</tr>
</tbody>
</table>

Values are expressed as mean ± S.D. of six animals in each group. Statistical analysis ANOVA followed by Dunnett t-test. N= 6 *P < 0.01 as compared with control, †P < 0.01 as compared with standard, ns = non significant.

**Histopathology of stomach region**

![Fig 1. GROUP – I-(Control)](image1)

![Fig 2. GROUP - II (Indomethacine induced)](image2)

![Fig 3. GROUP – III-(Standard)](image3)

![Fig 4. GROUP – IV-(EECS)](image4)
REFERENCES


