

The Anti-ulcerogenic Activity of Aqueous Extract of Carica Papaya Fruit on Aspirin – Induced Ulcer In Rats

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Abstract

The antiulcerogenic activities of Carica papaya extract on aspirin-induced ulcer in rats was examined in this study. The rats were treated with 400 mg kg⁻¹ body weight of aqueous extract of Carica papaya for 7 days after which they were fasted for 48h. Aspirin (400 mg kg body weight) was then given to the animals. 4h later the animals were sacrificed and gastric mucosa tissues were excised and screened for biochemical markers like ulcer index, lipid peroxide, alkaline phosphatase and catalase activities. The data generated show that Carica papaya extract significantly reduced the ulcer index, lipid peroxide levels and alkaline phosphatase activity in the rats. It also maintained the activity of the antioxidant enzyme, catalase in the gastric mucosa, to near normalcy when compared with water controls. The results indicate that Carica papaya may exert its gastroprotective effect by a free radical scavenging action. This study suggested that Carica papaya may have considerable therapeutic potential in the treatment of gastric diseases.

INTRODUCTION

Oxygen free radicals are considered to be important factors in the pathogenesis of gastrointestinal disorders ¹. Non-steroidal anti-inflammatory drugs (NSAIDs) are recognized as the most common etiologic factors associated with gastric ulcer ². Aspirin induces the formation of the reactive oxygen metabolites in animal models, which may contribute to mucosal injury ³. Furthermore aspirin causes a dose – dependent reduction in mucosal prostaglandin E₂ (PGE₂) and PGI₂ biosynthesis accompanied by an increase in the mean area of gastric ulcerations ⁴. This effect has been attributed to the fact that aspirin irreversibly inactivates the prostaglandin (PG) synthetase system which mediates synthesis of prostaglandin in the mucosa ⁴. So the observed gastric mucosal lesions induced by aspirin may also be due to the deficiency of mucosal prostaglandin.

Carica papaya (family Caricaceae) is an evergreen tree that originated in Central America. It is a herbaceous, dicotyledonous plant that may produce fruits for more than 20 years i.e. it is perennial. The chemical constituents of Carica papaya include papain and chymopapain, which are suggested to aid digestion. Others include phenolic compounds such as flavonoids, flavanol, benzyglucosinolate and alkaloids ⁵, and ?-lipoic acid, ? – carotene and lycopene, which are natural antioxidants ⁶. Extract of Carica papaya

fruits has been used in traditional medicine in Panama (USDA Phytochemical and Ethnobotanical data bases), and in Nigeria, for antiulcer remedy. Therefore the present study provides biochemical evidence for the antiulcerogenic property of Carica papaya fruit extract.

MATERIALS AND METHODS

CHEMICALS

The chemicals used for this research were of the analytical grade. Diethylether, hydrochloric acid, trichloroacetic acid were obtained from Analar Analytical Reagents Ltd, England; Dichromate from M & B Laboratory, Dagenlam, England; acetlysalicylic acid (Aspirin) – Pharchem Ltd. Lagos, Nigeria; thiobarbituric acid from Koch – light Lab. Ltd. Colebrook Bucks, England and Alkaline phosphatase kit was purchased from Randox Laboratories Ltd, UK.

ANIMALS

Fifteen healthy male albino rats (Wistar strain) weighing 180-200g, used for this research were obtained from the animal unit of the Federal College of Agriculture, Akure, Ondo state, Nigeria. They were maintained at 12h light and 12h dark condition in the laboratory for 2 weeks before the commencement of the experiments. Food pellet (Growers' marsh, BFFM, Ewu, Nigeria) and water were given ad libitum.

PLANT MATERIALS

Fresh, unripe, mature fruits of *Carica papaya* (pawpaw) used for this work were obtained from the Mini Campus of Adekunle Ajasin University, Akungba – Akoko Ondo State, Nigeria.

PREPARATION OF EXTRACT

Extraction was done using the method described by Olagunju et al ⁷.

TREATMENT OF ANIMALS

The rats were divided into 3 groups of 5 rats each. Group 1 (Control) and group 2 rats were fed with normal diet, while rats in group 3 were treated with 200 mg kg⁻¹ body weight of the extract twice a day for 7 days. At the end of treatment, the rats were fasted for 48 h. After fasting the extract was given to the animals in group 3. Thirty minutes later, rats in group 2 and 3 were treated with 400 mg kg⁻¹ body weight of aspirin.

COLLECTION AND PREPARATION OF STOMACH SAMPLES

Five hour after aspirin treatment, the rats were anaesthetized by putting them inside a diethylether saturated chamber. While under anaesthesia, the abdominal region was opened and the stomach carefully removed from the body. An incision was made along the greater curvature to expose the mucosa layer of the lumen. The stomach was pinned to the surface of the board and the gastric lesions were then viewed with the aid of a magnifying lens (x10) and counted. The overall total, divided by a factor of 10 was designated as ulcer index for that stomach ⁸.

The glandular portion of the stomach was scrapped and 1g of the portion was suspended in 4ml of ice cold physiological saline and homogenized. The homogenate was then centrifuged at 3500rpm for 10 minutes and the supernatant was used for biochemical analyses ⁴.

BIOCHEMICAL ESTIMATION

Lipid peroxidation was estimated spectrophotometrically by thiobarbituric acid reactive substances (TBARS) method as described by Varshney and Kale ⁹ and results expressed in terms of malondialdehyde (MDA) formed per mg protein. Catalase activity was measured by following decomposition of H₂O₂ according to the method of Sinha ¹⁰. Alkaline Phosphatase (ALP) was determined using ALP kit by Randox, UK.

STATISTICAL ANALYSIS

The data obtained were subjected to standard statistical analysis using analysis of variance procedure of SAS ¹¹ while the treatment means were compared using the Duncan's procedure of the same software.

RESULTS AND DISCUSSION

Results of table 1 show that the extract significantly reduced ulcer index and lipid peroxidation (estimated by measuring malondialdehyde (MDA) formation) when compared with aspirin alone treated rats (Group 2). Also, there was significant increase in activity of alkaline phosphatase but a decrease in the activity of the antioxidant enzyme, catalase in the mucosa of aspirin – treated rats relative to water controls. However, pretreatment of rats (Group 3) with the extract maintained the activity of the enzymes at near normalcy when compared with water controls.

Figure 1

Table: Effects of extract on aspirin-induced changes in ulcer index, alkaline phosphatase and catalase activities, and MDA levels.

Group	Treatment	Ulcer Index (n=5)	Alkaline phosphatase activity(U/L) (n=5)	Catalase activity (nM of H ₂ O ₂ decomposed /min/mg protein) (n=5)	Malondialdehyde (MDA nmole/mg protein) (n=5)
1	Water Control	-	670 ± 3.04	36.50 ± 1.12	0.66 ± 0.04
2	Aspirin only (400 mg kg ⁻¹ body wt.)	5.0 ± 0.5*	1035 ± 1.84*	28.80 ± 2.56*	14.50 ± 0.43*
3	Aspirin (400 mg kg ⁻¹ body wt.) + Extract (400 mg kg ⁻¹ body wt.)	1.30 ± 0.29*	706 ± 2.18	35.60 ± 1.14	1.25 ± 0.21

Values carrying notations are statistically (p<0.05) different from Water Control (Group 1).

The antiulcerogenicity of *Carica papaya* fruit extract and its effect on various biochemical markers like ulcer index, alkaline phosphatase activity, catalase activity and lipid peroxide levels were investigated using a model of aspirin – induced ulcer. The aqueous extract of *Carica papaya* has significant antiulcer properties as suggested by the result of this research.

The extract significantly ($p < 0.05$) reduced the ulcer index and alkaline phosphatase activity in the rats pretreated with the extract, (Group 3) when compared with those treated with aspirin only (Group 2). The release of alkaline phosphatase has been suggested to play a role in tissue necrosis associated with various models of gastrointestinal ulceration¹². The increased activity of this enzyme found in the group treated with aspirin only is in agreement with the above statement. When aspirin is in the lipid-soluble undissociated form it can damage the gastric mucosa¹³. Aspirin causes a dose – dependent reduction in mucosal prostaglandin E₂ (PGE₂) and PGI₂ biosynthesis accompanied by an increase in the mean of gastric ulceration⁴. Aspirin is known to irreversibly inactivate the PG synthetase system; which mediates synthesis of prostaglandin in the mucosa⁴. It is therefore reasonable to assume that the observed gastric mucosal lesion induced by aspirin is due to a deficiency of mucosal prostaglandin.

Antioxidant enzymes such as catalase, superoxide dismutase, glutathione-S-transferase and glutathione are present in oxygen handling cells which are the first line of cellular defense against oxidative injury, decomposing superoxide ion and H₂O₂ before they interact to form more reactive radicals¹⁴. Catalase is highly specific in its catalytic mode of action and it decreases the gastric mucosal damaging effect of aspirin¹⁵. The increase in catalase activity in extract pretreated rats compared to aspirin models is necessary for effective antioxidant activity. Hence the antioxidant activity of *Carica papaya* may be one of the important defensive factors involved in its ulceroprotective effect.

Furthermore, the extract significantly reduced the formation of lipid peroxide, MDA and so offers gastro-protection against aspirin induced ulcer. In the present study, aspirin treatment significantly increased the formation of MDA which is highly indicative of oxidative damage which may be due to accumulation of toxic free radicals in the mucosal cell. *Carica papaya* pretreatment of rats provided protection against the action of aspirin by blocking lipid peroxidation which was revealed by significantly reduced MDA level. This apparently points to the antioxidant bioactivity of the extract.

CONCLUSION

In conclusion, it can be said that *Carica papaya* extract exhibits a protective effects through free radical scavenging

properties and reduces oxidative damage or gastric ulceration caused by aspirin. These results provide scientific support for the use of this plant as an antiulcer remedy in the Nigerian traditional medicine. A further detailed study on various other parameters of mucosal defensive factors could elucidate their exact mechanism of action and their usefulness in the treatment of ulcer.

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