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Antihyperlipidemic Activity of *Murraya koenigii* Extracts in Triton Induced Hyperlipidemic Rats

Shrinivas K Sarje[1*], Shagufta Farooqui[1], Purushottam Punde[1] and Aparna Suryawanshi[1]
[1]Department of Pharmacology, Nanded Pharmacy College, Nanded, Maharashtra.

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Corresponding Author Email: shriniwas.sarje@gmail.com

Abstract
Hyperlipidemia is common in both insulin Dependent and insulin non-dependent diabetes mellitus and are related to the degree of glycemic control. In the present investigation, the antihyperlipidemic activity of *MurrayaKoenjii* extracts on Triton induced Hyperlipidemic Rats was carried out. Chloroform, ethylacetate, ethanolic extracts of *Murrayakoenjii* (350mg/kg body weight) was administered orally to Triton induced Hyperlipidemic rats for days to investigate antihyperlipedemic activity of the plant. Biochemical parameters were studied including total cholesterol, triglycerides, HDL and LDL in control, treated and diabetic rats. The results of the experiment suggest that chloroform, ethylacetate, ethanolic extracts of *Murrayakoenjii* exerts significant antihyperlipedemic effects in Triton induced hyperlipidemic rats.

Keywords
Antihyperlipidemic Activity, Antidiabetic Activity, Triton*, MurrayaKoenjii.*

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INTRODUCTION:
Diabetes mellitus is a non-communicable disease, which is considered as one of the five leading causes of death in the world. Diabetes mellitus is caused by the abnormality of carbohydrate metabolism which is linked to low blood insulin level or insensitivity of target organs to insulin. Due to this disorder, body fails to make proper use of sugar (loss of ability to metabolize sugar). The excessive amount of sugar accumulates in the blood and often assess in the urine. Diabetes mellitus is also often linked with abnormal lipid metabolism. The abnormality of lipid metabolism is common in both insulin dependent and non-insulin dependent diabetes mellitus and is related to the degree of hyperlipidemia. Hyperlipidemia is a major risk factor for initiation and progression of cardiovascular disease (The lipid research clinics program, 1981; National Cholesterol Education Program Expert Panel, 1994). Accelerated cardiovascular disease is a leading cause of both morbidity and mortality in diabetic patients. The investigation on plant drugs will be useful strategy in

the discovery of new lead molecules eliciting improved activity by regulating the different mechanisms maintain the lipid metabolism and thus can be used in treating hyperlipidemia of varied etiology. Recently herbal hypolipidemics have gained importance to fill the lacunae created by the allopathic drugs. Murrayakoenjii is an, medicinal plants belonging to family Rutaceae. The scientific knowledge on antihyperlipidemic efficacy of Murrayakoenjiiis very scanty. So the present study was carried out to evaluate the antihyperlipedemic activity of Murrayakoenjii extracts on Triton induced Hyperlipidemic rats.

MATERIALS AND METHODS:

Plant Materials:

The leaves of *Murrayakoenigii,* had been selected for present project. The crude drugs were collected from local region of Nanded and identified on the basis of its morphological features.

Preparation of Extracts:

Murrayakoenigii Leaves were shade dried, leaned and pulverized by hands made to obtain coarse powder of mesh size #40. Coarse powder (1000 g) of MKL was exhaustively defatted using petroleum ether (60-80 ^{o}C) (MKL-PE) and extracted successively with chloroform (MKL-CH), Ethyl Acetate (SOL-EA) and ethanol (MKL-ET) using Soxhlet apparatus. All the extracts were collected, filtered through whatman filter paper, concentrated and stored in tight desiccator and percentage yield was calculated.

Chemicals:

Ethanol, Chloroform, Pet-ether (60-80°C), Acetone, Methanol, Toluene, Butanol, Glacial acetic acid, Phloroglucinol, Hydrochloric acid, Glycerin, Iodine solution, n-hexane, benzene, ethyl acetate, Sodium carbonate, Sodium nitrate, Sodium hydroxide, Aluminum trichloride from Fine Chem Industries, Mumbai.All other chemicals and reagents were of analytical grade.

Animals:

For the study rats (Wistar), of weight 150-250 gm were selected. The rats were obtained and brought to the laboratory and were maintained under controlled environment. All animals were fed with standard pellet feed and water ad libitum. The study was approved by the Animal Ethical Committee of the Institute (790/03/ac/CPCSEA). The principles of animal care were followed throughout the experimental period.

Acute Toxicity Study:

Acute oral toxicity study for the MKL-EA, MKL-ET was carried out to find out safe experimental dose of extracts and observed for toxicity. Determination of safe dose calculation is usually an initial screening step in the assessment and the evaluation of the toxic characteristics of all compounds. The types of toxicity tests which are routinely performed in the investigation of a new drug involve acute, sub-acute and chronic toxicity. Safe dose calculation involves estimation of LD_{50} (the dose which has proved to be lethal (causing death) to 50% of the tested group of animals).

Organization for Economic Co-Operation and Development (OECD) regulates guideline for Oral Acute Toxicity study. It is an international organization which works with the aim of reducing both the number of animals and the level of pain associated with safe dose calculation.

Evaluation of Antihyperlipidemic Activity:

The animals were divided into fifteen groups of six rats each. Animals were weighed before the experiment, a single dose (350 mg/kg body weight i.p) of Triton WR-1339 dissolved in 0.15 N NaCl solution was used for induction of hyperlipidaemia in rats. Hyperlipidaemia was confirmed after 48 hours triton injection by determining the blood cholesterol level. The drug was administered continuously for 7 days by oral feeding needle. Group A rats received DMSO as a vehicle and Group B to O received toxicant with control, standard drug and test respectively.

On 7th day, after 1hr of administration of the last dose, blood samples were collected from overnight fasted rats by retro-orbital puncture. Blood parameters were measured by semi-autoanalyser using commercially available assay kits.

Biochemical Estimation:

Evaluation was carried out over lipid profile parameters as Serum Triglyceride, Serum Total Cholesterol, Serum LDL, Serum HDL, VLDL, etc. by using enzymatic kit and over morphological parameters as body weight.

Statistical Analysis:

Values were represented as Mean + Standard Error. To compare the means of different experimental groups with normal groups, One Way Analysis of Variance (ANOVA) was performed. The Tukey test was performed to investigate the influence of the Murrayakoenjii plant extracts on various biochemical parameters in the extract treated rats. All statistical analyses were performed by using Windows based SPSS package (Statistical Packages for Social Sciences and now it is called Statistical Product and Service Solutions).

RESULTS:

Antihyperlipidemic Actvity of Triton induced Hyperlipidemic rats.

Antihyperlipidemic activity of Murrayakoenjii was evaluated by analyzing abnormalities in serum cholesterol level, triglyceride level, HDL level and VLDL levels in diabetic rats, extract treated rats and were compared with the normal rats. Lipid profiles were measured in control and all experimental rats on the 7th day of treatment. Effect of Murrayakoeinjii extracts on the serum cholesterol, triglyceride, HDL and VLDL levels in Triton induced Hyperlipidemic rats are presents in the table 2.

Change in Body weight of triton Induced Hyperlipidemic rats:

In present study the effect of MKL-EA, MKL-ET, was studied for its antihyperlipidemic activity using triton (WR-1339) induced hyperlipidemia where rats were treated with single dose of triton (WR-1339) and further treatment continued for 7 days. At the end of the treatment rats were evaluated over change in body weight

and over lipid profile parameters as Serum Triglyceride, Serum Total Cholesterol, Serum LDL, Serum HDL, VLDL.

Table No.1: Effect of MKL-EA, MKL-ET, on change in body weight in Triton-induced hyperlipidemic rats.

Groups	Change in Body Weight (gm)
Control	02.32±0.44
Positive Control	33.43±2.63
Atorvastatin	2.21±0.41**
MKL-EA100	18.77±0.37**
MKL-EA200	16.53±0.33**
MKL-ET100	12.59±0.39**
MKL-ET200	5.79±0.31**#

Values are expressed as Mean±SEM. (n=6), ANOVA followed by Tukey test. *p<0.05 significant difference, **p<0.001 highly significant difference when compared with Positive-control. #p>0.05 non-significant difference when compared with standard **MKL-*Murrayakoenigii leaves*** extract, **EA-** ethyl acetate, **ET**- ethanol Change in body weight was measured on day 7. Normal control shown body weight change 2.32 gm on day 7 while Positive control shown body weight change 33.43 gm, Atorvastatin (2.21), MKL-ET 200 (5.79), MKL-ET 100 (12.59), shown (p<0.001) significant change in body weight over positive control while MKL-ET 200 shown (p>0.05) significance over standard on day 7.

Effect of *MurrayaKoenjii*on total Cholesterol levels.

In the normal rats the total cholesterol levels were to be found be79.93±0.6263. Treatment with Triton-X-100 caused a significant rise in the levels of cholesterol (189.83±0.49). Administration of various doses of the plant extract after the treatment with Titon-X-100 resulted in the lowering of Cholesterol levels in a dose dependent manner. The total cholesterol levels of groups treated with 100 and 200 mg/kg were extract was significant at (p<0.05).

Effect of *Murraya Koenjii*on Triglyceride levels.

Induction of hyperlipidemia resulted in significantly raised triglyceride levels (194.55±3.42) compared to the normal 62.51±0.49. Administration of various doses of the plant extract was able to produce a dose dependent decrease in the triglyceride levels. The respective triglyceride values for rats treated with 100 and 200 mg/kg of extract was significant at (p<0.05).

Effect of *Murraya Koenjii*on serum LDL levels.

The LDL levels in normal rats were found to be .07.51±0.17 Administration of Triton-X-100 resulted in a rise in LDL levels (119.43±2.19). In Atorvastatin group the LDL was reduced to34.03±0.73** whereas groups treated with 100 and 200 mg/kg of extract showed a dose dependent decrease in the LDL levels (83.62±0.77**52.52±0.45**respectively)

Effect of *Murraya Koenjii*on serum VLDL levels.

The VLDL levels in normal rats were found X-100 resulted in a rise in VLDL levels (12.51±0.98). In Atorvastatin group the VLDL was reduced to 24.71±0.78**whereas groups treated with 100 and 200 mg/kg of extract showed a dose dependent decrease in the VLDL levels (32.68±0.72*27.68±0. 72**#respectively)

Effect of *Murraya Koenjii*on serum HDL levels.

The HDL levels in normal rats were found to be59.93±3.65. Administration of Triton-X-100 resulted in a fall in HDL levels (31.55±1.82). In Atorvastatin group the LDL was elevated to66.54±3.58** , whereas groups treated with 100 and 200 mg/kg of extract showed a dose dependant

increase in the HDL levels (53.55±0.88**63.44± 0.32**respectively).

Table 2: Effect of MKL-EA, MKL-ET, on lipid profile level in Triton-induced hyperlipidemic rats

Groups	Serum Triglycerides (mg/dl)	Serum Total Cholesterol (mg/dl)	Serum LDL Cholesterol (mg/dl)	Serum HDL Cholesterol (mg/dl)	Serum VLDL Cholesterol (mg/dl)
Control	62.51±0.49	79.93±0.62	07.51±0.17	59.93±3.65	12.51±0.98
Positive Control	194.55±3.42	189.83±0.49	119.43±2.19	31.55±1.82	38.91±0.74
Atorvastatin	123.52±3.61**	128.29±0.77**	34.03±0.73**	69.53±0.31**	24.71±0.78**
MKL-EA100	182.44±3.17	181.74±0.44*	105.41±0.88*	39.83±0.32	36.48±0.73
MKL-EA200	172.33±3.53*	173.44±0.52**	94.64±0.55**	44.33±0.53**	34.46±0.78*
MKL-ET100	163.44±3.41**	169.81±0.82**	83.62±0.77**	53.55±0.88**	32.68±0.72*
MKL-ET200	138.47±3.27**#	143.63±0.51**	52.52±0.45**	63.44±0.32**	27.68±0.72**#

Values are expressed as Mean±SEM. (n=6), ANOVA followed by Tukey test. *p<0.05 significant difference, **p<0.001 highly significant difference when compared with Positive-control. #p>0.05 non-significant difference when compared with standard; **MKL-*Murrayakoenigii leaves*** extracts **EA-**ethyl acetate, **ET**- ethanol, Serum lipid profile viz., serum triglycerides, serum total cholesterol, serum LDL, serum HDL, VLDL was measured on day 7. Positive control shown 194.55, 189.83, 119.43, 31.55, 38.91, Atorvastatin shown 123.52, 128.29, 34.03, 69.53, 24.71, MKL-ET 200 shown 138.47, 143.63, 52.52, 63.44, 27.68, significant change (p<0.001) in lipid profile over positive control equal to standard.

CONCLUSION:

The results obtained from the pharmacological screening have led to the conclusions that, ethanolic extract of leaves of *Murrayakoenigii* has significant antihyperlipidemicactivity. Hence it can be exploited as an anti-hyperlipidemic therapeutic agent or adjuvant in existing therapy for the treatment of hyperlipidemia.

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