



Effect of Three Plant Extracts and Atorvastatin on Serum Lipids and Lipoproteins in Rats Fed High Cholesterol Diet

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Abstract

Introduction: To evaluate the relative efficacy of *Gloriosa superba*, *Valeriana wallichii* and *Odenlandia corymbosa* extracts and atorvastatin in correcting the dyslipidemia induced by feeding high cholesterol diet to rats.

Methods: The study was carried out on healthy male adult rats of Wistar strain. Dyslipidemia was induced by feeding them fructose-rich high fat diet (F-HFD). *Gloriosa superba* extract, *Valeriana wallichii* extract, *Odenlandia corymbosa* extract and atorvastatin were given orally for 30 days along with F-HFD to four different groups. Serum lipids and lipoproteins were measured.

Results: Feeding F-HFD for 30 days led to dyslipidemia in the form of raised serum cholesterol, triglycerides, LDL-cholesterol, VLDL-cholesterol and free fatty acids. In the rats fed F-HFD + *Valeriana wallichii* extract, serum cholesterol, triglycerides and VLDL-cholesterol were significantly lower as compared to rats fed F-HFD alone. No such effect was seen in the rats given F-HFD + *Gloriosa superba* extract and F-HFD + *Odenlandia corymbosa* extract. In the rats fed F-HFD + atorvastatin, serum lipids were significantly lower as compared to rats fed F-HFD alone and the effect was stronger than that of *Valeriana wallichii*.

Conclusion: *Valeriana wallichii* possesses anti-dyslipidemic activity but is not as effective as atorvastatin.

Keywords: Anti-dyslipidemic, *Gloriosa superba*, *Valeriana wallichii*, *Odenlandia corymbosa*.

Introduction

Dyslipidemia is an abnormality of plasma lipids in which plasma total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), very low-density lipoprotein cholesterol (VLDL-C) and triglycerides (TG) are elevated and high-density lipoprotein cholesterol (HDL-C) is lowered, either singly or in combination¹. Detection and correction of this condition is important for prevention and control of cardiovascular disease (CVD) and its sequelae. In 80% cases, lipid abnormalities are related to diet and lifestyle while heredity plays a role in the remaining cases². The prevalence of dyslipidemia is increasing worldwide^{3,4}. Studies have shown increased

prevalence of dyslipidemia and have attributed it to increasing prevalence of obesity and type 2 diabetes mellitus, which are linked to changes in lifestyle associated with modernization and socioeconomic development⁵.

A number of anti-dyslipidemic drugs are available in modern medicine to treat abnormal plasma lipids. The drugs used for controlling dyslipidemia include fibrates, statins and bile acid-binding resins. The statins are the most widely used out of these. However, long-term use of these drugs is not free from undesirable effects.

Atorvastatin, a widely used lipid-lowering agent, is an inhibitor of HMG-CoA reductase, which catalyzes the conversion of HMG-CoA to

mevalonate. Inhibition of HMG-CoA reductase decreases cholesterol synthesis and leads to upregulation of LDL cholesterol (LDL-C) receptors in the liver, mediated by activation of sterol regulatory element binding protein resulting in enhanced clearance of LDL from the circulation, thus playing an important role in preventing atherosclerosis⁶.

Some indigenous plants are supposed to possess cardio-protective properties e.g. *Gloriosa superba*, *Valeriana wallichii* and *Odenlandia corymbosa*. *Gloriosa superba* is commonly known as Glory Lily (Bachnag in Hindi) and belongs to family Liliaceae. It is found commonly in forest and is under cultivation in fairly large areas of India. *Valeriana wallichii* belongs to Valerianeaceae family and grows in temperate Himalayas from Kashmir to Bhutan. It has been used in the Ayurvedic system of medicine for centuries. Its native names include Tagara, Nata, Vakra etc. *Odenlandia corymbosa* belongs to family Rubiaceae and is commonly known as Diamond Flower (Daman Pappar in Hindi). It is found all over India⁷.

Since plant products are generally safe, the present study was undertaken to evaluate the effectiveness of *Gloriosa superba*, *Valeriana wallichii* and *Odenlandia corymbosa* extracts in correcting the dyslipidaemia resulting from feeding fructose-rich high fat diet to rats and to compare their effect with that of atorvastatin.

Material and Methods

Authenticated samples of *Gloriosa superba*, *Valeriana wallichii* and *Odenlandia corymbosa* were procured. The plant samples were dried under shade. They were ground by an electric blender, and the resulting powder (200 g) was extracted with one liter of 70% alcohol for 72 hours at room temperature. The extract was filtered and the solvent was evaporated to dryness. The yield of extract was calculated and stored at 2-8°C for further use.

The study was carried out on healthy male adult rats of Wistar strain (200-225 g) obtained from the

Animal House of King George's Medical University, Lucknow (U.P.). The study was started after obtaining permission from the Animal Ethics Committee of the University. All the rats were initially maintained on Hindustan Lever Food Pellets diet and water ad libitum. The cages were kept in a temperature and humidity controlled room with a 12-hour light-dark cycle. The rats were divided into six groups of six rats each and were fed as follows for 30 days:

Group 1- Control rats fed normal pellet diet.

Group 2- Rats fed fructose-rich high fat diet (F-HFD).

Group 3- Rats fed F-HFD and given extract of *Gloriosa superba* (250 mg/kg of body weight orally once a day).

Group 4 - Rats fed F-HFD and given extract of *Valeriana wallichii* (250 mg/kg of body weight orally once a day).

Group 5- Rats fed F-HFD and given extract of *Odenlandia corymbosa* (250 mg/kg of body weight orally once a day).

Group 6- Rats fed F-HFD and given atorvastatin (10 mg/kg of body weight orally once a day).

After 30 days, serum total cholesterol (TC), triglycerides (TG) and high density lipoprotein-cholesterol (HDL-C) were quantified by CHOD-PAP, GPO-POD and PEG-PAP methods respectively, and low density lipoprotein cholesterol (LDL-C) by immuno-turbidimetric assay⁸. Very low density lipoprotein cholesterol (VLDL-C) was calculated by Friedewald's formula⁹. Serum free fatty acids (FFA) were measured by the method of Monsinger et al¹⁰ and phospholipids (PL) by malachite green method¹¹. Plasmalecithin cholesterol acyl transferase (LCAT) activity was measured according to Albers et al¹² and post heparin lipolytic activity (PHLA) according to Wind and Robinson¹³.

Statistical Analysis

Student's unpaired t-test was used for comparison. The p value < 0.05 was considered significant. Analysis was carried out on SPSS 16.0 version.

Results

The rats fed F-HFD for 30 days had significantly higher serum TC, TG, LDL-C, VLDL-C, HDL-C and FFA than the rats fed normal pellet diet. No significant difference was seen in serum PL, LCAT and PHLA (Table 1). Thus, feeding F-HFD for 30 days produced significant dyslipidemia.

Table 1: Final levels of serum total cholesterol (TC), triglycerides (TG), high density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol (LDL-C), very low density lipoprotein cholesterol (VLDL-C), free fatty acids (FFA), phospholipids (PL), lecithin cholesterol acyl transferase (LCAT) and post heparin lipolytic activity (PHLA) in rats fed normal diet and rats fed fructose-rich high fat diet (F-HFD) for 30 days (all the values are mean±SD).

	Rats on normal diet	Rats on F-HFD
TC (mg/dL)	62.6±9.72	128±18.2**
TG (mg/dL)	48.1±11.2	110±16.6**
HDL-C (mg/dL)	28.3±8.61	40.5±6.86*
LDL-C (mg/dL)	24.6±8.2	65.5±19.2**
VLDL-C(mg/dL)	9.6±2.2	22±3.3**
FFA (mg/dL)	62.5±18.9	90.1±11.6*
PL (mg/dL)	102.3±23.7	128.1±26.3 [#]
LCAT (nmol/mL/h)	36.3±14.7	44.1±13.4 [#]
PHLA (nmol/mL/h)	21.0±3.8	21.6±5.50 [#]

*p<0.05, **p<0.001 and [#]p>0.05 as compared to normal diet group

Table 2: Final levels of serum total cholesterol (TC), triglycerides (TG), high density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol (LDL-C), very low density lipoprotein cholesterol (VLDL-C), free fatty acids (FFA), phospholipids (PL), lecithin cholesterol acyl transferase (LCAT) and post heparin lipolytic activity (PHLA) in rats fed fructose-rich high fat diet (F-HFD), F-HFD + *G.superba* extract (250 mg/kg BW/day), F-HFD + *V. wallichii* extract (250 mg/kg BW/day), F-HFD+ *O. corymbosa* extract (250 mg/kg BW/day) and F-HFD + atorvastatin (10 mg/kg BW/day) for 30 days (all the values are mean±SD).

	F-HFD	F-HFD + <i>G. superba</i> extract	F-HFD + <i>V. wallichii</i> extract	F-HFD + <i>O. corymbosa</i> extract	F-HFD + atorvastatin
TC (mg/dL)	128±18.2	120±16.6 [#]	91.5±14.6**	124.6±17.0 [#]	68.3±11.6***
TG (mg/dL)	110±16.6	90±11.8 [#]	70.5±12.1***	99.1±12.8 [#]	57±4.73***
HDL-C (mg/dL)	40.5±6.86	31.6±5.00 [#]	30.1±6.61 [#]	38.1±2.85 [#]	29.1±6.79*
LDL-C (mg/dL)	65.5±19.2	71.8±14.9 [#]	47.2±11.2 [#]	70±17.6 [#]	27.7±12.3***
VLDL-C(mg/dL)	22.0±3.3	18.±2.3 [#]	14.1±2.4***	19.8±2.5 [#]	11.4±0.94***
FFA (mg/dL)	90.1±11.6	84.1±12.4 [#]	71.5±11.0 [#]	86.6±11.8 [#]	59.1±17.1*
PL (mg/dL)	128.1±26.3	102.6±17.8 [#]	92.1±15.7 [#]	120±27.1 [#]	80.6±3.14**
LCAT (nmol/mL/h)	44.1±13.4	50±12.9 [#]	54.1±11.5 [#]	49.1±9.96 [#]	59.8±10.4 [#]
PHLA (nmol/mL/h)	21.6±5.50	16.8±5.07 [#]	13.6±3.14*	17.8±4.16 [#]	11.8±2.63*

*p<0.05, **p<0.01, ***p<0.001 and [#]p>0.05 as compared to F-HFD group

Discussion

Dyslipidemia in the form of elevated total cholesterol, low density lipoprotein (LDL)

The serum levels of TC, TG, HDL-C, LDL-C, VLDL-C, FFA, PL, LCAT and PHLA of rats given F-HFD + *Gloriosa superba* extract, F-HFD + *Valeriana wallichii* extract, F-HFD + *Oldenlandia corymbosa* extract, and F-HFD + atorvastatin for 30 days were compared with those of rats fed F-HFD alone. No significant difference was seen in the groups fed F-HFD + *Gloriosa superba* and F-HFD + *Oldenlandia corymbosa*, and the group fed F-HFD alone. Thus, these two plant extracts had no effect on the serum lipid levels. In the rats fed F-HFD + *Valeriana wallichii* extract, serum TC, TG, and VLDL-C were significantly lower as compared to the rats fed F-HFD alone. In the rats fed F-HFD + atorvastatin, serum TC, TG, LDL-C, VLDL-C, HDL-C, FFA and PL were significantly lower as compared to rats fed F-HFD alone. Thus both *Valeriana wallichii* and atorvastatin showed anti-dyslipidemic effect but the effect of atorvastatin was stronger than that of *Valeriana wallichii* (Table 2).

cholesterol, very low density lipoprotein (VLDL) cholesterol and triglycerides and decreased high density lipoprotein (HDL) cholesterol is one of the

major coronary risk factors. There is a strong pathophysiological association between raised LDL cholesterol level and initiation and progression of coronary atherosclerosis¹⁴.

Currently available therapies for dyslipidemia in modern medicine, e.g. fibrates, statins and bile acid sequestrates, correct lipid abnormalities to a significant extent but can also produce adverse effects. Therefore, there is a need to develop safe and effective treatment modalities for dyslipidemia. Medicinal plants can provide drugs that are less toxic, have fewer side effects and are cost effective. Some plants are supposed to have cardio-protective effects. If we can find plant products with lipid-lowering effect, they can provide a new option for the treatment of dyslipidemia.

We explored three plants viz. *Gloriosa superba*, *Valeriana wallichii* and *Oldenlandia corymbosa* for their possible anti-dyslipidemic effect in rats. For comparison, we took a standard drug i.e. atorvastatin. *Gloriosa superba* and *Oldenlandia corymbosa* did not show an anti-dyslipidemic effect but *Valeriana wallichii* was found to have a significant anti-dyslipidemic effect. When *Valeriana wallichii* extract and atorvastatin were compared, it was seen that the effect of atorvastatin was stronger. This finding is in agreement with the report of Zanguei and Jowhary who had investigated the effect of a different species of the same genus i.e. *Valeriana officinalis*¹⁵.

The results of the present study show that *Valeriana wallichii* extract can favorably modify the dyslipidemia resulting from feeding high cholesterol diet to rats. The extract was somewhat less effective than atorvastatin but if we can isolate the active compound from the plant, it may turn out to be more effective. One of the limitations of the present study was small sample size. Studies on larger samples are warranted for robust results.

Conclusion

Valeriana wallichii extract lowers serum lipid levels but is not as effective as atorvastatin.

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