Evaluation of the Ulcerogenic potential of the Aqueous extract of *Spondias mombin* and *Costus afer*.

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**ABSTRACT**

Ulcerogenic potential of the aqueous leaf extracts of *Spondias mombin* and aqueous stem extract of *Costus afer* was investigated in Wistar rats. Six groups of 5 healthy animals each received *Spondias mombin* (200 mg/kg and 400 mg/kg), *Costus afer* (200 mg/kg and 400 mg/kg), indomethacin 40 mg/kg, and normal saline respectively. After 3 hours, the stomach lining was evaluated for ulceration/scarring. This study showed that the aqueous extracts of both *Spondias mombin* and *Costus afer*, which are useful in the traditional treatment of various medical ailments, are less likely to cause ulceration on the gastric lining mucosa.

**Keywords:** Ulcerogenic potential, *Spondias mombin*, *Costus afer*, gastric lining mucosa.

**INTRODUCTION**

Herbal medicine has become the mainstay of the society, as majority of people in both developed and developing countries use plant drugs traditionally in the treatment of various diseases¹. In Nigeria, thousands of plants species have been claimed to possess medicinal properties and are employed in the treatment of many ailments². Though, numerous herbal remedies have been found to be effective, their safety is yet to be proven through research³. *Spondias mombin* (family: Anacardiaceae) commonly called hog plum or yellow mombin is a plant whose leaf, bark, roots and seeds are used for medicinal purposes such as treatment of pain, high blood pressure, diabetes, amongst others. Wound healing and anti-inflammatory⁴, anti-diabetic⁵, and blood lipid-lowering activity⁶ of *Spondias mombin* had been scientifically proven. *Costus afer* is a perennial tropical herbaceous plant from the costus family (Costaceae). It is commonly called bush cane, monkey sugar cane, ginger lily, and spiral ginger. The aqueous leaf and stem bark extracts of *Costus afer* are being used in the treatment of diabetes mellitus in folklore medicine⁷,⁸. The antimicrobial activity of the ethanolic extract of its leaves has been assessed⁹. Its stem extract has also been shown to have antioxidant effect¹⁰, as well as the anti-inflammatory activity of the rhizome of *Costus afer*¹¹. Both extracts have been reported to be useful in the traditional management of various medical ailments in Southern communities of Nigeria⁵,⁶,⁸, though, there is little concern on their ulcerogenic potential. Hence, this study is aimed at evaluating the ulcerogenic potential of the aqueous leaf extracts of *Spondias mombin* and aqueous stem extract of *Costus afer* in experimental rats, in order to validate their safety profile relating to gastric action.

**MATERIALS AND METHODS**

**Animals**

Wistar rats of both sexes weighing between 120-150 g were obtained from the colony breed of the animal...
The rats were kept in cages under standard conditions and fed with standard diet (Growers feed) and clean water *ad libitum*. The animals were allowed to acclimatization for two weeks prior to the commencement of the experiment. Animals were handled in compliance with NIH Guide for care and use of laboratory animals (pub. No. 85-23 revised 1985), and approved by the Faculty of Pharmaceutical Sciences, Nnamdi Azikiwe University’s ethical committee for the use of laboratory animals.

**Plant material**

Fresh leaves of *Spondias mombin* and stems of *Costus afer* were collected from the school garden of Delta State University, Abraka and were authenticated in the Department of Botany, Delta State University, Abraka. The plant materials were cut into pieces, air-dried at ambient temperature and blended into coarse powder.

**Plant Extraction**

The powdered *Spondias mombin* (500 g) was dissolved in 1500 mls of distilled water, while the powdered *Costus afer* (500 g) was dissolved in 2500 mls of distilled water. Both solutions were stirred every six hours. After 72 hours the solutions were then filtered and the filtrate concentrated to dryness using a freeze-dryer to yield a residue, 49.6 g (9.9% w/w) for *Spondias mombin* and 18.2 g (3.6% w/w) for *Costus afer*.

**Acute toxicity (LD$_{50}$):**

The acute toxicity (LD$_{50}$) study was carried on *Spondias mombin* and *Costus afer* using a modified Lorke’s method of 1983. Animals (rats and mice) of either sex were fasted overnight prior to the study. Dosage selection was based on the Organization of Economic Corporation and Development’s (OECD) guidelines.$^{12}$

**Phase 1:** In phase I, the rats and mice were placed in four groups ($n = 3$). Group 1 served as control and received 10 ml/kg of distilled water while groups 2, 3 and 4 received 10 mg/kg, 100 mg/kg, and 1000 mg/kg of the extracts respectively. The animals were observed and the number of death recorded after 24 hours.

**Phase 2:** In this phase, four groups ($n = 3$) of mice and rats were used. Doses were selected based on the lethality in Phase I. Absence of death in Phase 1 prompted the use of 2000, 3000, 4000, and 5000 mg/kg doses in Phase 2. The animals were observed and the number of death recorded after 24 hours. The LD$_{50}$ was calculated using the geometric mean of the highest non-lethal dose and the least toxic dose.

\[
LD_{50} = \sqrt{\text{highest non-lethal dose} \times \text{least toxic dose}}
\]

**Ulcerogenic Studies in Rats**

The method of Cashin *et al.*, 1979 [13] was used. Adult Wistar rats of both sexes (120-160 g) were divided into six groups (n=5) and fasted for 24 h.

Group 1 – Normal saline 10 ml/kg p.o. (negative control)

Group 2 – Indomethacin 40 mg/kg p.o. (positive control)

Group 3 – *Spondias mombin* 200 mg/kg

Group 4 – *Spondias mombin* 400 mg/kg

Group 5 – *Costus afer* 200 mg/kg

Group 6 – *Costus afer* 400 mg/kg

Three hours after drug administration, animals were sacrificed, and the stomach was removed, cut along the larger curvature and the mucosal surface was exposed. The mucosa was washed with normal saline and observed with magnifying lens. The ulcer index was determined according to the method described by Main and Whittle, 1975.$^{14}$

<table>
<thead>
<tr>
<th>Groups</th>
<th>Weight of Rats (g)</th>
<th>Scores</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1 (Normal Control)</td>
<td>134.58 ± 4.44</td>
<td>0.00 ± 0.00</td>
</tr>
<tr>
<td>Group 2 (Indomethacin 40 mg/kg)</td>
<td>141.50 ± 4.01</td>
<td>3.40 ± 0.68</td>
</tr>
<tr>
<td>Group 3 (SM 200 mg/kg)</td>
<td>133.16 ± 5.40</td>
<td>0.20 ± 0.20</td>
</tr>
<tr>
<td>Group 4 (SM 400 mg/kg)</td>
<td>129.62 ± 2.24</td>
<td>0.20 ± 0.20</td>
</tr>
<tr>
<td>Group 5 (CA 200 mg/kg)</td>
<td>132.08 ± 5.34</td>
<td>0.00 ± 0.00</td>
</tr>
<tr>
<td>Group 6 (CA 400 mg/kg)</td>
<td>128.70 ± 1.57</td>
<td>0.00 ± 0.00</td>
</tr>
</tbody>
</table>

Values are expressed as Mean ± SEM of sample replicates (n=5)

**Scoring of ulcer:** Normal colored stomach (0); Red coloration (1); Spot ulcer (2); Hemorrhagic speak (3); Deep ulcers (4); Perforation (5).
Fig 1.
Figures showing ulcer activity of both Spondias mombin and Costus afer
(A) Normal control. (B) Indomethacin treated - 40 mg/kg. (C) *Spondias mombin* extract, 200 mg/kg. (D) *Spondias mombin* extract, 400 mg/kg (E) *Costus afer* extract, 200 mg/kg. (F) *Costus afer* extract, 400 mg/kg.
Scoring of ulcer: Normal colored stomach (0), Red coloration (1), Spot ulcer (2), Hemorrhagic speck (3), Deep ulcers (4), Perforation (5).

Statistical analyses
All data obtained were expressed as Mean±SEM (standard error of mean).

RESULTS
Acute toxicity (LD$_{50}$):
Acute toxicity studies showed no obvious signs of toxicity in all treatment groups in both species (rat and mice) and phases (1 and 2) respectively following the administration of the aqueous extracts of Spondias mombin and Costus afer. The LD$_{50}$ of the extracts was greater than 5000 mg extract/kg body weight.

Ulcerogenic Study
Results on ulcerogenic study showed that indomethacin 40 mg/kg caused deep ulcer, while the Spondias mombin (SM) and Costus afer (CA) extracts at 200 mg/kg and 400 mg/kg produced a red coloration (hyperemia) in the stomach tissue in less than 50% of the animals tested (Table 1; Fig. 1).

DISCUSSION AND CONCLUSION
The absence of death in LD$_{50}$ study suggests the unlikelihood of Spondias mombin and Costus afer to cause short term toxicity on single administration. Absence of hemorrhagic speck, deep ulcer and perforation observed in the present study (Table 1 and Figure 1) suggests that these extracts do not have ulcerogenic effect on usage. This study has therefore shown that the aqueous extracts of both Spondias mombin and Costus afer which are useful in the traditional treatment of various medical ailments are less likely to be cause ulceration on the gastric lining mucosa.

RECOMMENDATIONS
This study recommends that both extracts are relatively safe for use, either individually or as a mixture (ratio 1:1), in the traditional management of medical ailments. Further studies are encouraged to ascertain the toxic effects of both plants extract on other organs such as the liver, kidneys, pancreas, as well as their mutagenic and teratogenic effects.

REFERENCES
13. Cashin CH, Dawson W, Kitchen EA. The pharmacology of benoxaprofen (2,4-chlorophenyl-methyl-5-benzoazole acetic acid) LRC.L3694, a new compound with anti-inflammatory activity apparently unrelated to