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RESEARCH ARTICLE

Comparative study of anti ulcer activity of aqueous extracts of leaves of *Piper betel* Linn and Dried fruits of *Cuminum cyminum Linn* and their combination in Rats

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Abstract

The antiulcer activity of the aqueous extracts of leaves of *piper betel* and dried fruits of *cumin* against the diclofenac sodium induced stomach ulceration has been studied and compared with omeprazole. All the test groups accelerated the healing process to different extents. Healing activity of the aqueous extracts of combination of *piper betel* and *cumin* was found to be good than healing activity of aqueous extracts of cumin and piper betel alone. Gastric mucin protection and regeneration was found to be due to aqueous extract administration was found to having good antiulcer property.

Introduction

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, leading to sour taste. Number of drugs including proton pump inhibitors, prostaglandin analogs, histamine recesptor antagonists and cytoprotective agents are available for the treatment of petic ulcer. But most of these drugs produce several adverse reactions including toxicities and even may alter biochemical mechanisms of the body upon chronic usage. Hence, herbal medicines are generally used in such cases when drugs are to be used for chronic periods. Several natural drugs have been reported to possess anti-ulcerogenic activity by virtue of their predominant effect on mucosal defensive factors.

From the centuries, Plants such as *Piper betel* Linn (piperaceae) and *Cuminum cyminum Linn* (umbelliferae) are using in treating peptic ulcers as folklore medicine. The leaves of *P. betel* with a strong pungent and aromatic flavour are widely consumed as a mouth freshner and credited with wound healing, digestive and pancreatic lipase stimulant activities in the traditional medicine. Its utility against various diseases can be traced in the ancient vedic literature, Atharved as early as 3000–2500 BC. Dried ripe fruits of *Cummin* are consumed as carminative and also used in treating diarrhea and dyspepsia. Cumin found to have Larvicidal activities, Antibacterial properties, Cancer Prevention, Antioxidant, Radical Scavenging Activity, Anti-fungal activity, Anti-microbial activity properties. The extracts of *P. betel* leaves are reported to provide cytoprotection against gastric lesions, and show digestive and antioxidative properties.

Based on these previous findings, we investigated the comparative evaluation the antiulcer activity of leaves of *Piper betel* and fruits of *Cuminum cyminum* for the additive effect.

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Materials and Methods

Plant material

Fresh leaves of piper betel and dried ripe fruits of cumin were purchased from the local market and were thoroughly authenticated in Pharmacognosy department of GCOP, Hyd. Material were dried under shade, dehydrated and powdered to a fine texture and subjected to hydro alcoholic extraction. The extract was concentrated under vacuum and the residue was used in the experiments. Formulations were made as suspension prepared in gum acacia 2%

w/v uniformly mixed. The formulations were fed to animals through gastric tube (9 mm) for rats and 2 – 3 cms polythene tubing sleeved on an 18-20 gauge blunted hypodermic needle for rats. The vehicle gum acacia (2% suspension) alone was used as a control in all the groups.

Animals

Healthy wister rats weighing 200- 250 grams were used for gastric tolerability test. Animals were housed in appropriate cages in uniform hygienic conditions and fed with standard pellet diet (liptonindia laboratories, Bangalore) and water *ad libitum* and were fasted overnight before the day of experiment. Animals were housed within the departmental animal house, and the room temperature was maintained at 27 degrees Celsius.

Experimental design:

Animals (n=30) were allocated to 6 groups (GC, GD, GO, GP, GCu, G PCu) of 5 animals each. Groups of five animals each receiving gum acacia as the control (GC), diclofenac sodium (GD), omeprazole (GO), extract of piper betel leaves (GP), extract of cumin dried ripe fruits (GCu), combination of extracts of piper betel leaves and cumin dried ripe fruits (G PCu) respectively.

Pylorus- ligation induced gastric ulcer:
Animals were anesthetized with ether and stomach exposed with small incision. Thread passed around the pyloric sphincter and applied a tight knot. After 4 hr of pyloric ligation, animals were sacrificed by decapitation method. Stomach was removed to collect the gastric contents. The mucosal surface was macroscopically observed and ulcer scores were determined.

Score the ulcers as below:

0= normal colored stomach
0.5=red coloration
1= spot ulcers
1.5= heamatologic streaks
2= ulcers≥3 but≤5
3=ulcers ≥5

The total volume of gastric content was measured. The gastric contents were centrifuged at 1000 rpm for 10 min. One ml of the supernatent liquid was pipetted out and diluted to 10 ml with distilled water. The solution was titrated against 0.01N NaOH using Topfer's reagent as indicator, to the endpoint when the solution turned to orange colour. The volume of NaOH needed was taken as corresponding to the free acidity. Titration was further continued till the solution regained pink colour. The volume of NaOH required was noted and was taken as corresponding to the total acidity.

Acidity was expressed as: Acidity = Volume of NaOH x Normality x 100 / 0.1

Carragennan induced paw oedema model in rat:
Animals were numberd and marked on both the hind paws (right and left) just beyond tibio-tarsal junction, so that every time the paw is dipped in the mercury column up to the fixed mark to ensure constant paw volume. The initial paw volume (both right and left) of each rat by mercury displacement method was noted for all groups. After 30min injected 0.1ml of 1% (w/v) carrageenan in the plantar region of the left paw of control as well as treated group. The right paw will serve as reference non-inflammaed paw for comparison. The paw volume of both legs of control and treated noted at 1hr, 3 hr and 6hr after carrageenan challenge. Calculated the percent difference in the right and left paw volumes of each animal of control and treated groups. Compared the mean per cent change in paw volume in control and treated animals and expressed as percent oedema inhibition by the drug.

Statistical analysis:

The values Mean±SEM are calculated for each parameter. For determining the significant inter group difference each parameter was analysed separately and one-way analysis of variance was carried out.

Results and Discussion:

1. Anti-ulcer activity of extracts of the plants

The gross appearance of Ulcer healing patterns was different depending on the type of treatments, and became more apparent in the aqueous extract of cumin. Diclofenac sodium caused a punctuate type clean eruptions. Combination of aqueous extracts of cumin and piper betel well tolerated to diclofenac sodium. Aqueous extract of piper betel group showed ulcer healing property than control group. All of the extract groups showed significantly higher ulcer protection values than the control group. That is, the plant extracts showed significant ulcer protection against diclofenac sodium and omeprazole treatment (Figure 1).

Figure 1: Ulcer index of the plant extracts

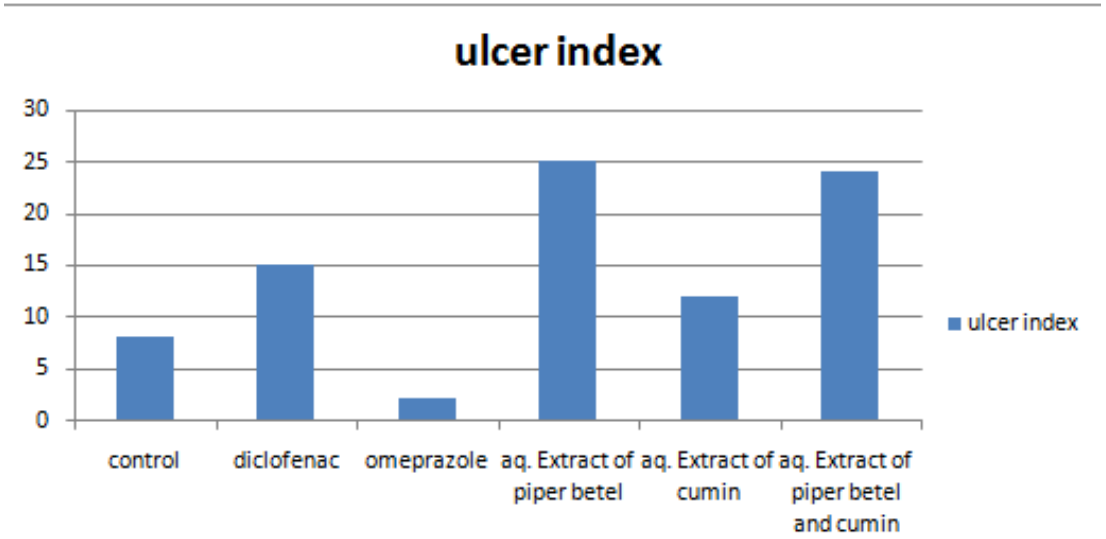

Table 1: Anti inflammatory activity of extracts of piper and cumin

GROUPS	Change in paw volume (ml) mean±SEM& % inhibition		
	1 hr	3 hr	6 hr
control	0.47±0.01	0.59±0.01	0.65±0.02
Diclofenac sodium	0.21±0.03 (55.32)	0.32±0.02 (45.77)	0.25±0.02 (61.54)
Aq. Extracts of Piper betel	0.28±0.02 (40.43)	0.45±0.01 (23.73)	0.32±0.02 (49.46)
Aq. extracts of Cumin	0.33±0.02 (29.78)	0.41±0.02 (30.51)	0.30±0.02 (53.38)
Aq. Extracts of Piper betel & cumin	0.28±0.02 (40.43)	0.36±0.01 (38.90)	0.29±0.01 (55.38)

Values are mean ±SEM, n=5, p<0.05 vs control

2. Anti inflammatory activity of extracts of plants:

All the extract groups of piper betel and cumin showed good anti-inflammatory action. Combination of plant extracts showed significant anti-inflammatory activity compared to individual treatments (table 1).

Conclusion:

From the above results we can state that cumin and piper betel having the anti-ulcer activity. And even they are effect in the treatment of NSAID Induced ulceration. But still exact mechanism for anti ulcerogenic activity has to be determined in safety parameters concerns.

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