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Research Article

Assessment of Hypolipidaemic Effect of Leptadenia Hastata Leaves in Albino Rats

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Abstract: This study was designed to determine the effect of *Leptadenia hastata* leaves on serum lipid profile and glucose in experimentally-induced hyperlipidemic Wistar rats. Sixteen adult Wistar rats were randomly assigned into four groups of four rats each. Group 1 was the hyperlipidemic group (positive control), Group 2 was the hyperlipidemic supplemented with *L. hastata* leaves group, Group 3 was the normolipidemic supplemented with *L. hastata* leaves group and Group 4 normal group fed on normal diet (negative control). The changes in the serum lipid profile and glucose were monitored after three weeks. The result of the serum lipid analysis showed a significant ($p<0.05$) reduction in the serum total cholesterol, low-density lipoprotein cholesterol with concurrent significant ($p<0.05$) increase in serum high density lipoprotein cholesterol in hyperlipidemic group treated with *L. hastata* leaves (group 2) compared with the hyperlipidemic group (group 1). Serum glucose level was also significantly higher in hyperlipidemic group ($p<0.05$) compared with other three groups. The result of this study suggests possible hypolipidemic effect of *L. hastata* leaves.

Keywords: Hyperlipidemia, *Leptadenia hastata*, lipoproteins

INTRODUCTION

Plants have been used for time immemorial by humans to meet basic necessities such as food, shelter, fuel and health. Though primitive societies had relied solely on plants for therapeutic management of diseases, in the recent past, there has been a growing interest in herbs either as alternative or complement to orthodox medicine in the management of myriad health problems (Baba *et al*., 1992).

Also basic information as a lead to scientific probing of medicinal plants in Africa has been obtained from herbalists or traditional medical practitioners, native herb sellers and the local indigenous people (Baba *et al*., 1992). By the early nineties, screening work on African medicinal plants has advanced with publications arising from the following research areas: antimicrobial (16%), molluscicidal (11%), antimalarial (7%), plant toxicology (7%), antitumour-related studies (4%) and others (54%) (Sofowora, 1993). For molluscicidal activity: *Phytolacca dodecandra*, *Tetrapleura tetraptera* and *Swartzia madagascariensis* had become an international research interest for the control of schistosomiasis (Adewunmi, 1991).

Hyperlipidemia is a condition associated with abnormally elevated levels of lipids in the blood. Lipids being non water soluble are transported in a protein capsule as lipoproteins whose densities are determined by the size of the capsules. The lipoprotein density and the type of apo-lipoprotein determine the fate of the particle and its influence on metabolism. The most dense and smallest are called High Density Lipoprotein (HDL), also known as good cholesterol. Lipoproteins that are a little dense are called Low-Density Lipoproteins (LDL). The least dense and the largest of the Lipoproteins are the very low-density Lipoproteins (Champe *et al*., 2008).

Cholesterol is required to build and regulate fluidity of cell membrane over the range of physiological temperatures. The hydroxyl group on cholesterol interacts with the polar head groups of the membrane phospholipids and sphingolipids, while the bulky steroid and the hydrocarbon chain are embedded in the membrane, alongside the non-polar fatty acid chain of the other lipids. Cholesterol reduces the permeability of the plasma membrane to protons, hydrogen ions and sodium ions (Haines, 2001). The insolubility of cholesterol in water is implicated as a factor in the development of atherosclerosis. It is characterized by pathological deposition of plaque of cholesterol and other lipid on the insides of major blood vessels, culminating in coronary artery disease. Atherosclerosis is initiated by inflammatory processes in the vessel wall in response to retained Low-Density Lipoprotein (LDL) molecules (Williams and Tabas, 1995). High density lipoprotein carries cholesterol away from the cells of the body while Low-Density Lipportein (LDL) carries it back into the system for use by the various body cells (Brown, 2007).

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Accumulation of LDL molecules on the vessel walls enhances their susceptibility to oxidation by free radicals and become potentially toxic to the cell leading to the damage of the arteries. Such damage caused by oxidized-LDL invokes immune system response by sending specialized white blood cells (macrophages and T-lymphocytes) to absorb the oxidized-LDL forming specialized foam cells. These white blood cells are not able to process the oxidized-LDL and ultimately grow and then rupture, depositing a greater amount of oxidized cholesterol into the artery wall. This triggers more white blood cells continuing the cycle (Sparrow and Olszewski, 1993).

Asciepiadaceae plants to which *Leptadenia hastata* is a family were associated with various potential therapeutic effects. *Leptadenia hastata* is a twiner with a corky on the older stems, well developed half succulent and persistent petiole leaves with a thick greenish sap. The leaves are more abundant and fresh during rainy season (Aliero *et al*., 2001). The plant has been reported to be safe with low LD 50 of 1513 mg/kg (Tambaura *et al*., 2005). It contains triterpenes, fatty acids, amino acids, polyoxypregnane, lutein and B-carotene (Aquino *et al*., 1996; Nikiema *et al*., 2007; Tambaura *et al*., 2005) and selenium and phosphorus (Freiberger *et al*., 1998).

In this study the possible hypolipidemic potential of *Leptadenia hastata* leaves were investigated in animal model of hyperlipidaemia, since it is being used in Hausa land in the treatment of hyperlipidemia.

MATERIALS AND METHODS

Chemicals: All chemicals unless otherwise stated were purchased from Randox Laboratories LTD (Ardmore, Diamond Road) United Kingdom.

Plant materials: The leaves of *L. hastata* were collected from natural habitat in Kano state, Nigeria in 2011. The leaves were sorted to remove the dead ones, washed to remove debris and dust particles and sun-dried for four days. The dried leaves were milled to get a course provider.

Study subject: Sixteen male albino rats weighing between 80-100 g purchased from Biology Laboratory Bayero University Kano were used. All aspect of animal care compiled with the ethical guidelines and technical requirement approved by the Institutional Animal Ethics Committee of the Department of Biochemistry, Bayero University, Kano, Nigeria.

The experiment was carried out in Biological science Laboratory after a week of purchased. The albino rats were divided into four groups of four rats per group (groups 1, 2, 3 and 4).

Animals in group 1, 2 and 3 were fed with different amount of supplement while group 4 animals serve as control. Group 1 was given cholesterol; butter and feed, group 2 were fed cholesterol, butter, feed and extract. Group 3 were given only feed and extract, then lastly the control were given only normal feed.

Experimental design:

Group 1: Hyperlipidemic and were not administered *Leptadenia hastata* (Hyperlipidemic control)
Group 2: Hyperlipidemic and were administered *Leptadenia hastate*
Group 3: Normal but administered *Leptadenia hastate*
Group 4: Normolipidemic not administered *Leptadenia hastata* but were only given water and food (Normolipidemic Control)

Group 1 and 2 were induced nutritionally to be hyperlipidemic by mixing the commercial feed with 40% butter 0.5% cholic acid and 5% cholesterol, but in which the diet of group two was supplemented with 20% *Leptadenia hastata* leaves. Group 3 were given commercial feed and 20% *Leptadenia hastata*. Group 4 was normolipidemic control fed on 100% normal commercial diet.

Sample collection: At the end of 21 days period, the rats were sacrificed by suffocation with carbon IV oxide to make the animals unconscious followed by surgical dislocation utilizing a stick. Blood samples were collected followed by centrifuging to collect serum for biochemical analysis.

Analytical procedures: The serum thus obtained was used for total cholesterol, HDL-Cholesterol and Triglycerides estimation. Serum total cholesterol was estimated using method of Flegg (1973), estimation of Triglycerides by Mendez *et al*. (1975) and HDL-cholesterol by Lopez-Vitrella *et al*. (1977), LDL-cholesterol values were estimated by a modification of Friedwald formula (Sandkamp *et al*., 1990). Serum glucose was estimated by the method of Glucose Oxidase Method (Barham and Trinder, 1972).

Phytochemical screening: The methods of Harborne (1973), Sofowora (1993) and Trease and Evans (1983) were used to identify the following phytochemicals in the extracts: Saponins, Tannins and Glycosides.

Statistical analysis of data: The data were analyzed using descriptive and inferential statistics. All values were presented as mean±Standard Error of Mean (S.E.M.) for four rats in each of the four groups of rats. The significance of difference in all the means of all parameters reported for the four groups of animals was determined using paired sample student t-test and a p-value of <0.05 (two failed) was considered as significant.

RESULTS

Table 1 shows the effect of *Leptadenia hastata* on serum lipid profile and serum glucose in both induced

Table 1: Effect of *Leptadenia hastata* on serum lipid profile and glucose in experimental rats

Group	Total cholesterol (mmol/L)	HDL chol. (mmol/L)	TRLG (mmol/L)	VLDL chol. (mmol/L)	LDL chol. (mmol/L)	Glucose (mmol/L)
Hyperlipidemic control	5.15±0.06	1.64±0.24	1.28±0.21	0.58±0.05	2.74±0.45	5.95±0.29
Hyperlipidemic on supplement	3.55±0.38*	2.82±0.12*	1.03±0.21	0.48±0.10	0.87±0.08*	4.89±0.24*
Normolipidemic on supplement	2.75±0.17	1.68±0.16	0.63±0.22*	0.32±0.21	0.41±0.02*	4.08±0.74*
Normolipidemic on normal diet	2.93±0.05	2.68±1.99	0.70±0.14*	0.35±0.04	0.30±0.11*	4.18±0.11*

*: Statistically significant at (p<0.05); Results are mean+S.E.M. (standard error of the mean); Number of experimental animals each group = 4

Table 2: Phytochemical screening of fresh and dried leaves extracts of *Leptadenia hastata*

Phytochemical	Relative amount of dried leaves
Tannins	++
Saponins	+++
Flavonoids	++
Volatile oils	+
Anthroquinones	-
Phenolic glycosides	+
Alkaloids	++

+: Trace amount; +++: Presence; -: Absence

hyperlipidemic and normolipidemic rats. The table shows that the administration of *Leptadenia hastata* leaves to the rats reduced the serum lipid profile of the rats. The HDL value for rats administered with *Leptadenia hastata* was higher than the hyperlipidemic control.

There was significant reduction of total cholesterol, triglycerides, LDL cholesterol and VLDL in hyperlipidemic rats administered *Leptadenia hastata* leaves compared with hyperlipidemic control ($p<0.05$). The total cholesterol level reduced from 5.15 mmol/L±0.06 to 3.55 mmol/L±0.38, the triglycerides level reduced from 1.28 mmol/L±0.21 to 1.03 mmol/L±0.2. Similarly the serum VLDL level was also reduced from 0.58 mmol/L±0.05 to 0.48 mmol/L±01.10, while the LDL level was reduced from 2.74 mmol/L±0.45 to 0.87 mmol/L±0.08. Serum glucose levels also decreases from 5.95 mmol/L±0.29 to 4.89 mmol/L±0.24. Conversely, the was a significant increase in HDL levels in hyperlipidaemic rats administered with *Leptadenia hastata* compared with hyperlipidaemic control ($p<0.05$).

Similarly there was significant difference in hyperlipidemic rats administered with *Leptadenia hastata* leaves in the level of serum glucose compared with hyperlipidemic control ($p<0.05$). For group 3, with also sub-groups on normal and administered *Leptadenia hastata* leaves, respectively, there was reduction in total cholesterol and LDL values, as well as serum glucose level compared with hyperlipidemic control group ($p<0.05$).

Table 2 shows the result of phytochemical analysis. The evaluation revealed the presence of flavanoids, tannins and alkaloids among other classes of compounds. Anthroquinones have not been identified.

DISCUSSION

Obesity and hyperlipidemia have been implicated as etiologic factors of atherosclerosis and heart attack. There is evidence both *in vitro* and in animal models of human atherosclerosis that oxidized lipids derived from LDL contribute to many of the stages of atherosclerotic development (Heineke, 1998). Mechanisms that have been proposed to result in enhanced Lipoprotein oxidation either locally and systemically and the progression and the development of atherosclerosis include increased production of tumour necrosis factor and other cytokines; up regulation of NADPH oxidase (s) and other oxidative enzymes in vascular tissues and increases in the renin angiotensin system (Brasier *et al*., 2002).

Overweight and obesity are associated with significantly increased mortality from atherosclerotic cardiovascular disease and other causes. Obesity is also associated with major risk factors for atherosclerosis including hyperlipidemia, diabetes mellitus, hypertension and metabolic syndrome (Brasier *et al*., 2002).

The human loss and financial cost associated with hyperlipidaemia is highly enormous in the United states, with estimated 100,00 death and management cost to the tune of $200 m annually (American Heart Association, 1997). The relationship between coronary heart disease and elevated serum cholesterol has been well established, prompting cardiologists to prescribe lipid lower agents to patients with coronary artery disease and hyperlipidemia (Daskalopoulou and Mikhailidis, 2006; Taylor *et al*., 2013). It is strongly associated with lifestyle characteristic of an affluent society and thus, rapid change of life style in developing countries predisposes people to hyperlipidemia and hence greater chances of developing heart attack (Taylor *et al*., 2013). Faulty diet is a very common cause of heart disease; therefore strong inclination to fast food rich in saturated fats has led to increase in Coronary Heart Disorder (CHD) in the developing countries (Kulkarni and Gurpreet, 1999). There is a reservoir of basic information on the use of herbs throughout the globe in the management or control of hyperlipidemia. Antihyperlipidemic activities of *Calotropis procera* and *Gymenma sylvestre* respectively were well reported (Bayala *et al*., 2011; Rachh *et al*., 2010). Chavda *et al*. (2010) found that *Calotropis procera* root bark has significant antioxidant and hepatoprotective potentials. However, *Leptadenia hastata* an edible plant of Tropical Africa has showed anti-inflammatory action (Nikiema *et al*., 2007) and its inhibitory effect on certain tumoral cells (Aquino *et al*., 1996). The plant is used in the treatment of scabies hypertension, catarrh and skin diseases (Thomas, 2012). Aqueous extract of leaf stem *Leptadenia hastata* has been reported to reduce the progressive velocity, linearity and sperm motility of male Wistar rats (Bayala *et al*., 2011). Though the plant has been associated with myriads of therapeutic functions, there is paucity of information on its use as hypolilpidemic agent. Though Bello *et al*. (2011) have reported reduction of serum VLDL-C in alloxan induced diabetes, it had not been shown to have the potential of reducing LDL-C. In Hausa land *Leptadenia hastata* is used in the management of hyperlipidemia.

In this study treatment with *Leptadenis hastata* produced a significant decrease in the serum lipids in induced hyperlipidemic rats which may be due to certain phytochemicals which act as primary antioxidant with high redox potentials and singlet oxygen quenching capacity (Kahkonen *et al*., 1999). *Leptadenis hastata* contain phytosterols which is reported as useful in the treatment of hyperlipidemia (Sudhessh *et al*., 1996).

From the present data the levels of total serum cholesterol, triglyceride and LDL lipoprotein had been lowered significantly with *Leptadenia hastata*. Hence, it can be utilized in providing dietary management in the prevention of atherosclerosis obesity and hyperlipidemia.

Phytochemicals such as flavonoids have been detected. Flavonoids are shown to act by inhibiting cholesterol esterase with the potential effect of treating obesity (Sivashanmugam *et al*., 2013) as well as inhibiting Coenzyme A reductase and Cholesterol acyl transferases thereby lowering serum cholesterol (Lee *et al*., 1999).

Flavonoids also activate cAMP synthesis, with subsequent activation of protein kinase. Protein kinase increases triacyglycerol hydrolysis with consequent reduction in blood and liver triglycerides and VLDL (Yang *et al*., 2004). Furthermore flavonoids activate LDL receptors (Kirk *et al*., 1998) as well as preventing the macrophage oxidation of LDL cholesterol, hence have the potential of inhibiting atherosclerosis (De Whalley *et al*., 1990).

Flavonoids are also reported to have anti atherogenic and thrombogenic effect on macrophage and platelet functions as well as inhibiting enzymes such as (phospholipase A2, cyclooxygenase and lipoxigenase (Frankel *et al*., 1993).

Polyphenols such as flavonoids and tannins have been shown to have numerous health protective benefits, which include lowering of blood lipids (Hayashi *et al*., 2002). Methoxylated flavonoids of citrus appear to have the potent effect of modulating liver lipid metabolism by suppressing apoB-containing lipoprotein secretion (Hayashi *et al*., 2002). Apolipo proteinB (apoB) is the primary lipid transport protein for Low Density Lipoproteins (LDL) and high levels are related to heart disease (Hayashi *et al*., 2002).

Citrus flavonoids such as tangeretin and nobelatin inhibit apoB secretion with modest reduction in cholesterol deposition by apoB, a key player play in LDL-cholesterol transport and removal. Reduction in Apo B synthesis is expected to reduce circulating LDL cholesterol, a proven risk factor of cardiovascular disease (Lin *et al*., 2011). Thus it can be suggested that the polyphenol contents in the extract may impact hypolipidaemic property of the leaves of *Leptadenia hastata*.

From the present data the levels of total serum total cholesterol and triglyceride were lowered significantly with *Leptadenia hastata*. These therapeutic effects are likely associated with the constituents phytochemicals such as flavonoids which were demonstrated to have the potentials of lowering serum lipid, due to their ability to enhance esterification of cholesterol, prevention of macrophage oxidation of lipids, increased triglycerides hydrolysis via induction of protein kinases and inhibition of oxidative enzymes. Thus, the use of leaves of *Leptadenia hastata* widely used in Hausaland as anti-hyperlipidaemic agent can be justifiably advocated as part of therapeutic measures to control hyperlipidaemia, with the anticipated consequence of reducing coronary heart disease, management of obesity and treatment of hypertensive complications.

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