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Indomethacin-induced gastric ulceration in rats: Protective roles of *Spondias mombin* and *Ficus exasperata*

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ABSTRACT

This study investigated the quantitative polyphenolic constituents and gastroprotective effects of aqueous leaf extracts of *Spondias mombin* and *Ficus exasperata* against indomethacin-induced gastric ulcer in rats. Ulceration was induced by a single oral administration of indomethacin (30 mg/kg body weight). Wistar rats were pretreated with esomeprazole (reference drug) at a dose of 20 mg/kg body weight, *S. mombin* or *F. exasperata* at 100 and 200 mg/kg body weight once daily for 21 days prior to ulcer induction. At the end of the experiment, gastric secretions and antioxidant parameters were evaluated. We observed that the significantly increased ($p < 0.05$) ulcer index, gastric volume, malondialdehyde level and pepsin activity were effectively reduced following treatment with *S. mombin* and *F. exasperata*. The extracts also markedly attenuated the reduced activity of superoxide dismutase as well as pH and mucin content in the ulcerated rats. These findings are indicative of gastroprotective and antioxidative potentials of the extracts which is also evident in the degree of % inhibition against ulceration. The available data in this study suggest that the extracts of *S. mombin* and *F. exasperata* proved to be capable of ameliorating indomethacin-induced gastric ulceration and the probable mechanisms are via antioxidative and proton pump inhibition.

1. Introduction

Gastric ulceration is a benign lesion on the mucosal epithelium upon exposure of the stomach to excess acid and aggressive pepsin activity [1]. It is the most prevalent gastrointestinal disorder ever known, accounting for an estimated 15 mortality out of every 15,000 complications yearly in the world [2,3]. In spite of the rapidly changing concept of gastric ulcer management from conventional vagotomy, prostaglandin analogs, H_2 receptor antagonists and antacids to proton pump inhibitors, gastrointestinal toxicity remains an impediment to their application in clinical practice. Specifically, gastrointestinal toxicity of nonsteroidal anti-inflammatory drugs (NSAIDs) origin may be as high as 4–8% per year and the complications are even higher for those with additional risk factors such as prior history of ulcer disease [4]. Various synthetic antiulcer drugs are presently available and some of these like cimetidine, misoprostol, ranitidine, omeprazole and esomeprazole are employed to manage and cure NSAID

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induced gastric ulcer. However, each of these drugs confers simpler to severe side effects, prompting a search for non-toxic, easily accessible and affordable antiulcer medication [5,6]. Investigation on the phytotherapy of medicinal plants that are highly valued and widely used in the traditional systems of medicine might provide efficient formulation for better management. *Spondias mombin* and *Ficus exasperata* belongs to this class of therapeutic plants.

S. mombin (SM) commonly known as "Iyeye" in the South-Western part of Nigeria is a fructiferous tree in the Family Anacardiaceae. The plant grows in rain forests and coastal areas, attaining a height of 15–22 m [7]. It is commonly used in folk medicine to cure many diseases due to its potent bioactive principles including tannins, saponins, flavonoids, phenolics and anthraquinone glycosides [8]. Antioxidant vitamins; alpha-tocopherol and ascorbic acid have been detected in its leaves extracts [9]. Tea from its flowers and leaves is taken as an analgesic and anti-inflammatory cure against stomach ache and discomfort [10]. Ayoka et al. [7] have also reported decoction from its leaves to be therapeutic against urethritis, cystitis as well as eye and throat inflammations. The gum from SM has also been exploited as an expectorant and vermifuge. The leaf extract of the plant has been outstandingly advocated for use in speedy wound healing processes, hemorrhoids and inflamed mucous membrane due to its tannin content [11]. Its pharmacological potencies such as antioxidative, antimicrobial, antimalarial and antibacterial have also been documented [8,10,12,13].

F. exasperata Valh (FE), called "Epin", "Anwerenwa" and "Kawusa" respectively among the Yorubas, Igbos and Hausas in Nigeria, is commonly known as 'sand paper tree' belonging to Moraceae Family. Phytochemical analysis of the leaf extract of FE has revealed the presence of flavonoids, tannins, saponnins, alkaloids and cyanogenic glycosides [14]. Its medicinal efficacy in treating many diseases has been researched. For instance, the South-Western people of Nigeria uses the decoction and infusion of FE leaves for the management, control and treatment of hypertension, diabetes mellitus and certain cardiovascular dysfunction [15]. Leaves of FE cooked with bananas are eaten for the treatment of gonorrhea [16]. Its leaf extract is also taken to suppress stomach ache, treat peptic ulcer and as antidote to poison [5].

With the remarkable attributes of SM and FE particularly in alleviating stomach ache related disorders and wound healing enhancement, the present study compared their therapeutic efficacy to a reference drug (esomeprazole) on indomethacin-induced gastric ulceration in rats.

2. Materials

2.1. Chemicals and drugs

Indomethacin and esomeprazole were respectively procured from Kapit Pharmaceutical Limited, Nigeria and Ranbaxy Laboratories, India. Trichloroacetic acid (TCA), dimethylaminobenzaldehyde, epinephrine, acetyl acetone, bovine serum albumin (BSA), gallic acid, aluminum chloride, quercetin and thiobarbituric acid (TBA) were products of Sigma Chemical Co. (St. Louis, MO, USA). Distilled water was obtained from Biochemistry Laboratory, Kwara State University, Malete, Nigeria. Assay kits used were from Randox Laboratories limited, United Kingdom. Other chemicals used were of analytical grade from reputable companies in the world.

2.2. Plant collection and authentication

Fresh leaves of SM and FE were collected in April 2014 following identification of the two plants at the botanical garden of University of Ilorin, Ilorin, Nigeria. The leaves were authenticated at the University's Herbarium, where voucher specimens (nos. 14/20567 and 14/20568) were prepared and deposited.

2.3. Experimental animals

Albino rats of the Wistar strain at a mean weight of 180.00 ± 1.85 g were used for the study. The animals were obtained and reared as described by Sabiu et al. [17], following approval from the Independent Ethical Committee on the Use and Care of Laboratory Animals of the Kwara State University, Malete, Nigeria. A certified number KSU/IECCULA/001/05/014 was assigned and issued for the research.

3. Methods

3.1. Preparation of extracts

Leaves of SM and FE were air-dried at room temperature for 10 days to constant weight. The dried samples were then pulverized with an electric blender (model MS-223; Blender/Miller III, Taiwan, China), weighed and kept air-tight prior to extraction. Powdered samples (500 g each) of both plants were separately extracted in 5 l of distilled water for 48 h with continuous shaking by orbital shaker maintained at 300 rpm. The solutions obtained were then filtered (with Whatman No. 1 filter paper) and the resulting filtrates lyophilized to give 15.5 g (SM) and 12.4 g (FE) residues, corresponding to yields of 3.1% and 2.48% respectively. The lyophilized samples were separately reconstituted in distilled water to give doses of 100 and 200 mg/kg body weight of each extract used in the study.

3.2. Determination of total phenolics

Following the reported method of Wolfe et al. [18], the total phenol contents in the plant extracts were determined. Briefly, an aliquot of each extract (1 ml) was mixed with 5 ml Folin-Ciocalteu reagent (previously diluted with water 1:10 v/v) and 4 ml (75 g/l) of sodium carbonate. The tubes were vortexed for 15 s and allowed to stand for 30 min at 40 °C for color development. Absorbance was read at 765 nm using a spectrophotometer (Beckman, DU 7400, USA). Extracts were evaluated at a final concentration of 1 mg/ml. Total phenolic content was expressed as mg/g gallic acid equivalent using the equation obtained from a calibration curve of gallic acid.