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Effects of *Spondias mombin* stem bark and *Senna alata* leaf extracts on some biochemical parameters in rats

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Abstract

Spondias mombin stem bark and *Senna alata* leaf ethanolic extracts, reputed for management of diabetes by traditional medicine practitioners, were investigated for effects on certain biochemical parameters in healthy rats at 150 mg/kg and 400 mg/kg for 28 days. Both plants significantly ($P<0.05$) lowered all lipid indices such as low density lipoprotein cholesterol, total cholesterol and triglycerides, but increased HDL-cholesterol level in treated rats. Hypoglycaemic effects of both extracts were comparable and peaked by the 4th week. PCV also increased significantly ($P<0.05$) following *Spondias mombin* administration in 4 weeks, and decreased with *Senna alata.* Weights of treated animals increased significantly ($P<0.05$) with 150 mg/kg of both extracts up to the 2nd week. This study suggests relevance of *Spondias mombin* and *Senna alata* in folkloric treatment of hyperglycaemia and associated conditions. Both plant extracts produced toxicity only in the kidney and heart of treated rats.

Keywords: *Spondias mombin; Senna alata;* Hypolipidemic effect; Hypoglycaemic effect.

Introduction

Spondias mombin L. (Anacardiaceae) is a tree, up to 20 m in height, widespread in farmlands and growing easily from stakes for making fence and enclosures (Burkill, 1985). It is a native of Caribbean and tropical America, but is now naturalized in West Africa. *Spondias mombin* is traditionally employed as a purgative, anthelmintic, analgesic, haemostatic and remedy for cough and gonorrhoea (Burkill, 1985). A wide variety of biological activities such as antidiabetic (Gbolade *et al*., 2008; Fred-Jaiyesimi *et al*., 2009), abortifacient (Offiah and Anyanwu, 1989), antianaemic (Adeyemi and Gbolade, 2006), anthelmintic (Gbolade and Adeyemi, 2008) and antiviral (Corthout *et al*., 1991) activities have been documented for *Spondias mombin*. Prominent among the chemical constituents of the plant are the phenolic compounds (Corthout *et al*., 1991).

Senna alata L. (Leguminosae) is traditionally employed as a purgative, anthelmintic, analgesic, haemostatic and remedy for cough and gonorrhoea (Burkill, 1985). Phytochemical investigations have revealed the presence of anthraquinones (Elujoba *et al*., 1989) amidst other constituents, responsible for laxative property. Most plants used in treating diabetes mellitus produce significant reductions in blood glucose, lipid levels, body weight and plasma

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protein levels (Lamba *et al*., 2000; Andrade-Cetto and Heinrich, 2005).

With the reported antidiabetic effects of *Spondias mombin in vivo* (Gbolade *et al*., 2008) and *in vitro* (Fred-Jaiyesimi *et al*., 2009), and listing of *Senna alata* as a principal antidiabetic plant in recent surveys of South-West Nigeria (Abo *et al*., 2008; Gbolade, 2009), biochemical effects of *Spondias mombin* stem bark and *Senna alata* leaf on fasted healthy normal rats, and the possible toxicological implications of oral administration of both extracts on vital body organs are hereby investigated.

Experimental

*Plant material and extraction***.** Fresh samples of *Spondias mombin* stem bark were collected from Olabisi Onabanjo University Teaching Hospital (OOUTH) premises, while *Senna alata* leaves were harvested along Lagos/ Benin expressway in the neighbourhood of the University (OOU) in Sagamu, Ogun State. Plants were authenticated at the herbarium of the Forestry Research Institute of Nigeria (FRIN), Ibadan (voucher nos: *Senna alata* FHI 107161 and *Spondias mombin* FHI 106132). Individual plant samples were cut into pieces, sun dried at ambient temperature and ground into coarse powder using a milling machine. Each sample (500 g) was macerated with 95% ethanol for a week and filtered. Further maceration of the marc for 5 days produced additional filtrates which were combined and concentrated *in vacuo* to yield dried residues (*Senna alata* 15%; *Spondias mombin* 16.5%).

*Phytochemical screening***.** Aqueous plant filtrates were screened for secondary metabolites as previously described (Dahiru *et al*., 2006). While *Senna alata* yielded anthraquinones, cyanogenetic glycosides and alkaloids, flavonoids, saponins and alkaloids were detected in *Spondias mombin.*

Animals. Albino rats of either sex weighing between 155-263 g were obtained from the colony breed of the animal house of the University of Ibadan, Ibadan, Oyo State. Rats were kept in cages at the animal house of Faculty of Pharmacy (OOU) under standard conditions and fed with standard diet (Growers feed) and water *ad libitum*. These normoglycaemic rats were divided into five groups (A-E) of eight animals each.

*Ethical clearance***.** The experiment was performed with the permission of the University's Animal Ethical Committee, and in accordance with approved institutional and national guidelines for the care and use of laboratory animals. The author declares no conflicting interest in this work.

Measurement of biochemical parameters. Fasting blood glucose was determined by the method of Gbolade *et al*. (2008). Animals were fasted for 18 h. (but allowed access to water) and divided into three groups A-C of eight animals each. Daily oral doses of 150 mg/kg and 400 mg/kg body weight of each of the aqueous filtrate were fed orally to separate groups A and B rats respectively, while group C rats received normal saline (1 ml/kg). Animals were also fed daily throughout the period of the experiment. Blood glucose was monitored before and 1, 2, 3 and 4 weeks after administration of extracts from samples collected after by amputation of the sterilised tail tip under mild anaesthesia. The blood was dropped onto LibertyR dextrostix (AgaMatrix, Inc, USA) reagent pad and values read using the micro processor digital LibertyR blood glucometer (AgaMatrix Inc, USA). For the determination of packed cell volume (PCV), blood was withdrawn using heparinised capillary tube. Tubes were sealed at one end and spun at 12,000 rpm for 5 min. in a microhaematocrit centrifuge (Hawksley, MK-5). PCV was read off using the haematocrit reader.

Lipid parameters such as total cholesterol (TC) and triglycerides (TG), as

well as high density lipoprotein (HDL)-cholesterol and low density lipoprotein (LDL)-cholesterol were determined according to Sophia and Manoharan (2007). Blood samples were collected from the heart of all treated rats after the 4th week under mild anaesthesia with diethyl ether, and transferred into lithium heparin bottle. Lipid analyses were done using a Hitachi Biochemical analyzer 902 (Germany) and TC, TG and HDL-cholesterol values read off, while LDL-cholesterol was calculated from the formula (Sophia and Manoharan, 2007):

LDL cholesterol = total cholesterol – HDL + (TG/5)

At the end of the experiment, animals were sacrificed and the heart, lungs, liver and kidney were isolated and preserved in formalin for histological analyses by conventional technique.

Statistical analysis. The Statistical Package for Social Sciences (SPSS) 10.0 was used for data entry. All values in the test were presented as mean±SEM (standard error of mean). Statistical differences between the means of the various groups were evaluated by one-way analysis of variance (ANOVA) and tested at 0.05 level of significance. The results were considered statistically significant if the p values were 0.05 or less.

Results

Effect on blood glucose: A comparison of biochemical effects of *Spondias mombin* and *Senna alata* extracts on fasted healthy rats revealed notable differences after oral dosing for 4 weeks. Progressive and significant ($P<0.05$) reduction in blood glucose from the 1st week in rats treated with 150 mg/kg and 400 mg/kg of *Spondias mombin* (Table 1) and *Senna alata* (Table 2) extracts was evident. Peak reductions in blood glucose by the 4th week was similar (27-32.2% for *Senna alata* and 20.2–25.6% for *Spondias mombin*) for both extracts, and this implies comparable hypoglycaemic potential. Significant difference in hypoglycaemic index, measured by percentage reduction in blood glucose, was evident at the two doses of both extracts.

While weight reduction was significant after the 4th week in rats fed with 400 mg/kg *Spondias mombin* (Table 1), it was unaltered at the same dose of *Senna alata* (Table 2). Hypoglycaemic potencies at the two doses were accompanied by significant increases in weights of animals up to 2nd week which was 2- to 4-times higher with 150 mg/kg *Senna alata* (Table 2). At 150 mg/kg, animals showed significant ($P<0.05$) weight gain within two weeks of feeding *Senna alata* and throughout the 4 weeks period in the case of *Spondias mombin*. Significant increases ($P<0.05$) at 150 mg/kg (20.9-35%) and 400 mg/kg (57.5% by the 4th week) were observed for *Spondias mombin* (Table 1), but this parameter was unchanged with both doses of *Senna alata* (Table 2).

Effect on lipids: In Table 3, there was significant lowering in total cholesterol (TC), total triglyceride (TG), low density lipoprotein-cholesterol (LDL) of animals treated with *Senna alata* extract which was higher at 150 mg/kg by the 4th week. Among these three lipid indices, LDL-cholesterol level was mostly affected (48.9-57.8% reductions) by administration of *Senna alata* at both doses. On the other hand, level of high density lipoprotein-cholesterol (HDL) increased (15.9–20.6%) significantly ($P<0.05$) at both doses by the 4th week. In the case of *Spondias mombin*, attenuation in TC, TG and LDL-cholesterol levels was significantly higher at 400 mg/kg, but HDL-cholesterol increased (32.9%) significantly at 400 mg/kg. Apart from signs of renotoxicity and cardiotoxicity, rats fed with both extracts showed near normal histology of most of the four organs examined.

Table 1: Effect of *Spondias mombin* on blood glucose, weight and PCV of rats treated for 4 weeks

Treatment	Baseline value	1st Week	2nd Week	3rd Week	4th Week
		Blood glucose (mg/dl)			
Extract (150 mg/kg)	133.4±0.2	104.3±8.4[b] (-21.8%)[a,c]	103.7±0.7[b] (-27.3%)[a,c]	101.0±0.3[b] (-24.3%)[a,c]	99.2±0.7[b] (-25.6%)[a]
Extract (400 mg/kg)	108.5±0.5	99.1±0.6 (-8.7%)[a]	97.9±1.2 (-9.8%)[a]	89.1±0.7[b] (-17.9%)[a]	86.6±17.2[b] (-20.2%)[a]
Normal saline (1 ml/kg)	133.8±0.4	137.0±0.4 (2.3%)	138.2±0.4 (3.3%)	138.2±0.4 (3.3%)	139.0±0.3 (3.9%)
Treatment		Weight changes (g)			
Extract (150 mg/kg)	156.3±0.5	193.6±0.2[b] (23.9%)[a,c]	192.1±0.3[b] (22.9%)[a,c]	190.8±0.5[b] (22.1%)[a,c]	189.1±0.7[b] (20.9%)[a,c]
Extract (400 mg/kg)	222.8±0.7	226.5±1.3 (1.7%)	222.8±0.7 (0%)	218.7±0.4 (-1.8%)	140.9±31.3[b] (-36.8%)[a]
Normal saline (1 ml/kg)	193.0±0.8	194.8±0.7 (0.9%)	195.8±0.7 (1.5%)	196.6±0.5 (1.9%)	195.6±0.7 (1.4%)
Treatment		Packed cell volume (%)			
Extract (150 mg/kg)	23.4±0.4	28.3±0.9 (20.9%)[a,c]	30.4±0.2[b] (29.9%)[a,c]	30.9±0.2[b] (32.1%)[a,c]	31.6±0.2[b] (35.0%)[a,c]
Extract (400 mg/kg)	24.7±0.3	33.9±0.3[b] (37.3%)[a]	24.6±0.3 (-0.4%)[a]	23.3±0.2 (-5.7%)[a]	38.9±8.8[b] (57.5%)[a]
Normal saline (1 ml/kg)	26.0±0.2	28.7±0.2 (10.4%)	29.0±0.2 (11.6%)	29.4±0.2 (13.2%)	29.6±1.8 (13.9%)

Results are expressed as mean±standard error of mean (S.E.M), n=8
Values in parentheses represent % decrease (-) or increase (+) in parameters
a, $p<0.05$ when % change in value for both doses were compared with the control
b, $p<0.05$ when values for all parameters for each week were compared with the baseline values
c, $p<0.05$ when % change in values at 150 mg/kg was compared with 400 mg/kg

Table 2: Effect of *Senna alata* extract on blood glucose, weight and packed cell volume in rats after 4 weeks

Treatment	Baseline value	1st Week	2nd Week	3rd Week	4th Week
		Blood glucose (mg/dl)			
Extract (150 mg/kg)	128.2±6.8	119.1±5.9[b] (-7.0%)[a,c]	121.4±3.2 (-5.3%)[a,c]	104.3±4.9[b] (-18.6%)[a,c]	93.5±2.8[b] (-27.0%)[a]
Extract (400 mg/kg)	136.5±9.6	118.3 ± 7.4[b] (-13.3%)[a]	121.0±7.9[b] (-11.4%)[a]	100.8±3.3[b] (-26.1%)[a]	92.5±2.2[b] (-32.2%)[a]
Normal saline (1 ml/kg)	133.8±0.4	137.0±0.4 (2.4%)	138.2±0.4 (3.3%)	138.2±0.4 (3.3%)	139.0±0.3 (3.8%)
Treatment		Weight changes (g)			
Extract (150 mg/kg)	162.0±5.8	190.5±7.4[b] (17.5%)[a,c]	205.0±7.2[b] (26.5%)[a,c]	176.6±7.0[b] (9.0%)[a,c]	162.5±11.3 (0.3%)
Extract (400 mg/kg)	212.1±12.9	229.5±13.2[b] (8.2%)[a]	226.7±3.2[b] (6.8%)[a]	195.7±10.9[b] (-7.7%)[a]	201.9±16.4 (-4.8%)[a]
Normal saline (1 ml/kg)	193.0±0.8	194.8±0.8 (0.9%)	195.8±0.7 (1.5%)	196.6±0.4 (1.9%)	195.6±0.7 (1.3%)
Treatment		Packed cell volume (%)			
Extract (150 mg/kg)	29.0±0.4	30.1±0.2	30.1±0.1	31.4±0.1	32.3±0.2
Extract (400 mg/kg)	36.5±0.3	37.8±0.2	38.0±0.2	31.5±0.3	32.8±0.2
Normal saline (1 ml/kg)	26.0±0.2	28.7±0.2	29.0± 0.2	29.4±0.2	27.6±1.8

Results are expressed in mean ± SEM, n=8
Values in parentheses represent % decrease (-) or increase (+) parameters when compared with baseline values.
a = $P < 0.05$ when % change in parameter at both doses were compared with control

b, P<0.05 when values for all parameters for each week were compared with the baseline values
c = P < 0.05 when % change in parameter at 150 mg/kg was compared with 400 mg/kg

Table 3: Effect of plant extracts on lipid parameters of rats after 4 weeks

Treatment	Baseline values (mg/dl)				Values after 4th week (mg/dl)			
	Senna alata							
	TC	TG	HDL	LDL	TC	TG	HDL	LDL
Extract (150 mg/kg)	103.2±0.9	78.7±3.3	45.9±2.3	41.5±2.7	81.2±0.7[a] (-21.3%)[b]	52.3±1.4[a,b] (-33.5%)[b]	53.2±2.4[a] (15.9%)[b]	17.5±2.3[a] (-57.8%)[b]
Extract (400 mg/kg)	103.2±0.9	78.7±3.3	45.9±2.3	41.5±2.7	89.1±0.5[a] (-13.6%)	62.3±3.7[a] (-20.8%)	55.4±1.6[a] (20.6%)	21.2±1.5[a] (-48.9%)
Normal aline (1 ml/kg)	104.6±1.7	81.8±6.3	42.4± 6.3	45.8±1.2	102.0±0.4 (-2.4%)	76.4±1.6 (-6.6%)	46.8±1.9 (10.3%)	40.5±2.3 (-11.5%)
	Spondias mombin							
Extract (150 mg/kg)	103.6±0.9	77.5±1.4	46.6±2.1	39.4±2.4	89.1± 2.6[a] (-13.9%)[b]	76.5±1.7 (-1.3%)[b]	46.5±0.8 (-0.2%)[b]	27.3±1.8[a] (-31%)
Extract (400mg/kg)	103.2±0.9	78.7±3.3	45.9±2.3	41.6±2.7	77.1±18.5[a] (-25.3%)	56.3±6.5[a] (-28.5%)	61.0±19.9[a] (32.9%)[b]	30.4±10.5[a] (-26.9%)
Normal aline (1 ml/kg)	104.0 ±1.7	81.8 ±6.3	42.4 ±0.9	45.8 ±1.1	102.0 ±0.4 (-2.5%)	76.4±1.6 (-6.6%)	46.8±1.9 (10.4%)[b]	40.5±2.3 (-11.6%)

Results are expressed in mean±SEM (standard error of mean), n=8
Values in parentheses represent % decrease (-) or increase (+) when compared with baseline values
TC= Total Cholesterol, TG= Triglycerides, HDL= High density lipoprotein-cholesterol, LDL= Low density lipoprotein-cholesterol
a = P <0.05 when extract groups were compared with control after 4 weeks
b = P<0.05 when % change in parameter at 150 mg/kg extract was compared with 400 mg/kg extract

Discussion

Results of hypoglycaemic and hypolipidemic effects of *Senna alata* and *Spondias mombin* when administered to fasted healthy rats for 4 weeks, suggest possible presence of active compounds in the polar extracting solvent. Bioactive compounds, such as the phenolic anthraquinones detected in *Senna alata,* and flavonoids in *Spondias mombin* extracts may produce insulin-like effects which in turn led to reduction in fasting blood glucose and lipid levels of experimental rats. Similarly, phenolic acids in rice bran (Jung *et al*., 2007) and flavonoids in *Helichrysum plicatum* (Aslan *et al*., 2007) have been shown to possess hypoglycaemic effect. Hypo glycaemic and hypocholesterolaemic effects of *Ageratum conyzoides* (Moura *et al*., 2005) and *Khaya grandifoliola* (Bumah *et al*., 2005) in fasted normal rats after chronic treatment are also reported. Olagunju *et al*. (2004) attributed altered metabolic activities in both the liver and kidney of rats treated with *Harungana madagascariensis* extract to hypercholesterolaemia and hypertriglyceridae mia, in addition to other biochemical effects. Hypoglycaemic effect of *Senna alata* is lacking in the literature, while that of *Spondias mombin* in *in vivo* (Gbolade *et al*., 2008) and *in vitro* (Fred-Jaiyesimi *et al*., 2009) models was recently published.

Hyperlipidemia is known to induce high damage, measurable by the changes on the liver weight, serum AST and ALT levels (Lee *et al*., 2006) and coronary heart disease (Manninen *et al*., 1992). Reduction in lipid levels by the plants investigated in this report may be linked with inhibition of endogenous synthesis of lipids probably by potentiating the secretion of insulin (Sophia and Manoharan, 2007), and hence offer protection prospects for vital body organs like liver and kidney.

Enhanced body weights in rats treated with lower dose of both plant extracts may

result from stimulation of appetite thereby leading to increased food consumption. The improved PCV in *Spondias mombin*-treated rats may suggest suitability as a blood enhancer and haematinic, while the unaltered parameter may support safety of *Senna alata* in treatment of disease conditions. Using normal rats, *Khaya gradifoliola* stem bark (Bumah *et al*., 2005) and *Murraya koenigii* extracts (Adebajo *et al*., 2006) were found to be effective in altering certain biochemical parameters including blood glucose, lipid levels and PCV after sub-chronic administration. Considering the effect on body organs, renotoxicity characterised by marked congestion and infiltration of the renal pelvis and associated chronic inflammation is now reported for these two plants. Signs of cardiotoxicity were also observed. Renotoxicity has been reported earlier by Adebajo *et al*. (2006) for *Murraya koenigii* in a sub-chronic model. This histopathological potential could be further substantiated by determining effect of *Senna alata* and *Spondias mombin* extracts on other animal organs like kidney and heart enzymes.

Conclusion

In the present investigation, *Spondias mombin* stem bark and *Senna alata* leaf extracts showed comparable hypoglycaemic effects when administered to fasted healthy rats during 4 weeks with accompanying reno- and cardiotoxicity. *Senna alata* appears to have relatively higher hypolipidemic effects and 150 mg/kg of the extract would suffice for further investigations. This study also suggests potential use of both plants in the treatment of hyperglycaemia and associated conditions.

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