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PHYTOCHEMICAL STUDIES, TOXICOLOGICAL CHARACTERIZATION AND ANTIULCEROGENIC EFFECTS OF AQUEOUS FRUIT EXTRACT OF SOLANUM MACROCARPON IN ALBINO RATS

Elendu Melford Uche[1], Uche Mercylyn Ezinne*[2], Ekweogu Celestine Nwabu[2]

[1]Department of Physiology, Imo State University, Owerri, Imo State.
[2]Department of Medical Biochemistry, Imo State University, Owerri, Imo State.

***Corresponding Author: Uche Mercylyn Ezinne**

Department of Medical Biochemistry, Imo State University, Owerri, Imo State.

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ABSTRACT

The fruit of *Solanum macrocarpon* is used in traditional medicine to treat sore throat, heart diseases and as an antihelminthic agent. The present research evaluated the phytochemistry, toxicity studies and antiulcerogenic effects of aqueous fruit extract of *Solanum macrocarpon* in rats. Animals were grouped (n=5/group) for acute toxicity test and treated with variuos doses of the fruit extract: 500mg/kg, 1000mg/kg and 2000mg/kg, 3000mg/kg, 4000mg/kg and 5000mg/kg according to the method described by OECD. For subacute toxicity and ulcer studies, rats were grouped (n=6/group). For toxicity study, group 1 served as the normal control while groups 2, 3 and 4 received 150mg/kg, 300mg/kg and 600mg/kg of *Solanum macrocarpon* fruit extract via daily gavage for 14 days respectively. For the ulcer experiment, groups 1,2 and 3 served as normal, negative and positive control respectively while groups 4, 5 and 6 received 150mg/kg, 300mg/kg and 600mg/kg of *Solanum macrocarpon* fruit extract respectively. All analysis and measurements were done using standard laboratory methods. In acute toxicity experiment, no signs of toxicity and no mortality was recorded. Animals evaluated for biomarkers: liver, kidney, lipid profile, haematological and antioxidant parameters did not show any sign of toxicity while ulcer study revealed antiulcer effect of *Solanum macrocarpon* fruit. This study shows that *Solanum macrocarpon* is safe with potent antiulcerogenic effects.

KEYWORDS: Antioxidant, toxicity, haematological, antiulcerogenic, *Solanum macrocarpon.*

INTRODUCTION

Medicinal plants are those species of the plant kingdom, whose parts (flowers, leaves, roots, stems, fruits, or seeds) are directly used or used in some preparation as a medicine to treat a condition or disease. Knowledge of the beneficial properties of medicinal plants to treat diseases represents a valuable resource to preserve the biological and cultural diversity of different ethnicities (Juan, 2021). They are a valuable source of a wide variety of chemical molecules having different structures and functionalities that exhibit important biological activities and are linked to a multitude of beneficial properties, such as antimicrobial, anticancer, antiviral, antioxidant and enzyme inhibitory, anti-aging, anti-inflammatory, antihypertensive, neuroprotective and anticoagulant effects (Lesellier et al., Ali et al., 2019; 2021). Both industrialized and developing countries are increasingly recognizing and developing these plants' medical properties and economic benefits (Refaz et al., 2017). Because plant products contain natural antioxidants, are easily affordable, readily available, have little to no side effects and contraindications, at least 80% of the world population especially those living in sub-saharan Africa rely on the use of medicinal plants as the mainstay in the cure of various diseases (Licciardi and Underwood, 2011; Ugbogu et al., 2018; Akubugwo et al., 2022). Life-threatening diseases such as cancer and stroke, hypertension and diabetes are managed using these plant constituents (Ugbogu et al., 2024). The seed, root, leaf, fruit, skin, flowers or even the whole plant may be used as raw materials in phytomedicine. In the body of these plants, certain materials are produced and

stored that are referred to as active compounds (substances), which have physiological effects on the living organisms (Kurek, 2019).

Solanum macrocarpon, also known as African eggplant or locally as akpuru-efe or Igbagba, is a plant of the family Solanaceae. *S. macrocarpon* is a tropical perennial plant that is closely related to the eggplant (Oboh et al., 2005). *S. macrocarpon* originated from West Africa, but is now widely distributed in Central and East Africa. *Solanum macrocarpon* can grow to a height of 1-1.5 m. It has an alternate leaf pattern with a blade width of 4–15 cm and a height of 10–30 cm. The shapes of the leaves are oval and lobed with a wavy margin. Both sides of the leaves are hairy with stellate or simple hairs. Prickles may or may not be present on the leaves depending on the cultivar. The roots, leaves, and fruit of *S. macrocarpon* contain medicinal qualities. In Nigeria, the fruit is used as a laxative, as a means to treat cardiac diseases and for weight loss (Ibrahim et al., 2024). The flowers are chewed to clean teeth (Oboh et al., 2005). In Sierra Leone the leaves are heated and then are chewed to ease throat pain. In Kenya the roots are boiled and the juice is then consumed to kill any hookworms in the stomach.

Ulcers are open sores that can develop on the skin, mucous membranes, or inner linings of organs. They can occur in various areas, such as the stomach (peptic ulcers), mouth (canker sores), and skin (pressure ulcers). Peptic ulcer disease refers to ulcerations in the stomach and duodenum and involves breaks in the full thickness of the gastrointestinal mucosa (i.e., extending into a deeper layer beneath the mucosa). Gastric acid and pepsin are central to the pathogenesis of peptic ulcer disease (James et al., 2017). *Helicobacter pylori* infection, the use of non-steroidal anti-inflammatory drugs (NSAIDs), and aspirin are leading causes of gastric and duodenal ulcers; idiopathic ulcers account for the remaining ulcers that occur in the absence of identifiable causes (Majid et al., 2024). Factors like bacterial infection, excessive acid production, poor circulation, or injuries can contribute to their formation. Ulcers can significantly impact a person's quality of life, causing discomfort, pain, adhesions, gastrointestinal tract bleeding and other complications (Jaiswal *et al*., 2021).

Most of the *Solanum* species have antiulcer properties and have also proven to be non-toxic in acute, subacute and sub-chronic studies (Anosike et al., 2011; El-Feky et al., 2024).

METHODOLOGY

Plant collection and identification

The fruits of *Solanum macrocarpon* was harvested from a farmland in Akanu Item, Bende Local Government of Abia State and identified by a taxonomist in the Department of Plant Science and Biotechnology, Imo State University, Owerri. Ethical clearance was be obtained from the Ethical Committee of Animal Care Use of the Faculty of Basic Medical Sciences, College of Medicine, Imo State University, Owerri for the use of these animals.

Sample Preparation

Freshly harvested *S. macrocarpon* fruits was cut into tiny pieces, sorted, washed, and air-dried for 24 hours. In line with the local herbal medicine preparation, 1kg of the cut fruit was boiled in a flask containing 2 litres of water for 1 hour. After cooling, the boiled extract was filtered using a Whatmann No1 and the filtrate freeze dried at -8^0C and then stored at 8^0C until when the need for use arises.

Phytochemical Screening of the Extract and Fractions

Qualitative and quantitative phytochemical screening of ASEPA and fractions were carried out according to the procedures outlined by Harborne (1998) to determine the presence and concentrations of the secondary metabolites.

Animal handling

Healthy male albino rats (200 - 240 g) was purchased from the animal house of the Department of Veterinary Medicine, College of Medicine, University of Nigeria for this study. The rats were allowed to acclimatize to laboratory conditions for two weeks prior to commencement of the experiment. They were kept under normal standard environmental condition of temperature (25-28^{o}C), humidity (35-60 %) and 12 h/12 h light/darkness cycles. Animals were fed *ad libitum* with standard rat were also allowed free access to water. Ethical principles World Health Organization of good laboratory practice regulations of 1998 and United States guidelines for experimental animals (Care Animal Use Committee, NRC, 2010) was strictly adhered to throughout the study.

Acute Toxicity Test

The acute toxicity study of the *Solanum macrocarpon* fruit extract was carried out by the methods described by OECD (2001) 423 (OECD, 2001; OECD 2008) guideline with little modifications. Forty-two male albino Wistar rats were randomly divided into 7 groups of 6 rats in each group. Group 1 served as a normal control received no treatment while groups 2-7 received a single oral administration of graded doses (500, 1000, 2000, 3000, 4000 and 5000 mg/kg respectively) of aqueous extract of *Solanum macrocarpon*. The rats were allowed free access to food and water *ad libitum* and monitored for a period of 24 h post-treatment. Within and after the period of 24 h, behavioural changes and signs of toxicity were assessed.

Subacute Toxicity Study

The method established by OECD guideline (OECD, 2001; OECD, 2008) 407 and 425 with some modifications was adopted for this study. Twenty (20)

male albino rats were randomly divided into four (4) groups of six rats each.
Group *I*: Normal control.
Group II: Treated orally with 150mg/kg body weight of Solanum macrocarpon aqueous fruit extract.
Group III*:* Treated orally with 300mg/kg body weight of Solanum macrocarpon aqueous fruit extract.
Group IV*:* Treated orally with 600mg/kg body weight of Solanum macrocarpon aqueous fruit extract.

The experimental animals for anti-ulcer determination were randomly divided into six (6) groups with six (6) rats per group

Experimental Design for Ibuprofen
Group I: Normal control rats will receive 0.2 ml of distilled water
Group II: Negative control (untreated ibuprofen induced ulcer rats)
Group III: Pretreated ibuprofen induced ulcer rats with 20mg/kg body weight of reference drug (omeprazole)
Group IV: Wistar rats that will be pretreated with 150mg/kg of *Solanum macrocarpon* aqueous fruit extract before ulcer induction.
Group V: Wistar rats that will be pretreated 300mg/kg of *Solanum macrocarpon* aqueous fruit extracts before ulcer induction.
Group VI: Wistar rats that will be pretreated with 600mg/kg of *Solanum macrocarpon* aqueous fruit extracts before ulcer induction.

Experimental Design for ethanol
Group I: Normal control rats that will receive 0.2 mL of distilled water
Group II: Negative control (untreated ethanol induced ulcer rats)
Group III: Pretreated ethanol induced ulcer rats with 20mg/kg body weight of reference drug (Omeprazole)
Group IV: Wistar rats that will be pretreated with 150mg/kg of *Solanum macrocarpon* aqueous fruit extract before ulcer induction.
Group V: Wistar rats that will be pretreated with 300mg/kgof *Solanum macrocarpon* aqueous fruit extract before ulcer induction.
Group V: Wistar rats that will be pretreated with 600mg/kg of *Solanum macrocarpon* aqueous fruit extract before ulcer induction.

Measurement of Body Weight
The experimental animals' body weights were measured on days 0, 7 and 14 during the administration of plant fruit extracts. The body weights are expressed as mean ± body weight (g).

Treatment of Experimental Animals
The experimental animals will be administered with the extract by oral gavage every day for 14 days. On the 14th day, the animals will be starved, anaesthetized with chloroform and sacrificed on the 15th day.

Blood Collection
Fourteen (14) days after feeding the rats with the aqueous extract, they were fasted overnight, anaesthetized with chloroform and sacrificed on the 15th day. Blood was collected by cardiac puncture using syringe and needle and blood samples from each animal collected into dry sample bottles for clinical chemistry analysis and EDTA (Ethylenediaminetetraacetic acid) container for haematological studies. The sample bottles with whole blood were allowed to stand for 15 minutes to clot and further spun at 12,000 rpm for 5minutes using the centrifuge. The serum was separated from the clotted blood with Pasteur pipette into sterile sample test tubes for the measurement of biochemical parameters.

Collection of Organs
The organs, namely, liver, kidney, heart and spleen were dissected and removed carefully and absolute weights of each organ determined. The relative organ weight of individual wistar rats was calculated as follows:
Relative organ weight = (Absolute organ weight (g) / Body weight of rat on sacrificed day (g) × 100

Haematological and Clinical Biochemical Analysis
Assessment of full blood count parameters which include haematocrit/packed cell volume (PCV), haemoglobin (Hb), white blood cell count (WBC), platelets, mean corpuscular haemoglobin (MCH), mean corpuscular haemoglobin concentration (MCHC), mean corpuscular volume (MCV), and WBC differentials was done using an automated haematocrit analyzer (model BC-2800 Mindray Company, China). Lipid profile (total cholesterol, triacylglycerol, high density lipoprotein cholesterol, low density lipoprotein cholesterol and very low density lipoprotein cholesterol), kidney function parameters (urea, creatinine, potassium, sodium, bicarbonate and chloride), liver function parameters (alkaline phosphatase, alanine aminotransferase, aspartate aminotransferase, total protein, albumin, globulin and bilirubin) were measured using standard laboratory kits by Randox Laboratory Ltd., Co., Antrim United Kingdom. The method described by Kanu et al. (2016), was used to assess the various antioxidant parameters: malondialdehyde, catalase, glutathione and superoxide dismutase.

Ibuprofen-Induced Ulcer
The rats were starved for 24 h prior to the commencement of this study, but had access to clean drinking water. Groups I and II rats were orally pretreated with 0.2 mL distilled water using a gavage tube. Group III animals were pretreated with omeprazole (a reference ulcer drug) at 20mg/kg body weight of rat. Groups IV, V and VI will receive 150mg/kg, 300mg/kg and 600mg/kg oral *Solanum macrocarpon* extract respectively. Thirty minutes after these pretreatments, all animals in groups II to VI were orally administered 1000mg/kg body weight of ibuprofen for ulcer induction, but none will be given to the group I rats. One hour after this induction; all the animals were anaesthetized with

chloroform and sacrificed by cervical dislocation. The stomach of each of the animals was carefully isolated and incised along the greater curvature and examined for ulcers. Ulcer index was calculated by putting into account the number of ulcers per animal and ulcer severity scores by observing the ulcers using a magnifying hand lens (Sivaraman and Muralidharan, 2010). Severity scores was recorded as shown below (Rasika *et al*., 2010).

Normal stomach = 0.0
Red colouration = 0.5
Spot ulcers = 1.0
Haemorrhagic streaks = 1.5
Ulcers > 3mm < 5mm = 2.0
Ulcers > 5mm = 3.0

Calculation of ulcer index

This was measured by the method described by Goel and Sairam (2002). The ulcerated lesion of the incised stomach was read using a magnifying hand glass.

$$\text{Ulcer index} = \frac{UA + US + UP}{10}$$

Where, UA = Average number of ulcers per animal, US = Ulcer severity score
UP = Percentage (%) of animals with ulcers

$$UP = \frac{\text{Total ulcers in a group}}{\text{Total number of animals}} \times \frac{100}{1}$$

$$\% \text{ inhibition} = \frac{UIC - UIT}{UIC} \times \frac{100}{1}$$

Where, UIC = Ulcer index of control group (Negative), UIT = Ulcer index of test group

Ethanol-Induced Ulcer

The rats were starved for 24 h prior to the commencement of this study, but had access to clean drinking water. Groups I and II rats were orally pretreated with 0.2 mL distilled water using a gavage tube. Group III animals were pretreated with omeprazole (a reference ulcer drug) at 20mg/kg body weight of rat. Groups IV, V and VI received 0.5ml, 1ml and 2ml oral *Solanum macrocarpon* extract doses respectively. Thirty minutes after these pre-treatments, all animals in groups II to VI were orally administered 1000mg/kg body weight of ethanol for ulcer induction, but none was given to the group I rats. One hour after this induction; all the animals were anaesthetized with chloroform and sacrificed by cervical dislocation. The stomach of each of the animals was carefully isolated and incised along the greater curvature and examined for ulcers. Ulcer index was calculated by putting into account the number of ulcers per animal and ulcer severity scores by observing the ulcers using a magnifying hand lens (Sivaraman and Muralidharan, 2010). Severity scores was recorded as shown below (Rasika *et al*., 2010).

Normal stomach = 0.0
Red colouration = 0.5
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Calculation of ulcer index

This was measured by the method described by Goel and Sairam (2002). The ulcerated lesion of the incised stomach was read using a magnifying hand glass.

$$\text{Ulcer index} = \frac{UA + US + UP}{10}$$

Where,
UA = Average number of ulcers per animal
US = Ulcer severity score
UP = Percentage (%) of animals with ulcers

$$UP = \frac{\text{Total ulcers in a group}}{\text{Total number of animals}} \times \frac{100}{1}$$

$$\% \text{ inhibition} = \frac{UIC - UIT}{UIC} \times \frac{100}{1}$$

UIC = Ulcer index of control group (Negative)
UIT = Ulcer index of test group

Statistical analysis

A one-way analysis of variance (ANOVA) and a Duncan multiple range comparison tests were carried out on the data generated from the animal study, with a statistical significance difference attained at a 95 % confidence level ($P < 0.05$) while the data for the qualitative phytochemicals were analysed using descriptive statistics. Statistical Products and Service Solutions (SPSS) version 22 was used for the data analysis.

RESULTS

Table 1: Phytochemical screening of the aqueous extract of *Solanum macrocarpon* fruit.

Phytochemicals	Qualitative test results	Amounts
Alkaloids	++	9.16±0.04
Tannins	+	2.69±0.05
Terpenoids	+	1.34±0.03
Saponins	+	3.39±0.05
Flavonoids	++	4.59±0.09
Phenols	++	5.35±0.06
Steroids	+	0.49±0.03
Cardiac glycosides	+	0.27±0.02

Key
+++ = present in high amount
++ = present in moderate amount
+ = present in little amount
- = not present

Table 2: Acute (oral) toxicity study of rats after 24 h administration of *Solanum macrocarpon* fruit extract.

Dose (mg/kg)	Death
0	0/5
500	0/5
1,000	0/5
2,000	0/5
3,000	0/5
4,000	0/5
5,000	0/5

No mortality was observed in all groups treated with the extract at all doses administered, even at 5000 mg/kg body weight. Animals instead remained active and showed no obvious signs of toxicity throughout the period of the acute toxicity test. Therefore, the lethal dose (LD_{50}) value of the extract was established to be >5000 mg/kg body weight.

Table 3: Effect of aqueous fruit extract of *Solanum macrocarpon* on body weight changes.

Treatment groups	Initial body weight (g)	Final body weight (g)	Weight gain (g)	Percentage weight gain (%)
Control	124.17±5.62^{a}	148.27±2.39^{b,c}	24.10±3.30^{b}	19.52±3.55^{b}
SM fruit extract, 150 mg/kg body weight	125.50±3.51^{a}	151.13±2.15^{c}	25.63±2.93^{b}	20.47±2.76^{b}
SM fruit extract, 300 mg/kg body weight	121.53±3.06^{a}	142.87±6.24^{a,b}	21.33±3.19^{a,b}	17.52±2.16^{a,b}
SM fruit extract, 600 mg/kg body weight	120.03±4.27^{a}	136.20±3.42^{a}	16.17±2 .20^{a}	13.51±2.20^{a}

Values are presented as mean ± standard deviation (n = 6), and values with different letter superscripts are significantly (P < 0.05) different within the column.

Result from table 3 shows that animals did not lose weight implying that *Solanum macrocarpon* fruit is non-toxic in the dosages given.

Table 4: Effect of aqueous fruit extract of *Solanum macrocarpon* on relative organ weight changes.

Treatment groups	Final body weight (g)	Liver (%)	Kidney (%)	Heart (%)	Spleen (%)
Control	148.27±2.39^{b,c}	6.08±0.12^{b}	1.11±0.09^{b}	0.61±0.03^{c}	1.38±0.03^{c}
SM fruit extract, 150 mg/kg body weight	151.13±2.15^{c}	6.18±0.07^{b}	1.03±0.03^{a,b}	0.58±0.03^{b,c}	1.30±0.02^{b,c}
SM fruit extract, 300 mg/kg body weight	142.87±6.24^{a,b}	5.73±0.13^{a}	1.03±0.12^{a,b}	0.54±0.05^{a,b}	1.21±0.07^{a,b}
SM fruit extract, 600 mg/kg body weight	136.20±3.42^{a}	5.63±0.26^{a}	0.94±0.02^{a}	0.51±0.01^{a}	1.17±0.08^{a}

Values are presented as mean ± standard deviation (n = 6), and values with different letter superscripts are significantly (P < 0.05) different within the column.

Body organs including the liver, kidneys, heart and spleen did not show any significant decrease (p>0.05) in weight when compared to the control animals. However, there was a significant decrease in the weight of the organs of animals treated with 600mg/kg when compared to the control.

Table 5: Effect of Aqueous Fruit Extract of *Solanum macrocarpon* on Haematological Parameters in Rats.

Treatment groups	Control	SM fruit extract, 150 mg/kg body weight	SM fruit extract, 300 mg/kg body weight	SM fruit extract, 600 mg/kg body weight
RBC ($x10^{6}/mm^{3}$)	6.30±0.26^{a}	6.72±0.14^{b}	7.03±0.05^{c}	7.17±0.04^{c}
PCV (%)	41.67±1.53^{a}	43.67±0.58^{b}	44.67±0.58^{b,c}	46.00±1.00^{c}
Hb (g/dl)	14.23±0.25^{a}	14.63±0.21^{a}	15.27±0.25^{b}	16.00±0.50^{c}
WBC ($x10^{3}/mm^{3}$)	8.54±0.23^{a}	8.78±0.16^{a,b}	9.04±0.10^{c}	9.06±0.11^{c}

PLT ($x10^3/mm^3$)	345.00±3.61[a]	338.67±9.45[a]	338.00±13.53[a]	330.00±9.85[a]
MCV (fl)	66.19±1.19[b]	65.02±0.55[a,b]	63.54±0.49[a]	64.12±1.04[a]
MCH (pg)	22.62±0.54[b]	21.79±0.17[a]	21.72±0.21[a]	22.30±0.57[a,b]
MCHC (g/dl)	34.18±0.71[a,b]	33.51±0.12[a]	34.18±0.23[a,b]	34.78±0.33[b]

Values are presented as mean ± standard deviation (n = 6), and values with different letter superscripts are significantly (P < 0.05) different across the row.

RBC, Red Blood Cells; PCV, Packed Cell Volume; Hb, Haemoglobin; MCV, Mean Corpuscular Volume; MCH, Mean Corpuscular Haemoglobin; MCHC, Mean Corpuscular Haemoglobin Concentration; WBC, White Blood Cell; PLT, Platelet.

Table 5 shows the effect of aqueous fruit extract of *Solanum macrocarpon* on haematological parameters in rats. There was a statistically significant increase ($p<0.05$) in the levels of RBC, PCV, Hb, WBC in extract treated animals when compared with the control. Changes in platelet level is not significant.

Table 6: Effect of aqueous fruit extract of *Solanum macrocarpon* on differential White Blood Cell count in rats.

Treatment groups	Neutrophils (%)	Lymphocytes (%)	Monocytesn (%)	Eosinophils (%)
Control	39.33±1.16[a]	55.00±2.00[a]	3.67±0.58[a]	1.67±0.58[a]
SM fruit extract, 150 mg/kg body weight	38.67±1.53[a]	56.67±1.53[a,b]	3.33±0.58[a]	1.33±0.58[a]
SM fruit extract, 300 mg/kg body weight	37.67±1.53[a]	57.67±0.58[a,b]	3.33±0.58[a]	1.33±0.58[a]
SM fruit extract, 600 mg/kg body weight	36.67±1.53[a]	59.33±1.53[b]	3.00±0.00[a]	1.00±0.00[a]

Values are presented as mean ± standard deviation (n = 6), and values with different letter superscripts are significantly (P < 0.05) different within the column.

Table 6 shows the effect of aqueous fruit extract of *Solanum macrocarpon* on WBC differential parameters in rats. No significant change ($p<0.05$) was seen in the levels of neutrophils, monocytes and eosinophils.

Table 7: Effect of aqueous fruit extract of *Solanum macrocarpon* on liver function parameters in rats.

Treatment groups	Control	SM fruit extract, 150 mg/kg body weight	SM fruit extract, 300 mg/kg body weight	SM fruit extract, 600 mg/kg body weight
Total protein (g/dl)	5.94±0.11[a]	5.98±0.19[a]	6.09±0.11[a]	6.15±0.10[a]
Albumin (g/dl)	3.24±0.03[a]	3.31±0.10[a]	3.34±0.09[a]	3.32±0.08[a]
Globulin (g/dl)	2.70±0.09[a]	2.67±0.16[a]	2.75±0.09[a]	2.83±0.07[a]
ALT (u/l)	25.67±2.08[a]	25.00±5.00[a]	24.00±2.00[a]	21.33±2.31[a]
AST (u/l)	36.33±2.31[b]	33.33±1.53[a,b]	32.67±2.52[a,b]	31.33±1.16[a]
ALP (u/l)	81.00±2.65[a]	78.67±1.53[a]	78.00±2.00[a]	77.33±1.53[a]
Total Bilirubin (mg/dl)	0.60±0.02[a]	0.59±0.04[a]	0.58±0.03[a]	0.55±0.03[a]

Values are presented as mean ± standard deviation (n = 6), and values with different letter superscripts are significantly (P < 0.05) different across the row.

AST, Aspartate Aminotransferase; ALT, Alanine Transaminase; ALP, Alkaline Phosphatase.

Table 7 shows the effect of aqueous fruit extract of *Solanum macrocarpon* on liver function parameters in rats. Treatment with 150mg/kg, 300mg/kg and 600mg/kg did not significantly increase the levels of total protein, albumin, globulin, ALT, AST, ALP and total bilirubin when compared to the control rats.

Table 8: Effect of aqueous fruit extract of *Solanum macrocarpon* on renal function parameters in rats.

Treatment groups	Control	SM fruit extract, 150 mg/kg body weight	SM fruit extract, 300 mg/kg body weight	SM fruit extract, 600 mg/kg body weight
Urea (mg/dl)	20.72±0.83[a]	19.06±1.37[a]	19.17±2.30[a]	19.04±1.00[a]
Creatinine (mg/dl)	0.70±0.03[a]	0.68±0.03[a]	0.67±0.02[a]	0.64±0.06[a]
Na^+ (mEq/L)	126.93±0.93[a]	128.93±1.17[a,b]	130.33±1.01[b,c]	131.87±1.14[c]
K^+ (mEq/L)	4.46±0.08[a]	4.55±0.05[a]	4.50±0.11[a]	4.61±0.07[a]
Cl^- (mEq/L)	86.87±1.32[a]	88.20±0.70[a]	88.47±0.96[a]	88.70±0.56[a]
HCO_3^- (mmol/L)	19.90±0.26[a]	19.80±0.20[a]	19.93±0.25[a]	19.83±0.32[a]

Values are presented as mean ± standard deviation (n = 6), and values with different letter superscripts are significantly (P < 0.05) different across the row.

Table 8 shows the effect of aqueous fruit extract of *Solanum macrocarpon* on renal function parameters in rats. Treatment did not significantly affect the levels of urea, creatinine, potassium, chloride and bicarbonate when compared to the control animals.

Table 9: Effect of aqueous fruit extract of *Solanum macrocarpon* on lipid profile parameters in rats.

Treatment groups	Total cholesterol (mg/dl)	HDL-C (mg/dl)	TAG (mg/dl)	LDL-C (mg/dl)	VLDL-C (mg/dl)
Control	110.43±1.90^{c}	61.13±1.14^{a}	84.87±4.22^{b}	32.33±1.79^{c}	16.97±0.84^{b}
SM fruit extract, 150 mg/kg body weight	103.37±2.93^{b}	62.23±1.51^{a}	79.27±2.21^{a}	25.28±2.58^{b}	15.85±0.44^{a}
SM fruit extract, 300 mg/kg body weight	98.93±3.19^{a,b}	62.77±0.70^{a}	78.37±1.37^{a}	20.49±3.53^{a}	15.67±0.27^{a}
SM fruit extract, 600 mg/kg body weight	97.03±1.88^{a}	63.47±1.17^{a}	77.47±2.50^{a}	18.07±0.77^{a}	15.49±0.50^{a}

Values are presented as mean ± standard deviation (n = 6), and values with different letter superscripts are significantly (P < 0.05) different within the column.

TC Total Cholesterol; HDL-C, High-Density Lipoprotein Cholesterol; TAG, Triacylglycerol; LDL-C, Low-Density Lipoprotein Cholesterol; VLDL-C, Very Low-Density Lipoprotein Cholesterol.

Table 9 shows the effect of aqueous fruit extract of *Solanum macrocarpon* on lipid profile parameters in rats. The result shows a significant decrease in the levels of total cholesterol, triacylglycerol, low-density lipoprotein cholesterol and very low-density lipoprotein cholesterol in animals that received 150mg/kg when compared to the control. Level of HDL-C shows a marginal increase when control group is compared with test group.

Table 10: Effect of aqueous fruit extract of *Solanum macrocarpon* on serum antioxidant parameters in rats.

Treatment	GSH (mg/dl)	GPx (u/l)	SOD (u/l)	CAT (u/l)	MDA (mmol/L)
Control	8.75±0.35^{a}	50.13±2.03^{a}	38.60±0.72^{a}	18.63±0.59^{a}	0.31±0.03^{a}
SM fruit extract, 150 mg/kg body weight	9.30±0.24^{a,b}	53.20±0.98^{a,b}	41.17±1.47^{a,b}	20.27±0.49^{b}	0.28±0.02^{a}
SM fruit extract, 300 mg/kg body weight	9.39±0.48^{b}	52.13±2.84^{a,b}	42.20±0.96^{b}	20.37±0.80^{b}	0.29±0.02^{a}
SM fruit extract, 600 mg/kg body weight	9.68±0.14^{b}	55.87±1.81^{b}	42.77±2.33^{b}	21.13±0.67^{b}	0.28±0.02^{a}

Values are presented as mean ± standard deviation (n = 6), and values with different letter superscripts are significantly (P < 0.05) different within the column.

Group. GSH, Glutathione; SOD, Superoxide Dismutase; CAT, Catalase; MDA, Malondialdehyde; GPx, Glutathione Peroxidase.

Table 10 shows the effect of aqueous fruit extract of *Solanum macrocarpon* on antioxidant parameters in rats. Treated rats showed a significant increase in the levels of GSH, GPx, SOD and CAT when compared with control animals. However, there was no significant change (p>0.05) in the level of MDA when the *Solanum macrocarpon* treated groups are compared with the normal control.

Table 11: Effect of aqueous fruit extract of *Solanum macrocarpon* on ethanol-induced ulcer in rats.

Treatment groups	UN	US	UP	UI	Percentage inhibition of ulcer
Normal control	0.00±0.00^{a}	0.00±0.00^{a}	0.00±0.00^{a}	0.00±0.00^{a}	100.00±0.00^{d}
Ulcer control	5.67±0.58^{d}	14.33±0.58^{e}	80.00±0.00^{a}	10.00±0.10^{d}	0.00±0.00^{a}
Omeprazole, 20 mg/kg body weight	4.00±1.00^{c}	8.00±2.00^{c}	80.00±0.00^{a}	9.0±0.30^{c}	8.00±03.00^{b}
SM fruit extract, 150 mg/kg body weight	4.67±1.16^{c,d}	6.67±1.16^{b,c}	80.00±0.00^{a}	9.13±0.23^{c}	8.67±2.31^{b}
SM fruit extract, 300 mg/kg body weight	4.33±0.58^{c,d}	10.33±1.53^{d}	80.00±0.00^{a}	9.47±0.21^{c}	5.33±2.08^{b}
SM fruit extract, 600 mg/kg body weight	2.67±0.58^{b}	5.33±0.58^{b}	80.00±0.00^{a}	8.80±0.10^{b}	12.00±1.00^{c}

Values are presented as mean ± standard deviation (n = 6), and values with different letter superscripts are significantly (P < 0.05) different within the column.

UI= Ulcer Index; UN = total number of ulcers per animal; US = total number of severity score for each animal. UP = Percentage (%) of animals with ulcers.

Table 11 shows the effect of aqueous fruit extract of *Solanum macrocarpon* on ethanol-induced ulcer in rats. The percentage ulcer inhibition seen in animals that received various doses of *Solanum macrocarpon* is favourably comparable to that of animals that received the standard drug omeprazole.

Table 12: Protective effect of *Solanum macrocarpon* extract against ibuprofen-induced ulcer in rats.

Treatment groups	UN	US	UP	UI	Percentage inhibition of ulcer
Normal control	0.00 ± 0.00^{a}	0.00 ± 0.00^{a}	0.00±0.00	0.00 ± 0.00^{a}	100.00 ± 0.00^{d}
Ulcer control	6.67 ± 0.58^{d}	14.67 ± 1.04^{e}	80.00±0.00	10.13 ± 0.16^{d}	0.00 ± 0.00^{a}
Omeprazole, 20 mg/kg body weight	4.67 ± 0.58^{c}	11.50 ± 1.32^{d}	75.00±0.00	9.12 ± 0.16^{c}	10.00 ± 1.59^{b}
MP extract (150 mg/kg body weight)	2.67 ± 0.58^{b}	7.67 ± 1.53^{c}	70.00±0.00	8.03 ± 0.21^{b}	20.70 ± 2.06^{c}
MP extract (300 mg/kg body weight)	3.00 ± 1.00^{b}	7.00 ± 2.00^{b}	70.00±0.00	8.00 ± 0.30^{b}	21.03 ± 2.96^{c}
MP extract (600 mg/kg body weight)	2.67 ± 0.58^{b}	4.67 ± 0.58^{b}	70.00±0.00	7.73 ± 0.06^{b}	23.66 ± 0.57^{c}

Values are presented as mean ± standard deviation (n = 6), and values with different letter superscripts are significantly ($P < 0.05$) different within the column.

Table 12 shows the protective effect of *Solanum macrocarpon* extract against ibuprofen-induced ulcer in rats. The percentage ulcer inhibition seen in treated groups is significantly higher ($p<0.05$) in extract treated groups when compared to the omeprazole treated group.

DISCUSSION

Ulcer is erosion in the lining of the stomach or duodenum. It is caused by disruption of the gastric mucosal defense and repair systems. Peptic ulcer disease (PUD) affects 5–10% of Nigerians annually, which is comparable to the global norm. Antiulcer agents are used in the treatment of gastric and duodenal (peptic) ulcers, reflux esophagitis, Zollinger-Ellison syndrome, and other gastrointestinal conditions where gastric acid reduction is beneficial but the use of these agents are always limited by side effects, high cost of procurement and unavailab ility. This present study evaluated the phytochemistry, toxicological characterization and antiulcerogenic effects of aqueous fruit extract of *Solanum macrocarpon* in albino rats. Phytochemical screening of aqueous stem extract of *Solanum macrocarpon* fruit showed the presence of alkaloids (9.16), phenols (5.35) and flavonoids (4.59) while the least present phytochemical was cardiac glycosides (0.27).

Extended administration of a xenobiotic up to 90 days may result in some adverse effects, generally classified as subacute toxicity (Cheng et al, 2018). Acute and subacute toxicity studies give an insight into the maximum dosage of an extract an animal can tolerate and the number of days over which a substance should not be used in order not to cause toxicity and adverse effects. They provide an estimate of the safety margin of exogenous chemical compounds. No death was recorded in the acute toxicity study when up to a maximum dosage of 5000mg/kg of extract was administered to the animals. Also, animals did not lose weight implying the non-toxic nature of the extract of *Solanum macrocarpon* fruit but rather percentage increase in the body and organ weights were seen in animals upon administration of 150mg/kg, 300mg/kg and 600mg/kg of extract.

Blood parameters such as RBC, Hb, PCV, MCH, MCHC, MCV and iron concentration serve as viable tools used to assess the level of anaemia and the efficacy of treatment in human and experimental animals (Lee et al, 2014). Significant increase in the levels of PCV, RBC and Hb was seen in rats treated with aqueous extract of *S. macrocarpon* fruit when compared to the normal control. This suggests that *S. macrocarpon* may have haematopoietic potentials. Previously studies showed that *S. macrocarpon* administration led to an increase in RBC level in Wistar rats after induction of anaemia by exposure to urban air pollution (Olajire and Azeez, 2012). This erythropoietic capability of *S. macrocarpon* may be as a result of their bio-constituents such as minerals (Fe^{2+}, Zn^{2+} and Cu^{2+}), vitamins (A, C, E, B) and phytochemicals such as polyphenols and flavonoids which are potent antioxidants (Anosike et al, 2011). These antioxidants may have moped up free radicals (Aduwamai et al, 2018) and the minerals and vitamins help to increase haematopoiesis and erythropoiesis in the bone marrow (Olajire and Azeez, 2012). Iron is known as an important integral part of haemoglobin, myoglobin and cytochrome, while zinc is RBC-SOD cofactor which plays essential role in the synthesis of haemoglobin, protects the integrity of erythrocytes and reduces oxidative stress (Fukushima et al, 2009). Administration of extract did not significantly affect the WBC differentials.

The liver is the organ responsible for xenobiotic metabolism/detoxification, secretion of bile, bilirubin metabolism, synthesis and storage of biomolecules (Adeyemi et al, 2015). ALP, AST, ALT and bilirubin levels are known to increase following cellular damage and tissue necrosis of the liver (Adeyemi et al, 2015).. In the index study, a significant ($P < 0.05$) decrease in serum levels of AST was seen especially in animals that received the maximum dose of 600mg/kg when compared with the control. Serum levels of ALT, ALP and bilirubin did not significantly change when experimental rats were compared to the control. This suggests that the extract at the doses given did not cause any liver damage, but rather possesses hepato-protective properties. Therefore, it could be suggested that the *S. macrocarpon* has both hepatoprotective properties.

Changes in biochemical parameters of the liver and kidney are relevant risk assessment tools in ascertaining extract's efficacy in animal model (Olson et al, 2000). Serum urea, creatinine and electrolytes such as sodium, chloride, bicarbonate, potassium and inorganic phosphate level elevation are pivotal indicators for kidney dysfunction (Kong et al, 2016). This study showed that the administration of the extract did not significantly affect the levels of urea, creatinine, sodium and potassium in animals treated with 250 mg/kg and 300 mg/kg and 600mg/kg of the extract. This suggests that *S. macrocarpon* does not have a negative effect but rather can protect the kidneys against toxic substances since a clinical decrease in creatinine was seen in extract treated animals when compared with the control rats. The extracts enhanced the ability of the kidneys to excrete these toxic wastes (urea, creatinine) and did not cause renal damage or impairment in rats.

Dietary and lifestyle modifications are among the efficient ways of managing hyperlipidaemia. Hypertension and cardiovascular diseases are associated complications of hyperlipidaemia (Eneche and Ozougwu, 2014). Dyslipidaemia is characterized by elevated levels of cholesterol, phospholipids, triacylglycerol and variations in lipoprotein levels (Bagade et al, 1991) with plasma LDL level, VLDL and cholesterol levels directly related to coronary heart disease (CHD) while high HDL level protects against heart diseases (Eneche and Ozougwu, 2014).. Our findings clearly indicate that the administration of aqueous stem extract of *Solanum macrocarpon* triggered hypolipidaemic effect in experimental animals irrespective of sex. While there was a significant decrease in the levels of TC, TAG, LDL-C, and VLDL-C in the experimental animals fed with 150mg/kg of extract compared to the control, the treated animals showed a marginal increase in the levels of high-density lipoprotein compared to the control. This suggests that *S. macrocarpon* has anti-hyperlipidaemic properties. This finding may be as a result of the extract constituents such as phytochemicals and fibre. *S. macrocarpon* has been shown to contain flavonoids, tannins, alkaloids, saponins, steroids in the index study. Previous studies have demonstrated that phytochemicals may act wholly or partly as anti-hyperlipidaemic agents (Gaamoussi et al, 2010) through the inhibition of absorption of lipid (cholesterol) by saponin, absorption of bound bile acids leading to increase bile acid excretion. Saponins may also cause decrease in fatty acid synthesis, enhance LDL receptors, activation of lipase acetyl-CoA carboxylase as well as lecithin-cholesterol acetyl transferase (LCAT) (Sharmila et al, 2007). Flavonoids and saponins may also inhibit synthesis of HMG-CoA both at the mRNA and protein levels thereby leading to decrease in endogenous cholesterol synthesis and the mobilization of cholesterol from the extra-hepatic tissues to the liver for the synthesis of bile acid Sharmila et al, 2007).. In addition, dietary fibre present in *Solanum macrocarpon* may also lower plasma cholesterol and triacylglycerol levels by production of short chain fatty acids when fermented in the colon (Sharmila et al, 2007). The findings of this present study are similar to the results of other researchers (Edijala et al, 2005; Ogunka-Nnoka, 2018) who reported a lipid-lowering effect of the extracts of *S. macrocarpon*.

Administration of aqueous fruit extract of *Solanum macrocarpon* significantly reduced the levels of superoxide dismutase, catalase, reduced glutathione and glutathione peroxidase while the level of malondialdehyde was elevated. While free radicals are a natural phenomenon that occurs in cells, an excessive amount can have a negative effect. Antioxidants are phytochemicals that protect cells against damage caused by the activity of free radicals (Chandimali et al, 2025). The antioxidant abilities of plants to remove free radicals that may be found in animals and humans are dependent on their constituents. Accoding to a study by Owusu et al, (2023), among the three vegetables studied, *S. macrocarpon* showed the most potent antioxidant capability as shown by its DPPH scavenging activity (Sieniawska, 2015). Also, in a previous study to access the antioxidant potential of the ethanolic extract of *S. macrocarpon*, Eletta *et al*, (2017) reported a percentage inhibition of 75.61%. Previous studies have shown a positive correlation between alkaloids and DPPH scavenging ability. Alkaloids, phenols, flavonoids and tannins present in *Solanum macrocarpon* can protect the body tissues against the action of free radicals and have potent antioxidant activities (Sieniawska, 2015; Gan et al, 2017).

Phytochemical screening of *Solanum macrocarpon* fruit showed the presence of bioactive compounds that have been previously shown to be gastro protective. These constituents are alkaloids, saponins, flavonoids, terpenoids and tannins. Saponins abundantly present in this extract has been shown to possess both antibacterial and trigger mucous membrane protective factors (Lanzotti et al., 2006; Borrelli and Izzo 2000). The ability of flavonoids to increase microcirculation in the gastric mucosa has also been reported (Jarial et al 2018). Flavonoids act as free radical scavengers and are powerful anti-oxidants (Galleano et al 2010). The anti-bacterial effect of flavonoids has also been demonstrated (Jarial et al., 2018). Tannins are known for their antioxidant effects and astringent property. They act by rendering the outermost layer of the mucosa less permeable to chemical irritants due to their astringent property. Tannins can also hasten the healing of wounds and inflamed mucous membrane due to their anti-inflammatory effects (Cheng et al., 2002) and their ability to form a protective layer over the exposed tissue hence keeping the wound from being infected (Stéphane et al., 2004). Terpenoids have shown anti-bacterial activity and wound-healing activity (Mai et al., 2003). They have also been reported to possess potent activity against gastric ulcers (Mitra et al., 2014). Anti-oxidants accelerate wound healing (Yen et al., 2018) and

compounds that act as antioxidants or activate the redox system are important for restoring gastric tissue (Hussain et al., 2015). Therefore, the presence of these bioactive substances may be an indication for the peptic-ulcer healing activity of the extract especially when bacterial infection by *Helicobacter pylori* and the exposure of the gastric mucosa by ethanol have all been implicated in gastric ulceration.

CONCLUSION

The extract of *Solanum macrocarpon* fruits is relatively safe with lipid lowering, renal, hepatoprotective and antioxidant capabilities which is attributable to the presence of bioactive phytochemicals. The use of the extract in ethnopharmacology for the management of peptic ulcer disease may therefore be justified and this peptic ulcer-healing effects could be related to the anti-bacterial, anti-oxidant as well as the combined pharmacological activities of the phytochemicals present in it. The ulcer-healing and gastroprotective effects of this seed extract have been demonstrated by the results of this study beyond doubt. A sub-chronic and chronic toxicity studies and further gas chromatography and mass spectrometry and pharmacological evaluation on fruit extract of *Solanum macrocarpon* with aim of developing a novel anti-ulcer agent is recommended.

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