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Xylopia aethiopica fruit extract lowers uric acid levels in wistar albino rats

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Abstract: *The effect of aqueous fruit extract of Xylopia aethiopica on bile, serum and fecal uric acid levels as well as bile secretion and cholesterol (LDL, VLDL, HDL and triglycerides) were studied in wistar albino rats. Thirty (30) wistar albino rats were divided into three groups of ten (10) rats each after an acclimatization period of seven (7) days. The control group received normal rat chow and water freely. The two test group's ii and iii received daily oral administration of 100mg/kg b.w and 200mg/kg b.w/day respectively of the fruit extract for 28 days, water and standard feed given ad libitum. At the end of the experimental period, bile, serum and feces from the three groups were analyzed for bilirubin and uric acid. Bile flow rate (ml/h) was significantly ($p<0.05$) lower in the test groups when compared with control. Total and unconjugated bile bilirubin in group ii were significantly ($p<0.001$) lower than control, while total, conjugated and unconjugated bile bilirubin in group iii was significantly ($p<0.001$) higher when compared with control. In the serum, total, conjugated and unconjugated biliribin was significantly ($p<0.05$, 0.001) higher in the group iii when compared with the control. Serum and fecal uric acid levels in the test groups were significantly ($p<0.001$) lower than in their control. The plasma cholesterol, LDL, HDL and triglycerides were significantly decreased in group i while the extract significant increased plasma triglyceride, VLDL but increased plasma LDL and HDL. It appears that low and high doses of aqueous fruit extract of Xylopia aethiopica caused the lowering of uric acid levels in serum and feces, and this might be a panacea to arthritis and gout , atherosclerosis, coronary heart diseases and other cardiovascular related disorders.*

Keywords: *bilebilirubin, rats, Xylopia aethiopica, , uric acid*

I. Introduction

Xylopia aethiopica, (Negro pepper) is one of the plants man has discovered in the search for food and health care. The essential oils from the fruits, bark and seeds have been shown to have antiseptic or anti-bacterial properties, and some are valuable in medicine [1,2,3]. *Xylopia aethiopica* is most commonly used for the treatment of lumbago, stomach and joint pains, [4,5]. Apart from its medicinal uses, it has several social uses that may be due its hotness and spicy flavour.

Joint pain (gout) is a group of disorders that produces hyperuricaemia. Crystal of salts is deposited in the joints causing acute and chronic joint disorders. Some of these endogenous crystals such as monosodium urates are known to be pathogenic [6]. Both endogenous and exogenous crystals produce disease by triggering a cascade that results in cytokine-mediated cartilage destruction. Arthritis is one of the common causes of joint pain in young men [7]. Joint pains are also common in middle-aged men, as well as older women [7, 6, 8]. Some evidence suggests that the disease is caused by an autoimmune reaction initiated by prior infection and that the organisms are associated with enteric infections that have oligosaccharide as their major component in their outer cell membrane and their derived antigens stimulate an array of immunologic responses [7]. Joint stiffness and low back pain are said to be common early symptoms as well as effect on ankles, knees and feet. The prevalence of joint pains varies among populations, with a strong male dominance that increases with age and increased concentration of serum uric acid [6]. Often the aim of relieving acute arthritis is to decrease the uric acid levels in blood.

The medicinal uses of many plants are still unknown. Diverse illnesses such as pains and infections are common in rural areas and a lot of people rely on medicinal plant care especially in the South Eastern Nigeria where some herbalists use *Xylopia aethiopica* to treat arthritis. The aim of this study was to find out the effect of aqueous fruit extract of *Xylopia aethiopica* on uric acid levels in bile and serum in rat. No scientific validation has been done to show whether the treatment could be related to its effect on uric acid and cholesterol levels in blood, hence, paucity of this study.

II. Materials and Methods

Collection and preparation of *Xylopia aethiopica* fruit extract

Dried fruits of *Xylopia aethiopica* were purchased from Watt Market, Calabar, Cross River State, Nigeria and were authenticated at the Department of Botany, University of Calabar, Calabar, Nigeria. They were pulverized and macerated 100g/litre of solvent (w/v) for 12h in water. It was filtered using Whatman No 1 filter paper (England). The filtrate was dried in an aerated oven to constant weight and the dried extract was stored in screwed-cap bottle until use.

Experimental animals

Thirty Albino Wistar rats weighing 280 – 300g were obtained from the Animal house of the Department of Physiology, College of Medical Sciences, University of Calabar, Calabar-Nigeria and used for this study. The rats were divided into three groups of 10 rats each as follows; Group i (control), Group ii and Group iii . Group ii received 100mg/kg body weight of *Xylopia aethiopica* extract while Group iii received 200mg/kg body of *Xylopia aethiopica* extract oral gavages daily. The rats were acclimatized in the animal house for one week before the start of the experiments. The animals were housed in stainless steel cages under standard conditions (ambient temperature, 28 ± 2^{o}C and humidity 46%, with a 12h light/dark cycle) and were fed normal rat pellet (Pfizer, Nigeria). All the rats in both test and control groups were allowed free access to food and water *ad libitum* throughout the 28 day experimental period. All the animal experiments were conducted following the guidelines of the Institutions Animal Ethical Committee.

Collection of bile

Collection of bile was carried out following the method described by [9].The rats were fasted for 12-18 hours and were anaesthetized by intraperitoneal administration of thiopentone sodium, (60mg/kg body weight) before the experiment. The anaesthetized rats were quickly pinned to a dissecting board, tracheotomy and laparatomy were performed and liver lobes were deflected anterolaterally to expose the common bile duct. The common bile duct was then cannulated with a portex cannnula (0.5mm diameter) after a semi transection was made on it. The cannula was held in place with a thread tied over it and around the bile duct. The bile was collected for an hour from each of the rats studied. The bile flow rate was noted and the samples were stored in the refrigerator for biochemical analysis.

Collection and preparation of blood samples for analysis

Blood samples were collected by cardiac puncture into plain screw-cap sample bottles. The blood samples collected were allowed to clot and the serum extracted with Pasteur pipette after spinning with MSC model (England) table top centrifuge at 2000rpm for 5minutes. The serum collected was used for biochemical studies.

Fecal uric acid

One gramme of fecal material was collected from the different groups and allowed to homogenize for 30 minutes in 15ml of water. The homogenate was filtered using Whatman No 1 filter paper (England). The supernatant was then transferred into plastic containers and refrigerated and used for fecal analysis according to the method of [10].

Biochemical analyses

Bile, serum and fecal samples were analyzed for total bilirubin, conjugated, unconjugated bilirubin uric acid and cholesterol in the Department of Chemical Pathology Laboratory, University of Calabar Teaching Hospital, Calabar, using standard procedures.

Statistical analysis

Data were presented as mean ± SEM. The significant differences between the means were evaluated using the student's t-test and analysis of variance (ANOVA). P values of less than 0.05 were considered statistically significant.

III. Results

The bile flow rate (ml/hr) of control, low and high dose groups are shown in Fig.1 following the administration of aqueous extract of *Xylopia aethiopica*. The rate of biliary secretion was significantly lower in both group ii ($P<0.05$) and groups iii ($P<0.01$) when compared with the control group.

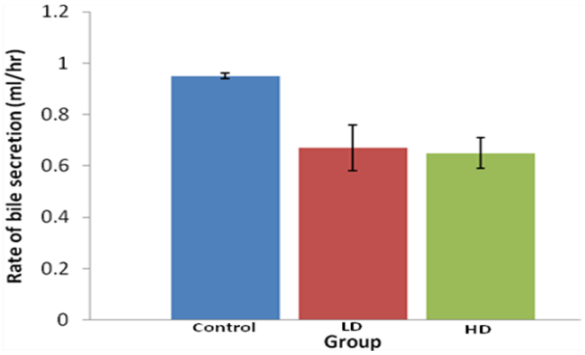

Fig. 1: Comparison of bile flow rate in group i (control), ii (low dose) and iii (high dose) *Xylopia aethiopica*-treated wistar albino rats.

Table 1 shows that the total bile bilirubin, conjugated and unconjugated bilirubin levels in the (high dose) group iii were all significantly (P<0.05, 0.01 and 0.001) respectively higher than control whereas, total bilirubin and unconjugated bilirubin were significantly (P<0.001) lower respectively in (low dose) group ii than control. *Ta*ble 2 shows that total, conjugated and unconjugated bilirubin levels in serum were significantly (P<0.001) higher in group iii, but there was no significant differences between all the bilirubin level in the serum of group ii compared with control. Table 3 shows the uric acid levels in serum, bile and feces of *Xylopia aethiopica* fed rats. Serum uric acid and fecal uric acid levels in treated groups were significantly lower than in control (p<0.01 – 0.001). However, biliary uric acid levels was higher in group ii than in control (p<0.001). (Table 4) shows the effect of aqueous fruit extract of *Xylopia aethiopica* on biliary concentrations of total cholesterol (TC) ,High density lipoprotein (HDL) ,low density lipoprotein (LDL),very low density lipoprotein (VLDL) .HDL concentrations in test groups were significantly (P<0.01) higher than in control. However, TG, VLDL and concentration in the two treated groups were significantly lower (P<0.001) than in control group. Likewise TC and LDL concentration in group ii were significantly (P<0.001) lower when compared with the control group while LDL concentration in the Group iii treated with the extract was significantly (P<0.01) higher than the control. The mean total cholesterol (TC)level in group I (control),ii and iii were 4.00±0.04,3.07±0.02 and 4.05 ±0.02mMol/L (Table5).Group ii (treated with 100mg/kg b.w) significantly P<0.001) lower TC level when compared with the control and groups iii .HDL levels in the test groups were significantly P<0.01 higher than control. The triglycerides (TG), low density lipoprotein (LDL) and VLDL levels in test group were significantly (P<0.001) lower than the control

Table 1 showing bile bilirubim levels in *Xylopia aethiopica* – treated wistar albino rats

Parameter	Control	Groupii	Group iii
Total bilirubin	22.77 ± 0.02	19.73 ± 0.97***	28.87 ± 2.53*[a]
Conjugated bilirubin	15.95 ± 1.01	15.18 ± 1.51[NS]	18.33 ± 1.66**
Unconjugated bilirubin	6.82 ± 1.0	3.18 ± 0.87***	10.53 ± .1.83**[a]

NS: not significant, * = p<0.05 ** p<0.01; *** = p<0.001 vs control, [a]p<0.001 vs. low dose; n = 10 values in Mean ± SEM

.**Table 2 showing the effect of *Xylopia aethiopica on serum bilirubin of wistar albino rats***

Parameter	Control	Low dose	High dose
Total bilirubin	11.50 ± 0.94	10.63 ± 0.97[NS]	17.45 ± 0.75***[a]
Conjugated bilirubin	6.85 ± 101	6.13 ± 0.94[NS]	9.85 ± 1.40***
Uncongugated bilirubin	4.05 ± 1.18	4.50 ± 1.18[NS]	7.57 ± 1.51**

NS: not significant, *** = p<0.001; **=p<0.01; [a]p<0.001; n = 10 value in Mean ± SEM.

Table 3 showing the effect *Xylopia aethiopica* on biliary and fecal uric acid levels of wistar albino rats

Parameter	Control	Low dose	High dose
Serum uric acid	0.30 ± 0.003	0.18 ± 0.008***	0.21 ± 0.004***[a]
Biliary uric acid	0.26 ± 0.02	6.13 ± 0.004*	0.28 ± 0.003**[a]
Fecal uric acid	0.14 ± 0.003	0.01 ± 0.003**	0.06 ± 0.003***[a]

*** = p<0.01; *** = p<0.001; *= p<0.05; [a] p<0.001; n = 10; value in Mean ± SEM.

Table 4: Effect of *Xylopia aethiopica* on bile lipid profile in wistar albino rats

Parameters	Control	Group ii (Treated with 100 mg/kg b.w	Group iii (Treated with 200mg/kg b.w)
TC	1.45±0.02	1.57±0.03***	1.70±0.001***
HDL	0.44±0.02	1.33±8.009**	0.62±0.01**
TG	0.47±0.01	0.4±0.09***	0.48±0.003***
LDL	0.87±0.11	0.79±0.03	0.85±.02
VLDL	0.68±0.03	O.21±0.02***	0.21±0.005***

*=P<0.05,***= P<0.01 VS control. Values are mean ± SEM,n=10.

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Table 5: Effect of aqueous extract of *Xylopia aethiopica on plasma lipid profile in wistar albino rats*

Parameter	Control	Group ii (Treated with 100 mg/kg b.w	Group iii (Treated with 200 mg/kg b.w
TC	4.00±0.04	3.07±0.02 ***	4.05±0.02[c]
HDL	1.20±0.001	1.30±0.002***	1.40± 0.03***
TG	1.53±0.02	0.77±0.02***	0.80±0.03***
LDL	1.73±0.33	1.42±0.02***	2.30±0.01***
VLDL	O.68±0.03	0.32±0.02***	0.37±0.02***

=P< 0.01,*= P<0.001 VS Control * = P<0.001 vs Group ii, NS =not significantly different values are mean ± SEM, n=10

IV. Discussion

Xylopia aethiopica treated groups showed a significant decrease in bile flow rate when compared with control. Bile is secreted by the liver cells into bile duct. Although the mechanism was not studied, the decrease in bile, flow rate or secretion in test animals might be caused by the inhibitory effect of the extract on the synthesis of the constituent's bile.

The total, conjugated and unconjugated bilirubin levels in the bile were significantly high in the high dose treated group while these parameters were low and non-significant in the low dose-treated group. Generally high bilirubin levels may be due to increase destruction of red blood cells. When red blood cells are haemolyzed, bilirubin is formed [11]. So, the extract at high doses may lead to haemolysis of red blood cells giving rise to high bilirubin levels in plasma or serum. The high unconjugated bilirubin levels will also signal liver disease since the liver is the site for conjugation of bilirubin and if the liver is damaged it is unable to conjugate.

Serum levels of uric acid were reduced in this study following treatment with *Xylopia aethiopica*. Uric acid is the end product of purine metabolism [7,8]. The reduction noticed here may therefore be caused by the effect of the aqueous fruit extract of *Xylopia aethiopica.* Serum levels of uric acid are usually raised in patients with acute gout and the aim usually is to prevent complication by lowering uric acid levels in blood [6,7]. The plasma lipid profile result indicates that the extract treated rats had low total cholesterol, triglycerides, low density lipoprotein, very low density lipoproteins and a high level of high density lipoprotein in treated groups. Taking the lipid fractions together increased HDL-the good cholesterol, the extract maybe beneficial to the rats. This is because increase in TC, TG, and LDL promotes atherosclerosis which may lead to hypertension, cardiac arrest and shock. Epidemiological studies show an inverse relationship between HDL and the development of atherosclerosis [8,12,13].It holds that HDL which is low in cholesterol and rich in surface phospholipids facilitates the clearance of cholesterol from bloodstream and transport to the liver where it may be excreted rather than re use in the formation of VLDL .HDL is believed to inhibit cellular uptake of LDL .LDL sometimes called bad cholesterol is the main carrier of cholesterol . increased LDL has been implicated in the development of atherosclerosis .The significance of most dietary therapy is to reduce total LDL cholesterol and increased HDL cholesterol levels [14].Therefore, since the aqueous fruit extract had strong impact on HDL,It appears it can be used to manage atherosclerosis, Coronary heart diseases and other Cardiovascular related disorders.

In conclusion, it may be held that the fruit extract has agents that lower serum uric acid level in blood and LDL level. Further researches may require the isolation of these agents and the mechanism of action.

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