

SHORT COMMUNICATION

The Antiulcer Activity of *Garcinia cambogia* Extract Against Indomethacin Induced Gastric Ulcer in Rats

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Garcinia cambogia extract is a herbal preparation that has been suggested as useful in the treatment of gastrointestinal disorders. In the present study this drug was tested for its antiulcerogenic effect. Oral pretreatment with *Garcinia cambogia* fruit extract (1 g/kg body wt/day) for 5, 10 or 15 days protected the gastric mucosa against the damage induced by indomethacin (20 mg/kg body wt). The volume and acidity of the gastric juice decreased in the pretreated rats. The glycoprotein levels of the gastric contents which were decreased in the untreated rats, maintained near normal levels in the pretreated rats. Protein which was elevated in the gastric juice of untreated rats, showed near normal levels in the pretreated rats. *Garcinia cambogia* was able to decrease the acidity and to increase the mucosal defence in the gastric areas, thereby justifying its use as an antiulcerogenic agent. Copyright 2002 John Wiley & Sons, Ltd.

Keywords: gastric ulcer; *Garcinia cambogia*; indomethacin; antiulcer activity.

INTRODUCTION

Peptic ulcer is a conglomerate of heterogenous disorders, which manifests itself as a break in the lining of the gastrointestinal mucosa bathed by acid and/or pepsin. NSAID ingestion is associated with erosions, petechiae, type C gastritis, ulceration, interference with ulcer healing, ulcer complications and injury to the small and large intestine (Wallace, 1992). Although a number of antiulcer drugs such as H₂ receptor antagonists, proton pump inhibitors and cytoprotectants are available for ulceration all these drugs have side effects and limitations (Ariyoshi *et al.*, 1986).

Herbal medicine deals with plants and plant extracts in treating diseases. These medicines are considered safer because of the natural ingredients with no side effects (Clouatre and Rosenbaum, 1994). *Garcinia cambogia* (Gaertn.) Desr. (Clusiaceae) fruit extract containing the principle organic acid (-)-erythro-L_α-hydroxycitric acid, is one such herbal preparation that has been used traditionally in treating ulcers, diarrhoea, dysentery, haemorrhoids, tumours and also as an antimicrobial agent (Warrier *et al.*, 1995; CSIR, 1985). This study was undertaken to assess the efficacy of *Garcinia cambogia* fruit extract in the treatment of gastric ulcer.

MATERIALS AND METHODS

Animals. Male Wistar rats (weighing 150–180 g) were

fed with standard pelleted diet (M/s Hindustan Lever Foods, Bangalore, India) and water *ad libitum* and housed under standard environmental conditions. The animals were deprived of food for 24 h prior to ulcer induction.

Drugs and chemicals. *Garcinia cambogia* fruit extract was obtained from Siris Herbex, Vijayawada, India, indomethacin was obtained from SRL, India. All other chemicals were of analytical grade.

Dosage fixation. *Garcinia cambogia* fruit extract was administered at different dosages (0.5, 1, 1.5 g/kg, p.o./day). The dosage and duration of the treatment period that exhibited the maximum antiulcer activity (based on ulcer index, volume of gastric juice, peptic activity and acid output) was fixed as the optimum dosage schedule for the drug. The optimum dosage was found to be 1 g/kg body wt/day orally for 15 days.

Grouping. The following groups of animals were used. Group I, normal control; Group II, ulcer: indomethacin (20 mg/kg body wt, p.o); Group III, drug control: *Garcinia cambogia* fruit extract (1 g/kg body wt/day) alone for 15 days; Group IV, pretreated ulcer: *Garcinia cambogia* fruit extract (1 g/kg body wt/day) for 5 days + indomethacin (20 mg/kg body wt, p.o); Group V, pretreated ulcer: *Garcinia cambogia* fruit extract (1 g/kg body wt/day) for 10 days + indomethacin (20 mg/kg body wt, p.o); Group VI, pretreated ulcer: *Garcinia cambogia* fruit extract (1 g/kg body wt/day) for 15 days + indomethacin (20 mg/kg body wt, p.o).

Experimental procedure. After 24 h of fasting at the end of the experimental period (5, 10, 15 days) with water provided, indomethacin at an oral dosage of 20 mg/kg

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Table 1. The effect of doses of *Garcinia cambogia* fruit extract (0.5, 1, 1.5 g/kg, p.o.) on the number of lesions, activity of pepsin, volume of gastric juice and acid output on indomethacin (20 mg/kg p.o.) induced gastric ulcer

Parameter	<i>Garcinia cambogia</i> (g/kg body wt)									
	Indomethacin induced ulcer		5 days		10 days		15 days			
	0.5	1.5	0.5	1.5	1.0	1.5	0.5	1.5		
No of lesions	10.24 ± 1.44	9.82 ± 1.16 ^{NS}	8.36 ± 0.87 ^a	8.29 ± 0.81 ^a	8.16 ± 0.80 ^a	6.12 ± 0.72 ^c	6.07 ± 0.68 ^c	6.98 ± 0.75 ^a	3.02 ± 0.64 ^c	2.98 ± 0.61 ^c
Pepsin (µmol tyrosine/4h)	675.80 ± 43.60	670.6 ± 45.4 ^{NS}	624.6 ± 30.6 ^a	618.4 ± 28.71 ^a	638.7 ± 31.5 ^{NS}	582.1 ± 29.7 ^b	577.4 ± 29.3 ^b	611.3 ± 28.4 ^b	561.2 ± 31.8 ^c	556.4 ± 30.7 ^c
Volume of gastric juice (mL/4h)	3.28 ± 0.33	3.11 ± 0.32 ^{NS}	2.88 ± 0.24 ^a	2.81 ± 0.20 ^a	2.86 ± 0.22 ^a	2.56 ± 0.21 ^b	2.50 ± 0.22 ^b	2.77 ± 0.25 ^a	2.21 ± 0.20 ^c	2.17 ± 0.19 ^c
Acid output µeq/4h	257.60 ± 25.40	248.5 ± 23.7 ^{NS}	219.3 ± 16.2 ^a	214.5 ± 16.8 ^a	236.4 ± 24.4 ^{NS}	203.50 ± 15.1 ^b	200.20 ± 15.90 ^b	218.3 ± 19.2 ^c	196.7 ± 16.5 ^c	191.6 ± 16.1 ^c

Values are expressed as mean ± SE; $n = 6$.

Student's t -test: ^a $p < 0.05$, ^b $p < 0.01$, ^c $p < 0.001$ vs ulcer (indomethacin) NS, non-significant.

Table 2. Effect of *Garcinia cambogia* fruit extract (1 g/kg, p.o./day) on indomethacin (20 mg/kg, p.o.) induced gastric ulcer in rats^a

Parameter	Group I Normal	Group II Ulcer indomethacin	Group III <i>Garcinia cambogia</i> alone	Group IV		Group V		Group VI		ANOVA F value
				Pretreated ulcer 5 days	indomethacin + <i>G. cambogia</i>	Pretreated ulcer 10 days	indomethacin + <i>G. cambogia</i>	Pretreated ulcer 15 days	indomethacin + <i>G. cambogia</i>	
No. of lesions	0	10.24 ± 1.44 ^c	0	8.36 ± 0.87 ^a	6.12 ± 0.72 ^a	3.02 ± 0.64 ^c	4.34 ^y			
Volume of gastric juice (mL/4h)	2.16 ± 0.18	3.28 ± 0.33 ^c	2.07 ± 0.26 ^{NS}	2.88 ± 0.24 ^a	2.56 ± 0.21 ^b	2.21 ± 0.20 ^c	3.56 ^x			
Acid output (µEq/4h)	193.40 ± 16.20	257.60 ± 25.40 ^c	187.20 ± 15.60 ^{NS}	219.30 ± 16.20 ^a	203.50 ± 15.10 ^b	196.70 ± 16.80 ^c	4.28 ^y			
Pepsin (µ mol tyrosine/4 h)	534.70 ± 32.10	675.80 ± 43.60 ^c	522.20 ± 31.50 ^{NS}	624.60 ± 30.60 ^a	582.10 ± 29.70 ^b	561.20 ± 31.80 ^c	3.12 ^x			
Protein (µg/mL)	256.80 ± 15.70	341.50 ± 21.30 ^c	262.40 ± 16.60 ^{NS}	298.10 ± 18.90 ^b	281.30 ± 18.20 ^c	267.80 ± 17.40 ^c	4.67 ^y			
Hexose (µg/mL)	387.30 ± 25.50	291.20 ± 36.40 ^c	393.50 ± 24.50 ^{NS}	314.60 ± 27.80 ^{NS}	358.70 ± 26.20 ^b	379.40 ± 30.30 ^c	2.83 ^x			
Hexosamine (µg/mL)	184.90 ± 15.20	106.40 ± 16.6 ^c	188.20 ± 16.1 ^{NS}	130.50 ± 16.10 ^a	152.80 ± 17.50 ^c	176.20 ± 17.10 ^c	4.30 ^y			
Sialic acid (µg/mL)	46.20 ± 2.10	33.70 ± 3.80 ^c	47.60 ± 2.50 ^{NS}	35.30 ± 2.90 ^{NS}	38.10 ± 2.70 ^a	43.70 ± 2.20 ^c	2.79 ^x			
Fucose (µg/mL)	40.40 ± 3.40	31.60 ± 2.80 ^a	41.20 ± 3.10 ^{NS}	32.20 ± 3.0 ^{NS}	33.70 ± 2.90 ^{NS}	35.30 ± 2.40 ^a	1.91 ^{NS}			
Total carbohydrate (µg/mL)	612.00 ± 35.3	434.00 ± 28.4 ^c	619.10 ± 34.60 ^{NS}	470.20 ± 32.30 ^{NS}	506.71 ± 29.50 ^b	596.00 ± 30.70 ^c	2.98 ^x			
TC:P	2.48 ± 0.26	1.37 ± 0.33 ^a	2.51 ± 0.29 ^{NS}	1.64 ± 0.21 ^{NS}	1.91 ± 0.24 ^b	2.28 ± 0.22 ^c	3.04 ^x			

Values are expressed as mean ± SE; $n = 6$.

Student's t test: group I vs group II & III; group II vs group IV, V and VI. ^a $p < 0.05$, ^b $p < 0.01$, ^c $p < 0.001$

NS, non-significant; TC, total carbohydrate.

F-test: ^x Significant at level of 5% (2.77); ^y Significant at level of 1% (4.25).

body weight was given. After the treatment period all groups underwent surgery. Group IV underwent surgery after 5 days, group V after 10 days and group VI after 15 days of pretreatment and ulcer induction.

The operative procedure adopted was that of Takeuchi *et al.*, (1976). The rats were quickly and mildly anaesthetized with ether and the abdomen was cut open through a midline incision. The pylorus was secured and ligated with silk sutures, after which the wound was closed and the animals were allowed to recover from anaesthesia. After ligation of the pylorus, drinking water was withheld and the gastric juice was collected for a period of 4 h. The rats were killed by cervical decapitation and the stomach was removed after clamping the oesophagus. The gastric contents were collected through the oesophagus. The gastric juice was centrifuged and the volume was noted. The stomach was then inflated with formal saline and then incised through the greater curvature and examined for the number of lesions under the dissecting microscope.

The total acidity was determined by titrating with 0.01N NaOH using phenolphthalein as an indicator. The gastric juice was estimated for its protein (Lowry *et al.*, 1951), pepsin (Anson, 1938), hexose and hexosamine (Winzler, 1958), sialic acid (Warren, 1959) and fucose (Dische and Schettles, 1948) contents. The ratio of total carbohydrate (sum of hexose, hexosamine, fucose and sialic acid) to protein was taken as the index of mucin activity.

Statistical analysis. The data were analysed by a one-way analysis of variance (ANOVA), followed by Student's *t*-test. The results are expressed as mean \pm SE.

RESULTS

The results of the initial trials carried out with different dosages of *Garcinia cambogia* extract (0.5, 1, 1.5 g/kg, p.o./day) for different periods of time are presented in Table 1. From the Table it is evident that a dosage of 1 g/kg, p.o./day of *Garcinia cambogia* markedly inhibited the acid output, the number of lesions along with a reduction in the volume of gastric juice and pepsin, reflecting a positive effect of *Garcinia cambogia* on indomethacin induced gastric ulcer.

In Table 2, the oral administration of indomethacin (20 mg/kg body wt) caused a significant ($p < 0.001$) increase in the number of lesions in the gastric mucosa, an increase in the volume of gastric juice and increased activity of pepsin. The level of protein in the gastric juice was significantly ($p < 0.001$) increased, while the carbohydrate:protein ratio and glycoprotein levels were significantly ($p < 0.001$) decreased in the ulcerated rats. Oral pretreatment with *Garcinia cambogia* fruit extract (1 g/kg body wt/day) for 15 days significantly ($p < 0.001$) prevented the adverse changes and maintained the rats at near normal status, while the group pretreated for 10 days (group V) had a marginal but significant ($p < 0.01$) increase in the prevention of adverse changes. The group pretreated for 5 days (group IV) did not reveal any significant change except for a marginal decrease in pepsin and acid output.

DISCUSSION

Although in most of the cases the aetiology of the ulcers is unknown, it is generally accepted that they result from an imbalance between aggressive factors and the maintenance of mucosal integrity through endogenous defence mechanisms (Bettarello, 1985; Piper and Stiel, 1986).

To regain the balance, different therapeutic agents including plant extracts are used. *Garcinia cambogia* fruit extract is one such herbal drug undertaken for the present study primarily to evaluate its antiulcerogenic potential.

The number of lesions in the untreated ulcer group was quite high and among the treated groups, the group pretreated for 15 days (group VI) had a dramatic decrease in the number of lesions. The group pretreated for 10 days (group V) had a notable decrease and the group pretreated for 5 days (group IV) had a marginal decrease, while the number of lesions in the untreated ulcer group remained high. The number of lesions present on the gastric mucosa are indicative of the ulcer severity (West, 1982). A significant reduction in the number of lesions in the pretreated *Garcinia cambogia* groups may be due to the appetite suppressant effect of the drug, thereby inhibiting gastric acid secretion, an important factor in ulcer formation (Clouatre and Rosenbaum, 1994).

The volume and total acidity were significantly increased in the untreated ulcer group relative to the normal group. The 10 day (group V) and 15 day (group VI) group showed a marked decrease both in volume and total activity. The increase in volume of the untreated ulcer rats is undoubtedly due to the increased production of HCl, as is evident from the total acidity of the gastric juice. The volume of gastric juice in indomethacin induced ulcer rats was significantly reduced by *Garcinia cambogia* pretreatment.

Garcinia cambogia extract which contains the principle organic acid (-)-erythro-hydroxycitric acid (HCA) significantly increased the production of glycogen in the liver (Sullivan *et al.*, 1974). The increased production of glycogen and the concomitant stimulation of gluco-receptors in the liver, results in early satiety through signals sent to the brain via the vagus nerve (Harvey Anderson, 1994). HCA induces inhibition of lipid biosynthesis and diverts the metabolism of carbohydrate towards glycogen production in the liver thereby controlling the appetite (Sullivan and Gruen, 1985) and HCl output. In the present study, HCA present in the fruit rind has been speculated to possess antiulcerogenic potential. A related species of the Guttiferaceae family, *Garcinia mangostana* Linn., containing the active principle mangostin, a xanthone present in the fruit rind has been reported to have an antiulcer property (Shankaranarayan *et al.*, 1979).

The carbohydrate: protein (C:P) ratio serves as a good indicator of gastric mucosal defence and an increase represents augmented mucosal protective activity (Venkataranganna *et al.*, 1998). A near normal C:P ratio was observed in indomethacin + pylorus ligated rats (group VI) pretreated with *Garcinia cambogia*, which indicates its mucoprotective property.

Relative to the normal levels the hexose, hexosamine and sialic acid content of the gastric juice decreased considerably in the ulcer group while the protein level

increased. The increase in protein content of the gastric juice indicates damage to the gastric mucosa as a result of which plasma protein leaks into the gastric juice (Goel *et al.*, 1985). The decrease in the glycoprotein moieties in the gastric juice may be attributed to the decreased activity of defence mechanisms as a result of damage to the gastric mucosa. In other words disintegration and degradation of glycoprotein moieties into their simpler components in the process of indomethacin induced injury might have resulted in minimal quantities of glycoprotein in the gastric juice. The levels of protein, hexose and hexosamine were maintained at near normal

levels in the group pretreated with *Garcinia cambogia* (group VI). *Garcinia cambogia* inhibits vagus nerve stimulation, thereby reducing the HCl output and acidity. Being an effective appetite suppressor (Clouatre and Rosenbaum, 1994), it protects the quantity and quality of mucus secretion against the offensive assault of acid.

Garcinia appears to regulate both acid output and mucus secretion. As *Garcinia cambogia* is far from toxic with antiulcerogenic potency, it could be a prospective substitute for the existing antiulcer drugs which have maximal side effects.

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