African Journal of Biotechnology Vol. 11(34), pp. 8612-8615, 26 April, 2012
Available online at http://www.academicjournals.org/AJB
DOI: 10.5897/AJB12.034
ISSN 1684–5315 © 2012 Academic Journals

Full Length Research Paper

Gastro-protective activity of aqueous *Carica papaya* seed extract on ethanol induced gastric ulcer in male rats

OKEWUMI Tolunigba Abisola and OYEYEMI Adekunle Wahab*

Department of Physiology, College of Medicine, Madonna University, Elele, Rivers state, Nigeria.

Accepted 27 February, 2012

Gastro protective effects of aqueous *Carica papaya* seed extract on ethanol induced gastric ulcer were investigated in male rats. Thirty two (32) male rats weighing between 180 and 250 g were randomly divided into four groups. Group 1 served as the negative control (distilled water), groups 2 and 3 received 50mg/kg and 100mg/kg *Carica papaya* seed extract respectively, while group 4 received 200mg/kg cimetidine (positive control). Two weeks after the oral administration, gastric ulcer was induced in all rats with ethanol (1 ml of 80% orally). Gastric juice volume, gastric acidity, ulcer index and percentage ulcer inhibition were determined. The results showed that the extract protected the gastric mucosa against ethanol effect. *C. papaya* extract significantly reduced the gastric juice volume and gastric acidity ($p<0.05$) in dose dependent manner when compared with the control. The percentage ulcer inhibition was significantly high ($p<0.05$) in rats treated with the extract when compared with the control and the effect is similar to that of rats treated with cimetidine. This study shows that *C. papaya* seed extract may possess gastro protective effects against ethanol induced gastric ulcer in male rats.

Key words: *Carica papaya*, gastro protective, gastric ulcer.

INTRODUCTION

Carica papaya Linn (family: *Carica*ceae) is a tropical and herbaceous succulent plants that posses self supporting stems (Dick, 2003), which grows in all tropical countries and many sub-tropical regions of the world, and it is largely used in tropical folk medicines (Jaime et al., 2007). The ripe fruit is edible and unripe (which is a rich source of vitamin A) can be eaten cooked (Lohiya et al., 2002). It contains bioactive compounds, namely, papain, chymopapain, alkaloids, flavonoids, benzylisothiocyanate and phenolic (Anaga and Onehi, 2010; Jaime et al., 2007). *C. papaya* fruits consist mostly of water and carbohydrate, low in calories and rich in natural vitamins and minerals, particularly vitamins A and C, ascorbic acid and potassium (Jaime et al., 2007).

The plant has different traditional medicinal values. It is used in treating malarial fever, diabetes mellitus, bacterial infections and as a de-wormer agent (Lohiya and Goya, 1992; Kinyuy, 1993; Chinoy et al., 1985). It also improves digestion. Its fresh leaves are also efficacious in the treatment of gonorrhea, syphilis and amoebic dysentery (Gill, 1992). The seed is used for intestinal worms when chewed (Ayoola and Adeyeye, 2010).

Scientific evidences have shown that *C. papaya* has the following activities: anti-diabetes (Gbolade, 2009; Robert et al., 2008), diuretic (Spripanidkulchai, 2001), antihyperlipidemic (Banerjee et al., 2006), antihelminthic, anti-amoebic (Okeniyi et al., 2007), contraceptive in mice rats (Verma et al*.,* 2006; Lohiya et al., 2006; Chinoy et al., 1985), hypoglycemic (Adeneye and Olagunju, 2009), nephroprotective (Olagunju et al., 2009), bactericidal (Emeruwa, 1982) wound and burn healing (Nayak et al., 2007; Hewitt et al., 2000), anti-oxidant (Majdi and Luciana, 2010), anti-nociceptive, anti-inflammatory (Anaga and Onehi, 2010) and anti-ulcer (Ezike et al., 2009; Indran et al., 2008). Chymopapain and papain which are among the plant constituents are being useful for digestive disorders and disturbances of the

*Corresponding author. E-mail: oyeyemiwahab@gmail.com. Tel: +2347034891903.

gastrointestinal tract (Huet et al., 2006). There is no scientific report on the anti-ulcer activity of aqueous extract of *C. papaya* seed extract.

This study aimed at investigating the gastric acid secretion and gastro-protective activity of aqueous extract of *C. papaya* seeds on male rats with ethanol induced acute gastric damage.

MATERIALS AND METHODS

The unripe fruits of *C. papaya* were bought from Elele market, Rivers state, Nigeria. They were cut open and the seeds were collected, dried on top of laboratory bench and pulverized into coarse powder using a hammer mill. About 200 g of the coarse powder was soaked in 1.0 L of distilled water with intermittent shaking for 48 h. The extract was filtered and the filtrate was evaporated to dryness using rotary evaporator. The yield was calculated to be 5.61 w/w dry matters and the extract was stored in a refrigerator at 4°C.

Thirty two albino Wistar male rats weighing between 180 and 250 g were procured from the Laboratory Animal Unit of the Faculty of Veterinary Medicine, University of Nigeria, Nsukka. The rats were housed in wire mesh cages under standard laboratory conditions (temperature 25 to 29°C, 12 h light and 12 h darkness cycles) with standard feeds and had free access to tap water *ad libitum*. They were maintained in accordance with the recommendation in the Guidelines for the Care and Use of Laboratory Animals (DHHS, NIH Publication No. 85-23, 1985). They were allowed to acclimatize for 2 weeks before the start of the experiments.

Experimental procedure

Thirty-two male rats were divided into four (4) groups, each group consisting of eight animals. Group 1 received distilled water (negative control), group 2 received 50 mg/kg of *C. papaya* seed extract, group 3 rats were given 100 mg/kg of *C. papaya* seed extract and the group 4 received 200 mg/kg of cimetidine (positive control). The dose of *C. papaya* extract used in this study has been reported by Adeneye and Olagunju, (2009) and Verma et al. (2006). The treatment in all the groups was single dose for fourteen consecutive days through gavages.

Ethanol-induced gastric ulcer

After two weeks of treatment, all the rats were fasted for 24 h with free access to water. Gastric ulcer was induced with 1 ml of 80% ethanol which was administered orally to each animal after 24 h fasting (Hawk and Ostor, 1995).

Determination of gastric secretion and ulcer index

This assay was performed as earlier described by Gehan et al. (2009). Four (4) hours after the induction of gastric ulcer, the rats were killed by cervical dislocation, the abdomen was opened to remove the stomach and gastric content was collected to determine the gastric juice volume (ml/4 h). Five milliliters (5 ml) of distilled water was added to the gastric juice and the resultant solution was centrifuged at 3,000 rpm for 10 min. Gastric acidity in meq/l was determined in the supernatant volume by titration to pH 7 with 0.0025 N of sodium hydroxide.

After removal of gastric content from the stomach, the stomach was pinned onto a soft board. Scoring of ulcer was done by the Following method: 1 = erosions 1 mm or less, 2 = 1 to 2 mm, 3 = >2 mm. The overall score was divided by a factor of 10 which was designated as the ulcer index (Main and Whittle, 1975). The percentage of ulcer inhibition was calculated as follows:

$$\text{Ulcer inhibition (\%)} = \frac{\text{(Mean ulcer index of control - Mean ulcer index of test)} \times 100}{\text{Mean ulcer index of control}}$$

Statistical analysis

The results of this study were expressed as mean and standard error of mean (mean ± SEM). Statistical significant between the groups was assessed by one way analysis of variance (ANOVA) followed by least significant difference (LSD) test with the level of significant, $p< 0.01$ and $p< 0.05$ using SPSS 16.

RESULTS

Figure 1 shows the effect of *C. papaya* seed extract on gastric acidity in male rats with ethanol induced gastric ulcer, the gastric acidity was significantly reduced in rats treated with 100 mg/kg of the extract (0.43 ± 0.018 meq/l) when compared with the control (0.61 ± 0.01 meq/l), also there was significant different between the control and the rats treated with 50 mg/kg of the extract (0.50 ± 0.014 meq/l). The gastric acidity in the rats treated with 200 mg/kg of cimetidine was significantly reduced when compared with the control.

The gastric juice volume in ml/4 h reduced from 3.08 ± 0.037 in control rats to 2.82 ± 0.017, 2.42 ± 0.013 and 1.94 ± 0.022 in 50 mg/kg of extract, 100 mg/kg of extract and 200 mg/kg of cimetidine, respectively. The reduction in gastric juice observed in rats treated with the extract and cimetidine were significant ($p<0.05$) when compared with the control group (Table 1).

As shown in Table 1, the ulcer index significantly decreased in groups treated with the extract ($p<0.05$) when compared with the control. The percentage ulcer inhibition was 44.9 and 63.9% in rats treated with 50 mg/kg and 100 mg/kg of the extract respectively while cimetidine treated rats have higher percentage inhibition of 75.0% (Table 1). Both ulcer index and percentage ulcer inhibition effect in the rats treated with the extract were dose dependent.

DISCUSSION

The antiulcer activity of the *C. papaya* seed extract was studied using ethanol ulcer model. This model is one of the common causes of gastric ulcer in human. Ethanol induced gastric injury is associated with significant production of oxygen free radicals leading to increased lipid peroxidation, which causes damage to cell and cell membrane (Allison et al., 1992). The *C. papaya* seed extract has significantly protected the gastric mucosa against ethanol challenge as shown by significant

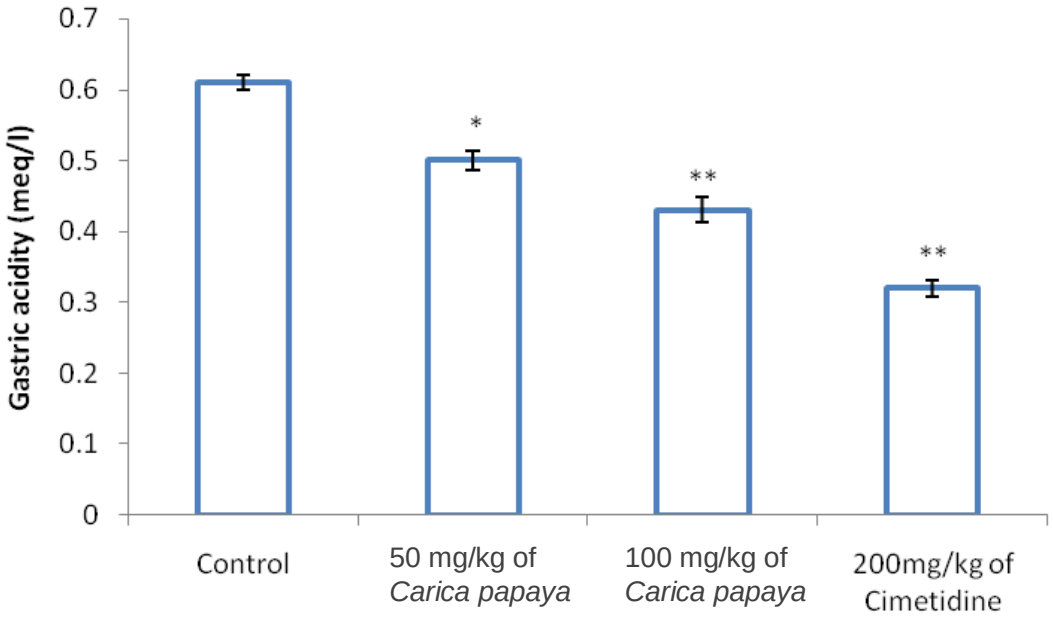

Figure 1. Effect of *C. papaya* seed extract on gastric acidity in meq/l in male rats' ethanol induced gastric ulcer. Each bar is expressed as mean ± SEM (n = 8). One way ANOVA and LSD revealed significant differences between the control and the treated groups with extract; **p<0.01, *p<0.05

Table 1. Effect of *C. papaya* seed extract on gastric juice volume, gastric ulcer index and percentage ulcer inhibition in male rats with ethanol induced gastric ulcer.

Group	Gastric juice volume (ml/4 h)	Ulcer index (mm)	Ulcer inhibition (%)
Control	3.08 ± 0.037	5.48 ± 0.32	-
50 mg/kg of extract	2.82 ± 0.017*	3.02 ± 0.12*	44.9%*
100 mg/kg of extract	2.42 ± 0.013*	1.98 ± 0.20**	63.9%**
200 mg/kg of cimetidine	1.94 ± 0.022**	1.37 ± 0.31**	75.0%**

Values are expressed as mean ± SEM of 8 rats per group. One way ANOVA and LSD revealed significant differences between the control and the treated groups with extract; **p<0.01, *p<0.05.

reduction in gastric juice volume, gastric acidity, ulcer index and percentage ulcer inhibition as compared to control group suggesting its potent gastro-protective effect on ethanol induced gastric ulcer in rats.

The observed effect of the extract is dose dependent, the high dose of the extract significantly produced more potent effect in reducing gastric secretion and protecting the gastric mucosa from noxious effect of ethanol, although the effect observed in rats treated with the extract were low as compared to that of cimetidine which is a well known drug for the treatment of gastric ulcer, there is tendency that further increase in the extract dose might produce the same effect as that of cimetidine. The mechanism of action of the extract in reducing gastric secretion may probably involve histaminic H_2 receptor since it produced effect that is similar to cimetidine, the H_2 antagonist. Also, is possible that the extract induced both mucous and HCO_3^- secretion to protect the stomach lining against alcohol assault apart from directly neutralizing the stomach acidity. Cimetidine is also known to act via the same mechanism (Indran, 2008).

Another possible reason for the action of this extract may be as a result of its antioxidant properties, although antioxidant assay was not investigated in this study, but some studies have revealed the antioxidant properties of the extract (Majdi and Luciana, 2010; Indrian et al., 2008). It is possible that the extract was able to reduce the noxious effect of ethanol by preventing the pro-oxidant effect of ethanol from damaging the gastric mucosa through its antioxidant effect that has been reported to be similar to that of vitamin C (Majdi and Luciana, 2010).

The gastro protective effect and the reduction in gastric secretion of the extract may also be attributed to the active compounds of the extract polyphenols (antioxidant), alkaloids and flavonoids (Tona et al., 1998) which are widely known as being useful for digestive disorders and disturbances of the gastrointestinal tract

(Jaime et al., 2007; Huet et al., 2006) In conclusion, the results suggest that *C.* papaya seed extract reduces gastric secretion and protects gastric mucosa from ethanol noxious effect.

REFERENCES

Adeneye AA, Olagunju JA (2009). Preliminary hypoglycemic and hypolipidemic activities of the aqueous seed extract of *Carica papaya* Linn. Wistar rats. Biol. Med. 1(1): 1-10.

Allison MC, Howastson AG, Torrance CJ, Lee FD, Russel RI (1992). N. Engl. J. Med. 327: 749-54.

Anaga AO, Onehi EV (2010). Antinociceptive and anti-inflammatory effects of the methanol seed extract of *Carica papaya* in mice and rats. Afr. J. Pharm. Pharmacol. 4(4): 140-144.

Ayoola PB, Adeyeye A (2010). Phytochemical and nutrient evaluation of *Carica papaya* (pawpaw) leaves. IJRRAS. 5 (3): 325-328.

Banerjee A, Vaghasiya R, Shrivastava N, Podn H, Nivsarkas M (2006). Anti-hyperlipidemic affect of *Carica papaya L*. in sprague dawley rats. Niger. J. Nat. Prod. Med. 10: 69-72.

Chinoy NJ, Verma RJ, Sam MG, Dsouza JM (1985). Reversible antifertility effects of papaya seed extract in male rodents. J. Androl. 6(2): 50.

Dick G (2003). Papaya: A tantalising taste of the Tropics. Maricopa County Master Gardener Volunteer information, University of Arizona Cooperative Extension. www.papaya Maricopa-hort@ag.arizo.edu.

Emeruwa AC (1982). Antibacterial substance from *Carica papaya* fruit extract. J. Nat. Prod. 45(2): 123-127.

Ezike AC, Akah PA, Okoli CO, Ezeuchenne NA, Ezeugwu S (2009). *Carica papaya* (paw paw) unripe fruit may be beneficial in ulcer. J. Med. Food. 12(6): 1268-1273.

Gbolade AA (2009). Inventory of antidiabetic plants in selected districts of Lagos state, Nigeria. J. Ethnopharmacol., 121 (1): 135-9.

Gehan H, Magdy KAH, Rauuia SA (2009). Gastroprotective effect of simvastatin against indomethacin-induced gastric ulcer in rats: Role of nitric oxide and prostaglandins. Eur. J. Pharmacol. 607: 188-193.

Gill LS (1992). *Carica papaya* L. In: Ethno-medicinal uses of plants in Nigeria.

Hawk PB, Ostor BL (1995). Hawk's Physiological Chemistry. 14th ed. New York, Mc Graw Hill.

Hewitt H, Whittle S, Lopez S, Bailey E, Weaver S (2000). Tropical use of papaya in chronic skin ulcer therapy in Jamaica. West Indian Med. J. 49: 32-33.

Huet J, Looze Y, Bartik K, Raussens V, Wintjens R, Boussard P (2006). Structural characterization of the papaya cysteine proteinases at low pH. Biochem. Biophysical Res. Commun., 341: 620-626.

Indran M, Mahmood AA, Kuppusamy UR (2008). Protective effect of *Carica papaya* L leaf extract against Alcohol Induced Acute gastric damage and blood oxidative stress in rats. West Indian Med. J. 57(4): 323.

Jaime A, Teixeira da S, Zinia R, Duong TN, Dharini S, Abed G, Manoel TS, Paula FT (2007). Papaya (*Carica papaya* L.) Biology and biotechnology. Tree Forest. Sci. Biotechnol. 1(1): 47-73.

Kinyuy WC (1993). Through integrated biomedical ethno-medical preparations and ethnotaxonomy, effective malaria and diabetic treatments have evolved. Acta. Hortic. 344: 205-214.

Lohiya NK, Goya BB (1992). Antifertility investigations on the crude chloroform extract of *Carica papaya* linn. seeds in male albino rats. Indian J. Exp. Biol. 30: 1051-1055.

Lohiya NK, Manivanna B, Mishra PK, Pathak N, Sriram S, Bhande SS, Panneerdoss S (2002). Chloroform extract of *Carica papaya* seeds induce long-term reversible azoospermia in Langur monkey. Asian J. Androl. 4: 17-26.

Lohiya NK, Manivannan B, Garg S (2006). Toxicological investigations on the methanol sub-fraction of the seeds of *Carica papaya* as a male contraceptive in albino rats. Reprod. Toxicol. 22(3): 461-468.

Main IHM, Whittle BJR (1975). Investigation of the vasodilator and antisecretory role of prostaglandins in the rats gastric mucosa by use of non-steroidal anti-inflammatory drugs. Br. J. Pharmacol. 53(2): 217-224.

Majdi D, Luciana D (2010). Antioxidant effect of Aqueous *Carica papaya* seeds extract. 2nd Conference on Biotechnology Research and Applications in Palestine, 26-27th September, 2010.

Nayak SB, Pinto PL, Maharaj D (2007). Wound healing activity of *Carica papaya L*. in experimentally induced diabetic rats. Indian J. Exp. Biol. 45(8): 739-743.

Okeniyi JA, Ogunlesi TA, Oyelami QA, Adeyemi LA (2007). Effectiveness of dried *Carica papaya* seeds against human intestinal parasitosis: a pilot study. J. Med. Food. 10(1): 194-196.

Olagunju JA, Adeneye AA, Fagbounka BS, Bisuga NA, Ketiku AO, Benebo AS, Olufowobi OM, Adeoye AG, Alimi MA, Adeleke AG (2009). Nephroprotective activities of the aqueous seed extract of *Carica papaya* Linn. in carbon tetrachloride induced renal injured wistar rats: a dose- and time dependent study. Biol. Med. 1(1): 11-19.

Robert SD, Ismail AA, Winn T, Wolever TM (2008). Glycemic index of common Malaysian fruits. Asia. Pac. J. Clin. Nutr. 17(1): 35-39.

Sripanidkulchai B, Wongpanich V, Laupattarakasem P, Suwansaksri J, Jirakulsomchok D (2001). Diuretic effects of selected Thai indigenous medicinal plants in rats. J. Ethnopharmacol. 75(3): 185-190.

Tona LK, Kambu N, Ngimbi K, Cimanga K, Vlietinck AJ (1998). Antiamoebic and phytochemical screening of some Congolese medicinal plants. J. Ethnopharmacol. 61: 57-65.

Verma RJ, Nambiar D, Chinoy NJ **(**2006). Toxicological effects of *Carica papaya* seed extract on spermatozoa of mice. J. Appl. Toxicol. 26(6): 533-535.