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(RESEARCH ARTICLE)

Histomorphological evaluation of the combined therapeutic potential of *Carica papaya* and *Musa paradisiaca* on indomethacin induced gastric injury

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Abstract

Background: Medicinal plants are often used for the preparation of remedies for the treatment of several ailments especially in rural areas.

Objective: The study investigated the combined effect of *Carica papaya* (pawpaw) and *Musa paradisiaca* (plantain) leaves extract on the stomach walls of albino rats against indomethacin induced gastric ulceration.

Materials and Methods: Twenty-five (n-25) albino rats were weighed and divided randomly into five groups. Each group consisted of five (n-5) rats. Group A served as negative control and received rat feeds and water *ad libitum*. Group B received feeds and a single dose of indomethacin (25 mg/kg body weight) via orogastric administration and organs were harvested 4 hours after administration. Group C rats were administered with *Carica papaya* leaf extract (250 mg/kg body weight) daily for 14 days. Group D was administered with *Musa paradisiaca* leaf extract (250 mg/kg body weight) for 14 days. Group E received combined extract of *Carica papaya* (250 mg/kg body weight) and *Musa paradisiaca* (250 mg/kg body weight) daily for 14 days. All the animals were allowed access to feed and water. The animals in groups C-E fasted for 24 hours and were administered with a single dose of indomethacin (25 mg/kg body weight). Four hours later, the animals were sacrificed under chloroform inhalation, organs harvested, processed and stained with haematoxylin and eosin for histomorphological evaluation.

Result: The result of the study shows that the single dose of indomethacin caused gastric ulceration within 4 hours. *Musa paradisiaca* leaf extract ameliorated the effect of indomethacin on the stomach. Combination of *Carica papaya* and *Musa paradisiaca* leaves extract exacerbated the effect of indomethacin on gastrointestinal tract ulcers.

Conclusion: The practice of using combined extract of *Carica papaya* and *Musa paradisiaca* should be avoided in ulcer patients or individuals on indomethacin therapy.

Keywords: Gastric ulcer; Indomethacin; *Carica papaya; Musa paradisiaca*

1 Introduction

Herbal remedies have been known to be effective in the treatment of various ailments [1, 2, 3, 4]. *Musa paradisiaca and Carica papya* have been noted for their therapeutic effects in herbal medicine. The extracts of *C. papaya* contain

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terpenoids, alkaloids, flavonoids, carbohydrates, glycosides, saponins, and steroids. The gastro-protective properties of unripe pawpaw fruit may be implicated on its anti-gastric motility and cytoprotective potentials [5,6, 7]. Scientific evidence shows that *Carica papaya* possesses antidiabetic, diuretic, anti-hyperlipidemic antihelminthic, anti-amoebic, hypoglycemic and wound healing properties (8, 9, 10, 11]. The leaves, fruits and latex obtained from the *C*. *papaya* plant are used medicinally and for various purposes. The fruit have been found to contain certain immune stimulating and anti-oxidant agents. Immature fruits and roots are used for their abortifacient activity [12]. The leaves of *C. papaya* have been found to be efficacious in wound healing and ameliorating inflammatory conditions such as arthritis, rheumatism and asthma [13]. On the other hand, the seeds, pulp and latex of *C. papaya* are also used by African traditionalists for the treatment of infertility in males, wounds and as an antihelminthic [14]. However, there are limited studies on the biological activities of the dried leaves widely used by traditional healers for the treatment of inflammatory conditions [13].

Musa paradisiaca (common name: plantain) can serve the dual purpose of dietary/nutritional and therapeutic roles for both humans and livestocks [15, 16]. So many phytochemicals and nutrients vital to human health are contained in plantain mostly on the peel [17, 18]. The health benefits of plantain are a product of its antioxidant properties and phytochemicals like flavonoids, carotenoids, and polysaccharides [19, 20].

In Nigeria, traditional medicine practitioners have used the leaf decoction of plantain and banana for treatment of typhoid fever, diarrhoea, malaria, stomach ache and ulcers [21]. Leaf extract of plantain is found to be effective against *Escherichia coli, Staphylococcus aureus, Pseudomonas aeruginosa* and *Salmonella* infections [22]. Antifungal properties of the peel and stalk extracts of *M. paradisiaca* have also been reported [23, 24, 25].

Many medicinal plants have shown protection against gastric ulcer, however the combined therapeutic effect of *Musa paradisiaca* and *Carica papaya* leaf extract have not been evaluated. This study explored the therapeutic potential of the combined extracts of *Musa paradisiaca* and *Carica papaya* leaves on indomethacin induced gastric injury in adult albino rats.

2 Materials and methods

2.1 Collection and Extraction of *Carica papaya* and *Musa paradisiaca* Leaves

Fresh leaves of *Carica papaya* and *Musa paradisiaca* were collected from the Niger Delta University campus, Wilberforce Island, Amassoma, Bayelsa State and identified by the Pharmacognosy Department, Faculty of Pharmacy, Niger Delta University, Wilberforce Island, Amassoma, Bayelsa State and voucher specimen deposited in the herbarium. The plants were processed and extracted according to the method of [26].

2.2 Animals

Twenty-five (25) healthy adult albino rats weighing between 120- 170g were procured from the animal house of the Department of Pharmacology, Niger Delta University, Wilberforce Island, Amassoma, Bayelsa State. The rats were housed in the animal house of the Department of Medical Laboratory Science, Niger Delta University (NDU), Wilberforce Island, Amassoma, Bayelsa State, in well aerated laboratory cages in a room under standard conditions, with temperature range of 25 ± 30 °C and a 12/12 hours of light and dark cycle. The rats were fed with feeds and water *ad libitum* during the experimental period. They were allowed to acclimatize to the laboratory environment for a period of two weeks before the commencement of the experimental protocol.

2.3 Animal Grouping and Experimental Design

The albino rats were weighed and assigned randomly into five groups. Each group consisted of five rats. Group A (negative control) was exposed to rat feeds and water *ad libitum.* Group B received rat feeds and was gavaged with a single dose of indomethacin (25 mg/kg body weight) via orogastric administration and organs harvested after 4 hours. Group C received rat feeds and was administered with *Carica papaya* leaf extract (250 mg/kg body weight) daily for two weeks. Group D received feeds and was administered with *Musa paradisiaca* leaf extract (250 mg/kg body weight) for two weeks. Group E received rat feeds and was administered with combined leaves extract of *Carica papaya* (250 mg/kg body weight) and *Musa paradisiaca* (250 mg/kg body weight) for two weeks. The animals in groups C-E were allowed to fast for 24 hours and administered with a single dose of indomethacin (25 mg/kg body weight). Four hours later, the animals were sacrificed via chloroform inhalation, organs harvested, processed and stained using haematoxylin and eosin for histomorphological evaluation of the stomach.

2.4 Histomorphological Studies

At the end of the experimental period, animals were sacrificed using chloroform inhalation method and the stomach of each animal of control and treatment groups were collected and fixed in 10% formal saline solution. Routine tissue processing was carried out using automatic tissue processor; Histokinette (LEICA TP 1020). The tissues were embedded in paraffin wax in tissue embedder (LE1CA EG 1160) and trimmed in a rotary microtome (LEICA P.M 2125 RTS) at 20 microns and sectioned at 5 microns thickness. The sectioned tissues were attached to slides and subsequently dewaxed in xylene and stained in Haematoxylin and Eosin using the method of [27] for general tissue architecture. The stained slides were then examined using compound light microscope at X400 magnification.

3 Results

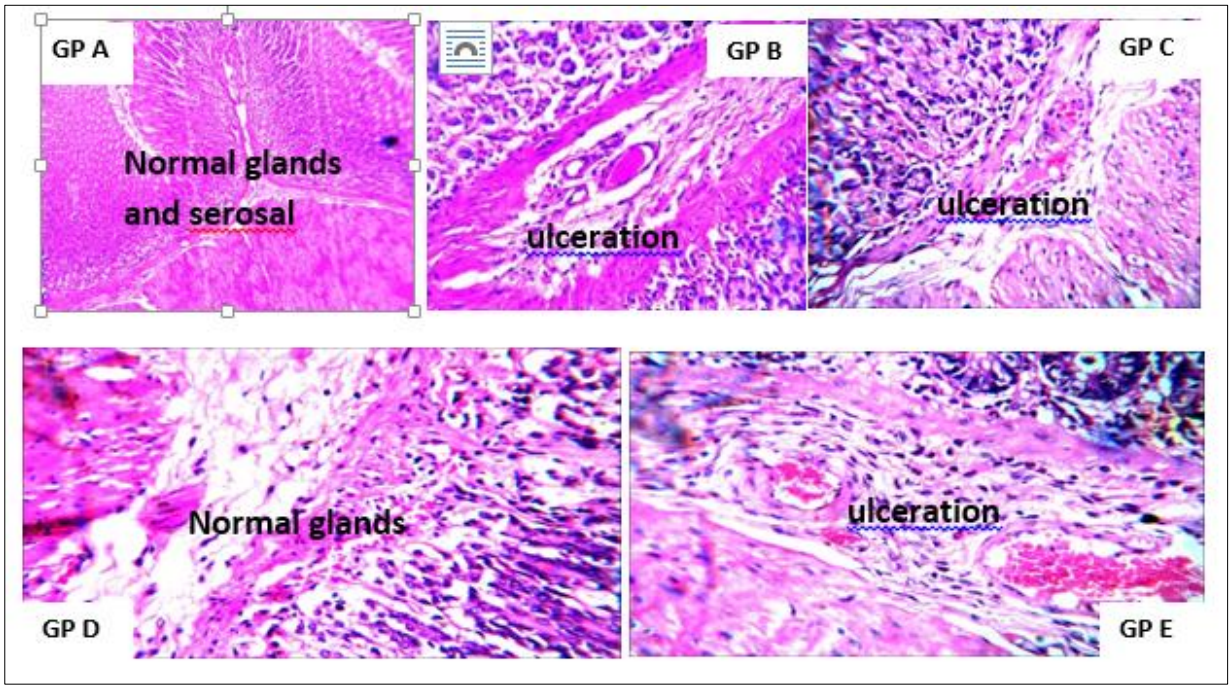

Figure 1. The morphology of the stomach of adult rat stained with haematoxylin and eosin (X400 magnification). Group A (negative control) shows normal histology of the stomach. Group B shows ulceration of the serosa with pyloric rings in rats induced with indomethacin without treatment. Group C shows ulceration of the serosa with pyloric rings. Group D shows normal serosa and glands. Group E shows the morphology of the stomach with extensive ulceration.

4 Discussion

Indomethacin is a non-steroidal anti-inflammatory drug (NSAID) that is indiscriminately used by individuals for the treatment of fever, pain, stiffness and swelling due to inflammation. Its mechanism of action involves the inhibition of prostaglandins production, a known endogenous signaling molecule that cause these symptoms [28]. This is achieved by inhibiting cyclooxygenase, an enzyme that catalyzes the production of prostaglandins. Cyclooxygenase-1 and 2 inhibits the production of prostaglandins responsible for maintaining the mucous lining of the gastrointestinal tract and can cause peptic or gastric ulcer which is the most prevalent disorder of the human gastrointestinal tract with grave complications-bleeding and perforation of the ulcer with prolonged hospitalization and high mortality rate [29].

This study observed ulceration of the serosa with classic pyloric rings following indomethacin administration which may be connected to either free radicals formation or inhibition of prostaglandin synthesis. This study corroborates the reports of other studies where indomethacin was also found to have caused ulceration, gastro-intestinal bleeding or gastric injury [30, 31].

Carica papaya and *Musa paradisiaca* are herbal remedies known for their efficiency and effectiveness in treating several ailments. They contain certain phytochemicals that helps in protecting the mucosa wall of the gastrointestinal tract [25]. Extracts of unripe *C. papaya* contain terpenoids, alkaloids, flavonoids, carbohydrates, glycosides, saponins, and steroids. The cytoprotective and anti-motility properties of the extracts may account for the anti-ulcer property of the unripe

fruit. [32]. [33] opines that *Musa paradisiaca* exhibits its protective and healing activities through predominant effects on various mucosa defensive factors.

From the result of the present study; group A shows normal histology of the stomach. Groups B, C and E shows ulceration of the serosa with classic pyloric rings. Group D shows normal histology; revealing the ameliorative properties of *Musa paradisiaca*.

[34] noted that aqueous and methanol extract of whole pawpaw was able to significantly reduce the ulcer index in experimental animal models. However, this study observed that animals pretreated with *Carica papaya* leaf extract before ulcer induction showed ulceration of the serosa with pyloric rings. Thus, *Carica papaya* does not confer any protective effect on the gastric mucosa of experimental animal models.

This study also observed that animals pretreated with *Musa paradisiaca leaf* extracts maintained normal histology of the serosa and fundal glands. The findings of this study agree with other studies which reported that *Musa paradisiaca* inhibits ulcer which may be due to their high phytochemicals and phytonutrients with high antioxidant properties that play significant roles in alleviating toxicity related disorders [35, 36, 16]. [37] proposed that the ulcer healing potential of *Musa paradisiaca* might not be unconnected with basic fibroblast growth factors responsible for epithelial regeneration. Extracts of *Musa paradisiaca* contains phytochemicals like phenols and flavonoids and prevents gastric ulceration via gastric mucosa strengthening and gastric juice decreasing mechanisms in experimental rat models [38,19].

[39] experimented the wound healing potential of *Musa paradisiaca* in male wistar rats and observed that animals treated with methanolic and hexanoic extracts of *Musa paradisiaca* peel extract recorded more healing activity compared to group treated with chloroformic extract. Methanolic plantain pulp extracts exhibited significant anti-ulcer effect and antioxidant activity in gastric mucosal homogenates; ulcer index was reversed and lipid peroxidation and super oxide dismutase value induced by stress was decreased [34]. Also, [39] noted that dried unripe plantain powder exerted protective effect against aspirin induced erosions of the gastric mucosa.

Though, there is no known study on the combination of *C. papaya* and *M. paradisiaca*, this study observed that the combination of *Carica papaya* and *Musa paradisiaca* leaves extract was ineffective in the prevention of gastric injury whereas, *Musa paradisiaca* leaf extract alone ameliorated the effect of indomethacin on the stomach of the adult albino rats.

5 Conclusion

The combination of *Carica papaya* and *Musa paradisiaca* leaves exacerbates the effect of indomethacin on gastrointestinal tract ulcers. Thus, the practice of using combined extract of *Carica papaya* and *Musa paradisiaca* should be avoided in ulcer patients or individuals on indomethacin therapy.

Compliance with ethical standards

Acknowledgments

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Disclosure of conflict of interest

The authors declare that there is no conflict of interest.

Statement of ethical approval

The protocol for this study was approved by the Ethical and Research Committee of Niger Delta University, Bayelsa State, Nigeria. The study adhered strictly to the ethical principles for medical research involving animal subjects as outlined in the Helsinki declaration in 1975 and subsequent revisions.

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