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Effect of aqueous fruit extract of *Solanum macrocarpum* Linn. on cat blood pressure and rat gastrointestinal tract

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Abstract

Studies were conducted to assay the therapeutic potentials of the dried fruit of *Solanum macrocarpum* Linn. believed in traditional medicine to be useful both as a laxative and a hypotensive agent. The plant material was extracted with distilled water and the extract was concentrated *in vacuo* with a yield of 15.34%$^{w}/_{w}$. The effects of the extract on the gastrointestinal propulsion of charcoal meal for laxative effect and on blood pressure of albino rats at known concentrations were monitored. Also, phytochemical analysis to determine the chemical constituents of this extract was performed. The results showed that the extract dose-dependently decreased the adrenaline-induced hypertension in rats from 0.1 to 0.4 ml 2 mg/ml after which further increase in extract dose did not lead to a further reduction in blood pressure. The extract also dose-dependently increased intestinal propulsion from 25 mg/kg to 200 mg/kg ($p < 0.05$) with the charcoal meal after which there was no further increase. The dried powdered fruit was observed to contain alkaloids, cardiac glycosides, sterols, tannins, phlobatannins, flavonoids, saponins, reducing sugars, combined sugars and ketoses. The study shows that the aqueous fruit extract of *Solanum macrocarpum* could be useful as a laxative and hypotensive agent.

Keywords: *Solanum macrocarpum*, blood pressure, hypotensive effect, laxative effect; aqueous extract

Introduction

Many plants have been screened for their antihypertensive and laxative properties. Some of them have shown promising activities (Hikino *et al*., 1993; Ibarrola *et al*., 1996; Egesie *et al*., 2004). The unripe fruit of *Solanum macrocarpum* ("Gorongo" in Kanuri and garden egg in English) family Solanaceae, is basically taken as a laxative, to treat cardiac diseases and to clean the teeth (Grubben and Denton, 2004). It has wide patronage among the Kanuri women of Borno State in Nigeria in cleaning the teeth. In Sierra Leone, heated leaves are chewed to treat throat troubles. In Kenya, the juice of boiled roots is drunk to get rid of hookworm while crushed leaves are taken to treat stomach troubles. *Solanum macrocarpum* is occasionally grown as an ornamental herb. There are also claims that the young fruits of this plant are cooked and consumed as vegetable. The leaves are eaten as a separate dish or in sauces together with other ingredients. The taste is more or less bitter

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and very much liked. The leaves can either be steamed (as practiced in Uganda) or fried in oil with onions. In Uganda, it is mostly the leaves that are eaten, but the fruits are added to sauce (Grubben and Denton, 2004). There is however no reference in literature as to the possible hypotensive and laxative effects of the fruit either in human or animal studies. The present study was undertaken to establish if the unripe fruit possesses any true hypotensive and laxative properties.

Experimental

Plant material. The fruit of *Solanum macrocarpum* Linn. used in this study was obtained from Alau in Konduga Local Government Area, Borno State between October and November, 2007. The plant was identified and authenticated by Prof. S.S. Sanusi of Biological Sciences Department, University of Maiduguri, Nigeria. Specimen voucher No. 548 A was made and deposited at the Research Laboratory of the Department of Chemistry.

Preparation of extract. The fruit of *S. macrocarpum* was air-dried and the dried fruit was pulverised by grinding using pestle and mortar. Then 2.2 kg of the ground fruit was subjected to exhaustive extraction in distilled water maintained at 50-60°C to give the extract yield of 15.34%$^{w}/_{w}$ (Mittal *et al*., 1982; Fernando *et al*., 1991; Lin *et al*., 1999). The resultant solution was concentrated *in vacuo* and it was stored in a specimen bottle at room temperature until when required.

Phytochemical screening The phytochemical screening of the powdered *Solanum* fruit was carried out to determine the presence of sterol, alkaloids, tannins, flavonoids, saponins, steroidal glycosides, reducing compounds using standard procedures (Ioan, 1982; Williams *et al*., 1986).

Animals. A cat (2.10 kg) and albino rats (35) of Wistar strain, weighing about 160 to 200 g obtained from the Department of Veterinary Physiology and Pharmacology, University of Maiduguri, Maiduguri were used in this study. The animals were randomly quarantined under standard laboratory condition in plastic cages and were fed growers mash feed (ECWA Nig. Ltd. Jos, Nigeria) and water *ad libitum*. All the animals were handled according to the International Guiding Principle for Biomedical Research Involving Animals (CIOMS, 1985) as certified by the Animal Ethics Committee of the Faculty of Veterinary Medicine, University of Maiduguri, Maiduguri.

Blood pressure (B.P.) This was carried out by the methods employed by the Staff of the Department of Pharmacology, Edinburgh, (1970), Nwafor, (1998) and Dayom *et al*., (2004). The cat (2.10 kg) was anaesthetised (i.p.) with 60 mg/ml stock concentration of thiopentone at a dose of 45 mg/kg body weight. The femoral vein was canulated and connected to a 2 ml syringe containing heparinated saline to prevent intravascular clotting of blood. The carotid artery was canulated and connected to a microdynometer machine (7050 Italy) via a pressure transducer for B.P. recording. The trachea was exposed and canulated at 36 ± 0.5°C on a Bioscience heated small animal operating table (816.50301-1-kent). The drugs and extracts were administered after an equilibrium period of 30 minutes. The baseline reading was taken, followed by the reading on administration of normal saline. The standard negative control Adrenaline (Adr) 0.1 ml was administered to the cat from the stock (10 μg/ml) after serial dilution with distilled water had been carried out to give 1 mg/ml and the tracing was recorded. Then following serial dilution of the extract, 200 mg/ml, to obtain 1 mg/ml, 0.1 ml, 0.2 ml, 0.4 ml and 0.8 ml were administered to the cat (i.v.). The tracings were also recorded. Acetylcholine (ACh) 0.1 ml of 1 mg/ml solution prepared from the stock, 10 μg/ml was also administered to the

cat and the tracing was also recorded. Finally, the effect of the combination of 0.8 ml of the extract and 0.1 ml of the ACh was also determined.

Effect of aqueous extract on gastrointestinal propulsion (or transit) of charcoal meal. The method of Williamson *et al*., (1996), as modified by Egesie *et al*., (2004) was employed. The rats were fasted for 24 h but allowed free access to water. They were randomised and placed in cages of five rats per cage. Groups I to V were pre-treated (i.p.) with 25 mg/kg, 50 mg/kg, 100 mg/kg, 200 mg/kg and 400 mg/kg of extract respectively. One hour post extract administration, 1 ml charcoal meal (p.o.) was administered to the rats. Group VI, the negative control, was administered with 1 ml normal saline (i.p.) for 1 h before being treated with 1 ml charcoal meal (p.o.) Group VII, the positive control was administered with 1 ml/kg of $1MNa_2SO_4$ solution (i.p.) for 1 h before being given 1 ml charcoal meal orally (p.o.). The rats were humanely sacrificed 30 minutes later by cervical dislocation and bled, and the small intestine was rapidly dissected and placed on a clean surface. The intestine was carefully inspected and the distance traversed by the charcoal meal from the pylorus was measured. The length of the whole small intestine was also measured. The distance traversed by the charcoal meal from the pylorus was expressed as a percentage of the distance from the pylorus to the ilio-caecal junction using the formula below.

$$\% \text{ Intestinal Propulsion} = \frac{\text{Distance moved by charcoal head}}{\text{Whole length of small intestine}} \times 100$$

Statistical analysis. Test of significance between control and treatment means were carried out by the analysis of variance (ANOVA) using SPSS/PC 4 Package and difference between means were compared using Ozdamar's (1991) multiple range test.

Results

Phytochemical analysis. The constituents of the powdered fruit are shown in Table 1. The fruit contained alkaloids, cardiac glycosides, sterols, tannins, phlobatannins, flavonoids, saponins, reducing sugar, combined sugar and ketoses.

Blood pressure. The administration of aqueous fruit extract of *S. macrocarpum* produced a decrease in blood pressure of cat at concentration of 1 mg/ml when 0.1-0.2 ml of the extract was used (Fig. 1). However, increase in the concentration of the extract, 0.4-0.8 ml did not produce any further decrease in the blood pressure even though acetylcholine was administered prior to administration of the extract.

Gastrointestinal propulsion of charcoal meal. The effect of the aqueous extract on gastrointestinal propulsion of charcoal meal shows that at the doses of the extract used, the degree of propulsion exhibited by the charcoal meal was dose-dependent, with 200 mg/kg dose of the extract having the highest degree of propulsion (100.00 ± 2.94), followed by 100 mg/kg (84.35 ± 0.16) (Table 2). The extract at the dose of 25 mg/kg and 50 mg/kg exhibited intestinal propulsion of 46.08 ± 10.53 and 50.68 ± 16.23 respectively which were lower than that of the normal saline of 59.72 ± 18.44. However, at 400 mg/kg, the sharp decrease observed was far below that of both the positive and negative controls ($p < 0.05$).

Table 1: Phytochemistry of the powdered extract of *Solanum macrocarpum* fruit

S/N	Class of chemical component	Result	Observation
1.	Alkaloids		
	General: Dragendorff's test	++	Precipitate
	: Mayer's test	++	Precipitate
2.	Cardiac glycosides		
	a) Keller-Killani's test for digitoxose	+++	Reddish brown
3.	Terpenes and Sterols		
	a) Lieberman-Burchard's test	–	No Green colour
	b) Salkowiski's test	+	Reddish brown
4.	Anthraquinone Derivatives		
	a) Free anthraquinone test	–	No Bright pink colour
	b) Free and/or combined anthraquinones	–	No Bright pink colour
	c) Anthraquinone derivatives in a reduced form which are not easily reduced	–	No Bright pink colour
5.	Tannins		
	a) Ferric chloride test	++	Blue
	b) Lead subacetate test	+	Coloured precipitate
6.	Phlobatannins		
	a) Hydrochloric acid test	–	No red precipitate
	b) Bromine water test (for condensed tannins)		
	c) Lime water test (for pseudotannins)	–	No precipitate
	d) Formaldehyde test (for hydrolysable tannins)	++	Precipitate
		–	No precipitate
7.	Flavonoids		
	a) Lead acetate test	+++	Coloured precipitate
	b) Sodium hydroxide test	–	No yellow solution
	c) Ferric chloride test	++	Green or blue solution
*	d) Shinoda's test	–	No green or blue solution
8.	Saponins (Froth test)	++	Honey comb froth
9.	Resins and Balsams		
*	a) Resins	–	No purple colour
*	b) Oleo-Gum resins	–	No violet colour
*	c) Balsams	+	Dark green
10.	Carbohydrates		
	a) General test (Molisch's test)	++	Purple ring
	b) Monosaccharides (Barfoed's test)	–	No red precipitate
	c) Reducing sugar (Fehling's test)	++	Brick red precipitate
	d) Combined sugars	++	Brick red precipitate
	e) Ketoses (resorcinol or Selivanoff's test)	+	Rose
	f) Pentoses	–	No rose colour

Key:

+++ = Copiously present
++ = Moderately present
+ = Slightly present
– = Absent

Table 2: Effect of graded doses of aq. extract of *Solanum macrocarpum* fruit on rat intestinal propulsion

Animals	Extract Dose/Drug Dose	% Intestinal Propulsion
Group 1	25 mg/kg	$46.08^{a} \pm 10.53$
Group 2	50 mg/kg	$50.68^{b} \pm 16.23$
Group 3	100 mg/kg	$84.35^{c} \pm 0.15$
Group 4	200 mg/kg	$100.00^{d} \pm 2.94$
Group 5	400 mg/kg	$19.37^{e} \pm 0.11$
Group 6	Normal saline 1 ml (–ve control)	$59.72^{f} \pm 18.44$
Group 7	1 M Na_2SO_4 1 ml/kg (+ve control)	$82.74^{g} \pm 12.51$

Within columns, means with different letters are statistically significant, $p < 0.05$
n = 5 (Where n is the number of animals in each group)

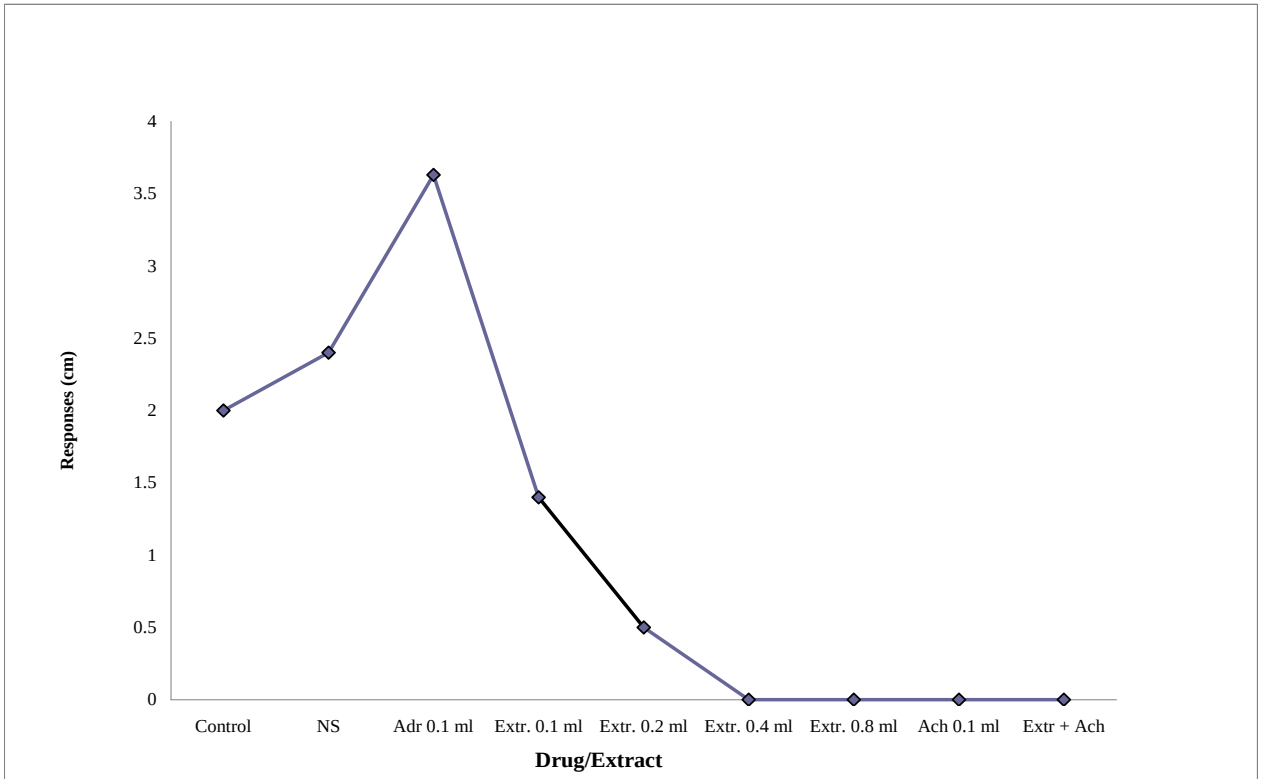

Fig. 1: Effect of graded doses of aqueous extract of *Solanum macrocarpum* on cat blood pressure

Discussion

Blood pressure measurements revealed that the aqueous extract of *Solanum macrocarpum* fruit decreased B.P. which was greater at lower doses of 0.1 ml and 0.2 ml extract than at higher doses of 0.4 ml and 0.8 ml. The direct action of cardiac stimulants especially those medicated by muscarinic stimulation include an important increase in membrane potassium permeability in arterial muscle cells and probably in the cells of the sinoatrial nodes as well (Katzung, 2004). These stimulants also decrease the slow inward calcium current in atrial and nodal cells of some species.

The observed reduction in B.P. exhibited by the extract may be attributed to either or both of these actions. Since whole animal was used, B.P. changes may be due to effect of the extract on any of the B.P. regulating sites from central nervous system (vasomotor centre) to extra-CNS sites such as

baroreceptors and action on the vascular smooth muscles. Several plant extracts have been shown to decrease blood pressure in rodents by different routes (Uguru and Okwuasaba, 1998; Ibarrola *et al.*, 1996). The crude root extract of *Solanum sysimbriifolium* (Solanaceae) also showed hypotensive effects in normo- and hypotensive rats (Ibarrola *et al*., 1996). The hypotensive effect of the extract may probably also be due to non-detections of Cd in the fruit of *S. macrocarpum* (Sodipo *et al*., 2008). It is known that accumulation of high concentration of Cd leads to hypertension with an enlarged heart and changes in blood vessels of the kidney (Schroeder, 1974).

Plant constituents like tannins, flavonoids, cardiac glycosides, saponins and alkaloids as found in powdered *Solanum macrocarpum* fruit have demonstrated diuretic properties which may account for the lowering of B.P. observed in this experiment (Dayom *et al*., 2004). Alkaloids of *Ephedra* roots have demonstrated hypotensive effects (Hikino *et al*., 1983) which may be due to their vasodilatory effects. This, in addition to effects of cardiac glycosides on the heart, may contribute to the hypotensive effect on the heart in this experiment. Flavonoids according to www.geocites.com, (2006) which are also found in *Solanum macrocarpum*, reduce capillary fragility and are thus employed in lowering blood pressure; in the treatment of hypertension as claimed in traditional medicine.

Acetylcholine, when applied in geometrical doses on isolated tissues, gives a graded dose-response in which the response obtained increases with the dose of the drug until such a time that no further increase in the dose increases the response. Hence when the maximum response is attained, a plateau is established and the response then starts to decrease with further increase in dose (Jacob, 1987). At this stage, all the receptors are said to be occupied. Probably at 0.4 ml of 1 mg/ml of the extract, all the receptors have been occupied by the extract and any further increase in the extract or addition of ACh could not bring about a further decrease in the B.P. of the cat.

When a combination of ACh and the extract were administered, a further decrease in B.P. was not observed. Thus the extract though produces hypotensive effect but in combination with ACh, it neither showed additive drug effect, synergism nor potentiation. More work needs to be done to explain this.

The results of the *in vivo* experiment for the charcoal meal showed that 30 minutes after administration of reference drug, sodium sulphate, Na_2SO_4, there was an increase in intestinal propulsion with the charcoal meal when compared with the negative control, normal saline. The propulsion recorded for Na_2SO_4 was 82.74 ± 12.51 whilst that of normal saline was 59.72 ± 18.44, indicating an increase in motility of the intestine.

Egesie *et al*., (2004) had demonstrated that the ethanolic stem bark of *Khaya senegalensis* A. Juss caused an increase in amplitude on isolated rat jejunum similar to that produced by ACh, which is a muscarinic receptor against whose activity increased the contraction of the rat jejunum via muscarinic receptors (Lawrence et al., 1997; Ganong, 1998). Thus, the extract of *Solanum macrocarpum* fruit may probably be acting through the same mechanism.

The percentage propulsion of charcoal meal showed that the extract exerted similar effect with the reference drug, Na_2SO_4, which is an osmotic laxative (Lawrence, *et al*., 1997).

At 400 mg/kg dose of the *Solanum macrocarpum* aqueous fruit extract, the propulsion decreased to 19.37 ± 0.11 after the maximum propulsion of 100.00 ± 2.94 had been reached. This may probably imply that the 200 mg/kg extract was the ceiling dose which corresponded to the maximum

response, in which case all the receptors might have been fully occupied (Jacob, 1987; Okenwa, 1997; Katzung, 2004). At the 400 mg/kg dose, the extract is now probably acting as an antidiarrhoeal because according to Williamson *et al*., (1996), a decrease in intestinal propulsion corresponds to a constipating effect.

Egesie *et al*., (2004) demonstrated that 400 mg/kg and 600 mg/kg ethanolic stem bark of *Khaya senegalensis* could be used in constipating crisis which is characterised by difficulty in defecation. The overall evaluation of the aqueous fruit extract of *Solanum macrocarpum* compared with the reference drug showed that at 100 mg/kg and 200 mg/kg, the propulsion obtained were higher and were dose dependent. Thus 100 mg/kg and 200 mg/kg aqueous fruit extract of *S. macrocarpum* could be used in constipating crisis.

Sodium sulphate as an osmotic laxative exerts its effects by preventing water absorption in the gastrointestinal tract (GIT) (Lawrence *et al*., 1997). These osmotic properties cause water retention in the GIT, thereby increasing the bulk of the intestinal content which causes a stretch of the intestinal walls, the reflex stimulation resulting in normal contractility and defecation. Acetylcholine and histamine act via muscarinic and histamine receptors respectively, they bind and stimulate these receptors, causing the smooth muscles of the GIT to contract (Lawrence *et al*., 1997; Ganong, 1998).

Conclusion

In conclusion, the results have provided information on the presence of substances in the fruit of *Solanum macrocarpum* whose pharmacological actions can be exploited into beneficial effects with clinical application.

From the results obtained, it can be deduced that the aqueous extract of *Solanum macrocarpum* fruit is an osmotic laxative when compared to actions of other similar plants like the ethanolic stem bark of *Khaya senegalensis* (Egesie *et al*., 2004). It may also be deduced that the mechanism of action of the extract might be by binding to muscarinic and histamine receptors and causing the smooth muscle of the GIT to contract. More work needs to be done to elucidate this mechanism of action of the extract and other pharmacological properties of the extract.

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