Effect of Stem Bark Extract of *Fagara zanthoxyloides* on Bile Secretion in Rats

Umaru H.A., Clarkson W.P. and *Christopher K.

Department of Biochemistry, Modibbo Adama University of Technology, Yola, Nigeria.
*Corresponding author: E-mail: kwansaichris@gmail.com

Abstract

This study was designed to evaluate the effect of stem bark extract of *Fagara zanthoxyloides* on bile secretion in rats. Twenty five albino rats weighing 135±15 g were randomly divided into five groups of five animals each: group I was administered water and normal feed (control), while group II, III, IV and V were administered 100 mg/kg, 200 mg/kg, 300 mg/kg, and 400 mg/kg of extract respectively. The aqueous extract was administered daily for 21 days after which the animals were sacrificed. The effect of the aqueous extract on bile secretion: Total, conjugated and unconjugated bilirubin, cholesterol, phospholipids, potassium, sodium, bicarbonate, chloride ions were analysed. Results obtained shows significant ($p<0.05$) decrease in total, conjugated and unconjugated bilirubin, cholesterol, phospholipids, sodium, bicarbonate, chloride ions and Bile output in a dose depended manner when compared to the control group. However, there was no significant difference ($p<0.05$) between the value of potassium ion of the test groups and that of the control group. From the result obtained in this study, it shows that aqueous extract of *Fagara zanthoxyloides* has an effect on bile secretion hence its used as spice should be with caution.

Key Words: *Fagara zanthoxyloides,* Extract, electrolytes, Billiary output, Bile, Albino Rats

{**Citation:** Umaru H.A., Clarkson W.P., Christopher K. Effect of Stem Bark Extract of Fagara zanthoxyloides on Bile Secretion in Rats. American Journal of Research Communication, 2019, Vol 7(7): 1-9} www.usa.journals.com, ISSN: 2325-4076.

1.0 Introduction

Medicinal plants play a key role in the human health care. Ameesh and Murugan (2016) reported that, about 80% of the world population rely on traditional medicine,

predominantly plants. These practices incorporated ancient beliefs and were passed on from one generation to another by oral tradition and/or guarded literature. Most of these plants are use routinely without consideration of their safety largely due perhaps to their long history of application and availability in local communities. However, literature on the safety of these medicinal plants is usually inadequate or unavailable.

Fagara zanthoxyloides Lam also known as *Zanthoxylum zanthoxyloides* belongs to the genus Zanthoxylum, sub-family Rutoideae, family Rutaceae. This plant is an indigenous plant used widely as chewing sticks for teeth cleansing in West Africa (Adebiyi *et al.,* 2009). Itemire *et al.,* (2013), reported that, the plant is well known for its varied uses in trado-medical practice, the root, root-bark and other parts of the plant are used in treating dental diseases, various medical problems and bio-pesticide for stored food protection.

The plant has been used as components of antiseptic, anti-parasitic and analgesic preparations for managing small pox, syphilis and related disease conditions (Anne *et al.,* 2013). Traditional healers throughout Nigeria have used different parts of *Zanthoxylum* for the treatment of a wide range of disorders, including toothache, urinary and venereal diseases and rheumatism (Adesina, 2005). Metabolites isolated from *Zanthoxylum* stem bark have shown anticonvulsant, antisickling, anaesthetic, antibacterial, anti-hypertensive and anti-inflammatory properties. The extract contains flavonoids, chelerythrine, berberine and phenol (Adebiyi *et al.,* 2009).

The liver is the largest organ in the abdominal cavity and the most complex with more functions than any other human organ. It consists of a myriad of individual microscopic functional units called lobules. The liver performs a variety of functions including the removal of endogenous and exogenous materials from the blood, complex metabolic processes including bile production/secretion, carbohydrate homeostasis, lipid metabolism, urea formation, and immune functions and is the main target of a number of toxicants (Meyer and Kulkarni, 2001).

Bile is a dark green or yellowish brown fluid, produced by the liver continuously and stored in the gallbladder. After eating this stored bile is discharged into the duodenum, and the gallbladder bile composition is: 97% water, 0.7% bile salts, 0.2% bilirubin, 0.51% fats (cholesterol, fatty acids and lecithin) and 200 meq/inorganic salts (Guyton and Hall, 2011; Barrett and Kim, 2012). Many factors may tend to alter the rate of bile secretion which may be either primary from the liver (liver bile) or secondary from gallbladder (gallbladder bile) and consequently lead to excess or low bile secretion.

Bile which facilitates the digestion and dispersion of consumed fats, when secreted above or below the body's need may lead to clinical conditions such as; jaundice caused by the accumulation of bilirubin, when the liver produces high amount of cholesterol in the bile gallstones (cholelithiasis) are formed which causes blockage of the biliary duct and heartburn. Other complications associated with bile secretion are; gastric surgery, peptic ulcer, cirrhosis, vomiting (emesis) etc. This study intends to evaluate the effect of stem bark extract of *Fagara zanthoxyloides* on bile secretion in rats so as to justify the safety of the plant in line with bile secretion.

2.0 Material and Methods

2.1 Sample Collection and Preparation

Fresh mature stem bark samples of *Fagara zanthoxyloides* collected from Jimeta modern market, Yola south local government area of Adamawa state, Nigeria. The botanical identification of the plant was done at the department of Plant Sciences, Modibbo Adama University of Technology Yola, Nigeria. The fresh stem samples were dried at room temperature and pulverized to dry powder using pestle and mortar. About 200 g of the powdered material was macerated in 1000 mls of distilled water over 24 hours and filtered using Watman No.1 filter paper. The filtrate was evaporated to dryness at 50°C on a water bath.

2.2 Animals

Twenty five (25) male albino Wister rats weighing 135±15 g were obtained from National Veterinary and Research Institute (NVRI) Vom, Jos, Plateau State, Nigeria. The rats were acclimatized for one week, kept in plastic cages at room temperature and fed pelleted diet (Grand Cereal Limited, Jos, Nigeria) and water *ad libitum* throughout the experimental period.

2.3 Chemicals

All reagents used in the study were of high purity and purchased from SIGMA Chemicals Co. (Dorset, UK).

2.4 Experimental Design

The experimental animals were randomly divided into five groups of five animals each. The treatment protocol is given below;

Group I (Control): Received water and Normal feed.

Group II: Received 100mg/Kg body weight of extract (*Fagara zanthoxyloides*).

Group III: Received 200mg/Kg body weight of extract (*Fagara zanthoxyloides*).

Group IV: Received 300mg/Kg body weight of extract (*Fagara zanthoxyloides*).

Group V: Received 400mg/Kg body weight of extract (*Fagara zanthoxyloides*).

The duration of treatment in all groups was 21 days.

2.5 Biochemical Assay

At the end of twenty one days, the animals were anaesthetised in chloroform vapour, dissected and blood samples collected by cardiac puncture into plain blood bottles. The blood was allowed to clot for few minutes. Serum samples were extracted by centrifuging the clotted blood at 3000 g for 10 min using a bench top centrifuge. Serum biliary bilirubin, cholesterol concentration was estimated using calorimetric method as described by Allain *et al.*, (1974). Serum biliary electrolytes Cl^-, Na^+ and K^+ were measured using a flame emission spectrophotometer as described by Tietz *et al.*, (1994) and HCO_3^- was estimated using a titrimetric method as described by Cheesbrough, (1992).

2.6 Statistical Analysis

All results were expressed as the mean ± standard error of mean for five replicates. Statistical analysis of variance was carried out using one way ANOVA (SPSS 22.0) followed by Duncan multiple range tests to determine significant differences in all the parameters. A value of $p< 0.05$ was used as the level of significance.

Table I. Effect of Stem Bark Aqueous Extract of *Fagara zanthoxyloides* on Biliary Concentration of Total, Conjugated and Unconjugated Bilirubin

DOSE (mg/kg body wt)	TOTAL BILIRUBIN	CONJUGATED BILIRUBIN	UNCONJUGATED BILIRUBIN
0 (control)	58.85±3.30	31.10±1.05	27.75±0.02
100	49.34±0.12*	27.23±0.15*	23.11±0.18*
200	46.31±1.10*	25.97±2.12*	20.34±0.10*
300	36.18±0.03*	20.47±0.23*	15.71±1.04*
400	27.14±2.08*	15.11±0.25*	12.03±0.20*

Values are expressed as mean ± SEM, n=5, $p<0.05$

* Significantly lower when compared to the control group.

Table II. Effect of Stem Bark Aqueous Extract of *Fagara zanthoxyloides* on the Biliary Cholesterol and Phospholipid in mmol/L.

DOSE (mg/kg body wt)	CHOLESTEROL	PHOSPHOLIPIDS
0 (control)	2.04±0.02	104.00±1.16
100	1.92±0.05	95.01±0.20*
200	1.69±1.04*	89.01±0.04*
300	1.42±0.10*	81.34±2.07*
400	1.38±0.13*	74.15±2.47*

Values are expressed as mean ± SEM, n=5, $p<0.05$
* Significantly lower when compared to the control group.

Table III. Effect of Stem Bark Aqueous Extract of *Fagara zanthoxyloides* on Biliary Electrolytes in mmol/L.

DOSE (mg/kg body wt)	Na^+	HCO_3^-	K^+	Cl^-
0 (control)	129.00±1.89	28.08±0.67	5.00±3.12	98.15±1.13
100	126.06±0.12*	26.20±0.05*	5.01±0.01#	97.06±2.08*
200	125.98±0.67*	24.24±0.01*	5.02±1.16#	88.79±0.49*
300	122.31±1.09*	21.05±1.12*	5.03±2.68#	69.23±1.16*
400	119.01±1.25*	15.23±1.00*	5.04±1.08#	61.18±0.11*

Values are expressed as mean ± SEM, n=5, $p<0.05$
* Significantly lower when compared to the control group.
# No significant difference when compared to the control group.

Table IV. Effect of Stem Bark Aqueous Extract of *Fagara zanthoxyloides* on Bile Output in ml/hr.

DOSE (mg/kg body wt)	BILE OUTPUT (ml/hr)
0 (control)	3.00±0.01
100	2.30±0.04*
200	2.10±1.03*
300	1.40±2.01*
400	0.90±0.04*

Values are expressed as mean ± SEM, n=5, $p<0.05$
* Significantly lower when compared to the control group.

3.0 Results and Discussion

The results of the effect of stem bark aqueous extract of *Fagara zanthoxyloides* on biliary concentration of total, conjugated and unconjugated bilirubin is presented in Table I. The different doses of *Fagara zanthoxyloide* given to the rats affect the biliary concentration of total, conjugated and unconjugated bilirubin. They are significantly ($p>0.05$) lower when compared with the control group.

Bilirubin has biological and diagnostic values being an important catabolic product of blood. Obasi *et al.*, (2016) report that hepatocytes convert bilirubin to a polar form via phase II mechanism of biotransformation by adding glucuronic acid or sulfate molecules to it in a process referred to as conjugation. This reaction increases its solubility in water and thus enhances the ease with which bilirubin becomes excreted in the bile (Murray *et al*., 2000). The results suggest an increase in the levels of conjugated bilirubin in a dose dependent manner which may increase the ease with which bilirubin becomes excreted in the bile, and this may explain the dose dependent decrease in the level of total bilirubin observed in this study.

The results of the effect of stem bark aqueous extract of *Fagara zanthoxyloides* on the biliary cholesterol and phospholipid is presented in Table II. The results observed after 21 days of administration of the extract showed a dose dependent significant decrease in biliary cholesterol and phospholipids level across the experimental groups ($p>0.05$).

Decreased level of biliary cholesterol may be due to biliary sludge, which tends to inhibit and absorb the bile pigments towards the formation of either cholesterol or pigment gallstones. Biliary sludge is a crucial intermediate stage in the pathogenesis of both cholesterol and pigments gallstones, because it facilitates crystallization and agglomeration of solid plate-lik cholesterol monohydrate crystals, as well as precipitation of calcium billirubinate and ultimately develops into macroscopic stones (Lee *et al.*, 2015)

The results of the Effect of stem bark aqueous extract of *Fagara zanthoxyloides* on biliary electrolytes is presented in Table III. The results observed after 21 days of administration of the extract showed a dose dependent significant decrease in Na^+, HCO_3^- and Cl^- concentration across the experimental groups ($p>0.05$) while the concentration of potassium ion is not significantly different ($p>0.05$) when compared to the control group.

Obasi *et al.,* (2016) report that, inorganic electrolytes occur in large quantities in both extracellular and intracellular fluids. They comprise the single most important factor in the transfer and movement of water and electrolytes between the three divisions of the extracellular and intracellular compartments. Our study shows that, there was a significant

decrease in the concentration of Na^+, HCO_3^- and Cl^- and this could lead to some health challenges. Obembe *et al*., (2015) report that, increase in the concentration of potassium (K^+) and bicarbonate (HCO_3^-) could be useful as bicarbonate have been known to curb the harsh acidic condition in the duodenum and avert factors that may bring about duodenal ulceration following gastric emptying.

The results of effect of stem bark aqueous extract of *Fagara zanthoxyloides* on bile output are presented in Table IV. The results observed after 21 days of administration of the extract showed a dose dependent significant decrease in biliary secretion across the experimental groups ($p>0.05$).

Bile is an exceptional and very important aqueous secretion of the liver that is formed by the hepatocytes and modified downstream by absorptive and secretory properties of the bile duct epithelium. Bile acid formation and secretion serves the intestinal digestion of lipids and absorption of lipid-soluble nutrients. In addition, unessential and potentially poisonous material is disposed of in bile, including cholesterol, bilirubin, and an abundance of xenobiotics such as drugs and environmental chemicals as well as their metabolites (Obembe *et al*., 2015). An alteration in the process of biliary synthesis as well as its secretion will lead to an impaired gastrointestinal metabolism of fats which may result to steatorrhoea.

Biliary output was observed to be reduced in our study and this may be as a result of altered hepatic function thereby accounting for the decrease in its synthetic function (Obembe *et al.,* 2010; Guyton and Hall, 2011). They also report that, prostaglandins cause decrease in bile secretion in rats *in vivo* and *in vitro*. These prostaglandins are formed from polyunsaturated lipids being one of the phytochemical constituents.

Conclusion

Although chronic administration of *Fagara zanthoxyloides* reduces bile secretion which may lead to poor gastrointestinal fat metabolism, it also affects electrolytes balance which will affect duodenal stability (health). Hence, its use in the study area as a major spice should be properly guided as it may bring about abnormal conditions like steatorrhoea, duodenal ulceration, etc.

References

Adebiyi A.O., Koekemoer T., Adebiyi A.P., Smith N., Baxter E., Naude R.J. and Vande-Venter M. (2009). Antimicrobial and antioxidant activities of crude extracts of two Nigerian chewing sticks. *Pharmaceutical Biology.* 47(4):320-327. 2009.

Adesina S.K. (2005). The Nigerian *Zanthoxylum*; Chemical and biological values. *Afr. J. Trad. Med*. 2 (3), 282-301.

Allain C.C., Poon L.S., Chan C.S.G., Richmond W. and Fu P.C. (1974). Enzymatic determination of total serum cholesterol. *Clinical chemistry.* 20:470-475.

Ameesh M. and Murugan S. (2016). Protective Role of Ethanolic xtract of TridaxProcumbens in Experimental Hepatocellular Carcinoma in Rats. *IOSR Journal of Dental and Medical Sciences (IOSR-JDMS).* 15(4): 32-38.

Anne I.O., Andrew O.O. and Idu M. (2013). Phytochemistry and antimicrobial activity of *Zanthoxylum zanthoxyloides root* used as chewing stick in Nigeria. *The Journal of Phytopharmacology* 2(6): 1-7.

Barrett K.E.,Barman S.M., Boitano S. and Brooks H.L. (2012). Ganong's Review of Medical Physiology. Twenty-Third Edition. New York: McGraw-Hill Companies, Inc. 512.

Cheesbrough, M. (1992). Medical Laboratory Manual for Tropical Countries, vol. 1, EESB, Cambridge, UK, 2nd edition.

Guyton C. and Hall J.E. (2011). The liver as an organ in: Textbook of Medical Physiology. 12th ed. Elsevier Saunders,Philadelphia, 859-864.

Itemire O. A., Ogbimi O. A. and MacDonald I. (2013). Phytochemistry and antimicrobial activity of *Zanthoxylum zanthoxyloides* root used as chewing stick in Nigeria. *The Journal of Phytopharmacology*. 2(6): 1-7

Lee J.Y., Keane M.G., Pereira S. (2015). Diagnostic and treatment of gallstone disease. *Practioner.* 259(1783):15-19.

Meyer S and Kulkarni A (2001). Hepatotoxicity in: Introduction to biochemical toxicology. 3rd edition. New York: John Wiley and Sons, 487.

Murray R.K., Granner D.K., Mayes P.A. and Rodwell V.W. (2000). Harper's Biochemistry (20th ed). McGraw-Hill, New York., 594–602.

Obasi N.A., Obasi S.E., C.O. Egwu, G. Otuchristian and F.N. Nkasi (2016). Effects of oral administration of ethanolic leaf extract of *Mucana puriens o*btained from Afikpo on serum Biochemical Parameters and electrolytes in Albino Wistar Rats. *European Journal of Pharmaceutical and Medical Research.* 3(4), 82-88.

Obembe A. O, Ofutet E. O., Okon V. E. and Okpo-ene A. I. (2015). *Xylopia aethiopica* reduces the rate of bile secretion and increases biliary bicarbonate concentration in albino rats. *Der Pharmacia Lettre,* 7(8):85-91.

Obembe A.O., Antai A.B., Owu D.U., Okwari O.O., Eteng M.U. and Osim E.E. (2010). Bile secretion and palm oil diets in Wistar rats. *Nutrition and food Science.* 40(4): 388-394.

Tietz, N.W. E.L. Pruden and O. Siggaard-Anderson. (1994). In: "Tietz textbook of Clinical Chemistry" (Bur tis, G. A. and Ashwood, E. R. eds.) W. B. Saunders company, London. pp. 1354-1374.