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EFFECTS OF EXTRACTS OF *HYPODAPHNIS ZENKERI* AND *XYLOPIA AETHIOPICA* ON BLOOD LIPIDS, GLYCEMIA AND BODY WEIGHT OF TRITON WR-1339 AND INSULINO RESISTANT RATS

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ABSTRACT

Obesity is a complicated multifaceted problem generally accompanied by disturbances in carbohydrate and fat metabolism, insulin resistance as well as an increase in oxidative stress. The bark of *Hypodaphnis zenkeri* (HZ) and dry fruits of *Xylopia aethiopica* (XA) commonly used as spices in Cameroonian cuisine also have applications in traditional medicine. This study evaluates their effects on some biological parameters of acute hyperlipidemic rats and on rats fed with High Fat High Sucrose (HFHS) diet. The spices were extracted in water, water/ethanol (50/50) and ethanol. The first part of the work was the *in vitro* study where, the partial phytochemical composition as well as the antioxidant potential of extracts were studied, using folin Ciocalteu's phenol method and ABTS (3-ethyl-benzothiazoline-6-sulfonic acid) assay. The best extract for each spice was selected and used for the "*in vivo*" study which consisted in studying their effect on weight and biochemical parameters in acute hyperlipidemic rats and insulin resistant rats. The extracts contained phenols like flavonoids. They also showed free radical scavenging properties *in vitro*. Total phenolic content were higher particularly for the hydroethanolic extract (HEE) of *Hypodaphnis zenkeri* (413.87 ± 13.19 mg Eq catechin/g of extract), but lowest for the water extract (WE) of *Xylopia aethiopica* (63.07 ± 1.60 mg Eq catechin/g of extract). At a concentration of 400 mg/kg, the HEE extract of *Hypodaphnis zenkeri* showed a hypotriglyceridemic activity on rats with hypertriglyceridemia induced by triton WR-1339 unlike the EE of *Xylopia aethiopica*. But these two extracts inhibited weight gain and reduced postprandial glycemia in insulin resistant rats. The bark of *Hypodaphnis zenkeri*, and dry fruits of *Xylopia aethiopica* contained bioactive ingredients; they ameliorated the glucose uptake and the evolution of weight impaired by the chronic consumption of HFHS diet in rats.

Keywords: *Hypodaphnis zenkeri*, *Xylopia aethiopica*, hyperlipidemia, insulino resistant, antioxidant.

INTRODUCTION

Obesity is a major public health problem, both in developed and developing countries. It is associated with many diseases (cardiovascular diseases, hypertension, diabetes, breast cancer, joint problems) originating from mechanical, metabolic, cardiovascular, or endocrine problems.[1] One of these problems is insulin resistance which is a pre-diabetic state that can predict the incident of type 2 diabetes relatively far into the future.[2] There is a relationship between obesity, insulin resistance and the development of type II diabetes. However, all obese do not necessarily develop type II diabetes and therefore, genetic influence can be involved. Hyperlipidemia observed in obese subjects causes this insulin resistance and can also lead to coronary heart diseases which are always associated with oxidative stress. Oxidative stress impairs glucose uptake in muscle and fat and decreases insulin secretion from pancreatic β cells. Increased oxidative stress also underlies the physiopathology of late diabetic complications directly affecting vascular wall.[3] Previous research works carrying out the lipid lowering effect of some spices and their compounds have been reported. *Ocimum basilicum* uses as spice or medicinal plant in Cameroon reduce plasma total cholesterol, HDL-Cholesterol in triton-treated rats.[4] Some common dietary compound like capsaicin, curcumin, ferulic acid have shown a lipid lowering action in rats fed with high fat diet.[5] One study revealed that aqueous extract of *Xylopia aethiopica* decreased the plasma cholesterol and triglyceride levels of normal rats and is attributable to the presence of hypolipidemic agent in the extract.[6] However, the mechanisms explaining the potential hypolipidaemic or hypoglycemic effect of *Hypodaphnis zenkeri* or *Xylopia aethiopica* have not been reported. Increasing evidence in both experimental and clinical studies suggests that oxidative stress - the consequence of an imbalance between prooxidants and antioxidants in the organism - plays a major role in the pathogenesis of both types of diabetes mellitus. Free radicals are formed disproportionately in diabetes by glucose oxidation, non enzymatic glycation of proteins, and the subsequent oxidative degradation of glycated proteins.[7] So oxidative stress is rapidly gaining recognition as a key phenomen in chronic diseases. To prevent its negative effects, one can help their body to defend itself by increasing their dietary intake of antioxidants which are largely found in plant foods.[8] Considering the availability as well as the wide use of spices in Cameroon, this study, explores the antioxidant capability of the barks of *Hypodaphnis zenkeri* and dry fruits of *Xylopia aethiopica*. It also investigated their hypolipidaemic potential on acute hyperlipidaemia induced by Triton WR-1339 in rats and

their effects on some biological parameters in insulin resistant rats.

MATERIALS AND METHODS

Preparation of extracts

The spice samples were bought from the Mokolo market in the town of Yaounde, Cameroon. Identification was done at the National Herbarium of Cameroon with voucher specimen numbers 16419/SRF/CAM and 16459/SRF/CAM. Each spice was crushed and 100 g of powder weighed. For water extract (WE), 400 ml (1:4, P/V) of water was added. For ethanolic extract (EE), 400 ml (1:4, P/V) of ethanol was added, and for the hydroethanolic extract (HEE), 400 ml of solvent (50:50, V/V) was added to the powder. The different mixtures were macerated for 48 h after which, they were filtered and the obtained solutions were concentrated under vacuum at 65°C during 48 h to obtain dry extracts.

In vitro study

Phytochemical tests

The methods of Trease and Evans[9] were used. These methods, which are qualitative, are based on the color changes; and distilled water was used as control for each test.

Determination of total phenolics

The amount of total phenolics in extracts was determined according to the Folin- ciocalteu procedure.[10] Samples (20 µl, three replicate) were introduced into test tubes; 1 ml of Folin- ciocalteu's reageant (diluted 10 times), were added and the mixture left at room temperature for 30 minutes after which absorption was measured at 750 nm. The total phenolic content was expressed in mg equivalent catechin per gram of extract.

ABTS [2,2'-Azino-bis (3-ethylbenzo-thiazoline-6-sulfonic acid)] assay

The antioxidant capacity of the samples in the reaction with stable $ABTS^+$ radical cation was determined according to the method described by Re *et al*.[11] with some modifications. The stock solutions included 7.4 mM $ABTS^+$ solution and 2.6 mM potassium per sulfate solution. The working solution was then prepared by mixing the two solutions in equal quantities and allowing them to react for 14 h at room temperature in the dark. The solution was then diluted 10 times with distilled water to obtain an absorbance of 1.956 at 734 nm. The prepared solution was then used for the assay. Different volumes of extracts (10 µl, 20 µl, 40 µl, 60 µl, 80 µl and 100 µl) were allowed to react with 1000 µl of $ABTS^+$ for 30 minutes. Then, the absorbance was taken at 734 nm. The percentage decrease of the absorbance at 734 nm was calculated by the formula $I = (A_B - A_A)/A_B * 100$, where I = $ABTS^+$ inhibition percentage, A_B = absorbance of blank at t = 0 minute, A_A = absorbance of a tested samples at the end of the reaction (t = 30 minutes).

In vivo study

Preparation of dose of extract

For the "*in vivo*" study, the prepared extracts were dissolved in DMSO 10 % before giving to the rats in order to obtain a single dose of 400 mg/Kg body weight with 1ml as volume of administration.

Diet composition

Table 1 present the different diets used for the animals experimentations. The composition of HFHS diet was prepared as described by Chalkley *et al*.[12] and Shoumin *et al*.[13] with some modifications.

Hypolipidemic effect of selected extracts of *Hypodaphnis zenkeri* and *Xylopia aethiopica* in triton WR-1339 induced acute hyperlipidemic rats

Animals

Adult male Wistar rats weighing 190 – 205 g were used for this study. The animals were given standard diet and water *ad libitum* throughout the study.

Experimental design

Hyperlipidemia was induced with a single intraperitoneal injection of 850 mg/Kg /Body weight of triton WR-1339 (Tyloxapol, Sigma-Aldrich, USA) in normal saline, in triton control and test group. Normal control was injected with normal saline. 24, 30 and 36 h after triton injection, the test group received a dose (400 mg/Kg) of the selected extracts of *Hypodaphnis zenkeri* and *Xylopia aethiopica* via gavages. Forty-four hours after triton injection, after an overnight fasting period, rats were sacrificed. The blood sample collected was immediately centrifuged (3400 rpm). The obtained plasma was used for lipids analysis.

Lipids analysis

The amount of total cholesterol, triglycerides, high density lipoprotein, was assayed by enzymatic kits. LDL cholesterol was calculated using the Friedewald formula.[14]

Effect of the selected extracts on post-prandial glycemia, weight and some biochemical parameters of insulin resistant (IR) rats

Induction of insulin resistance

The rats (150 – 190 g) were divided into two groups: a normal group fed standard laboratory diet and the other group received the high fat high sucrose diet (HFHS) for four months.

Oral glucose tolerance test

After four months of feeding, the HFHS fed rats were divided in groups for the investigation of an oral glucose tolerance test. The rats showing an abnormal evolution of post prandial glycemia were considered IR.

Effect on weight and some biochemical parameters of IR rats

We have investigated the effect of sub acute treatment (30 days) with the selected extract of *Hypodaphnis zenkeri* and *Xylopia aethiopica* on body weight and blood lipid of the IR rats.

Table 1: Composition of Diets Use for the Animal Experimentation

	Standard diet (%)	HFHS diet (%)
Maize (starch)	53	35
Sucrose	14.74	20
Proteins	19.25	15
Lipids	5.7	20
Vitamins	0.3	1.5
Minerals	3.21	3.5
Fibers	3.8	5
Energy (Kcal/g)	3.40	4.64

Table 2: Phytochemical Constituent of Different Extracts

Extract	Spice	Alk	Gly	Fl	CGly	Sa	Ta	Ph	Li	St	Ant	Qu	Phl	Rsu
WE	*Hypodaphnis zenkeri*	+	+	+	+	+	+	+	-	+	-	+	+	+
	Xylopia aethiopica	+	-	-	+	-	+	+	+	-	+	+	+	+
HEE	*Hypodaphnis zenkeri*	-	+	+	+	-	+	+	-	+	+	+	+	+
	Xylopia aethiopica	+	-	+	+	+	+	+	+	+	-	+	+	+
EE	*Hypodaphnis zenkeri*	+	+	+	+	+	+	+	-	+	+	+	+	+
	Xylopia aethiopica	+	+	+	+	+	+	+	+	+	-	+	+	+

(+) = present; (-) = absent, WE = Water extract, HEE = Hydroethanolic extract, EE = Ethanolic extract, Alk: Alkaloids, Gly: Glycosides, Fl: Flavonoids, CGly: Cardiac Glycosides, Sa: Saponins, Ta: Tanins, Ph: Phenols, Li: Lipids, St: Sterols and Triterpenes, Ant: Anthocyanins, Qu: Quinones, Phl: Phlobatannins, Rsu: Reducing sugar

Table 3: Polyphenolic Content and Abts^{+} Radical Scavenging Activity of Each Extract

Extracts	Spices	Phenol concentration (mg Eq catechin/g of extract)	ABTS• radicals scavenging activity. IC_{50} (mg)
WE	*Hypodaphnis zenkeri*	278.60 ± 10.96^{c}	$7.66\ E\text{-}07 \pm 0.01^{a}$
	Xylopia aethiopica	63.07 ± 1.60^{a}	$37.35 \pm 1{,}49^{b}$
HEE	*Hypodaphnis zenkeri*	354.96 ± 3.94^{c}	1760.47 ± 12.045^{d}
	Xylopia aethiopica	82.43 ± 5.71^{a}	$12.40 \pm 0{,}06^{b}$
EE	*Hypodaphnis zenkeri*	413.87 ± 13.19^{d}	$1.22\ E\text{-}45^{*} \pm 0.000^{a}$
	Xylopia aethiopica	179.72 ± 16.01^{b}	397.44 ± 38.12^{c}

EE = Ethanolic extract, WE = Water extract, HEE = Hydoethanolic extract, Values shown are mean ± SD (n = 5), Different letters ($p < 0.05$)

Table 4: Effect of Selected Extracts on Blood Lipids of Rats after Administration of Triton Wr-1339

Groups	Total cholesterol	Triglycerides	HDL-Cholesterol
Normal diet rats	54.75 ± 2.5^{a}	27.5 ± 6.35^{a}	41.21 ± 6.021^{a}
HFHS diet rats untreated	319.00 ± 131.45^{b}	1494 ± 367.88^{b}	135.00 ± 38.79^{b}
HFHS diet rats + HEE of *Hypodaphnis zenkeri*	38.25 ± 12.42^{a}	32.75 ± 23.39^{a}	36.50 ± 10.85^{a}
HFHS diet rats + EE of *Xylopia aethiopica*	400.14 ± 3.80^{b}	1348.50 ± 1278.39^{b}	256.75 ± 155.91^{b}

Values shown are mean ± SD (n = 5) Different letters ($p < 0.05$)

Table 5: Effect of Selected Extract on Some Markers of Toxicity on Rats after Injection of Wr-1339

Groups	Proteins (g/L)	GPT(UI)	GOT(UI)	Creatinin (mg/dL)
Normal diet rats	$51{,}7 \pm 3{,}5^{b}$	$29{,}8 \pm 5{,}4^{b}$	31.04 ± 7.67^{b}	$3{,}1 \pm 0{,}2^{c}$
HFHS diet rats untreated	$68{,}3 \pm 0{,}7^{a}$	$73{,}1 \pm 23{,}5^{a}$	$85{,}3 \pm 13{,}7^{a}$	$15{,}3 \pm 5{,}6^{a}$
HFHS diet rats + HEE of *Hypodaphnis zenkeri*	$53{,}1 \pm 2{,}8^{b}$	$28{,}7 \pm 5{,}7^{b}$	22.34 ± 4.4^{d}	$3{,}8 \pm 0{,}6^{c}$
HFHS diet rats + EE of *Xylopia aethiopica*	59.2 ± 7.6^{b}	49.92 ± 15.69^{c}	40.36 ± 27.9^{c}	27.78 ± 13.02^{b}

Values shown are mean ± SD (n = 5), Different letters ($p < 0.05$)

Table 6: Effect of the Extracts on Glucose Tolerance of Rats Consuming HFHS Diet

	Glycaemia (mg/ml)				
	0 minute	30 minutes	60 minutes	120 minutes	240 minutes
Normal diet rats	72.67 ± 5.13^{a}	75.00 ± 11.27^{b}	70.67 ± 10.69^{a}	63.33 ± 4.51^{a}	48.67 ± 10.69^{e}
HFHS diet rats untreated	70.50 ± 4.95^{a}	122.5 ± 9.19^{c}	118.50 ± 13.44^{c}	116.00 ± 4.24^{c}	99.5 ± 0.71^{d}
HFHS diet rats + HEE of *Hypodaphnis zenkeri*	71.20 ± 14.04^{a}	113.6 ± 15.01^{c}	115.60 ± 11.10^{c}	92.40 ± 18.40^{b}	80.20 ± 12.19^{b}
HFHS diet rats + EE of *Xylopia aethiopica*	74.20 ± 8.38^{a}	108.00 ± 10.63^{c}	100.40 ± 7.83^{d}	87.60 ± 7.40^{b}	83.00 ± 12.59^{b}

Values shown are mean ± SD (n = 5), Different letters ($p < 0.05$)

Table 7: Effect of Sub Acute Treatment with HEE of *Hypodaphnis zenkeri* and EE of *Xylopia aethiopica* on Evolution of Weight of HFHS Diet Rats

	Variation percentage of weight (%)		
Time (Days)	7	21	28
Normal diet rats	0.16	-1.19	-0.65
HFHS diet rats untreated	9.40	22.24	24.64
HFHS diet rats + HEE of *Hypodaphnis zenkeri*	5.69	7.56	6.83
HFHS diet rats + EE of *Xylopia aethiopica*	-2.05	-0.23	-1.04

Table 8: Effect of HEE of *Hypodaphnis zenkeri* and EE of *Xylopia aethiopica* on Blood Lipids of HFHS Diet Rats

Groups	Total cholesterol	Triglycerides	HDL-Cholesterol
Normal diet rats	46.25 ± 6.35^{a}	67.00 ± 2.89^{a}	41.25 ± 7.37^{a}
HFHS diet rats untreated	59.25 ± 16.38^{b}	110.25 ± 42.94^{b}	21.43 ± 7.94^{b}
HFHS diet rats + HEE of *Hypodaphnis zenkeri*	45.82 ± 10.29^{a}	61.20 ± 14.90^{a}	37.66 ± 17.59^{a}
HFHS diet rats + EE of *Xylopia aethiopica*	53.32 ± 11.19^{c}	41.20 ± 20.41^{c}	26.2 ± 8.24^{c}

Values shown are mean ± SD (n = 5), Different letters ($p < 0.05$)

Experimental design

Twenty IR rats divided into four groups of five rats each received corresponding extracts during 30 days in the following order:

- Group 1: 1 ml of *Hypodaphnis zenkeri* extract (400 mg/kg/body weight)
- Group 2: 1 ml of *Xylopia aethiopica* extract (400 mg/kg/body weight)
- Group 3: 1 ml of distillated water
- Group 4: DMSO 10 %.

Body weight was measured at the beginning, and every week during the experimentation. After thirty days of feeding, rats were sacrificed after an overnight fasting period. The blood sample were collected and used for blood lipid analysis.

Statistical analysis

The data was expressed as mean ± Standard deviation (SD). Statistical significance was calculated using one-way analysis of variance (ANOVA). Significance was accepted at $p < 0.05$.

RESULTS

Phytochemical constituents

The different extracts contained active compounds. Our extracts contain molecules like quinons, tannins, reducing sugars. Except the water extract of *Xylopia aethiopica*, all the extracts contained sterols, triterpenes and flavonoids. Lipids were found in the three extracts of *Xylopia aethiopica* (Table 2).

Polyphenolic content and ABTS radical scavenging activity

HEE of *Hypodaphnis zenkeri* had the highest level of polyphenols (413.87 ± 13.19 mg Eq catechin/g of extract) followed by the EE (Table 3). The water extract of *Xylopia aethiopica* showed the lowest concentration ($P < 0.05$). For the ability of the extracts to reduce the ABTS radical, the EE and the WE of *Hypodaphnis zenkeri* showed the lowest IC_{50}, followed by the HEE of *Xylopia aethiopica*. The highest IC_{50} was obtained with the hydroethanolic extract ($P < 0.05$) of *Hypodaphnis zenkeri*.

***In vivo* Expérimentations**

The administrations of triton lead to the significant ($P < 0.05$) rise of TC, TG, and HDL cholesterol in untreated rats. The tritonized rats treated with HEE of *Hypodaphnis zenkeri*, had the value of these parameters not different ($P > 0.05$) from the one of untritonized rats (Table 4). The administration of EE of *Xylopia aethiopica* on tritonized rats had no effect on these parameters. Tyloxapol (triton WR-1339) elevated the plasma levels of some toxicity markers namely GPT, GOT or creatinin compared to the untritonized rats ($P < 0.05$). The administration of our extracts in tritonized rats reduced ($P < 0.05$) the concentration of GOT and GPT, but as for the plasma creatinin, only the treatment with *Hypodaphnis zenkeri* led to its reduction. While, the rats treated with *Xylopia aethiopica* had a high level of plasma creatinin than untreated rats ($P < 0.05$) (Table 5). During the glucose tolerance test of rats fed with HFHS diet, glycaemia did not differ between the different groups at basal conditions. Blood glucose levels of rats consuming HFHS diet which were not treated with extracts, remained high over time and did not return to the baseline ($P < 0.05$). Oral administration of HEE of *Hypodaphnis zenkeri* to HFHS diet rats reduced significantly ($P < 0.05$) blood glucose levels at 120 minutes and 240 minutes, whereas the EE of *Xylopia aethiopica* reduced it since the sixtieth minute until the end of the experimentation. No difference ($P > 0,005$) was observed between untreated and treated rats at 30 minutes (Table 6). The rate of weight gain increased in untreated HFHS diet rats compared to that of rats consuming normal diet at the 7^{th}, 21^{th} and 28^{th} days. Sub acute (30 days) treatment with HEE of *Hypodaphnis zenkeri* and EE of *Xylopia aethiopica* led to the inhibition of exponential body weight gain induced by the HFHS diet. We noticed that the inhibition of body weight was more pronounce for rats treated with *Xylopia aethiopica* (Table7). Table 8 show the effect of *Hypodaphnis zenkeri* and *Xylopia aethiopica* on blood lipids of HFHS diet rats. The four months consumption of HFHS diet induces an increase of total cholesterol and triglycerides; it also decreased the concentration of plasma HDL cholesterol. Groups treated with HEE of *Hypodaphnis zenkeri* and the EE of *Xylopia aethiopica* reduced significantly plasma TG and TC ($p < 0.05$) and increased HDL cholesterol compared to untreated group. But the increment of HDL cholesterol was more prominent for groups treated with *Xylopia aethiopica*; decrease of TG was more visible with *Xylopia aethiopica* treatment, whereas TC concentration in group treated with *Hypodaphnis zenkeri* was not different from the groups consuming normal diet.

DISCUSSION

Knowledge of the chemical constituents of plants is important not only for the discovery of therapeutic agents, but also because it reveals new sources of materials such as tannins, oils, precursors for the synthesis of chemicals. In addition, it could be very useful in the discovery of the current quality of traditional medicines.[15] A triterpenoid has been isolated from the stem bark of *Hypodaphnis zenkeri*.[16] Several studies on the phytochemical screening of plants have been conducted and published consisting of random sampling involving some plants from all parts of the world. It was noted that the main chemicals of interest of these screenings were alkaloids, saponins, and other various groups of phytochemicals such as flavonoids, tannins, triterpenes that we have also found in our extracts. These phytochemical showed a significant

polyphenol concentration, as well as a radical scavenging activity of $ABTS^{+}$. These two parameters were negatively correlated. It means that, when the concentration of polyphenols was high, the IC_{50} of the reduction ability decreased, suggesting the action of polyphenols in the antioxidant activity. Some spices like dried fruits of *Xylopia aethiopica* contain antioxidants such as ascorbic acid and carotenoids.[17] Phenolic compounds that have antioxidant activity are known to be mainly phenolic acids and flavonoids.[18] Both were revealed during our phytochemical screening. Tyloxapol is a detergent that is commonly used for acute studies on rats but not for sub-acute and chronic studies.[19] Several studies have shown that intravenous injection of Triton WR-1339 resulted in a significant increase in the concentration of plasma triglycerides and cholesterol. In 2006, Amrani *et al*.[4] indicated an increase of 358 % and 334 % of triglycerides and cholesterol respectively, 24 h after injection of triton. We observed an increase ($P < 0.05$) in plasma triglycerides after intraperitoneal injection of tyloxapol in rats. An explanation of this can be the fact that, Tyloxapol have a trapping mechanism of cholesterol and triglycerides in the blood and reduced the flux of triglycerides plasma in the liver.[20] In addition, it has been shown that Triton WR-1339 increased the activity of the hydroxylmethylglutaryl coenzyme A reductase in the liver.[21] There is also an increase in triglycerides concentration which is the result of an inhibition activity on lipoprotein lipase.[22] It is well known that high serum total cholesterol, triglycerides, and LDL cholesterol are the primary risk factors of vascular disease and high levels of serum HDL cholesterol confer a protective effect against their development.[23] Many herbs and spices have shown hypolipidemic effects in animals after triton WR-1339 injection; namely *Ocimum basilicum*,[4] *Phyllanthus niruri*.[24] Since the injection of triton influences lipoprotein metabolism by the above mechanisms, we suggest the influence of HEE of *Hypodaphnis zenkeri* on them. Additionally, these extracts have reduced the plasma concentration of markers of liver and kidneys damage like GOT, GPT, creatinin,[25] suggesting the protective effect of *Hypodaphnis zenkeri* and *Xylopia aethiopica* on these organs. The tested extracts were benefit to the rats fed with HFHS diet. We noted that, in rats consuming a diet rich in sugar and fat, blood glucose remained high over time after administration of glucose and does not return to baseline even after 240 minutes of experiment; suggesting that this diet causes a deficiency in the uptake of glucose in the blood. This was not the case in rats consuming a normal diet. We consider three hypotheses that prolonged hyperglycemia in the HFHS diet rats: (I) the insulin is abnormal ie modified or inactive, (ii) the insulin receptors in target cells is insufficient or defective - Indeed, diet rich in sugar and fat in rats causes a deactivation of insulin in the liver and muscles,[26] (iii) a decrease of function of pancreatic β cells.[13] Shoumin *et al*.[13] after giving a diet rich in fat to pigs, also found the deficiency of uptake of glucose in blood as well as a decrease in plasma insulin. He explained this by the fact that, the administration of a diet high in fat and sugar would induce insulin resistance that follows a decrease in the functioning of the pancreatic β cells. Thus, the administration of our extracts for a period of 30 days to the HFHS diet rats improved the removal of glucose in the blood. We suggest through following mechanisms of action: (i) Activation of β cells of the pancreas (ii) an effect on the insulin receptor or action in the activation of insulin. The lowering effect of the rate of body weight gain in treated rats observed in a period of 30 days shows the potential value of the extracts in minimizing TG. The increase in body weight was also observed in several studies where rats were fed with diets rich in fat or sugar.[27-28] The authors found their explanation in the fact that carbohydrates are known to induce hyperinsulinemia, which increases the accumulation state of fat by activation of adipocyte lipoprotein lipase.[27] So our extracts may act at this level to prevent formation of adipose tissue. Scientific supports referring to the influence of spices on lipid metabolism are limited, but the cholesterol and lipid lowering effects of some spices have been shown.[29] Curcuminoids present in many herbs and spices showed lipid-lowering effect in rats consuming a high-fat diet.[30] The HEE of *Hypodaphnis zenkeri* and the EE of *Xylopia aethiopica* have reduced triglycerides; only treatment with *Hypodaphnis zenkeri* led to the significant ($P < 0.05$) reduction of TC compared to the untreated group, suggesting that the administration of these spices could prevent the accumulation of fat in the liver. The reduction of TG may be associated with the inhibition of fat absorption[31] inhibition of fat synthesis, or increasing beta-oxidation.[32]

CONCLUSION

Our extracts showed significant biological properties at a concentration of 400 mg/kg; on the contrary to the ethanolic extract of *Hypodaphnis zenkeri*, the hydroethanolic extract of *Hypodaphnis zenkeri* showed a hypolipidemic activity on rats with hyperlipidemia induced by triton WR-1339. The two extracts reduced the elevation of triglyceride observed in rats consuming a HFHS diet. The administration of our extracts in tritonized rats reduced the concentration of GOT and GPT raised by the injection of triton WR-1339. Rats treated with *Xylopia aethiopica* showed an increase in plasma creatinin but the treatment with *Hypodaphnis zenkeri* led to its reduction. Our results also indicate that, the barks of *Hypodaphnis zenkeri*, and dry fruits of *Xylopia aethiopica* ameliorated the uptake of glucose impaired by the effect of HFHS diet on rats by inhibiting the elevation of blood glucose during a glucose tolerance test. The mechanisms studied here, suggest the use of these spices as functional foods representing a significant contribution to the enhancement of the Cameroonian spices and the use of natural products to combat some complications such as hyperlipidemia and insulin resistance related to obesity.

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