

ASSESSMENT OF ANTI-HYPERLIPIDEMIC ACTIVITY OF A POLYHERBAL FORMULATION BA019

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Received on: 11/12/2019

Revised on: 01/01/2020

Accepted on: 22/01/2020

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ABSTRACT

In this study, anti-hyperlipidemic activity of polyherbal formulation BA019 was assessed by two animal models, Triton induced hyperlipidaemia and fructose diet induced hyperlipidaemia in wistar rats. In both animal models, BA019 produced a significant reduction in serum concentration of cholesterol and triglycerides. The effect of 200 mg/kg of BA019 was significant when compared to vehicle treated group. The effect of 400mg/kg of BA019 was nearly equal to standard drug Atrovastatin (10mg/kg, p.o). These results showed that polyherbal formulation BA019 possessed anti-hyperlipidemic activity.

KEYWORDS: Anti-hyperlipidemic, Triton, fructose, BA019, Atrovastatin, rats, cholesterol, triglycerides.

INTRODUCTION

Hyperlipidemia is a broad term which is the major cause of coronary heart disease.^[1] Several classes of anti-hyperlipidemics are used to treat hyperlipidemia and obesity but they have side effects such as headache, nausea, bowel upset, rashes, sleepy disturbances, muscle tenderness and myopathy. To reduce the impact of hyperlipidaemia there is an urge to provide a cost effective treatment to the public. With the increased incidence of hyperlipidaemia and obesity recently, natural herbs that have anti-hyperlipidemic effect have gain more attention as alternative treatment for hyperlipidaemia and obesity Herbal medicines exhibit low toxicity and cheaper cost when compared to synthetic drugs. As per traditional practitioners, a combination of plant extracts or herbs show increased therapeutic efficacy than a single plant extract or herb.

The polyherbal formulation BA019 contains: *Psidium guajava*, *Carica papaya* and *Cinnamomum verum* had already been shown to exhibit antihyperlipidemic activity in experimental models in previous studies.^[2,3,4] In the present study, an attempt has been made to investigate the anti-hyperlipidemic activity of a polyherbal formulation BC019 in treating hyperlipidemic rats by employing Triton induced hyperlipidemic model and fructose induced hyperlipidemic method. The standard drug, Atrovastatin which was used as a positive control to compare the efficacy of a polyherbal formulation BA019 as an anti-hyperlipidemic agent.

MATERIALS AND METHODS

Collection and Authentication

The plants *Psidium guajava*, *Carica papaya* and *Cinnamomum verum* were collected from Guntur, Andhra Pradesh, India. The plants were identified and authenticated by Dr.P.Satya Narayana Raju, Plant Taxonomist, Department of Botany and Microbiology, Acharya Nagarjuna University, Nagarjuna Nagar, Guntur, Andhra Pradesh, India.

Preparation of Polyherbal formulation BA019

The dried fruits of *Psidium guajava*, leaves of *Carica papaya* and bark of *Cinnamomum verum* *Acorus calamus* were washed and cleaned separately. The powdered plant materials were used for the preparation of ethanolic extracts. 500 gms of each plant material was weighed and extracted with 95% ethanol by maceration process separately for 4 days and filtered with whatman filter paper. The extracts were concentrated under reduced pressure and stored in vacuum dessicators for complete removal of solvent. Each extract was weighed and percentage yield was calculated.^[5]

The polyherbal formulation which contains equal proportions of the ethanolic extract of *Psidium guajava* (fruits), *Carica papaya* (leaves) and *Cinnamomum verum* (bark) was called as BA019.

Qualitative Phytochemical Analysis

Phytochemical analysis of Polyherbal formulation BA019 was carried out by using standard procedures to identify the presence of various phytoconstituents.^[6]

IN-VIVO Studies**Experimental Animals**

Adult wistar albino rats (150-180 g) of either sex were procured from the laboratory animal house, Hindu College of Pharmacy, Guntur, Andhra Pradesh, India and used in the study. The animals were kept under standard environmental conditions of room temperature (22± 2°C), relative humidity (50% ± 5%) and 12 h light and dark cycle. The animals were housed in the colony cages (three rats per cage) and provided feed (commercial pellets contain a balanced ration obtained from Mahaveera Enterprises, Hyderabad) and water *ad libitum*.

All the animals were acclimatized to the laboratory environment 5 days prior to experiment. The animals were fasted overnight just prior to the experiment but allowed free access to drinking water. All the experiments were carried out in accordance with the guidelines of Institutional Animal Ethics Committee.

The study was conducted after obtaining ethical committee clearance from the Institutional Animal Ethics Committee No: HCOP/IAEC/PR-3/2019.

Anti-Hyperlipidemic Activity**1. Triton X100 (Tr) Induced Hyperlipidemia Model**

Thirty wistar rats weighing 150-200 gm were randomly divided into 5 groups of 6 each. The first group was administered with normal saline (p.o). The II, III and IV,

and V group animals were injected i.p. with 10% aqueous solution of triton (100mg/kg body weight). After 72 hours of triton injection, the second group was received a daily dose of normal saline (p.o) for 7 days, the third group was given the Polyherbal formulation-BA019 (200 mg/kg; p.o), fourth group received Polyherbal formulation-BA019 (400 mg/kg; p.o) and the fifth group was administered a daily dose of standard Atorvastatin (10mg/kg; p.o.) for 7 days. Food was withdrawn 10 h prior to the blood sampling.

Group I: Normal control

Group II: Triton control

Group III: Triton+Polyherbal formulation-BA019 (200 mg/kg, p.o)

Group IV: Triton+Polyherbal formulation- BA019 (400 mg/kg, p.o)

Group V: Triton+Atorvastatin (10mg/kg, p.o)

On 8th day, blood was collected by retro orbital sinus puncture, under mild ether anaesthesia. The collected blood samples were centrifuged for 15 minutes at 2500rpm. Then serum samples were estimated for Total Cholesterol, Triglycerides, HDL, LDL and VLDL.^[7]

Statistical analysis

Results were analyzed by one-way ANOVA followed by Dunnett's multiple comparison test and the values P< 0.05 were considered significant (Table 1).

Table 1: Effect of Polyherbal Formulation BA019 on Serum Lipid parameters levels in Triton induced Hyperlipidemic rats.

No.	Groups	Serum Lipid parameters (mg/dl)				
		Total cholesterol	Triglycerides	HDL-C	LDL-C	VLDL-C
I	Normal control	82.8 ±3.5	70.2±6.4	51.1± 5.30	26.1±2.2	15.6±2.9
II	Hyperlipidemic control	210.6 ±11.4	128.1±9.2	35.4±5.2	152.1±12.3	27.6±1.7
III	BA019 (200mg/kg)	92.5±13.7*	90.7±1.2*	46.4±6.3**	47.2±7.82*	20.1±1.5*
IV	BA019 (400mg/kg)	70.1±9.3**	86.5±1.7**	49.8±4.4**	41.6±9.5**	18.5±0.5**
V	Atorvastatin (10mg/kg)	76.2±11.4*	80.9±1.9*	50.8±6.8*	35.2±10.7*	15.4±1.4*

All values are mean ± SEM. (n=6).One-way ANOVA followed by Dunnett's test.*P< 0.05,** P<0.01 when compared to vehicle treated (control) animals.

2. Fructose Induced Hyperlipidemia Model

Wistar rats weighing between 150-200 gm were divided into five groups of six animals each. The first group was fed with standard pellet diet and water *ad libitum*. The 1st was administered with normal saline (p.o).10% fructose was used as inducing agent for hyperlipidemia. The 2nd, 3rd,4th and 5th groups were fed with 10% fructose in drinking water for a period of one week. Third group was received Polyherbal formulation-BA019 (200 mg/kg; p.o), fourth group was received Polyherbal formulation-BA019 (400 mg/kg; p.o) and the fifth group was administered a daily dose of standard Atorvastatin (10mg/kg; p.o.) along with fructose diet simultaneously for 7 days.

Group I: Control (normal saline)

Group II: Fructose control

Group III: Fructose + Polyherbal formulation-BA019 (200 mg/kg, p.o)

Group IV: Fructose + Polyherbal formulation- BA019 (400 mg/kg, p.o)

Group V: Fructose + Atorvastatin (10mg/kg, p.o)

On 8th day, blood was collected by retro orbital sinus puncture, under mild ether anaesthesia. The collected blood samples were centrifuged for 15 minutes at 2500rpm. Then serum samples were estimated for Total Cholesterol, Triglycerides, HDL, LDL and VLDL.^[8]

Statistical analysis

Results were analyzed by one-way ANOVA followed by Dunnett's multiple comparison test and the values P< 0.05 were considered significant (Table 2).

Table 2: Effect of Polyherbal Formulation BA019 on Serum Lipid parameters levels in fructose induced Hyperlipidemic rats.

No.	Groups	Serum Lipid parameters (mg/dl)				
		Total cholesterol	Triglycerides	HDL-C	LDL-C	VLDL-C
I	Normal control	81.9±2.7	60.7±9.1	46.1±6.5	23.7±2.6	11.7±2.6
II	Hyperlipidemic control	195.0±13.5	114.2±6.2	28.2±5.3	145.4±1.0	22.4±0.4
III	BA019 (200mg/kg)	118.3±7.7*	90.4±6.4*	33.1±4.4*	57.8±6.4*	24.0±1.3*
IV	BA019 (400mg/kg)	111.2±6.3**	82.2±5.1**	37.4±5.7**	50.1±2.1**	20.2±1.2**
V	Atorvastatin (10mg/kg)	91.1±12.2*	75.4±5.4*	40.1±3.5*	43.3±15.2*	16.1±0.7*

All values are mean ± SEM. (n=6). One-way ANOVA followed by Dunnett's test. * $P < 0.05$, ** $P < 0.01$ when compared to vehicle treated (control) animals.

RESULTS AND DISCUSSION

The air dried and finely ground plant parts of *Psidium guajava* (fruits), *Carica papaya* (leaves) and *Cinnamomum verum* (bark) was extracted by maceration process with 95% ethanol for 4 days, when filtered and concentrated under reduced pressure gave the yield of 12% w/w and 8% w/w and 12% w/w respectively. This was kept in dark place at 4°C until tested. Hence forth, the polyherbal formulation which contains equal proportions of the ethanolic extract of *Psidium guajava* (fruits), *Carica papaya* (leaves) and *Cinnamomum verum* (bark) was called as BA019.

Preliminary phytochemical analysis revealed the presence of carbohydrates, volatile oils, tannins & phenolic compounds, sterols and flavonoids in BA019.

The importance of new products in the treatment and prevention of hyperlipidemias becomes essential to reduce the mortality and morbidity due to cardiovascular complications. The search for low toxic drugs for hyperlipidaemia has increased the interest of the research scientists for natural herbal products. The polyherbal formulation BA019 showed to be able to manage hyperlipidemia induced by Triton and high-fructose diet, reducing serum levels of total cholesterol and triglycerides.

The natural herbal products produce anti-hyperlipidemic activity due to their phyconstituents which inhibit cholesterol biosynthesis and absorption and modify the activity of lipogenic and lipolytic enzymes, leading to reduced lipid metabolism. In this study, hyperlipidemic rats treated with BA019 exhibited significant reduction in the levels of total cholesterol and triglycerides.

Our results showed that polyherbal formulation BA019 was also able to manage hyperlipidemia by decreasing serum level of cholesterol and triglycerides and were similar to standard drug Atrovastatin.

CONCLUSION

From the results of our studies, it can be concluded that Polyherbal formulation BA019 exhibited significant anti-

hyperlipidemic activity. The observed effects are nearly equal to the existed familiar standard drug Atorvastatin. However, further studies are necessary to find the exact mechanism of anti-hyperlipidemic effect.

ACKNOWLEDGEMENT

The authors are thankful to Dr. S. Madhusudana Rao, M.B.B.S, Secretary and Correspondent and Sri. Jupudi Rangaraju B.com., B.L, Chairman, Hindu College of Pharmacy, Guntur for providing necessary facilities to carry out the present research work.

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