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Ethanol-induced gastric ulceration in rats: Protective roles of methanol and water extracts of *Cyathula prostrata* Linn Blume

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Abstract

The study investigated gastro protective effect of methanol and water, crude extract of *Cyathula prostrata* against ethanol induced gastric ulcer in rats. Ulceration was induced by oral administration of absolute ethanol (1cm³/kg body weight). Wistar rats were pre-treated with Omeprazole 20mg/kg body weight, 50mg/kg, 100mg/kg and 150mg/kg per body weight of methanol and water extract separately. These extracts showed a marked deduction in the mean ulcer index parameter studied on the test animals in a dose dependence manner with a significant increase in percentage preventive index. In conclusion, it was observed that the methanol and water extract of *Cyathula prostrata* provides a significant anti-ulcer effect against ulcer in rats, a fact that supports the traditional use of hot water extract of the whole plants for its anti-ulcer effect.

Keywords: Gastroprotective, NSAIDS, *Cyathula prostrata*, ulcer.

Introduction

Gastric ulceration is a benign lesion of the mucosal epithelium upon exposure of the stomach to excess acid and aggressive pepsin activity Khazaei and Salehi (2006) [12]. It is the most prevalent gastrointestinal disorder ever known, accounting for an estimated 15 mortality rate of every 15,000 complications yearly in the world Sonnenberg (1996) [19] and Shristi, *et al.*, (2012) [18]. In spite of the rapidly changing concept of gastric ulcer management from conventional vagotomy, prostaglandin analogs, H₂ receptor antagonist 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 Griffin and Scheima (2001) [8]. Various synthetic anti-ulcer drugs are presently available and some of these like cimetidine, misoprostol, ranitidine, omeprazole and esomeprazole are employed to manage and cure NSAID 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 Akah *et al.*, (1998) [1], Hawkin and Hanks (2002) [9]. Investigation on the phytotherapy of medicinal plants that are highly valued and widely used in the traditional systems of medicine might provide efficient formation for better management.

Cyathulaprostrata is an annual perennial herb, which can grow up to the height of 30-50 cm tall. It is an erect or ascending herb with its rooting at the nodes, the stem obtusely quadrangular thickened above the nodes, often tinged with red, covered with patent and fine hairs (Daizial, 1937). The leaves arrangement is opposite, simple and rhomboid-aborate to rhomboid oblong form.

In Nigeria, the Igbo (Owerri) called it 'agbirigba', the fula-fulfulde called it 'Kebbedoombi', the Hausa's called it 'da'nka' dafi, and Yoruba's called it 'cawerepepe'. In Gambia, the Manding-mandinka called it 'naninjon'. In west Cameroon, the Kpe called it 'krokos', and in Ghana the Akan – Asante called it 'mpupua'. The plant has analgesic and antiseptic properties. The "Kru" people of Guinea, use the ash of the burnt plant with water to smear on the body for scabies and in Nigeria the leaves are applied to scabies, the sap is applied to sores and cancers and used as eardrop for otitis and headache (Daizial, 1937).

It is commonly used in folk medicine to cure many diseases due to it potent bioactive components such as Tannins, Saponins, flavonoids, Alkaloids, phenolic, Anthraquinone and glycosides Anthony *et al.*, (2016) [2]. Its medicinal efficacy in treating many diseases have been researched. For instance, *Cyathula prostrata* has been documented to be relatively non-toxic in albino mice, Kannppan and Sundaram (2009) [11].

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Methanol extract of *Cyathula prostrata* is known to possess anti-inflammatory and analgetic properties, justifying its application in the management of ailment associated with pain among others, Ibrahim *et al.*, (2012) [10]. It is a novel potential plant use as a source of anti-oxidant in the fight against the incident of free radical implicated in so many degenerative disease Olawale *et al.*, (2012) [16].

2. Materials and Methods

2.1 Plant Identification

The plant *Cyathulaprostrata* was identified through analysis of its macro morphological features and its botanical profile, in the Herbarium Section of Forestry Research Institute of Nigeria Ibadan, where vouches specimen FHI 110263 was deposited.

2.2 Animals

Inbred matured albino wister rat of both sexes weighing 150 – 230 g, bred in the laboratory animal unit of Faculty of Pharmaceutical Sciences, University of Jos were used in the experiments. The rats were kept in the same room with a varying temperature between 28 – 30 °c, lighting period was between 15 – 17 hours daily. The rats were kept in stainless steel wire mesh cage which separated them from their faeces to prevent coprohagy. They were supplied clean drinking water and fed with standard feed. Ethical rules guiding the use of animals for the experiment was strictly adhered to.

2.3 Sample Collection and Treatment

Fresh whole plant of *Cyathula prostrata* were collected from Umuosisi – Obizi in Mbaise Local Government Area of Imo State, Nigeria. The plants were air-dried under shade and ground in to powder using mortar and pestle.

2.4 Extraction

The powdered plant sample was extracted using methanol and water sequentially. The powered plant sample (78g) was packed in a muslin cloth and inserted in to soxhlet extractor. Methanol (150cm³) was used for extraction in a soxhlet for 8 hours. At the end of the period, the solvent was recovered by rotatory evaporator and the methanol extract was collected. The methanol sample was air dried under shade for methanol to evaporate. The sample (free of methanol) was weighed, packed in a muslin cloth and inserted into soxhlet extractor. Water (150 cm³) was used for extraction for 8 hours and the solvent was recovered by rotatory evaporator and water extract was collected. The extracts were placed in a desiccator to dry for further analysis

2.5 Effect of Methanol and water crude extracts of *Cyathula prostrata* on Ethanol – Induced Gastric Ulcer in Rats

Ethanol – induced ulcer in rats were valued as described by Ode and Asuzu (2011) [15]. For each extract, Adult wistar rats of either sex were marked, weighed and randomly assorted into eight groups with each group containing five rats. The rats were fasted for 24 hours. One group was orally administered with distilled water and another with Omeprazole (20mg/kg). For the three groups, 50, 100 and 150mg/kg of methanol extracts were administered respectively. After an hour, 1.0 cm³/kg of absolute ethanol was administered orally to all the rats. Two hours after drenching the rats with ethanol, they were killed and their stomach were carefully removed and rinsed with distilled water. Each was cut open through the grater curvature with a

scalpel blade and again rinsed with distilled water. Each stomach was pinned to a white background on a wooden board for examinations and assessment of ulcer. This procedure was repeated using water extracts on the rest of the rat groups.

The stomachs were examined for ulcer with the aid of a magnifying lens (x10). The ulcer index was assessed as follows:

< 1.0 mm = 1, between 1 and 2mm = 2, ≥3mm = 3.

The sum of the scores were divided by 10 (magnification of the lens) to obtain the ulcer index in rat (Main and White, 1975) [13].

The mean ulcer index for each group was subject to Anova and Dunnett's multiple comparison test and the effectiveness of the each extract and drug was calculated, using equation 2.

$$\text{Preventive index \%} = \frac{U_1 - U_2}{U_1} \times 100 \dots \dots \dots (2)$$

where, U_1 = Ulcer index of control

U_2 = Ulcer index of treated

3. Results

3.1 Effect of methanol and water extracts of *Cyathula Prostrata* on rats in ethanol induced gastric ulcer.

The effect of crude extracts of methanol and water of *Cyathula prostrata* on the ulcer index and percentage inhibition against ulcer in experimental animals are shown in table 1 and 2.

Table 1: Effect of Methanol Extract of *Cyathula prostrata* on Ethanol Induced Gastric Ulcer in Rats

Treatment	No of animal	Mean ulcer index ± SE	Preventive index %
Distilled water as control	5	1.40 ± 0.11	0
Omeprazole (20 mg/kg)	5	0.32 ± 0.08	77.14
Methanol extract (50 mg/kg)	5	0.80 ± 0.27*	42.00
Methanol extract (100 mg/kg)	5	0.26± 0.12*	81.42
Methanol (150 mg/kg)	5	0.14 ± 0.07*	90.00

Superscript indicates significant difference at P< 0.05 when compared with the control.

Table 2: Effect of Water Extract of *Cyathula prostrata* on Ethanol Induced Gastric Ulcer in Rats

Treatment	No of animal	Mean ulcer index± SE	Preventive index (%)
Distilled water as control	5	1.40 ± 0.11	0
Omeprazole (20 mg/kg)	5	0.32 ± 0.08	77.14
Water extract (50 mg/kg)	5	0.92 ± 0.24*	34.28
Water extract (100 mg/kg)	5	0.30 ± 0.08*	78.7
Water extract (150 mg/kg)	5	0.12 ± 0.07*	91.42

Superscript indicates significant difference at P< 0.05 when compared with the control

Oral administration of 1.0cm³/kg of absolute ethanol increase the degree of ulceration (Ulcer index) in the rats while a significant improvement in the level of inhibition against

ulceration was however observed in the extracts-treated animals. Administration of 100 and 150mg/kg of all the extract produced significant reduction in the mean ulcer index ranging from 0.12 ± 0.07 to 0.92 ± 24 compare with 1.40 ± 11 in distilled water treated rats. These extracts at a dosage of 100mg/kg and 150mg/kg had better gastro protective effect with preventative index ranging from 78.70 to 92.85% over omeprazole. However at a dosage of 50mg/kg methanol extracts produced 0.80 ± 29 and water extract produce 0.92 ± 24 mean ulcer index respectively, while omeprazole 20mg/kg had mean ulcer index of 0.32 ± 0.08 .

Discussion

In the present study, the significant increase in ulcer index and gastric volume following oral administration of ethanol in the ulcerated rats may be attributed to either free radicals formation or inhibition of prostaglandin synthesis. Decreased prostaglandin level has been attributed to impaired gastro protection and increased gastric secretion which are important events in the etiology of mucosal ulceration. This agrees with the reports of Ode and Azuzu (2011) [15]. Where Ethanol was reported to have caused alterations in gastric secretions in rats. Phytochemical analysis of the whole plant of *Cyathula prostrata* showed that the plant contain bioactive compounds Anthony *et al.*, (2016) [2]. Flavonoids are found to increase mucosal Prostaglandin content (Alkaraz and Houl, 1985). Decrease histidinedecabonylases, Bronnes and landry, (1985) [4] and are free radical Scavengers (Cavallini *et al.*, 1978) [6], the activity of Saponin against ulcer is due to activity of mucous membrane protective factor (Saito *et al.*, 1977) [17]. Tannins are known to tan the outer layer of the mucosa and render it less permeable and more resistant to chemical and mechanical injury or irritation (Asuzu and Onu, 1990) [3].

Conclusion

Overall, the attenuation of gastric affronts of ethanol by administration of extracts of *Cyathula prostrata* at various concentration regimen is indicative of its excellent gastroprotective and antioxidant potential in rats, which laid credence to traditional use of hot water extracts of *Cyathula prostrata* in the treatment of ulcer.

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