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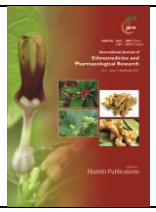

Anti-dyslipidemic activity of Siddha herbal formulation Vaeppampoovathy Mathirai in Animal model

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ABSTRACT

Life style disorders in other words called as diseases of civilization, diseases of modernization and diseases of more industrialization. Dyslipidemia indicates an abnormal lipid level that is increase or decrease in lipid levels. One of the polyherbal kayakalpa drug mentioned in siddha literature is *Vaeppampoovathy mathirai*, which includes 14 herbal drugs with rich anti-oxidant property and it is indicated for adiposity, kapha-pitha diseases, hypertension and obesity. In this study the test drug *Vaeppampoovathy Mathirai*, is taken for anti-dyslipidemic activity. The aim of the present study was to screen the drug for its acute toxicity in animal model and Anti-dyslipidemic activity in Triton WR-1339 induced hyperlipidemia in animal model Wistar albino rats. The animals were selected randomly and divided into four groups with six animals in each group. Group 1 taken as normal control, group 2 taken as control, group 3 taken as standard and group 4 taken as test drug *Vaeppampoovathy Mathirai* (200mg/kg). The results were tabulated and it reveals the potency of the drug. *Vaeppampoovathy mathirai* showed significant ($P<0.05$) hypolipidemic effect as it decreased the level of total cholesterol, triglyceride level and LDL cholesterol and increased in HDL cholesterol level compared to the standard drug Atorvastatin.

Keywords: Dyslipidemia, Triton, Atorvastatin, Triglyceride.

INTRODUCTION

Today the world encounters innumerable problems including health concerns among them lifestyle disorders play a major role in threatening the whole world. Life style disorders in other words called as diseases of civilization, diseases of modernization and diseases of more industrialization. Life style diseases are dyslipidemia, arthritis, depression, diabetes mellitus and hypertension. Among them, obesity is becoming the main precursor of many diseases and death.

Dyslipidemia indicates an abnormal lipid level that is increase or decrease in lipid levels. Dyslipidemia is one of the major risk factor for coronary artery diseases associated with atherosclerosis, obesity, coronary artery disease and metabolic disorders like diabetes mellitus and polycystic ovary diseases. It was projected that by 2030 there will be about 23.3 million CVD deaths worldwide (Mathers CD, Loncar D., 2006)

The holistic approach of siddha medicine treating the patient as a whole, meaning intervention targeted towards complete physical, psychological and spiritual well-being makes this science a wonderful option in lifestyle disorders.

Siddha system of medicine is based on hypothetical and biological laws of nature. The Siddhars were pioneers in the world in the field of minerals, metals and medicinal herbs.

Modern therapy for hyperlipidemia is effective associated with side effects. Lipid lowering drugs fibrates, status and bile acid sequestrants do not possess antioxidant property and therefore a drug having a dual property of both antioxidant and lipid lowering effect is an ideal remedy for dyslipidemic population. One of the polyherbal kayakalpa drug mentioned in siddha literature is *Vaeppampoovathy mathirai*, which includes 14 herbal drugs with rich anti-oxidant property and it is indicated for adiposity, kapha-pitha diseases, hypertension and obesity.

In this study the test drug *Vaeppampoovathy Mathirai*, is taken for anti-dyslipidemic activity. Most of the herbs included in this drug are Kayakalpam which not only reduced dyslipidemia related obesity but also enhance a healthy body to lead a long life. The trial drug *Vaeppampoovathy Mathirai* is unique and safe. It improves the overall health with no adverse effects and it is not cost effective. But its effectiveness is not supported by sufficient scientific evidence. So an attempt was made to evaluate the anti-dyslipidemic activity of *Vaeppampoovathy Mathirai* in Triton induced dyslipidemic wistar albino rats.

MATERIAL AND METHODS

The polyherbal preparation Vaeppampoovathy Mathirai was selected from the siddha literature (Shanmugavelu M, 1973).

INGREDIENTS

Neem flowers (*Azadirachta indica*), dried Ginger (*Zingiber officinalis*), Pepper (*Piper longum*), long pepper (*Piper longum*), Chebulic myrobalan (*Terminalia chebula*), Indian gooseberry (*Embelica officinalis*), Bellaric myrobalan (*Terminalia bellaric*), Cloves (*Syzigium aromaticum*), Cinnamomum (*Cinnamomumverum*), Cardamom (*Elaterria cardamom*), cuscus grass (*Vetiveria zizanoides*), climbing brinjal (*Solanum trilobatum*), Indian Phyllanthus (*Phyllanthus niruri*), Wedeliachinensis (*Chinensis wedelia*) and lemon (*Citrus limon*)

COLLECTION OF PLANT & RAW MATERIAL

Drugs were procured from Nagercoil, they were identified and authenticated by botanist of Central Research Institute Chennai and faculties of the department of Gunapadam, Govt Siddha Medical College Chennai, Tamilnadu. Specimens of each sample have been kept in the Post graduate department of Gunapadam for future reference.

PREPARATION OF POLYHERBAL FORMULATION

All the ingredients were cleaned well and dried in sun shade. After complete drying each ingredient was taken separately and purified as per Siddha classical literature (Sarakku Suthi Muraigal 2008). After purification the ingredients were grounded separately to powder. The powder was sieved through a white cloth and then 64gms of Neem flower powder, 32gms of powder of Indian Phyllanthus, climbing brinjal, chinens is wedelia and 8gms powder of remaining ingredients were mixed thoroughly in stone mortar and rubbed with sufficient quantity of lemon juice for 3 days and rolled into size of 130 mg. The pills were stored in airtight container and labeled as VPM.

ANIMALS

The animal model for this activity was the Wistar albino rat of either sex. The weight of each animal ranges from 120-200gm. The animals were purchased from the animal house of king institute of preventive medicine, Guindy, Chennai for the experimental study. The animals were kept in the ventilated room under normal laboratory condition with food and water *ad libitum.* The animals were acclimatized 2 weeks before they were exposed to the experiment.

The experimental protocol was approved by the institutional ethical committee (IAEC) under CPCSEA (approval no: 1545/PO/a11/CPCSEA)

ACUTE ORAL TOXICITY STUDY

The study was conducted as per the guidelines of Organization for Economic Cooperation and Development (OECD, 2000). VPM prepared as per the classical Siddha

literature was suspended in 2% CMC with uniform mixing and was administered to the groups of Wistar albino rats. It is given in a in a single oral dose by gavage using a feeding needle. After the substance has been administered, food was withheld for a further 3-4 hours. Observations were made and recorded systematically and continuously observed as per the guideline. The toxicological effect was assessed on the basis of mortality. Since this test drug has been under practice for long time and likely to be non-toxic, a limit test at one dose level of 2000 mg/kg body weight will be carried out.

PHARMACOLOGICAL ACTIVITY

Anti-Dyslipidemic activity of VPM

Triton WR 1339 induced hyperlipidemia in Wistar Albino Rats

Drug and Stock solution

The VPM was prepared as per the procedure in traditional Siddha text recommendation and made into suspension form with using CMC as a suspending agent and used in this study. The resulting suspension was then grounded and filtered. The filtrate was stored in a refrigerator until use. The suspension was further diluted with 2% CMC so as to achieve 200mg/ml stock concentration.

Induction of hyperlipidemia

Hyperlipidemia was induced in wistar albino rats by a single injection of Triton WR-1339(400 mg/kg body weight). Triton was diluted with normal saline (400 mg ml^{-1}) and injected $1mlkg^{-1}$ b.w to each rat intra-peritoneally**.** (Khanna *et al.*,2002) After 72 hours of triton injection received a daily dose of 2% CMC.

Procedure

The animal model Wistar albino rats were taken. The rats weighing around 200-300 g were taken. Then they were injected intravenously with 400 mg/kg Triton WR 1 339 (isooctyl-polyoxyethylene phenol). Two phases of reaction takes place after the administration. In phase I Serum cholesterol levels increase sharply 2-3 times after 24 h. In phase II, hypercholesterolemia decreases nearly to control levels within the next 24 h. The test drugs employed or the solvent for the controls are administered simultaneously with the Triton injection or 22 h thereafter. Serum cholesterol analyses are made 6, 24, and 48 h after Triton injection.

EXPERIMENTAL DESIGN

The animals were divided into 3 groups with 6 animals in each group.

Group I: Received 2% CMC (Control)
Group II: Received triton 400mg/kg b.wt (Triton control)
Group III: Hyperlipidemic rat treated with Standard Atorvastatin- 10 mg/kg b.wt were administered orally
Group IV: Hyperlipidemic rats treated with test drug Vaeppampoovathy mathirai (VPM) 200 mg/kg b.w orally.

All the animals after 72 hours of Triton injection (ie. after inducing hyperlipidemia) the respective treatment was continued for 7 days.

Collection of blood

On the 8^{th} day the blood was collected by retro orbital sinus puncture, under mild ether anesthesia. The collected samples were centrifuged for 10 minutes. Then serum samples were collected and it is used for various biochemical experiments.

Biochemical analysis

- Total cholesterol (Zak's, 1977)
- High-density lipoprotein (varley et.al., 1980)
- Low-density lipoprotein (Friedwald Levy and Frederickson, 1972)
- Very low density lipoprotein (Henry et.al.,1998)
- Triglycerides (Rice, 1970)

STATISTICAL ANALYSIS

All values were expressed as mean ± SEM. Data were analyzed using the repeated measures ANOVA followed by the Dunnets multiple comparison test. *P* value <0.05 was considered significant.

RESULT AND DISCUSSION

Acute oral toxicity in rats – OECD 423

Wistar albino rat was treated with the test drug AVC of single dose of 2000mg/kg in 2%CMC as suspention. This study was conducted as per the OECD guidelines. The acute toxicity result shows no mortality rate up to 2000mg/kg. The behavioural changes are normal. Hence the test drug VPM is a safe herbal drug and can be used for long time administration.

Anti-dyslipidemic activity

The Anti-Dyslipidemic activity of VPM has been studied in Triton WR-1339 induced hyperlipidemic rats. It effectively increased the total cholesterol, triglycerides, LDL, VLDL levels and decreased the HDL level compared to control groups.

Triton WR-1339 has been widely used to induce acute hyperlipidemia in animal models particularly in rats for screening natural or chemical hyperlipidemic drugs (Harbowy and Balentine, 1997).

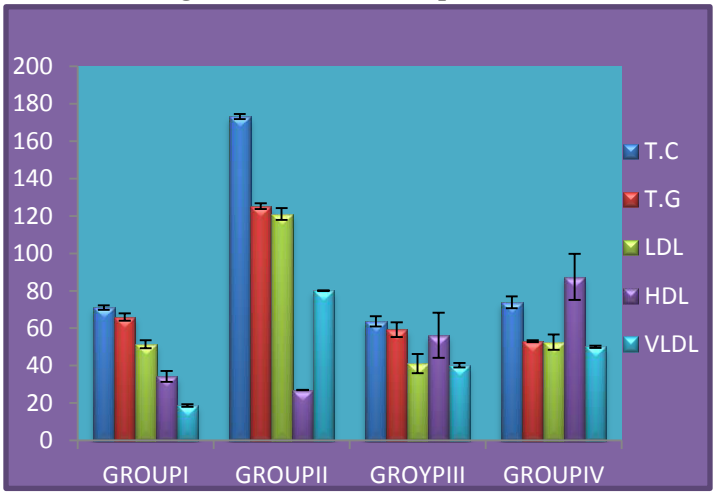
Oral administration of the test drug VPM taken in the dose of 200mg/kg showed significant decrease in the level of cholesterol, triglycerides, LDL, VLDL and increase in the level of HDL. The test drug showed a significant change which may be probably due to the synergetic effect of Flavonoids, Tannins and Triterpenoids. Flavonoids are reported to lower LDL-C and increase HDL-C concentration in hypercholesterolemic animals. Tannins can reduce cholesterol absorption in intestinal to lower lipid concentrations and reduce the incidence of cardiovascular diseases.

Table-1. Effect of VPM on serum lipid profile in Triton- induced hyperlipidemic rats

Treatment	T.C	T.G	LDL	HDL	VLDL
NormalControl	70.98±1.2	66.01±1.98	51.43±2.1	34.22±2.9	18.73±0.7
Triton treated	173.12±1.39^{++} +	125.25±1.52^{+++}	121.03±3.12^{+++}	27.04±0.11^{++}	80.12.±0.21^{+++}
Hyperplipidemic rats+ atorvastatin	63.63±2.7**	59.23±3.91**	41.09±5.2***	56.21±12.1** *	40.23±1.2**
Hyperlipidemic rats VPM 200 mg/kg	73.88±3.2**	53.12±0.5**	52.42±4.1***	87.42±12.3**	50.11±0.6**

*Values are as mean ± SEM (n=6). Hyperlipidemic control was compared with control rats. Values are statistically significant at +P<0.05, ++P<0.01, +++P<0.00 Experimental groups (G III &IV) were compared with hyperlipidemic control rats. Values are statistically significant at *P<0.05, **P<0.01, ***P<0.001*

Fig-1. VPM on Serum Lipid Profile



CONCLUSION

Anti-dyslipidemic activity of *Vaeppampoovathy mathirai* was screened by triton induced hyperlipidemia in wistar albino rats and serum level of total cholesterol, triglycerides, LDL, HDL cholesterol was determined. *Vaeppampoovathy mathirai* showed significant ($P<0.05$) effect as it decreased the level of total cholesterol, triglyceride level and LDL cholesterol and increased in HDL cholesterol level which is almost equal to the standard drug.Further comprehensive chemical and pharmacological investigations are needed to elucidate the exact mechanism of the hypoglycemic effect of AVC and the drug bear the potential for further research.

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