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Lipid lowering effect of aqueous leaves extract of *Murraya koenigii* (curry leaf) on alloxan-induced male diabetic rats

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ABSTRACT - *Murraya koenigii* leaves is considered extensively in the indigenous system of medicine as an antidiabetic agent in many Asian countries. The current investigation focuses attention on the lipid lowering property of the aqueous extract of *Murraya koenigii* leaves on experimentally induced diabetes in rats. The lipid parameters studied are plasma total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), very low density cholesterol (VLDL-C), triglyceride (TG) and phospholipids (PL). Extracts were orally administered daily for 8 weeks at dose of 600 mg/kg in alloxan diabetic rats. The levels of TC, LDL-C, HDL-C, VLDL-C, triglyceride and phospholipids were reduced significantly ($P<0.05$), while HDL-C levels did not alter significantly in rats given, aqueous extracts of *Murraya koenigii* when compared to diabetic control rats. In conclusion, these results showed that *Murraya koenigii* leaves extract when administered orally, can reduce plasma lipids level. These results further suggest that *Murraya koenigii* may be useful in the therapy and management of diabetic hyperlipidemia through reducing lipid levels.

KEY WORDS: alloxan, diabetes mellitus, hyperlipidemia, *Murraya koenigii*,

INTRODUCTION

Diabetes mellitus is a syndrome resulting from a variable interaction of hereditary and environmental factors and characterized by depleted insulin secretion, hyperglycaemia and altered metabolism of lipids, carbohydrates and proteins, in addition to damaged β-cells of pancreas and an increased risk of complications of vascular diseases (1). A number of pharmacological and chemical agents act as diabetogenic and produce variety of diabetic complications. Alloxan induction of diabetes is an experimental model widely used to study glycemic and lipidemic changes in plasma. Many species of plants and herbs are known to act as anti-diabetic agents, but only a few of them have been investigated (2).

Murraya koenigii (family, *Rutaceae*), popularly known as curry leaf is a medicinal plant that grows throughout the greater parts of India and South East Asia (3). This species is known to possess anti-inflammatory, antidysenteric, antioxidant, antidiabetic and diverse pharmacological properties (4-6). Several studies also shown that curry leaf decreased blood glucose significantly in different animal models (7-9). *Murraya koenigii* leaves have been shown to prevent hyperglycemia and pancreatic damage induced by alloxan in rats (10). Dietary supplement with curry leaves has been shown to reduced total serum cholesterol, LDL + VLDL, increased HDL, decreased the release of lipoproteins into circulation and increased catalase activity in rats (11). The present study was carried out in Sprague-Dawley rats to explore the effects of *Murraya koenigii* aqueous leaf extract on plasma lipid profile changes associated with diabetes.

MATERIALS AND METHODS

Plant material: Leaves of *Murraya koenigii* were collected fresh from plants grown in University of Agricultural Sciences campus, Bangalore, Karnataka, India. Taxonomic identification was authenticated by the Department of Botany, University of Agricultural Science, Bangalore, Karnataka, India. The leaves were air dried, reduced to powder and were kept separately in airtight containers until the time of use.

Preparation of aqueous extract

Powder of *Murraya koenigii* leaves (100 g) was taken and 200 ml of distilled water was added and boiled and later it was filtered off by using filter. The final concentration of the extract was 150 mg/ml. The filtrate obtained served as crude extract and administered orally into the experimental animals at the concentration of 600 mg/kg body weight per day for 8 weeks.

Animals

Experimental animals and induction of diabetes

Adult male Sprague-Dawley rats (200-300 g) bred in the Central Animal House, University of Agricultural Sciences campus, Bangalore, were used in this study. The animals were housed in polypropylene cages under

controlled conditions of 12-h light/dark cycle, and at 24 ± 2ºC. They were maintained on standard pellet diet containing 22% protein, 4.28% oil, 3.02% fiber, 7.8% ash and 1.3% silica (Amrut Laboratory Animal Feed, Nav Maharashtra Chakan Oil Mill Ltd, Pune, India) and water *ad libitum*.

Diabetes was induced in rats by intraperitoneal injection of 100 mg/kg body weight of alloxan monohydrate (5% w/v), freshly dissolved in physiological saline immediately before use (12-14). The diabetic state was confirmed 48 h after alloxan injection by weight loss, glucosuria (15) and hyperglycemia (16) and the animals, which presented blood glucose level above 200 mg/dl, as well as with the clinical signs of polydypsia, polyuria and polyphagia were selected for the experiment.

Treatment

Animals were divided into following 3 groups of 6 each. Group I: Normal rats received only physiological saline, Group II: Control diabetic rats received only physiological saline, Group III: Diabetic rats received aqueous extract of *Murraya koenigii* leaves (600 mg/kg body weight) per orally daily. This study was carried out for 8 weeks according to the guidelines of the Institutional Animal Ethical Committee.

Animals were anaesthetized with ether after which blood from retro orbital venous plexus was collected for estimation of plasma lipid profile.

Biochemical analysis

Plasma TC (17), HDL-C (17) and TG (18) estimation were carried out using respective diagnostic commercial kits from Accurex Biomedical Pvt. Ltd., Bombay, India. Phospholipids (19) level was estimated in plasma. VLDL-C and LDL-C in plasma were also calculated as per Friedewald's equation (20).

Statistical analysis

The results were expressed as mean ± SEM. Statistically analysis was carried out using one-way ANOVA followed by Bonferroni's test. Differences below $P<0.05$ implied significance (21).

RESULTS AND DISCUSSION

Table 1a & 1b. Shows the effect of oral administration of aqueous extract of *Murraya koenigii* on plasma lipids. The rats of Group II, diabetic control showed a marked increase in plasma TC, LDL-C, VLDL-C, TG and PL and a fall in HDL-C levels when compared to normal control group. However, following treatment with aqueous extract of *Murraya koenigii* (600 mg/kg) for 8 weeks, the plasma TC, LDL-C, VLDL-C, TG and PL were reduced significantly ($P<0.05$), while HDL-C remains unchanged in extract treated group when compared to diabetic control group.

***Table 1a*. Effect of aqueous extract of *Murraya koenigii* on the lipid profile of alloxan diabetic male rats.**

Treatment group	TC	TG	PL
Group I	71.48 ± 0.82	78.43 ± 1.35	75.95 ± 1.07
Group II	94.69 ± 2.23*[a]	155.10 ± 2.17*[a]	126.00 ± 2.15*[a]
Group III	80.18 ± 3.01*[b]	125.10 ± 6.33*[b]	99.80 ± 3.59*[b]

***Table 1b*. Effect of aqueous extract of *Murraya koenigii* on the lipid profile of alloxan diabetic male rats.**

Treatment group	LDL-C	HDL-C	VLDL-C
Group I	25.13 ± 1.30	43.36 ± 0.73	19.73 ± 0.63
Group II	28.51 ± 1.34*[a]	34.62 ± 0.46*[a]	31.04 ± 0.43*[a]
Group III	25.38 ± 1.40*[b]	29.83 ± 0.41	25.02 ± 1.27*[b]

The values are expressed in mg/dl. Values are expressed as mean ± SEM for six animals in each group.
**[a] values are significantly different from normal control (Group I) rats.*
**[b] values are significantly different from diabetic control (Group II) rats.*
Bonferroni's test (<0.05) was used ; Group I (normal control rats), Group II (diabetic control rats), Group III (aqueous extract treated diabetic rats), TC - total cholesterol, TG - triglycerides, PL - phospholipids, LDL-C - LDL-cholesterol, HDL-C - HDL-cholesterol, VLDL-C - VLDL-cholesterol

Studies in human and animals demonstrated that alteration of blood lipid profiles in condition of diabetes represents a risk factor for cardiovascular diseases (22). A number of pharmacological and chemical agents act as diabetogenic and produce variety of diabetic complications. Alloxan induction of diabetes is an experimental model widely used to study glycemic and lipidemic changes in plasma. Previous study demonstrated that aqueous extract of *Murraya koenigii* had a hypoglycemic effect in diabetic rats (10). The present study evaluated the effect of *Murraya koenigii* aqueous leaf extract on lipid parameters such as plasma TC, LDL-C, VLDL-C, HDL-C, TG and PL in alloxan-induced experimental diabetic rats.

Following the treatment with alloxan to rats a remarkable rise in the levels of plasma TC, LDL-C, were observed. Previous reports suggest that, elevated TC and LDL-C levels in the plasma of diabetic are considered to be a prime cause of coronary heart disease (CHD) (23-25). Many epidemiological studies showed that drug or diet induced reduction of TC and LDL-C could reduce the risk of CHD (26-28). In the present study, its recovery towards normal levels in aqueous extract administered diabetic rats coincides with the above observations, thus unearthing the cardioprotective effect of *Murraya koenigii*. The TG, PL and VLDL-C content in plasma registered a significant hike in diabetic control group, which was retrieved to near normalcy in aqueous extract treated diabetic rats. This observation also indicates the lipid lowering potential of *Murraya koenigii*.

Phytochemical analysis of *Murraya koenigii* leaf shows the presence of alkaloids, flavonoids, glycosides, minerals, vitamins and many other compounds (3, 29, 30). It has been reported the effect of tertiary and quaternary alkaloids, flavonoids and glycoside components reduces lipid levels in animals (31, 32). The varied chemical composition found in this leaf extract assigns to its lipid lowering property. This property of *Murraya koenigii* leaf extract may also be because of its other properties like antiinflammatory property which may prevent inflammatory pancreatic damage, immunomodulating property and antioxidant property (33) thereby reducing the oxidative stress imposed by the chemicals (alloxan); this antioxidant mechanism seems to be important as *Murraya koenigii* leaves has been shown to reduce oxidative stress (6) and oxidative stress has been found to be the most important mechanism in diabetic condition.

In conclusion, this study has shown that, oral administration of the aqueous extract of *Murraya koenigii* leaves have significantly reduced plasma lipid levels associated with diabetes mellitus. Thus it can be concluded that extract of *Murraya koenigii* leaves prevents as well as reverse the plasma lipid profile, thus emphasizing the protective role against diabetes induced hyperlipidemia. Further studies on the active components of *Murraya koenigii* and mechanism(s) of its protective effect against diabetic hyperlipidemia are needed.

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