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Hypolipidaemic Activity of *Rauwolfia serpentina* Benth

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Abstract: Hypolipidaemic activity of *Rauwolfia serpentina* benth was investigated to provide a base for isolation of active principle and to validate its use for the control of hyperlipidaemia, the major cause of cardiovascular diseases prevailing worldwide. Twelve days trial was done with oral administration of root powder of *R. serpentina* (30 mg/kg) and distilled water (1 ml/kg) in test and control rabbits respectively. The blood was collected from each group on 1st, 4th, 8th and 12th day to estimate serum Triglycerides (TG), Total Cholesterol (TC), Low Density Lipoprotein (LDL-C), High Density Lipoprotein Cholesterol (HDL-C), Alanine Aminotransferase (ALT) and Lactate Dehydrogenase (LDH). Gradual decrease observed in TG and LDL-C levels from 204.76-111.94 and 33.31-10.85 mg/dL, respectively in test when compared with control rabbits ($p<0.0001$). Similarly, TC was significantly decreased when compared 1st-12th day of treatment in test group ($p<0.0001$) and test on 12 day compared with control ($p<0.05$). However, HDL-C remained constant in test rabbits throughout the study but found higher than control ($p<0.05$). ALT and LDH levels were found normal. According to the data, root powder of *R. serpentina* has hypotriglyceridemic and hypocholesterolemic effects with undetectable side effects on liver and cardiac functions.

Key words: Cholesterol, triglycerides, LDL-C, HDL-C, ALT, LDH

INTRODUCTION

High lipid content (hyperlipidaemia) leads to many life threatening conditions such as atherosclerosis, myocardial infarction, ischemic heart disease, stroke and other vascular diseases (Davignon and Cohn, 1996; Frishman, 1998). In all over the world the prevalence of hyperlipidaemia increases day by day either due to the genetic factor, unhealthy lifestyle or secondary to other diseases (Arif *et al*., 1990; El-Hazmi and Warsy, 2001) and becomes one of the major causes of death (Parab and Mengi, 2002; Aziz *et al*., 2004). Pakistan is also facing the same threat (Iqbal *et al*., 2004; Aziz *et al*., 2004; Jafary *et al.,* 2007).

Rauwolfia serpentina benth (*family: Apocynaceae*) is a medicinally famous herb (Salma *et al.*, 2008). Almost, 50 alkaloids have been isolated from root bark of this plant including reserpine, yohimbine, serpentine, deserpidine, ajmalicine, etc. (Klyushnichenko *et al*., 1995) which are used to treat hypertension (Von Poser *et al*., 1990) and breast cancer (Stanford *et al*., 1986). Beside hypertension, roots of this plant are also reported for the treatment of number of diseases such as insomnia, anxiety, excitement, schizophrenia, insanity, epilepsy, hypochondria, diarrhea, dysentery etc in Ayurveda medicines (Dastur, 1988; Kirtikar and Basu, 1993; Bhatara *et al*., 1997; Ghani, 1998; Tona *et al*., 1999).

The current research was conducted to investigate the effect of root powder of *R.serpentina* on lipid profile *viz*., triglycerides, total cholesterol, LDL-C, HDL-C and on enzymes *viz*., Alanine aminotransferase (ALT) and Lactate Dehydrogenase (LDH).

MATERIALS AND METHODS

Animals: Rabbits weighing from 1-1.5 kg were purchased from local supplier of University of Karachi and used in the whole experiment. The rabbits were housed under uniform hygienic conditions with continuous airflow and maintained on a standard laboratory diet and water *ad libitum.*

Plant material: Roots of *R. serpentina* was purchased from Hamdard Dawakana, Sardar, Karachi and identified by expert in Botany department, University of Karachi, Karachi-75270, Pakistan. The voucher specimen has been kept in our department (KU/BCH/SAQ/02).

Hypolipidemic activity: Experimental rabbits were divided into control and test groups. Each group contains six rabbits. The grinded root powder of *R. serpentina* (30 mg/kg) suspended in 1 ml distilled water administrated orally to the test group for 12 days consecutively. While same volume of only distilled water was administrated orally to the control group for the same period. The blood was collected from marginal ear vein of rabbits on each 1st, 4th, 8th and 12th day of the trial from each group. Sera were separated and used to analyze biochemical parameters on Spectro UV-Visible Auto, PC Scanning Spectrophotometer, Labomed, Inc.

Biochemical analysis: Triglycerides, total cholesterol, HDL-C, Alanine aminotransferase (ALT) and Lactate Dehydrogenase (LDH) were determined by

commercially available enzymatic kits (Human, USA). LDL-C was calculated by formula given in reagent kit (Randox, UK) as:

$$\text{LDL}-\text{C}(\text{mg}/\text{dL})=\text{Total cholesterol}-\frac{\text{TG}}{5}-\text{HDL}-\text{cholesterol}$$

Statistical analyses: The data were analyzed by *Student's t*-test (Graphpad Software, Quick Calcs *Online calculators for Scientists*). Differences considered significant with p<0.0001, p<0.01 and p<0.05. Values are expressed as Mean±standard Error Mean (S.E.M).

RESULTS

Effect of root powder of *R.serpentina* on lipid profile: A gradual significant decrease (p<0.0001) in triglyceride concentrations from 204.76-111.94 mg/dL were observed in test rabbits from 1st-12th day of oral treatment of root powder of *R.serpentina* (30 mg/kg). Whereas, the triglycerides were found in the range of 243.31-248.67 mg/dL in control rabbits treated with 1 mL distilled water orally for same period. The difference between control and test groups at each day interval was also found statistically significant with p<0.0001 (Table 1 and Fig. 1).

Oral administration of same dose of *Rauwolfia* was also induced a decrease in cholesterol concentrations of test rabbits from 184.76-151.08 mg/dL in 12 days trial (p<0.0001) as compared to control rabbits where it was ranging from 172.41-240.96 mg/dL (Table 1 and Fig. 2). The most striking feature of present investigation is the huge decrease found in LDL-cholesterol levels of test rabbits from 33.31-10.85 mg/dL (p<0.0001). However, HDL-cholesterol levels were remained constant in test rabbits especially at 4th, 8th and 12th day of oral treatment but found higher than their respective control with p<0.05 (Table 1). Observed readings of LDL- and HDL-cholesterol concentrations of control rabbits are mentioned in Table 1.

Effect of root powder of *R. serpentina* on cardiac and liver specific enyzmes: The LDH levels were found ranging from 33.33-50.00 U/L in control rabbits. Where, as a constant value of 29.70 U/L (p<0.0001) was observed in test rabbits treated with root powder (30 mg/kg) for 12 days consecutively (Table 2).

The ALT levels in control and test rabbits ranged between 18.52-23.18 and 17.84-27.79 U/L, respectively (Table 2).

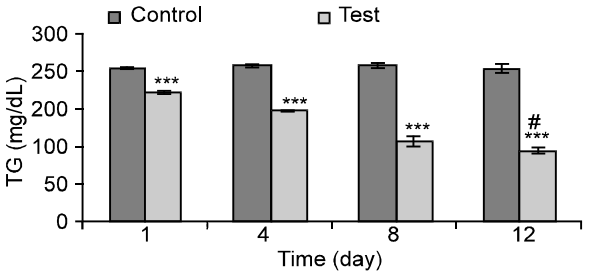

Fig. 1: Changes in triglycerides level (mg/dL) at different day intervals in control treated with distilled water (1 mL) and test rabbits treated with root powder of *R. serpentina* (30 mg/kg). Each column represents mean±SEM (n = 6). *** and # = p<0.0001= test compared with respective control and day 1 compared with day 12 in test rabbits, respectively

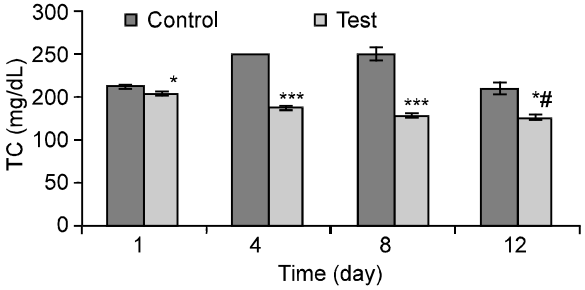

Fig. 2: Changes in cholesterol level (mg/dL) at different day intervals in control treated with distilled water (1 mL) and test rabbits treated with root powder of *R. serpentina* (30 mg/kg). Each column represents mean±SEM (n = 6). * = p<0.05 and *** = p<0.0001 represent significant differences from respective control and # = p<0.0001 represents difference between 1 and 12 day of treatment in test rabbits

DISCUSSION

Researchers have diverted their attention toward natural sources to find out new hypolipidaemic agent with less side effects (Mashour *et al*., 1998) because therapeutic uses of commercially available lipid lowering drugs are associated with side effects (Ghatak and Asthana, 1995). *Rauwolfia serpentina* has a significant place in the treatment of hypertension both Ayurvedic and Western medicines (Craig, 1999). The present investigation demonstrate the efficacy of root powder of *Rauwolfia* in lowering the serum levels of triglycerides, cholesterol, Low Density Lipoprotein Cholesterol (LDL-C) and increasing level of high density lipoprotein (HDL-C), is the promising feature of any drug that is necessary for the treatment of hyperlipidaemia and other cardiovascular diseases. It is widely accepted that high concentrations of cholesterol, triglycerides and LDL-C are the major risk factors of cardiovascular diseases including hypertension (Smith *et al*., 2004; Posta *et al*., 2006).

In the present study, a significant fall was observed in TG levels of test rabbits treated with root powder consecutively for 12 days. This decrease may be due to enhance the activity of lipase enzyme that hydrolyzes TG

Table 1: Effect of root powder of *Rauwolfia serpentina* on lipid profile (mg/dL)

	Control				Test			
	1st day	4th day	8th day	12th day	1st day	4th day	8th day	12th day
TG	243.3±2.1	247.5±1.4	248.6±5.09	243.4±5.5	204.7±3.2***	175.5±1.4***	126.7±8.5***	111.9±6.09***#
TC	194.3±2.9	240.9±0.03	240.6±10.0	172.4±7.8	184.7±2.4*	164.6±2.7***	153.5±3.3***	151.08±3.3*#
HDL-C	114.2±1.1	111.8±0.6	114.3±0.03	115.1±2.8	110.5±0.8	117.8±2.6*	117.8±2.6	117.8±2.6#
LDL-C	31.44±0.9	79.66±0.01	76.66±9.01	28.62±2.1	33.31±2.3	11.68±5.1***	10.31±7.3**	10.85±2.41**#

Each value is the mean±S.E.M. (n = 6). * = p<0.05, ** = p<0.01 and *** = p<0.0001 represent significant differences from respective control and # = p<0.0001 compared 12th day from 1st day of test

Table 2: Effect of root powder of *Rauwolfia serpentina* on enzyme level (U/L)

	Control				Test			
	1st day	4th day	8th day	12th day	1st day	4th day	8th day	12th day
ALT	18.5±1.3	21.1±1.3	19.8±0.0	23.1±3.1	21.8±5.7	17.8±3.4	26.8±1.5**	27.7±0.0
LDH	40.0±2.0	33.3±6.6	46.6±6.6	50.0±3.3	29.7±0.0**	29.7±0.0	29.7±0.0*	29.7±0.0***

Each value is the mean±S.E.M (n = 6). * = p<0.05, ** = p<0.01 and *** = p<0.0001 represent significant differences from respective control

under normal condition (Sharma *et al*., 1997) or increase excretion of TG via feces (Sukla *et al*., 2004). Where as the decrease in cholesterol level may be due to decrease in resorption of endogenous cholesterol or an increase in the rate of secretion into intestinal tract or both (Bahramika and Yazdanparast, 2008). The root powder of *R. serpentina* may also become a good agent for the treatment of atherosclerosis by showing a decrease in serum level of LDL-C of test rabbits. The relationship between LDL-C and atherosclerosis has already been reported (Frishman, 1998). On the other hand, oral administration of root powder consecutively for 12 days induce increase in HDL-C level of test rabbits as compared to control group but it remain constant from 4th-12th day. It might possible that HDL-C level may be increased if root powder is used for >12 days or it may restore. The research is still in progress to prove this claim.

The effect of root powder of *R. serpentina* on liver and cardiac function was evaluated by measuring the serum ALT and LDH levels respectively. Our study showed that normal activities of ALT and LDH were observed in both control and test rabbits. These observations proved that *R. serpentina* had no toxicity on both important organs of the body.

Conclusion: The data of present investigation clearly indicate that root powder of *R. serpentina* is a potent hypolipidaemic agent especially having hypotriglyceridemic and hypocholesterolemic effects with undetectable side effects on liver and cardiac functions. Due to the significant effect of root powder on lipid profile, research is still going on in lab to investigate the same hypolipidemic activity in different extracts of root powder. This may lead to activity-guided fractionation of that particular extract in order to know the phytochemical composition, isolation, structure elucidation of some of the bioactive constituents followed by establishing the most probable mechanism of action of reducing serum lipids.

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