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MORPHOLOGICAL ASSESSMENT OF THE PROTECTIVE EFFECTS OF *Annona muricata* SEED EXTRACT AGAINST POTASSIUM DICHROMATE STOMACH POISONING IN WISTAR RATS

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ABSTRACT
This study investigated the protective effects of *Annona muricata* seed extract against potassium dichromate ($K_2Cr_2O_7$) stomach poisoning in Wister rats. Seeds were extracted with ethanol, and 20 rats were divided into five groups. Group I received distilled water, Group II received 200 mg/kg extract, Group III received 20 mg/kg $K_2Cr_2O_7$, Group IV received 20 mg/kg pbw of $K_2Cr_2O_7$ followed by 200 mg/kg pbw of extract, and Group V received 200 mg/kg pbw of extract followed by 20 mg/kg pbw of $K_2Cr_2O_7$. Group I showed normal liver and stomach morphology. Group II showed normal stomach morphology. Group III showed stomach damage, disruption of surface epithelium, and leukocyte infiltration. Group IV showed normal stomach morphology, while Group V showed no pathological lesions. *Annona muricata* seed extract protects against $K_2Cr_2O_7$ stomach poisoning in Wistar rats, suggesting its potential against stomach poisoning in humans. Further molecular investigation is needed to understand the mechanism of action.

Keywords: *Annona muricata* seeds, morphology, stomach, Wistar rats, potassium dichromate, poisoning

INTRODUCTION
Annona muricata L. is a member of the Annonaceae family, and is widely distributed in Central and South America, including countries in the tropics (George *et al.*, 2012). Natives of varying countries have long cultivated this tropical tree plant due to its extensive applications in folk medicine (George *et al.*, 2014). It is commonly known as soursop, graviola, or custard apple by English-speaking people but is known locally as a shawa-shawa in Nigeria and can be found, grown or sold everywhere in the country (Moghadamtousi *et al.*, 2015). Other names in Nigeria-speaking dialects include ebo or apekan (Yoruba), sawanshop (Igbo), and fasadarur or tuwon biri (Hausa). Several preparations, especially decoctions from the bark, fruits, leaves, pericarp, seeds, and roots, have been extensively used in traditional medicine to treat multiple ailments, including cancers, by local communities in tropical Africa and South America (Rady *et al.*, 2018; Woode *et al.*, 2011). The aerial parts of *A. muricata* have several functions; the fruits have been widely used as food confectionaries while other parts like the barks have remarkable medicinal usage for varying ailments such as hypertension, diabetes, inflammation and parasitic infections (Pourmorad *et al.*, 2006; Omale *et al.*, 2008). The lanceolate dark green leaves of *A. muricata* are traditionally used as an antispasmodic nervine for heart conditions and as mild sedative (Coria-Téllez *et al.*, 2018). The leaves are applied to treat asthma, cough, fever, headache, hypertension, and toothache by herbalists (George *et al.*, 2012).

The use of other plants for medicine has greatly increased since it has been generally agreed that medicinal plants and their products are relatively safer than their synthetic counterpart drugs (Coria-Téllez *et al.*, 2018). *A. muricata* boasts a rich array of bioactive compounds, including acetogenins, alkaloids, flavonoids and essential oils, as well as vitamins and minerals, which exhibit potent antidiabetic, anticancer, anti-inflammatory, and antioxidant activities, making it a valuable resource for developing treatments for various diseases. Despite the numerous claims as documented in some literature, there are not enough scientific reports on the use of *A. muricata* seed extract in particular as far as this study can attest, which the major focus of this study is based. More so, information regarding the role of *A. muricata* seed extract in folk medicine relating to stomach injuries remains unclear. In addition, the incidence of abnormalities in cells/tissues is increasing, and generating concerns regarding the efficacy of the current treatment options. *A. muricata* is a plant traditionally used for its various medicinal benefits in synergy with other plants; they have been shown to have promising compounds that can be utilized in the treatment of cancers. Native to the tropical and subtropical parts of the world, *A. muricata* plant extracts contain compounds particularly effective against abnormal cells/tissues. Field research suggests that *muricata*-derived substances have potential properties that include anti-inflammatory, anti-diabetic, anticancer, and cytotoxic effects in laboratory experiments. In all of these, there are limited reports on

the seed extracts and possible regenerative or protective effects on hepatic and renal pathology. It is against this backdrop that the current study focused on one of the vital internal organs due to its vast functions in humans, which is always at the receiving end whenever there is an intake of poisonous substances whether consciously or unconsciously.

The potent antioxidant and anti-inflammatory properties of *A. muricata* seeds make them a promising natural remedy for treating stomach injuries, with potential for future therapeutic applications. Also, it may lead to a scientific breakthrough in the development of pharmacological products directed toward the aforementioned organ if properly harnessed. The general public stands to benefit from the data published on the use of *A. muricata* seed for preserving and or protecting the stomach. Data generated from this study will assist in making policymakers to make policies in the interest of the public.

MATERIALS AND METHODS

Plant collection and authentication

Annona muricata fruits were purchased from Benin City in New Benin local market. Samples of fresh fruits of *A. muricata* were identified and authenticated at the Department of Plant Biology and Biotechnology, University of Benin, by Prof. Henry A. Akinnibosun. Afterward, a sample plant was deposited at the Departmental Herbarium, and a voucher number, UBH**A**452, was assigned for referral and cross-reference of possible changes to any previously done research on *A. muricata*.

Experimental animals and grouping

Twenty healthy Wistar rats (*Rattus norvergicus*) of both sexes, aged 2-4 months old and weighing 130-180 g, were used for this study. They were housed in well-ventilated, standard, clean cages made of plastic and wire gauze. Wood shavings were used as bedding to keep each compartment dry. Normal standard ambient conditions of temperature between 28 - 31°C, relative humidity between 50 – 60%, and a photoperiodicity of 12 h of natural light and 12 h of darkness were maintained. Animals were allowed to acclimatize for 14 days to adapt to their new environment properly and were weighed fortnightly. They had access to pelletized feeds (growers mash feed) and tap water provided *ad libitum*. Animals were grouped into five cages and named (Group I to V), while each group consisted of 4 rats (n=4).

Physical and empirical measurements

The animals were monitored for behavioral uses of acute toxicity, such as reduced activity, dullness, restlessness, hair loss, and watery stool, following the method adopted by Atoigwe *et al.* (2016), Odigie *et al.* (2015). Activities like dullness and reduced activity were monitored a few hours after treatment. The method described by Ajiboso *et al.* (2007) was used to determine the body weight of experimental rats. Individual rats were monitored for daily gain in body weight using a digital electronic balance (Gilbertini, Italy).

Animal ethics statement and clearance

All ethical and human considerations, as well as euthanasia of the animals, were considered and performed according to humane conditions. Experimental procedures were carried out according to the Institutional Animal Ethics Committee (IAEC) guidelines, published by the US National Institute of Health (NIH publication No. 85-23, revised 1996), Ensuring respect for life of experimental animals, societal benefit of using these animals and non-maleficence of experimental animals. Ethical issues relating to animal experimentations were approved by the animal care ethics committee of the Ministry of Agriculture and Natural Resources (clearance No. V.1034/41).

Plant preparation and extraction

Seeds were removed from the freshly obtained fruits, washed, sterilized with 70% ethanol, and air-dried for two weeks. Dried samples were pulverized by blending into uniform powder with an electric blender. It was sieved and repeatedly pulverized into uniform powder until a pure, fine powdered particle was obtained (exhaustive pulverization). The powder was weighed with an electric weighing balance (electronic compact scale), which weighed 1.283 kg. The seeds were extracted using a Soxhlet extractor and ethanol as extraction solvent at 220 v. Afterward, the solution was filtered with a white sterile muslin cloth to obtain the filtrate. At the same time, the residue was re-airdried, transferred into the extractor, and re-filtered repeatedly until an exhaustive extraction was achieved, in which the solution became colorless after adding the solvent (ethanol). The filtrate was evaporated in a water bath at 56.4^{o}C to obtain the crude extract weighing 41.5 g, which was used to prepare the stock solution for this experiment.

Acute toxicity (LD50) testing

Before the experiment, the acute toxicity study of *A. muricata* was determined using an adaptation from Woode *et al.* (2011), low to moderate doses of the extract demonstrated no toxicity in animal tissues. Nine (9) rats were divided into three groups of three (3) rats per cage. In this progression, the rats were given extrapolated doses from the aqueous extract: 200, 400 and 800 mg/kg pbw. daily for two weeks, keenly observed for 24 h if there was mortality and intermittently after that. The estimated lethal dose of potassium dichromate was 0.1-1 g, adopted from Sharma *et al.* (1978).

Gross and histology

At the end of the experiment, all rats were sacrificed by cervical dislocation. Stomachs were excised from all animals; they were grossed and studied before fixing in 10% neutral buffered formalin for tissue processing after cutting tissues at 3-5 mm. Cut tissues were processed in an automatic tissue processor for dehydration, clearing, and impregnation using molten paraffin wax while embedding was done with an embedding machine. Sections were obtained at 3-5 microns with the digital (Hertz) rotary microtome (German mode) to produce serial ribbon while staining

of the sections was according to the H&E method (Avwioro, 2010; Baker *et al.*, 2001).

Microscopy and photomicrography

Two or more pathologists at the University of Benin Teaching Hospital (UBTH), Benin City, reviewed study slides. Sections were examined using a Leica DM500 Binocular microscope, and photomicrography was conducted with an Optic-shot: Al-triple camera attached to the eyepiece of the microscope.

Statistical analysis

Data were presented as Means ± SD and analyzed using one-way ANOVA and Duncan post hoc test. Significance was determined at $p < 0.05$ using Statistical Package for Social Sciences (SPSS) version 16.0 (Inc *et al.*, USA).

RESULTS AND DISCUSSION

Signs of acute toxicity were evident in rats administered with high dose of 20 mg/kg pbw of $\mathbf{K_2Cr_2O_7}$, indicating severe adverse effects such as prolonged sleep, dullness, and reduced activities. At the same time, empirical measurements showed increased weight in all treated animals, particularly in Group I and influentially in Group II. Physical activities of animals in Groups III, IV, and V treated with $\mathbf{K_2Cr_2O_7}$ showed signs of dullness and reduced activities but was more pronounced in Group III. The stomachs of rats treated with $\mathbf{K_2Cr_2O_7}$ showed slight variation in consistency but no changes in color, while the mean weight was 5.1 g. Each tissue was palpated and reported to have a soft tan consistency (Plate 1–4). The mean weights of the stomachs of animals in Group I and II (controls) were compared with those of other groups (III, IV, and V). There was a noticeable difference of 0.8 g decrease in the mean weight of rats in Group III (negative control). The cut surface of the stomach was smooth with a pale pinkish color with fine ridges (Plate 1). For rats in Group III treated with $\mathbf{K_2Cr_2O_7}$, their cut surfaces were smooth like other groups but appeared dull (Plate 2). Histopathology findings are in keeping with the normal histology of organs examined, and there was no evidence of necrosis or deleterious effects seen at the cellular level for sections from (Groups I, II, IV, and V). However, Group III showed evidence of pathologic effects: disruption of surface epithelium mucosa, mucosal damage, and leukocyte infiltration in sub-mucosa and muscularis mucosa, respectively. Photomicrographs of the test and control sections are shown below with their corresponding pathological effects (Plate 5–9).

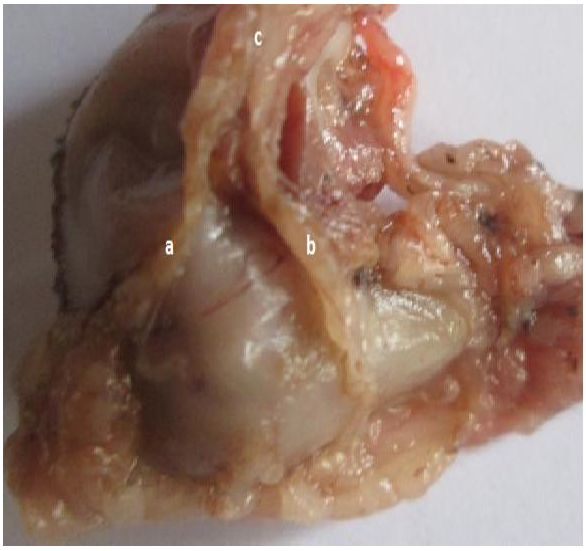

Plate 1: Gross examination of the stomach of rats in Group II treated with 200 mg/kg body weight (pbw) of extract once a week for two weeks (cut surface) Macro-anatomy revealed a normal pattern (a) = greater curvature (b) = lesser curvature and (c) = *incisura angularis* (Optic-shot: X5)

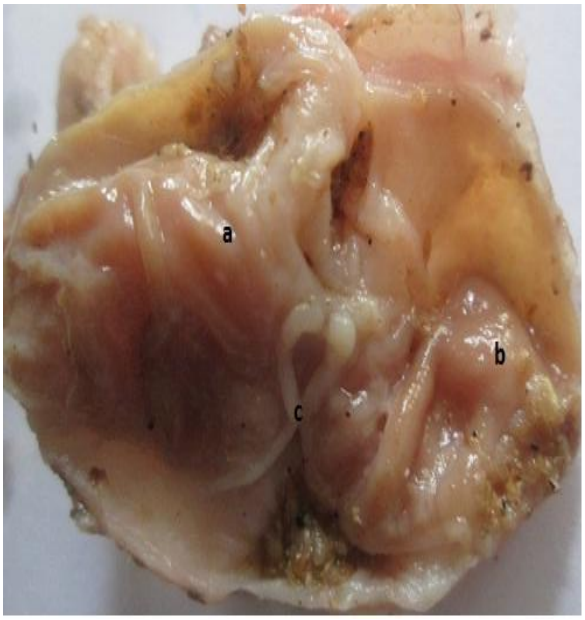

Plate 2: Gross examination of the stomach (cut surface) of rats in Group III (Negative Control). Macro-anatomy revealed a dull appearance but normal pattern (a) = greater curvature, (b) = lesser curvature, and (c) = *incisura angularis* (Optic-shot: X5)

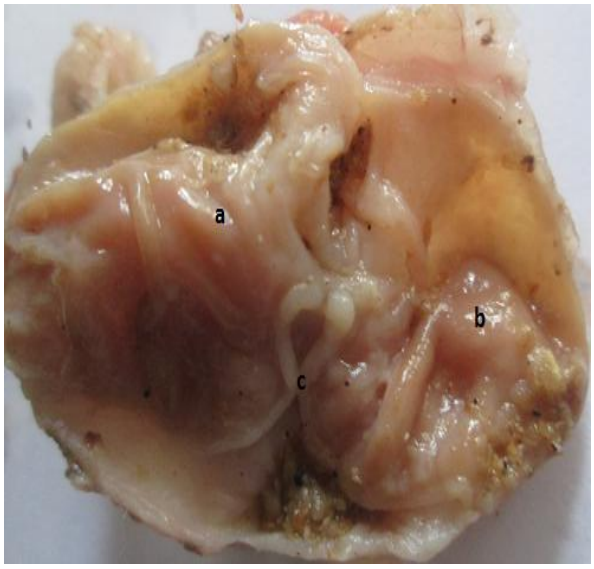

Plate 3: Gross examination of the stomach of animals in Group IV treated with a single dose of 20 mg/kg pbw of $K_2Cr_2O_7$ poison in the first week followed by 200 mg/kg pbw of extract daily in the second week (ventral views). Macro-anatomy revealed a normal pattern (a) = peritoneal folds, (b) = surrounding folds and (c) cardia - conical portion of the stomach (Optic-shot: X5)

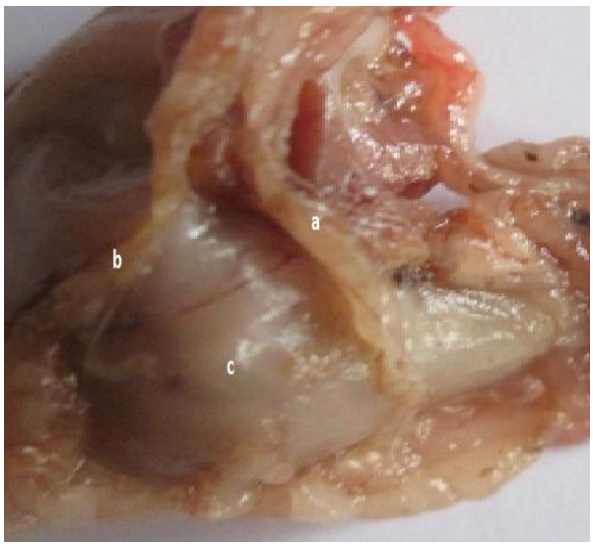

Plate 4: A gross examination of the stomach of rats in Group V administered 200 mg/kg pbw of extract once daily for one week followed by a single dose of 20 mg/kg pbw $K_2Cr_2O_7$ poison at the end of the week and was repeated in the second week (ventral view). Macro-anatomy revealed a dull appearance but with a normal pattern (a) = peritoneal folds, (b) = surrounding folds, and (c) the antrum (Optic-shot: X5)

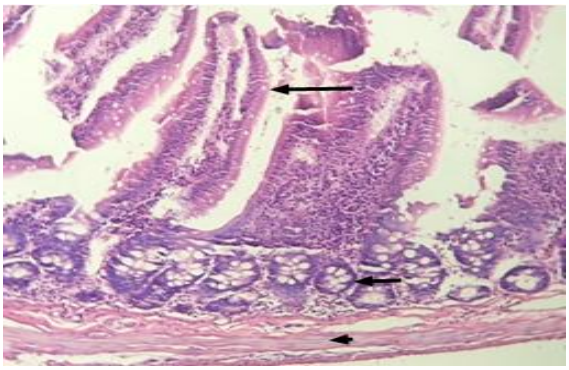

Plate 5: Photomicrograph of untreated rat's section of the stomach in Group I (control) showed normal stomach histology. It revealed visible mucosa containing a secretory sheath with prominent gastric pits (long arrow), which appeared lined with columnar epithelium. Above the muscularis mucosa are prominent gastric glands and below are connective tissues (short arrow). With H&E: x400 magnifications

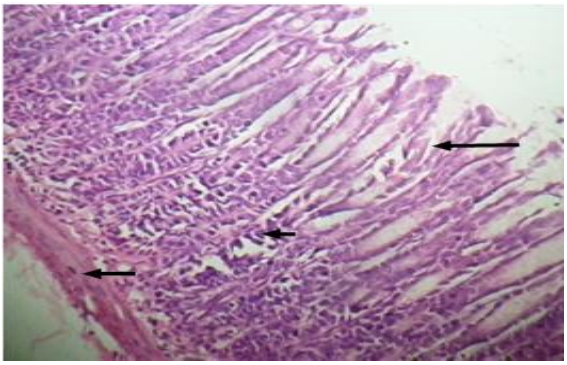

Plate 6: Photomicrograph of treated section of rat's stomach of animals in Group II (administered 200 mg/kg pbw *A. muricata* seed extract once daily for two weeks) showed the tissue appeared normal under histological examination. It revealed tightened surface epithelium mucosa and mucosal (long arrow) with prominent sub mucosa and muscularis mucosa (short arrow) without evidence of pathologic effects. With H&E: x400 magnification

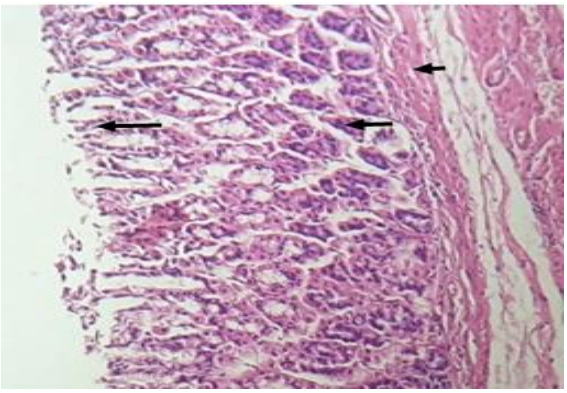

Plate 7: Photomicrograph of treated sections of the stomach of rats in Group III (administered 20 mg/kg pbw $K_2Cr_2O_7$ 20 mg/kg once a week for 2 weeks) revealed disruption of surface epithelium mucosa and visible mucosal damages (long arrow) with visible leukocyte infiltration in the submucosa and muscularis mucosa (medium arrow). The gastric glands appeared slightly disrupted in shape and colour with pathologic lesions. With H&E: x400 magnification

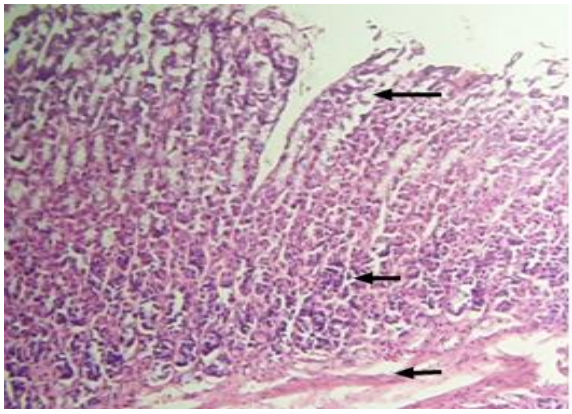

Plate 8: Photomicrograph of treated section of rat's stomach in Group IV (administered a single dose of 20 mg/kg pbw of $K_2Cr_2O_7$ in the first week followed by 200 mg/kg pbw of extract daily in the second week). It revealed normal histology of the epithelium mucosa and mucosal (long arrow), submucosa, and muscularis mucosa (with short arrow) With H&E: x400 magnification

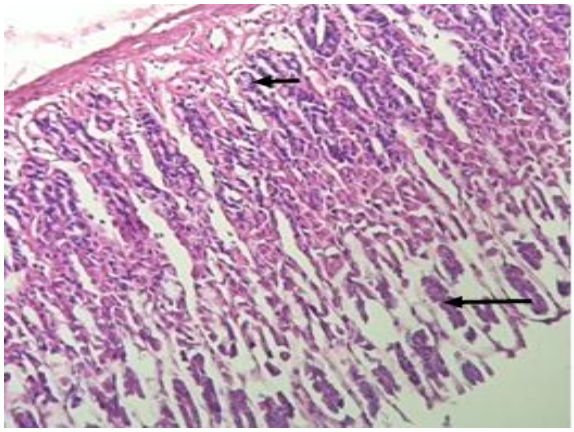

Plate 9: Photomicrograph of stained section of treated rat's stomach in Group V (administered 200 mg/kg pbw of extract once daily for one week and a single dose of 20 mg/kg pbw $K_2Cr_2O_7$ afterward) revealed no pathologic lesion in the surface of the epithelium mucosa and mucosal (long arrow) as well as submucosa and muscularis mucosa (short arrow) of the stomach. With H&E: x400 magnification

Annona muricata plays a significant role in traditional medicine, particularly in the treatment of cancer and various degenerative health disorders (Dreosti, 2000). The role of *A. muricata* aqueous seed extracts before and after $K_2Cr_2O_7$ poisoning in experimental animals was investigated in this study, which seeks to know if *A. muricata* aqueous seed extracts have ameliorative effects on the stomach of rats exposed to $K_2Cr_2O_7$ poisoning or protective effects in animal model. Potassium dichromate ($K_2Cr_2O_7$) is a known potent carcinogen used extensively in cancer research (Danadevi *et al.*, 2004). The observed significant increased body weight in the groups treated with *A. muricata* might have resulted from the high caloric value of the seed, as reported by Onimawo (2002), who found out that *A. muricata* seed has a high carbohydrate content (55.1%) which suggests a high caloric value of the seed compared to those treated with $K_2Cr_2O_7$ alone that resulted to reduced body weight. Treatment with ethanoic seed extract of *A. muricata* resulted in elevated body weight and organ weight in rats, suggesting that the extract increased appetite and feed efficiency, enhanced nutrient metabolism and utilization by tissues and cells of the body, and prevented loss of body nutrients (Osmund, 2001; Oyewole & Oladele, 2017).

In the present experiment, rats used as positive control fed with pellets and water only had normal histological appearance of the stomach walls; the mucosa, submucosa, muscularis externa and serosa. The histologic micrographs revealed the average and relative thickness of the four primary layers of the stomach: mucosa, submucosa, muscularis externa, and serosa, which appeared normal. Group II received 200 mg/kg pbw *A. muricata* seed extract once daily for two weeks compared with the positive control that was fed food and water, which only showed normal histology without evidence of necrosis or pathologic effects, suggesting that the seed extract is safe and consumable. There was also a noticeable increase in body weight from the initial body weight, which can be attributed to the high caloric value of the seed (Onimawo, 2002) and the presence of minerals such as calcium, sodium, iron, potassium, copper, and magnesium that suffice the supply of the essential nutrients upon consumption (Lererme *et al.*, 2006). This report is similar to the report by Omale *et al*. (2008) in which *A. muricata* has a remarkably satisfactory and refreshing taste.

Meanwhile, rats in Group III (Negative control) that received 20 mg/kg pbw $K_2Cr_2O_7$ showed disruption of surface epithelium mucosa and mucosal damages with visible leukocyte infiltration in the submucosa and muscular mucosa in the stomach, which is due to the effect of $K_2Cr_2O_7$ poisoning and further confirmed that animals in Group III were poisoned. The visible abnormality/degenerative changes in the stomach resulting in the erosive lesions of the mucosa that extended to deeper layers is also evidence of a severe pathologic effect from $K_2Cr_2O_7$ poisoning. The gastric glands that appeared severely disrupted in shape and color suggest stomach poisoning and have been reported earlier by Oyewole and Oladele (2017).

Stomach rats in group IV were administered a single dose of 20 mg/kg pbw of $K_2Cr_2O_7$ in the first week, followed by 200 mg/kg pbw of extract daily in the second week showed no pathologic effects, which strongly suggests that the action of the extract was able to overturn the effects of $K_2Cr_2O_7$ poisoning in this experiment. Therefore, the effects exerted by *A. muricata* seed extract in Group IV can be said to be ameliorative rather than protective. This action is made possible due to the possession of tannins widely available in all parts of the *A. muricata* plant. Tannins are known to be beneficial for preventing cancer and

treating inflamed or ulcerated tissues (Li & Liu, 2003; Okwu & Emenike, 2006). This is why there is a quick reversal of injured or damaged stomachs within two weeks of *A. muricata* treatment in experimental rats. Rats in Group V were administered 200 mg/kg pbw of extract once daily for a week, followed by a single dose of 20 mg/kg pbw **$K_2Cr_2O_7$**, revealing normal histology closely similar to those in Group IV.

Behavioral observations

Group III ($K_2Cr_2O_7$): The prolonged sleep, dullness, and reduced activity observed in this group indicate severe neurotoxicity and general systemic distress. These behavioral changes are consistent with the known toxic effects of potassium dichromate, which include oxidative stress and cellular damage (Pourmorad *et al.*, 2006; Coria-Téllez *et al.*, 2018).

Groups IV and V (*A. muricata* + $K_2Cr_2O_7$): The improved behavior in these groups suggests that *A. muricata* seed extract has neuroprotective properties, likely due to its antioxidant components, which mitigate oxidative stress and enhance neuronal function (Coria-Téllez *et al.*, 2018).

Weight changes

Group III ($K_2Cr_2O_7$): The significant weight loss observed in this group underscores the severe metabolic and systemic toxicity induced by potassium dichromate.

Groups IV and V (*A. muricata* + $K_2Cr_2O_7$**):** The recovery and increase in body weight in these groups suggest that *A. muricata* seed extract enhances metabolic efficiency and nutrient utilization, counteracting the catabolic effects of $K_2Cr_2O_7$.

Histopathological findings

Group III ($K_2Cr_2O_7$): The disruption of surface epithelium, mucosal damage, and leukocyte infiltration observed in this group are hallmarks of severe gastric toxicity. These findings are consistent with previous studies that have documented the corrosive and inflammatory effects of potassium dichromate on gastric tissues and other organs (Baker *et al.*, 2001).

Groups IV and V (*A. muricata* + $K_2Cr_2O_7$): The normal histology observed in these groups indicates that *A. muricata* seed extract effectively prevents and repairs gastric tissue damage. This protective effect is likely due to the presence of bioactive compounds such as tannins, flavonoids, and phenolics, which have known anti-inflammatory and antioxidant properties (Coria-Téllez *et al.*, 2018). This signifies a preventive effect of the extract against degenerative changes that may have occurred from stomach exposure to potassium dichromate. The effect can thus be attributed to the preventive functions of *A. muricata* seed extract due to the phytochemicals that contribute significantly to protection against degenerative diseases (Dreosti, 2000). One such phytochemicals is the flavonoids and phenolics, which are free radical scavengers that prevent oxidative cell damage and inhibit tumor invasion (Rafat *et al.*, 1987). Flavonoids and phenolics are free radical scavengers that prevent oxidative cell damage and have anticancer solid activities (Pourmorad *et al.*, 2006; Ugwu *et al.*, 2013). They might induce mechanisms that affect cancer cells and inhibit tumor invasion (Rafat *et al.*, 1987). Furthermore, their activities could be attributed to their ability to neutralize and quench free radicals (Ugwu *et al.*, 2013) and may be due partly to any of the following: redox properties of flavonoids and phenolics (Omale & Okafor, 2008), the presence of conjugated ring structures and carboxylic group (Pourmorad *et al.*, 2006), which have been reported to inhibit lipid peroxidation (Rice-Evans *et al.*, 1995). Therefore, the action of *A. muricata* before and after ($K_2Cr_2O_7$) treatment in this experiment buttresses the report relating to anticancer and anti-inflammatory activities of the present extract (Simpson and Amos, 2016). Similarly, Randy *et al.* (2018) reported that *A. muricata* leaf extract demonstrated notable protective effects on acute and chronic inflammations in experimental rats.

We have integrated a more thorough comparison of our findings with existing literature to highlight the significance of our study

Protective effects of *A. muricata*: Our findings align with previous research that has demonstrated the protective effects of *A. muricata* against various forms of toxicity. For instance, Rady *et al.* (2018) reported that *A. muricata* leaf extract has notable protective effects against acute and chronic inflammation in experimental rats. Our study extends these findings by demonstrating similar protective effects in the gastric context.

Antioxidant and anti-inflammatory properties: The observed protective effects of *A. muricata* seed extract can be attributed to its rich content of antioxidants and anti-inflammatory compounds. Studies by Pourmorad *et al.* (2006), Coria-Téllez *et al.* (2018) have documented the high antioxidant activity of *A. muricata*, which supports our findings of reduced oxidative stress and tissue damage in treated rats.

To elaborate more on the potential mechanisms through which *A. muricata* seed extract exerts its protective and ameliorative effects

Revised mechanisms discussion section: The presence of flavonoids and phenolics in *A. muricata* seed extract likely contributes to its antioxidant activity. These compounds are known to scavenge free radicals, reducing oxidative stress and preventing cellular damage (Coria-Téllez *et al.*, 2018). This mechanism is supported by the observed reduction in gastric tissue damage and improved overall health in treated rats.

Tannins and other polyphenolic compounds in *A. muricata* have anti-inflammatory properties that help reduce leukocyte infiltration and tissue inflammation (Rady *et al.*, 2018). This is a proof in the histological findings that, the treated rats showed normal gastric histology with no signs of inflammation.

The increase in body weight and improved behavior in treated rats suggest that *A. muricata* seed extract enhances nutrient absorption and metabolic efficiency, which could be due to the extract's ability to improve

gastrointestinal health and function (Oyewole and Oladele, 2017), thereby enhancing overall nutrient uptake and utilization.

CONCLUSION

This study provides conclusive evidence that *Annona muricata* (soursop) seed extract offers substantial protection and alleviation against stomach damage induced by potassium dichromate ($K_2Cr_2O_7$) in Wistar rats.

The key findings of this research are

Behavioral Observations: Rats treated with $K_2Cr_2O_7$ alone exhibited prolonged sleep, dullness, and reduced activity, indicating severe toxicity. In contrast, rats treated with *A. muricata* seed extract either before or after $K_2Cr_2O_7$ exposure showed normal behavior, suggesting a protective effect of the extract.

Weight Changes: There was a noticeable increase in body weight in rats treated with *A. muricata* seed extract, indicating enhanced nutrient metabolism and utilization. Conversely, rats exposed to $K_2Cr_2O_7$ alone experienced weight loss, highlighting the extract's role in mitigating the toxic effects of $K_2Cr_2O_7$.

Histopathological Findings: The stomachs of rats treated with $K_2Cr_2O_7$ alone displayed significant pathological changes, including disruption of the surface epithelium, mucosal damage, and leukocyte infiltration. However, rats treated with the seed extract either before or after $K_2Cr_2O_7$ exposure showed normal stomach histology, with no evidence of necrosis or deleterious effects.

Protective vs. Ameliorative Effects: The study found that *A. muricata* seed extract administered before $K_2Cr_2O_7$ exposure had a protective effect, preventing degenerative changes in the stomach. When administered after $K_2Cr_2O_7$ exposure, the extract exhibited ameliorative effects, reversing the toxic damage.

Significance and contribution

The significance of this study lies in its potential application for human health, particularly in the context of managing stomach poisoning and related gastrointestinal disorders. The findings contribute to the growing body of evidence supporting the use of medicinal plants in therapeutic settings. Specifically, the study highlights:

Therapeutic Potential: *A. muricata* seed extract could be developed as a natural therapeutic agent for protecting and treating stomach poisoning caused by toxic substances like potassium dichromate.

Nutritional Benefits: The extract's ability to enhance body weight and nutrient utilization suggests it could also be beneficial in improving overall nutritional status.

Phytochemical Efficacy: The presence of tannins, flavonoids, and phenolics in *A. muricata*, known for their antioxidant and anti-inflammatory properties, provides a scientific basis for its protective and ameliorative effects.

Future directions

Further molecular research is warranted to elucidate the mechanisms by which *A. muricata* seed extract exerts its protective effects. Long-term safety studies and comparative analyses with other therapeutic agents will help establish its efficacy and safety profile, potentially leading to its inclusion in clinical practice for managing stomach poisoning and other related conditions.

Recommendation

Future research should investigate the molecular mechanisms of *A. muricata* seed extract in protecting against stomach poisoning and explore its potential as a therapeutic agent. Additionally, exploring bioavailability and pharmacokinetics is crucial. These areas are justified as they will enhance understanding of the extract's therapeutic potential, ensure safety, optimize dosing, and validate its effectiveness in humans, thereby facilitating its clinical adoption. Methodologically, this involves advanced analytical techniques, randomized controlled trials, and longitudinal studies with rigorous monitoring.

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