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Full Length Research Paper

Effect of rosemary (*Rosmarinus officinalis*) on lipid profiles and blood glucose in human diabetic patients (type-2)

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Investigation of the effect of oral administration of rosemary (*Rosmarinus officinalis*) as powder on lipid profiles and blood glucose in healthy and type-2 diabetic human patients was done. Forty-five type-2 diabetic patients and 15 non-diabetic persons of age 40 years or older participated in the study. Patients selected in this study had fasting blood glucose in the range 160-300 mg/dl, and high lipid profiles levels. In addition, patients were allowed to take their routine diet and usual diabetic medicine but not any other health medication. All participants were told to take 3 g of rosemary per day for 4 weeks. Plasma lipid profiles and blood glucose were measured before and after rosemary administration. Significant effect of rosemary is obviously noticed in diabetic patients. Lipid profiles (low density lipoprotein LDL, triglycerides and cholesterol) decreased by 31-35%, and blood glucose decreased by 21%. In addition, high density lipoprotein (HDL) in both diabetic and non diabetic persons increased by 22%. Rosemary showed favorable changes in lipid profiles and blood glucose levels in type-2 diabetic patients.

Key words: Type-2 diabetes, rosemary, dyslipidemia, blood glucose.

INTRODUCTION

Diabetes mellitus (DM) is a group of metabolic disorders that share the common feature of hyperglycemia. The disease affects approximately 6.4% of the world's population with the highest prevalence in North America and Caribbean (10.2%) followed by middle East and North Africa (9.3%) (International Diabetes Federation, 2010). It is categorized as absolute (type 1) or relative (type 2) deficiencies in insulin secretion or receptor insensitivity to endogenous insulin, resulting in hyperglycemia (ELHilaly et al., 2007). Diabetic patients must have restrictive measures of diet to control blood glucose levels, normal body weight and prevent heart and vascular disease as well, (Melzig and Funki, 2007). Fruits, vegetables, herbs and spices are a promising alternative diet which were found to limit harsh metabolic disorders correlated to lipidemia (Miller et al., 2002) and cardiovascular diseases (Creager et al, 2003). Generally, these plants have a variety of high antioxidant concentrations that inhibit the

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Table 1. Effect of rosemary consumption on fasting blood glucose and lipid profiles

Test	Diabetic patients			Healthy persons		
	Before consumption	After consumption	Change (%)	Before consumption	After consumption	Change (%)
FBG	95.5±11.60	86.7±7.10	- 9	202.6±28.2	159.12±9.2*	-21
Triglycerides	170.7±13.6	145.4±6.23	- 15	240±17.1	163.8±9.8**	-32
Cholesterol	191.3±11.20	158± 12.10	-17	272±9.5	176±8.4**	-35
LDL	127.7±15.10	102.7± 10.70	-19	232.5±28.6	160.1±9.8**	-31
HDL	45.6± 3.2	57.3± 3.22	+20	37.2± 7.3	49.2±6.3*	+22

> Values equal means ± SD (mg/dl); * Significant (P<0.05); ** Highly significant (P<0.01).

oxidation of metabolites in biological pathways (Linda et al., 2006).

Rosemary (*Rosmarinus officinalis*) is an evergreen perennial aromatic shrub growing as decorating plant in gardens and used commonly as spice in food processing. Its effects are attributed to the different chemical constituents including monoterpenes, diterpenes and the phenolics derivatives -mainly caffeic acid known as rosmarinic or carnosic acid and gallic acid. Among these bioactive constituents, the pharmacologic properties have been suggested to be highly attributed to rosmarinic acid, the predominant secondary metabolite in rosemary. Biochemically, rosemarinic acid is an ester of caffeic acid, hydroxydihydrocaffeic acid, chlorogenic acid and their hydrolyzed metabolites (El Deeb, 1993; Herrero et al., 2010; Rababah et al., 2004; Wang et al., 2004). Rosmarinic acid has been suggested to have anti-atherogenic activity by preventing the oxidation. (Dubois et al., 2008; Furtado et al., 2010; Hadafi et al., 1998; Moon et al., 2010; Park et al., 2008; Shetty, 2007; Vanithadevi and Anuradha, 2008).

Ethanolic extract of rosemary leaves showed protective and anti mutagenic effects in rats and potential effect on glucose homeostasis in rabbits (Fahim et al., 1999; Bakirel et al., 2008). In recent study, Labban et al. (2014) found that 10 g of rosemary leaves powder for four weeks significantly improved lipid profiles and glucose level in human selected randomly. However, the present study aims to investigate the effect of powder consumption of whole rosemary (leaves and stems) on lipid profiles and blood glucose levels in human type- 2 diabetic patients.

MATERIALS AND METHODS

Data collection

A pre/post test randomized study design was utilized to show the impact of rosemary consumption on blood glucose and lipids levels among type-2 diabetic patients and non-diabetic persons.

Blood samples were collected in Al-Mafraq Governmental Hospital in Jordan. Forty-five patients recognized with type-2 diabetes of both sexes (25 males and 20 females) and 15 healthy subject (10 males and 5 females) of mean age 46 ± 6 years were recruited for the current study.

Diabetic patients who were encountered had fasting blood glucose in the range of 160-300 mg/dl, high lipids profile level, taking their routine diet and usual diabetic medicine but not any other medicinal drug health.

All participants were told to take two capsules (500 mg each) of whole rosemary (*R. officinalis*) powder three times daily after breakfast, lunch and dinner for a four week course. These capsules were prepared by the technician of the local pharmacy. Plasma lipid profile and blood glucose were measured before and after rosemary administration coarse. The study was approved by medical ethical committee of the Al-Ahliyya Amman University

Biochemical measurements

Approximately 7 ml samples of venous blood were taken into lithium heparin vacuum tubes for measurements of fasting blood glucose level (FBG), triglyceride (TG), total cholesterol (Ch), high-density lipoprotein (HDL) and low-density lipoprotein (LDL) before and after rosemary administration coarse. The blood was centrifuged at 2000 xg for 10 min at 4°C, and then after, the separated plasma was carried immediately by cold boxes filled with ice to the Jerusalem Consulting Laboratory (Zarka-Jordan). Measurements were achieved by using Chemiluminescence imunoassay; Immulite 2000 (Siemens Medical Solutions Diagnostics, Deerfield , IL).

Statistical analysis

Statistical analysis was conducted using descriptive statistics; means, and standard deviation (SD) of the means utilizing SPSS (version 14). A probability value (*P*) of < 0.05 was considered to be statistically significant.

RESULTS AND DISCUSSION

Changes in lipid profile and glucose levels due to rosemary administration are estimated in both sexes randomly and illustrated in Table 1. Significant effect of rosemary is noticeably seen in diabetic patients. Before rosemary administration, higher levels of FBG, TG, Ch, LDL with lower levels of HDL in diabetic patients when compared with levels of healthy persons was seen. However, after four weeks of consumption of rosemary, levels of FBG, TG, Ch and LDL were significantly reduced in 21, 32, 35, and 31%, respectively, and 22% increase in HDL. Nevertheless, healthy persons had an improvement in HDL level 20% without affecting other parameters.

The significant decline in the blood glucose, triglycerides, cholesterol, LDL and increase HDL cholesterol caused by rosemary may be an indication of progressive metabolic control of rosemary. Hypoglycemia effect of rosemary may be attributed to several metabolic mechanisms such as increasing the insulin level (Vanithadevi and Anuradha, 2008) due to regeneration or stimulation of the *β*-cells of the pancreas (Alnahdi, 2012) or by inhibiting the intestinal absorption of glucose by inhibition of intestinal amylase enzyme (McCue and Shetty, 2004)) or by potent anti-oxidant properties. Accordingly, changes in lipid profile could be established by different metabolic mechanisms, that is, inhibition of pancreatic lipase, a reduction in the absorption of dietary fat supported by an increase in fecal fat excretion (Ibarra et al., 2011), changed LDL receptor activity and uptake of LDL-C by hepatocytes (Attar, 2006), changed rate of fatty acids oxidation in the liver and reduced rate of triglycerides biosynthesis (Attar 2006). In addition, may be attributed to the antioxidant properties that inhibit lipid peroxidation**.**

Chemically, most important constituents of rosemary are caffeic acid and its derivatives such as rosmarinic acid which has antioxidant effect (Decker, 1995; Al-Sereiti et al., 1999) and polyphenols glabridin (derived from licorice). Moreover Fuhrman et al. (2000) reported that rosemary contains a mixture of natural antioxidants. Generally, antioxidants change dramatically metabolism of glucose, lipid and proteins associated with cardiac diseases. Antioxidants were found to perform several cardio protective properties including the ability to prevent LDL from oxidative modification by monitoring the levels of triglycerides, HDL and LDL. HDL (Nofer et al., 2002) or accumulation of lipid peroxides on LDL was shown (Mackness et al., 1993). More or less, rosemary may exerts antioxidant effects indirectly by increasing levels of anti-oxidants agents such as glutathione reductase, vitamin C and *β* carotene (Labban et al., 2014).

In conclusion, the present data demonstrated that consumption of rosemary may lead to reduction in the risk of hyperglycemic and hyperlipidemic symptoms associated with heart diseases. However, additional investigation will be needed to purify the bioactive constituents in the rosemary.

Conflict of Interests

The author has not declared any conflict of interests.

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Full Length Research Paper

Hypolipidemic effect of *Irvingia gabonensis* fruits juice on sodium fluoride induced dyslipidemia in rats

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Effect of *Irvingia gabonensis* fruit juice administration on serum lipid profile of sodium fluoride (NaF)-intoxicated rats was investigated. Twenty-four (24) male Wistar rats divided into four groups of six (6) animals each - one control and three intoxicated groups were used. The normal control (NC) group received only standard pelletized diet and water. All three intoxicated groups received 20 $mgkg^{-1}$ bodyweight of NaF daily by gavage for 35 days. While the first group (NaFC group) received only NaF, the second in addition was treated with *I. gabonensis* fruit juice (*I. gabonensis* group). The third received NaF plus 15 $mgkg^{-1}$ body weight Quercetin + 100 $mgkg^{-1}$ bodyweight vitamin E (Q+Vit E group). Result showed that LDL-C was significantly elevated, while HDL-C was markedly reduced in the NaFC group. In the *I. gabonensis*-treated group, lipoprotein phenotypes were normalized, with HDL-C increasing from 38.92±9.28 $mgdl^{-1}$ in NaF intoxicated group (NaFC) to 65.14±5.33 $mgdl^{-1}$, which was even higher than 60.83±4.56 $mgdl^{-1}$ obtained in the standard (Q+Vit E) group. Low density lipoprotein-cholesterol concentration also reduced from 17.3±3.2 $mgdl^{-1}$ in NaF-intoxicated group to 7.5±1.0 $mgdl^{-1}$ in *I. gabonensis*-treated group, which compared favourably with that of the standard. Furthermore, NaF toxicity resulted in the elevation of atherogenic index in the NaFC group. This was significantly ($p<0.05$) lowered in all other groups. The total non-HDLcholesterol and LDL/HDL ratio were significantly reduced in *I. gabonensis*-treated rats. This tends to suggest that the juice of *I. gabonensis* may be useful in alleviating and preventing cardiovascular diseases.

Key words: Sodium flouride, *Irvingia gabonensis,* cholesterol, high-density lipoprotein (HDL), low-density lipoprotein (LDL).

INTRODUCTION

Tropical Africa's rainforests hold a wide array of plants and biodiversity. About ¼ of all the medicines used around the world are from rainforest plants (Palande, 2010). Many of these plants have been identified, scientifically classified and widely applied for known therapeutic benefits (Fennell et al., 2004). Among the classified, some still possess many

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unidentified beneficial pharmacological properties. Some of these plants have long been used by the local people either for food or applied in the treatment of various ailments. With changing life pattern and increase in predisposing factors, atherosclerosis and cardiovascular diseases are fast becoming common decimals in both developed and underdeveloped nations. This is often as a result of changes in life style. For instance, with continuous increase in distances from homes to offices, most people resort to eating outside their homes, very often eating junk meals laden with saturated fats. This has led to the increased need for search for effective and natural hypolipidemic agents to reduce cholesterol in the blood. Atherosclerosis is usually linked to increased cholesterol, especially of LDL phenotype, as well as with triglycerides which is the main carrier of cholesterol in plasma (Nelson and Cox, 2005). LDL influences the plasma cholesterol concentration and is also closely implicated in the aetiology of atherosclerosis (Phil-Sun et al., 2006). Research in many countries show that increasing concentration of blood cholesterol is associated with a progressively increasing risk of coronary heart disease (CHD), even from concentrations regarded as absolutely normal such as 200 mg/100 ml (Tamas et al., 2002). Dyshomeostasis in serum lipids resulting in increased Non-HDL- cholesterol is also a risk factor. Diet plays a significant role in the onset of hypercholesterolemia, atherosclerosis and CHD, especially high saturated fat diets.

The plant *Irvingia gabonensis* is a tropical tree of the genius *Irvingia.* It is indigenous to west and central Africa. It is known by the common names 'bush mango' or 'wild mango' and indigenous names of *Ugiri, Ado, Dika* etc. It is widely distributed in the rain forest of Ghana, Nigeria, Cameroon, Ivory Coast, Uganda and Democratic republic of Congo (Ayivor et al., 2011). The tree *I. gabonensis* is about 15-40 m in height and 1 m in diameter; it may occur in gregarious clusters. They produce edible fruits similar to the mango fruit from which it derives the common name "bush mango". Different parts of the plant are used in traditional and modern medicine for the treatment of several illnesses and in industrial processes (Anegbeh et al., 2003). The fruits are nearly spherical, green when ripe with a bright orange pulp. This fleshy and succulent pulp is edible or can be processed into jelly, jam, juice or wine (Akubor, 1996). The seeds of *I. gabonensis* have a wide variety of application including its use as a thickener in soup and stews and a source of edible oil. The bark has been widely applied in the treatment of diarrhea (Ndoye and Tchamou, 1994), dysentery (Okolo, et al., 1995), scabby skin (Ndoye and Tchamou, 1994) and a potent anti-inflammatory agent (Okolo, et al., 1995). Leaf decoction of *I. gabonensis* and the seed extract have been reported to possess hypoglycaemic and hypolipidemic effect (Dzeufiet et al., 2009). In addition, antidiabetic effects of its bark and leaves on streptozocin-induced diabetic rats have been reported (Ngondi et al., 2006). *I. gabonensis* has also been shown to improve the haematopoietic system of rats (Omonkhua and Onoagbe, 2012). Since this fruit is relatively available but often less frequently consumed by people, and given the fact that available information on the hypolipidemic properties of the plant were on other plant parts (leaves, seed extract) and were all done outside the locality of this research (Dzeufiet et al., 2009; Oben, 2010), the present study was therefore designed to investigate the effect of *I. gabonensis* fruit juice on sodium fluoride-induced dyslipidaemia in Wistar albino rats.

Sodium fluoride is a well-known toxicant. Earlier studies showed that fluoride can produce abnormalities in the liver including degenerative and inflammatory changes (Chinoy et al., 1993; Parihar et al., 2013). Its ability to increase oxygen free radicals and consequent oxidative stress has been well demon-strated (Eşsiz et al., 2008). The neurotoxic effects of sodium fluoride in rats have been established since 1995 (Mullenix et al., 1995; Connett, 2012). More recently, low glucose utilization (Jiang et al., 2014), cognitive deficits and anxiety-depression-like behaviors have been described in mice treated with NaF (Liu et al., 2014). Use of sodium fluoride is on the increase in our world today and a lot of debate going-on on its continuous usage or non-use especially in fluoridation of water.

Children also consume a lot of fluoride through tooth pastes. Increased risk of flourosis due to high water-borne fluoride concentrations is threatening to many parts of the world (Vasant and Narasimhacharya, 2012), and black children are disproportionately affected (CDC, 2005; Connett, 2012). This is probably due to biologic susceptibility or greater fluoride intake (CDC, 2005). It therefore becomes pertinent to assess the effect of this fruit extract on sodium fluoride-induced toxicity.

MATERIALS AND METHODS

Plant materials

Ripe and edible fruits of *I. gabonensis* were collected from a local plantation in Ugiri-Ike, Ikeduru Local Government Area of Imo State. The plant material was authenticated by a plant taxonomist, at the Department of Plant Science and Biotechnology, Imo State University, Owerri, Imo State. These fruits were obtained fresh as when needed.

Animals

Twenty four healthy, male albino Wistar rats (*Rattus norvegicus*) weighing 115-150 g (averaging 6 weeks old) were used for this study. They were purchased from the animal house of the Department of Veterinary Medicine, University of Nigeria, Nsukka. They were housed in stainless steel cages under standard laboratory conditions of light, temperature (21±2°C) and relative humidity (55±5%). The animals were given standard rat pellets (Vital finisher) and tap water *ad libitum* and were left for a period of two weeks to acclimatize before commencement of the study. The rats were randomly divided into four (4) experimental groups and used for the determination of sodium fluoride toxicity and normalisation effect of *I. gabonensis*. The ethical committee of the university approved the study protocol prior to commencement of study and the study was carried out according to the guidelines of the Animal Welfare Act.

Preparation of fruit extracts

The ripe fruits of *I. gabonensis* were washed with clean tap water and peeled, seeds removed and the succulent pulp cut into small pieces. This was weighed and 250 g portion of the fleshy portion of the fruits was extracted with 250 g of distilled water in a juice extractor; Sinbo SJ3138 (Sinbo, China), to obtain the fruit juice (I.G). The resulting juice was then stored in a freezer (≤ 4.0°C) until needed. A fresh juice of the fruit was extracted each day of administration.

Grouping of animals

Twenty four (24) healthy, male albino Wistar rats were divided into four groups of six (6) animals each for the amelioration of sodium fluoride toxicity studies. Animals (rats) were separated into groups and treatments were as follows: Group I served as normal control (NC) which received standard pelletized diet and water only throughout the treatment period; Group II served as intoxicated control (NaFC) which received standard diet and water *ad libitum* and sodium fluoride toxicant (20 mg/kgbwt) by gavage daily; Groups III served as intoxicated tests (I.G) which received standard diet and water *ad libitum*, in addition to *I. gabonensis* fruit juice (IG) and sodium fluoride toxicant (20 mg/kgbwt) daily; Group IV served as intoxicated standard (Q +Vit E) which received standard diet and water *ad libitum*, in addition to Quercetin 15 mg/kgbwt + α-tocopherol 100 mg/kgbwt and toxicant sodium fluoride (20 mg/kgbwt) daily.

At the end of thirty five days of daily intoxication and treatment with *I. gabonensis* juice and standard for amelioration, the animals were fasted for 24 h after which they were lightly anaesthetized with dichloromethane and sacrificed by cervical dislocation and blood collected by cardiac puncture. Blood samples of each animal was taken and allowed to clot for 45 min at room temperature. Serum was separated by centrifugation at 600 ×*g* for 15 min and analyzed for the determination of serum total cholesterol, HDL-cholesterol, LDL-cholesterol and triglycerides (TG) levels using commercial diagnostic kits (Biosystem, Spain).

Biochemical estimations

Total cholesterol was determined by the enzymatic (cholesterol esterase/oxidase/peroxidase) method of Allain et al. (1974). Triglycerides was determined by the glycerol phosphate oxidase/peroxidase method as described by Bucalo and David (1973). Low-density lipoprotein –cholesterol (LDL-C) was determined according to the method of Assman et al. (1984) while high-density lipoprotein-cholesterol (HDL-C) was determined using the phosphotungstate/Mg-cholesterol oxidase and peroxidase method by Grove (1979) and Burstein et al. (1980).

Data analysis

Data was analyzed using the statistical software "Analyze-it" for Microsoft excel. Results were presented as mean ± SD and differences between the various groups and the control group were tested at (P<0.05) using one-way analysis of variance (ANOVA) statistic followed by Tukey test.

RESULTS

Results show that NaF toxicity caused significant (p<0.05) elevation of serum total cholesterol in all the treatment groups {NaF control group (NaFC = 74.86±6.26 mgdl^{-1}),

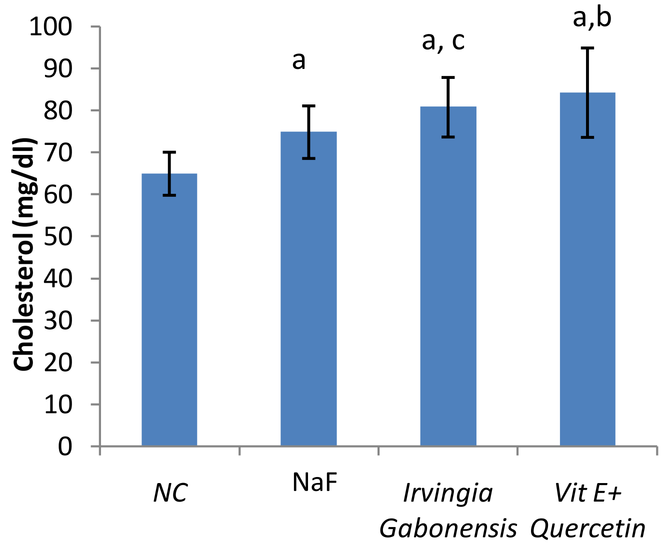

Figure 1. Effect of *I. gabonensis* fruit juice administration on serum total cholesterol in sodium fluoride (NaF)-induced dyslipidemia. Results are mean ± SD of 6 determinations, values with different superscript show significant difference at p<0.05. a=significantly (P<0.05) different from normal control (NC); b=significantly (P<0.05) different from NaF; c=significantly (P<0.05) different from VitE + Quercetin.

I. gabonensis treatment group (*I.G* = 80.8±7.09 mgdl^{-1}) and standard (Q+Vit.E = 107.20±9.73 mgdl^{-1})} as compared to normal control (NC = 64.96±5.13 mgdl^{-1}) (Figure 1). Although IG administration in NaF exposed rats resulted in significant (p=0.008) elevation of total serum cholesterol as compared to the control, no significant difference was obtained between the cholesterol levels of NaF control and I.G groups.

HDL cholesterol concentrations (Figure 2) were 44.02±8.18, 38.92±9.28, 65.14±5.33 and 60.83±4.56 mgdl^{-1} in NC, NaFC, I.G and Q+Vit E respectively. HDL-cholesterol was significantly (p<0.05) elevated in exposed groups administered with I.G and Q+Vit E as compared to NaF control and NC. Figure 3 shows the serum triglycerides concentration of the exposed animals. No significant (p>0.05) alteration in serum triglycerides concentration was seen across the groups.

LDL concentration (Figure 4) was 10.2±1.1 mgdl-^{1} in NC group, 17.3±3.2 mgdl-^{1} in NaFC group, 7.5±1.0 mgdl-^{1} in I.G group and 10.5±1.2 mgdl-^{1} in Q+Vit E-treated group. Result obtained demonstrated that NaF exposure resulted in a significant (p<0.05) elevation of LDL-cholesterol in NaFC as compared to NC, I.G and Q+Vit E groups. Also, *I.gabonensis* administration significantly (p<0.05) lowered LDL-cholesterol in exposed subjects and was even lower than that of the standard – treated group.

Effect of *I. gabonensis* fruit juice administration on LDL/HDL ratio in NaF-induced dyslipidemia (Figure 5) showed that NaF toxicity resulted in an elevation of LDL/HDL ratio in NaF control (0.44 ± 0.02) which was significantly

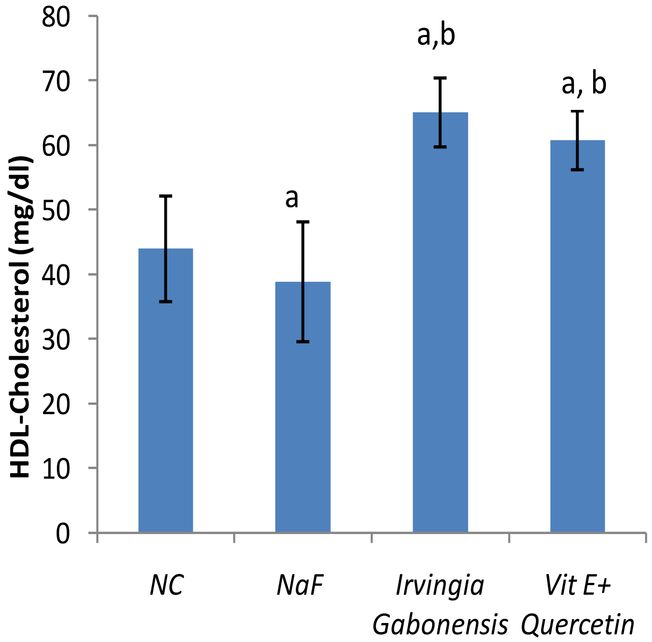

Figure 2. Effect of *I. gabonensis* fruit juice administration on serum high density lipoprotein (HDL)-cholesterol in sodium fluoride (NaF)-induced dyslipidemia. Results are mean ± SD of 6 determinations, values with different superscript show significant difference at p<0.05. a=significantly (P<0.05) different from normal control (NC); b=significantly (P<0.05) different from NaF; c=significantly (P<0.05) different from VitE + Quercetin.

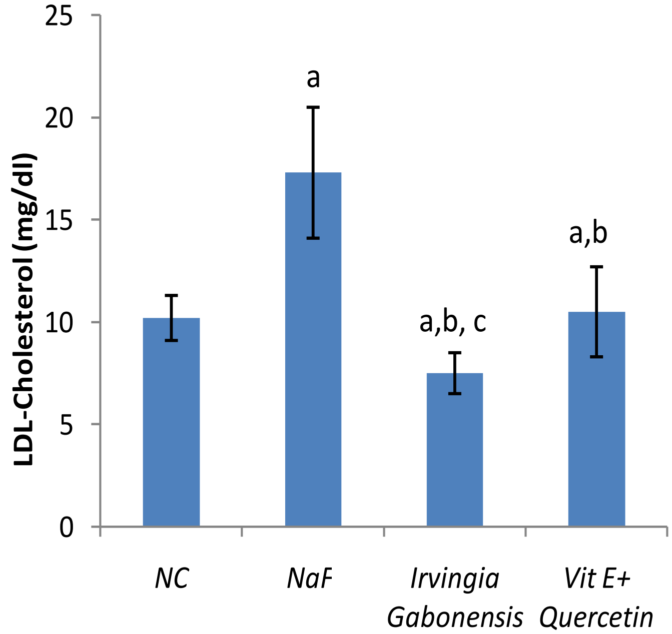

Figure 4. Effect of *I. gabonensis* fruit juice administration on serum low density lipoprotein (HDL)-Cholesterol in sodium fluoride (NaF)-induced dyslipidemia. Results are mean ± SD of 6 determinations, values with different superscript show significant difference at p<0.05. a=significantly (P<0.05) different from normal control (NC); b=significantly (P<0.05) different from NaF; c=significantly (P<0.05) different from VitE+Quercetin.

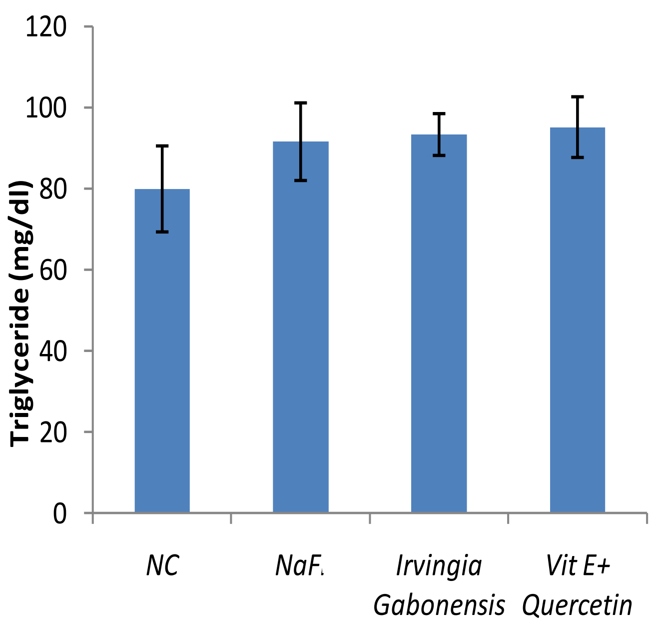

Figure 3. Effect of *I. gabonensis* fruit juice administration on serum Triglyceride in sodium fluoride (NaF)-induced dyslipidemia. Results are mean ± SD of 6 determinations, values with different superscript show significant difference at p<0.05. a=significantly (P<0.05) different from normal control (NC); b=significantly (P<0.05) different from NaF; c=significantly (P<0.05) different from VitE+Quercetin.

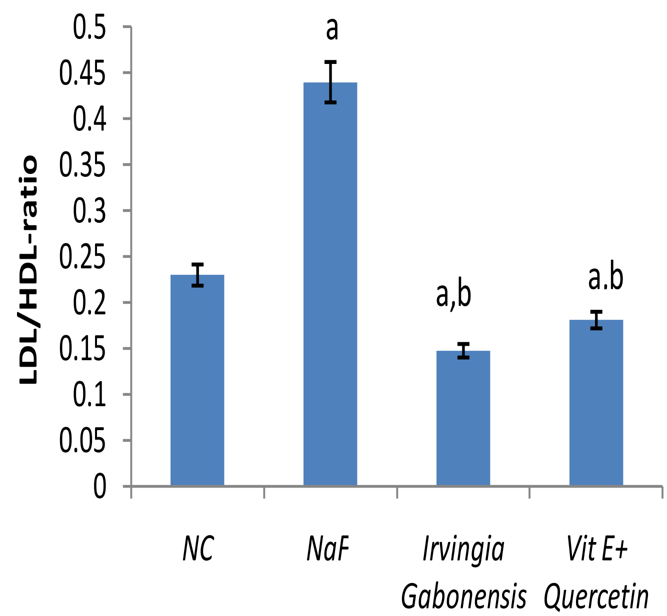

Figure 5. Effect of *I. gabonensis* fruit juice administration on low density lipoprotein/high density lipoprotein (LDL/HDL) ratio in sodium fluoride (NaF)-induced dyslipidemia. Results are mean ± SD of 6 determinations, values with different superscript show significant difference at p<0.05. a=significantly (P<0.05) different from normal control (NC); b=significantly (P<0.05) different from NaF; c=significantly (P<0.05) different from VitE+Quercetin.

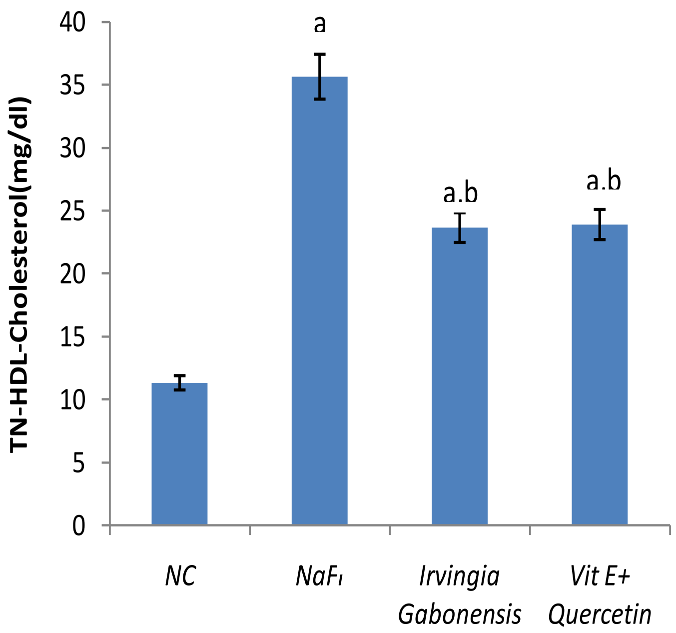

Figure 6. Effect of *I. gabonensis* fruit juice administration on total Non-HDL-cholesterol in sodium fluoride (NaF)-induced dyslipidemia. Results are mean ± SD of 6 determinations, values with different superscript show significant difference at p<0.05. a=significantly (P<0.05) different from normal control (NC); b=significantly (P<0.05) different from NaF; c=significantly (P<0.05) different from VitE+Quercetin.

(p<0.05) higher than in the normal control (0.23±0.01), I.G fruit juice - treated group (0.14±0.01) and Q+Vit E - treated group (0.180±0.01). Administration of I.G juice resulted in a significant (p<0.05) reduction of LDL/HDL ratio in intoxicated animals and again was lower than that of the standard-treated group. Total Non-HDL-Cholesterol was significantly (p<0.05) elevated in the NaF control group (35.64±1.78 $mgdl^{-1}$) as compared to normal control (20.94±1.0 $mgdl^{-1}$), I.G -treated group (23.66±1.2 $mgdl^{-1}$) and Q+Vit E- treated group (23.9±1.2 $mgdl^{-1}$) (Figure 6). *I. gabonensis* juice treatment also resulted in a reduced TN-HDL-cholesterol which was comparable to those of NaF exposed rats treated with the standard.

DISCUSSION

Fluoride toxicity in animals can be multifarious. It is implicated in inflammatory and degenerative changes in the liver (Anamika et al., 2012) and is known to result in abnormal metabolic function as well as histopathological changes in different species (kotodziejezyk et al., 2000). Acute and chronic exposure to NaF may differentially affect cardiovascular function (Bera et al., 2007), induce testicular damage and lipid peroxidation in mice and disrupt other biological functions (Ghosh et al., 2002). It is also known that acute fluoride intoxication leads to the progressive fall in arterial blood pressure responsible for cardiovascular damage (Strubelt, 1982). The present study examined the ability of *I. gabonensis* fruit juice to normalise serum lipid profile in NaF-induced dyslipidemia. Result of our study shows that NaF of 20 mg/kgbwt daily for 35 days induced a deranged lipid profile on our experimental animals. It is well known that dyslipidemia is a common feature of chemical toxicity-induced damages especially those affecting the liver (Alisi et al., 2011). Identification and management of dyslipidemia have gained importance for both primary as well as secondary prevention of recurrent events in atherogenesis.

In our study, serum total cholesterol was significantly (p<0.05) elevated in NaF challenged animals as compared to normal controls. Similar elevations were observed in the standard group treated with a combined dose of 20 mg/kgbwt Quercetin+100 mg/kg bwt α-Tocopherol, as well as the *I. gabonensis* group. Recall that the primary event in atherogenesis is cholesterol deposition in the arterial walls. Cholesterol originates from circulating plasma lipoproteins which contain both free and cholesteryl esters. LDL and lipolytic products of chylomicrons as well as very low density lipoproteins (VLDL) also contribute greatly to atherogenesis (Tabas, 2009).

It is important to note that increased TC in the NaFC group was contributed immensely by elevated LDL-C level which is a major risk factor in cardiovascular events. The *I. gabonensis* group and the standard group had HDL-C contributing highly to their elevated TC, sinceno changes were seen in their triglyceride levels. Conventional treatment of atherogenic lipid profile targets reduction in total cholesterol levels and LDL-cholesterol, or increasing HDL-cholesterol. Treatments often include statins, fibrates, niacin, resins and lifestyle modification (Sharma and Garg, 2012).

Lipid-lowering effect of plant extracts has been known to occur via reduced gastrointestinal absorption which is often reflected in the concurrent increase in fecal lipid load of the animals (Miettinen et al., 1995). This was however not investigated in our study. The hypolipidemic effect would have been exerted through increased catabolism of LDL or reduced activation (inactivation) of acetyl CoA carboxylase (McCarthy, 2001), thus leading to reduced cholesterol synthesis. On the other hand, the elevated total cholesterol level may suggest that the extract contains ingredients capable of enhancing the activities of hepatic lipogenic and cholesterogenic enzymes like malic enzyme, fatty acid synthase, glucose 6- phosphate dehydrogenase and HMG-CoA reductase (*Vega* et al., 2003) which are required for cholesterol synthesis.

HDL-cholesterol level in *I. gabonensis* juice- treated group was elevated more than that of the standard group receiving combined treatment of 20 mg/kg bwtquercetin + 100 mg/kg bwt α-tocopherol. A significant (p<0.05) lowering effect on LDL-cholesterol was also evident in *I. gabonensis* fruit juice-treated group as compared to the other three groups. This significant reduction of LDL cholesterol and increased HDL is indicative of a lowered negative atherogenic index shown as reduced LDL/HDL ratio in the *I. gabonensis* treated group. This could be related to presence in the plant of alkaloids, saponins, flavonoids and polyphenols commonly known to reduce serum lipids in animals (Ezekwe and Obioha, 2001).

The total non-HDL- cholesterol was significantly elevated in the NaF control group when compared to the others. Dyshomeostasis in serum lipids resulting in increased non-HDL- cholesterol is a risk factor in the onset of athero-sclerosis. Non-HDL cholesterol (which usually includes cholesterol in VLDL, VLDL remnants, IDL and LDL) may actually be more predictive of CAD risk than LDL chole-sterol (Goldberg, 2013).

Total non-HDL cholesterol was however significantly reduced by our juice. This was indeed remarkable and underscores the efficacy of *I. gabonensis* juice in CAD. Results of our study are in agreement with earlier reported studies on hypolipidemic properties of *I. gabonensis* carried out in other parts of Africa (Dzeufiet et al., 2009; Oben, 2010). Although a clearly reduced total cholesterol level may not have been seen from our study, the significantly reduced total non-HDL cholesterol makes up for it showing that increased HDL-C may have been contributory. Oben (2010) reported that *I. gabonensis* reduced total cholesterol and increased HDL-cholesterol and adiponectin levels in their study. This is indeed similar to our findings.

Plant polyphenols and ascorbic acid possess strong antioxidative potency responsible for their protective effect against various toxicants. Ascorbic acid-deficient diets have been associated with increased aortic accumulation of cholesterol. Our result showed an ameliorative potency of *I. gabonensis* fruit juice on NaF-induced lipidemia in rats. The ameliorative effect observed may be due to its reportedly rich vitamin C content and plant polyphenolics (Anil, 2007; Ebimieowei, 2012).

In conclusion, NaF which is usually incorporated as a component of dental products, drinks, dietary supplements and foods in general may not be as safe as it is consi-dered. It has been identified to cause systemic toxicity in the liver, induce testicular damage and lipid peroxidation in mice and disrupt other biological functions. Our study reveals that aqueous fruit juice extract of *I. gabonensis* has hypolipidemic effect on NaF induced dyslipidemia. The extract was able to normalise lipoprotein phenotype altered by NaF-induced toxicity in albino rats by enhancing HDL-C concentration and lowering serum LDL-C concentration and atherogenic index. Further studies are however required to determine the exact mechanism by which *I. gabonensis* may have affected cholesterol biosynthesis and in general lipoprotein metabolism.

Conflict of Interest

The authors declare that there is no conflict of interests regarding the publication of this paper.

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