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Evaluation of the Ulcer-healing Potential of *Chromolaena odorata* (Independent Plant) in Wistar Rats

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Authors' contributions:

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Gastric ulcer is a disease that affects the GIT notably the stomach. It has been implicated in numerous deaths both in the developing and developed countries. Plants are endowed with variety of compounds of immense health significance and could account for the multi-therapeutic potential. Thus, the aim of this study was to determine the ability of the *Chromolaena odorata* (Independent

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plant) to heal gastric ulcer and also protect the liver against damage. Freshly harvested *C. odorata* leaves were processed and extracted. A total of 25 adult Wistar rats were divided into five groups of five rats. Group I: (normal control) was administered 2 mL of distilled water, Groups II-V were administered 300 mg/kg of aspirin to induce gastric ulceration. However, while group II was not administered the said plant extract, group III and IV were administered 200 and 400 mg/kg of extract respectively, and group V was administered 20 µg/kg of misoprostol. Animals were treated for 10 days and afterwards, sacrificed. The stomach was harvested and opened, blood sample was collected. While ulcer index was performed on all groups, the activity of the serum hepato-markers was restricted to Groups I, II and III. The parameters were evaluated using standard procedures. The activities of alanine transaminase (ALT), aspartate transaminase (AST) and alkaline phosphatase (ALP) reported for rats administered extract were not significantly ($P>0.05$) different from those reported for the normal control. It was also observed that methanol leaf extract of *C. odorata* significantly ($p<0.05$) reduced ulcer index in a dose dependent manner. In conclusion, it can be deduced from this study that methanol leaf extract of *C. odorata* has the potential to heal gastric ulcer and as well protect the liver against insult.

Keywords: Chromolaena odorata; misoprostol; ulcer index; alkaline phosphate.

1. INTRODUCTION

The gastrointestinal tract is a highly specialized organ system that allows consumption of diverse array of food stuff in discrete meals to meet nutrient needs. In addition, the GIT participates in the metabolism and elimination of non-nutrients as well as toxic compounds [1]. Thus, a properly functioning GIT is translated into a healthy nutrition hence, the overall wellbeing of an individual [1].

The stomach is a sack-like organ and an important segment of the gastrointestinal tract that aid in the digestion of food through its muscular activities which results in mixing of food with juice [1]. Gastric ulcer as the name implies is an ulcer in the stomach. It occurs in both developed and developing countries of the world [2]. An estimated 80% of the populations of the developing countries suffer from this disease [3]. Risk factors for the development of ulcers include excessive use of non-steroidal anti-inflammatory drugs among others [4]. Among other symptoms, loss of appetite that generally characterizes ulcer conditions can result in inadequate food intake and consequently malnutrition. Although the etiology of gastric ulcer is not clearly defined, it is generally accepted that it results from an imbalance between the protective and aggressive factors [5].

Synthetic drugs available for the treatment of gastric ulcer have some shortcomings such as high cost, relapses after treatment, drug interactions and side effects such as arrhythmias, gynaecomastia and hematopoietic changes [6].

Natural products have been used for combating human diseases since they exhibit a wide range of biological activities that can be explored for medical applications. Plants have been a recognized source of natural product for the treatment of human and animal diseases [7].

The plant *Chromolaena odorata* popularly known as siam weed is native to South and Central Africa. It is a fast growing, invasive perennial plant that was introduced into the tropical region of Asia, Africa and other parts of the world [8]. The economic value of *C. odorata* is low [9]. Consequently, there is relatively paucity of research work on it [10].

Leaf extract of *C. odorata* has demonstrated wound healing activity. It is endowed with constituents that wield the potential to modulate one or more of the overlapping wound healing stages [11]. It has been established via in vitro and in vivo studies that extracts of the said plant enhance wound healing activities such as fibroblast, endothelial cell and keratinocyte proliferation [11]. On the basis of these findings, it is not out of place to investigate the possibility of its ability to address internal wound (gastric ulcer).

2. MATERIALS AND METHODS

Collection of plant material: Fresh leaves of *Chromolaena odorata* (Independent plant) were obtained from a bush within a residential area in Uturu, Isiukwuato Local Government Area of Abia State, Southeastern part of Nigeria. The leaves were conveyed in a dark polythene bag to the herbarium unit of the Department of Forestry,

Michael Okpara University of Agriculture, Umudike Abia State Southeast Nigeria for identification.

Extraction of plant material: Thoroughly washed leaves of *Chromolaena odorata* were spread on a flat surface in the laboratory to dry at room temperature. The dried leaves were subsequently transformed into a fine powder by grinding with the aid of an electrical blender. Exactly 500 g of powdered *C. odorata* leaf sample was soaked in a litre of 50% methanol for 3 days. The mixture was shaken twice daily and the solvent ridded through a layer of gauge, the filtrate was subjected to evaporation to dryness in vacuo at 55°C.

Median Lethal Dose: The medial lethal dose determination was performed in two phases. The initial phase was characterized by the division nine rats into three groups of three rats each which were separately administered with 10, 100 and 1000 mg/kg of extract orally. This was followed by the observation of the animals for 24 h. for possible signs of toxicities. Being that mortality was not recorded at the first phase, the second phase which involved three groups of one rat per group were separately administered 1600, 2900 and 5000 mg/kg of extract, after which signs of toxicities were watched for on the animals which were observed for 48 h for signs of toxicity according to Lorke [12].

Phytochemical screening: Methanol leaf extract obtained from the leaf of *Chromolaena odorata* (Independent leaf) was screened to identify the inherent phytochemicals according to the method of Trease and Evans [13].

Animals: Adult male Wistar rats weighing 130-160 g were obtained from a commercial Animal House in Okigwe, Imo State. The rats were kept in plastic cages under standard laboratory conditions. They were allowed access to food and water *ad-libthum.* Animals were allowed to acclimatize for 21 days.

Experimental Design: Twenty five adult Wistar rats were divided into five groups of five rats each.

Group I: (Normal control) was administered 2 ml of distilled water
Group II: was induced ulcer without treatment (IGUWT)
Group III: Rats with ulcerated stomach were treated with 200 mg/kg of INDPE

Group IV: Rats with ulcerated stomach were treated with 400 mg/kg of INDPE

Group V: Rats with ulcerated stomach treated with 20 µg /kg of INDPE

Animals with ulcerated stomach were treated for 10 days after which they were sacrificed and subsequently processed for the determination of ulcer index.

Determination of ulcer index: Gastric lesions in the glandular region of the stomach were located in the gastric mucosa as elongated dark red lines parallel to the long axis of the stomach. The length (mm) of each lesion was measured and lesion index was calculated by adding the length of all lesions in the fundic region of the stomach [14].

Liver function test: To perform liver function test, exactly 2 mL of blood introduced into the EDTA tube was centrifuge at 4,000 rpm for 15 min and the resulting plasma was analyzed using kits to determine the activity of aspartate aminotransferase (AST), alanine transaminase (ALT), alkaline phosphatase (ALP).

Statistical Analysis: Data obtained from the study were expressed as mean ± standard deviation using SPSS (Ver. 23). Data were analysed using one way analysis of variance (ANOVA). Variation in mean values was compared using Tukey Test. *P-values* less than 0.05 was considered statistically significant.

3. RESULTS

Table 1 shows that the leaf of *C. odorata* contains alkaloids, flavonoids, glycosides, tannins, saponins and phenols with flavonoids being the most abundant of all phytochemicals reportedly present.

Table 1. Outcome of Qualitative Phytochemical Screening on the Methanol Leaf Extract of *Chromolaena odorata*

Phytochemicals	Result
Alkaloids	++
Flavonoids	+++
Glycosides	+
Tannins	++
Saponins	+
Phenols	+

+ [abundant] ++ [more abundant] +++ [most abundant]

Table 2. Effect of oral administration of *Chromolaena odorata* on the Hepatic Health

Groups	ALT (IU/L)	AST (IU/L)	ALP (IU/L)
Normal control	61.96 ± 1.10[a]	181.10 ± 0.80 [a]	223.32± 1.20[a]
INDP 200mg/kg	62.31± 3.10[a]	180.12 ± 2.90 [a]	225.22 ±1.50[ab]
INDP 400mg/kg	63.21± 2.16[a]	182.22± 2.80 [ab]	224.01 ± 2.10[a]

Results are expressed as mean ± standard deviation of three determinations. Values with the same superscript in a column are not significantly (P>0.05) different

Table 3: Ulcer Index of the Ulcerated Stomach of rats administered Methanol Leaf Extract of *C. odorota*

Grouping	Treatment	Ulcer index
Group I	2 ml of distilled water	0.00±0.00[a]
Group II	300 mg/kg of asprin	7.82±0.96[d]
Group III	Asprin + 200 mg/kg INDP	5.28±0.27[c]
Group IV	Asprin + 400 mg/kg INDP	3.64±0.56[bc]
Group V	Asprin + 20µg/kg Misoprostol	3.02±0.36[b]

Results are expressed as mean ± standard deviation of three determinations. Values with the same superscript in a column are not significantly (P>0.05) different

Table 2 shows the effect of *C. odorata* administration on hepatic health indicating that oral administration of 200 and 400 mg/kg of *C. odorata* (independent plant) leaf extract did not inflict injury on the hepatocytes, evident by the fact that the activity of ALT, AST and ALP reported for groups administered with extract was not significantly (P>0.05) different from that reported for the normal control.

Table 3 shows the ulcer index of the ulcerated stomach of rats treated with methanol extract of *C. odorata* leaf showing that the high ulcer index recorded following the administration of 300 mg/kg of aspirin was significantly (P<0.05) reduced in a dose dependent manner following oral administration of 200 and 400 mg/kg of extract of *C. odorata* and was not significantly (P>0.05) different from that reported the group administered 20µg/mg of misoprostol which however was significantly (P<0.05) higher than that reported for the normal control.

4. DISCUSSION

A number of synthetic drugs have been developed for the treatment of gastric ulcer. Unfortunately, these drugs have demonstrated certain side effects which are of concern to global health care systems and necessitate the need to probe certain plants with wound healing ability for possible development of safer alternatives. The efficiency with which a plant extract achieves wound healing is indisputably a function of the inherent antioxidants which facilitates the conservation of the fibroblast and keratinocyte proliferation on wounds [15]. Table 1 shows the result obtained following a qualitative phytochemical screening on *C. odorata* leaf showing that alkaloids, flavonoids, glycosides, tannins, saponins and phenols were reportedly present in the leaf of *Chromolena odorata*. However, of all the phytochemicals revealed through this study, flavonoids were the most abundant. This is consistent with the finding of Ukwueze et al. [8] which revealed that aqueous extract of *C. odorata* leaf contains salvigenin, sakuranetin, isosakuranetin, kaempferide and betulenol all of which are flavonoids. It is in tandem with the outcome of a work by Wenji et al. [16] which showed that flavonoids exhibit gastroprotective effects against peptic ulcer both in vivo and in vitro. Liver enzymes are membrane bound in the liver, and a distortion in the membrane architecture is implicated in their spillage into blood circulation [17]. Table 3 shows the activities the liver enzymes (AST, ALP and ALT) of rats administered methanol leaf extract of *C. odorata* (independent plant) indicating that the activities of the liver enzymes in groups administered extract were not significantly (P<0.05) different from that reported for the normal control implying that the leaf could possibly be devoid of hepatotoxins, hence absence of membrane distortions observed on the hepatocytes. This is consistent with the finding of Fidelis and Charlse [18] which reported decreased activity of AST, ALT and ALP in rats fed crude petroleum tainted feed that was treated with *C. Odorata*. Table 3 shows the ulcer index reported on the stomach of rats induced ulcer prior to treatment with the said extract indicating

that oral administration of 300 mg/kg body weight of aspirin significantly (P>0.05) increased ulcer index in rats. This affirms the ulcerogenic effect of aspirin. However, administration of extract significantly (P>0.05) reduced ulcer index in a dose dependent manner which establishes the ulcer healing potential of the said leaf. This could be attributed to the presence of flavonoids reportedly present in the extract which had been substantiated by Wenji et al. [17] who showed that flavonoids has gastroprotective potential.

5. CONCLUSION

It can be deduced from this study that methanol leaf extract of *Chromolaena odorata* could heal GIT wounds and does not inflict damage on the liver.

CONSENT

It is not applicable.

ETHICAL APPROVAL

Animal Ethic committee approval has been collected and preserved by the author(s).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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