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Hypolipidemic activity of gum ghatti of *Anogeissus latifolia*.

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ABSTRACT

Cardiovascular diseases are becoming an increasing problem worldwide and hypercholesterolemia has been correlated for coronary heart diseases. Currently available hypolipidemic drugs have been associated with number of side effects. Herbal treatment for hyperlipidemia poses no side effects and is relatively cheap and locally available. In view of this, the present study was carried out to investigate the effect of gum ghatti of *Anogeissus lalifolia* on serum lipid levels of albino rats. Rats were made hyperlipidemic by the oral administration of cholesterol (400mg/kg body weight/day) along with cholic acid (50mg/kg) in coconut oil. The hypolipidemic effect was compared with control. The rats were divided into six groups of six animals each. In atherogenic diet induced hyperlipidemic model, the rats receiving treatment with gum ghatti at 250 mg/kg dosage showed significant reduction in serum triglyceride (82.75±0.63) only and there was no significant changes either in serum total cholesterol or elevation in HDL. Whereas, at 500 and 750 mg/kg dosage showed significant reduction in serum total cholesterol (72.85±0.60, 68.17±0.95) and serum triglyceride (78.92±0.34, 75.93±1.05). Further, the 750 mg/kg dose has also exhibited significant elevation in high density lipoprotein cholesterol (41.13±0.37).

KEYWORDS: *Anogeissus lalifolia*, Hypolipidemic, Total cholesterol, Triglyceride, Gum-ghatti, HDL.

INTRODUCTION

Cardiovascular diseases with an incidence of approximately 50% are the main cause of death in most advanced countries and witnessing an increasing trend in the developing world also (1). The World Health Organization estimates that every year 12 million people worldwide die from cardiovascular diseases (2). The primary cause of cardiovascular disease is believed to be an atherosclerosis, a progressive multifactorial disease of the arterial wall (3, 4). Central to the pathogenesis of atherosclerosis is deposition of cholesterol in the arterial wall (5). Nearly all lipoproteins are involved in this process including cholesterol carried by very low density lipoproteins (VLDL), remnant lipoproteins and low density lipoproteins (LDL). Hypolipidemic therapy is highly effective in reducing the risk as has been demonstrated dramatically in the Scandinavian Simvastatin Survival Study (6).

In recent years different type of antihyperlipidemic agents have been developed and selected for such treatment, depending on symptoms and other conditions of the subjects (7). The inhibitors of 3-hydroxy–3methyl glicaryl coenzyme A reductase have high efficacy against hyperlipidemia (8, 9). These agents however, have serious adverse effects, including myopathy by destroying striated muscle in rare cases (9). Further, drug administration continues over a long period of time in this chronic disease and therefore adverse effects should be minimal

and as mild as possible. Hence other types of agents that are different in mechanism from the existing agents are also needed. Medicinal plants are part and parcel of human society to combat diseases from dawn of civilization (10). Pectin gums and soluble fiber have a serum cholesterol lowering effect. Mechanisms proposed to explain hypercholesterolemic effect of these include, 1) Altered intestinal absorption, metabolism and release of cholesterol through an influence on bile acids. 2) Altered hepatic metabolism and release of cholesterol with increased excretion of bile acids reducing the size of the bile acid pool and less cholesterol available for incorporation into lipoprotein and subsequent release into the circulation and 3) Altered peripheral metabolisms of lipoproteins. Fibers may also alter the proportion of cholesterol incorporated into chylomicrons and lipoprotein (11). Plant gums also provide the soluble fiber in a healthy diet by absorbing water and adding bulk to the large intestine. Epidemiological studies have indicated that a diet low in fiber is associated with the incidence of the adult disease including coronary heart disease (12) and a colon cancer (13).

Gum Ghatti is the amorphous translucent exudates of the *Anogeissus latifolia* (Roxb) wall ex. BEDD (Family: Combretaceae). It is a smaller or fairly large tree, commonly found in the forests of the sub-Himalayan region, Myanmar, Srilanka, Siwalik hills and throughout India up to 1200 m. It is an important timber and the leaves and bark are used for tanning. The bark was first examined by Reddy et al. in 1965 who isolated (+) leucocyanidin. Later ellagic acid and two new glycosides of ellagic and flavellagic acid were reported (14). Ethnobotanically, the bark has been reported to be used in the treatment of various disorders like skin diseases such as sores, boils and itching (15), snake and scorpion bite, stomach diseases (16), colic (17), cough (18), diarrhoea (19). Further, antioxidant and wound healing (20, 21) activities have been evaluated in *A. latifolia*.

The objectives of the study were to:

- Study the effect of gum ghatti on serum cholesterol, serum triglyceride and high density lipoproteins (HDL) in albino rats.
- Study the lipid lowering property of gum ghatti if any, along with standard atorvastatin.

MATERIALS AND METHODS

Collection of Gum Ghatti

Fresh gum ghatti of *Anogeissus latifolia* was collected from Thyaverekoppa village of Shivamogga District, Karnataka, India. The plant was authenticated by comparing with the herbarium voucher specimen deposited at Kuvempu University Herbaria, Department of Botany, Ku/sd/Tk/206. The gum ghatti was completely dried and powdered in a pulverizer as and when required, sieved, labelled and stored in PET Bottles (22).

Drug Formulation

Various concentrations of gum ghatti of *Anogeissus latifolia* was dissolved in water for oral suspension.

Animals

Wistar albino rats of either sex weighing 150-200g were brought from Venkateshwara enterprises, Bangalore, were housed in polypropylene cages in a room where the optimum temperature was 27°C±1°C and 12 hrs light and dark cycles were maintained. The animals were allowed to acclimatize to the environment for 7 days and supplied with a standard pellet diet (Hindustan Lever Limited, Bangalore) and water provided *ad libitum*. The experiment was approved by the institutional animal ethical committee (NCP/IAEC/CLEAR/01/06/2007-08).

Evaluation of Hypolipidemic Activity

Gum ghatti was used to study the effect on serum lipid profile. Rats were made hyperlipidemic by the oral administration of cholesterol (400mg/kg) along with cholic acid (50mg/kg) in coconut oil for 20 days, once daily (23). The rats were then given drug treatment for 10days. During these 10 days, all the groups also received cholesterol in the same dose as earlier. The animals were divided into following groups of six animals each.

Group I	:	Normal Diet.
Group II	:	Atherogenic control (400mg/kg body weight cholesterol p.o)
Group III	:	Atherogenic treated + standard Atorvastatin (5.5 mg/kg body weight i.p)
Group IV	:	Atherogenic treated + 250mg/kg body weight gum ghatti (p.o).
Group V	:	Atherogenic treated + 500mg/kg body weight gum ghatti (p.o).
Group VI	:	Atherogenic treated + 750mg/kg body weight gum ghatti (p.o).

Collection of blood

On the 30th day blood samples were withdrawn from rats, by retro orbital sinus puncture under mild ether anesthesia after an overnight fasting. The collected samples were centrifuged for 10 minutes. Then serum samples were

Table 1: Hypolipidemic effect of Gum Ghatti of *Anogeissus latifolia* on Total Cholesterol, Triglyceride and HDL in Albino Rats

SL.NO	GROUPS	TOTAL CHOLESTROL	TRIGLYCERIDE	HDL
1	Group I(Normal Diet)	58.33±2.11	65.83±1.47	55.10±2.89
2	Group III(Atherogenic Control)	81.83±3.17	96.17±2.89	34.20±1.16
3	Group III(Atherogenic Control Atorvastatin)	63.50±1.18*	70.17±2.44*	45.50±0.76*
4	Group IV(Atherogenic Control Gum Ghatti 250mg/kg)	74.92±1.32	82.75±0.63*	35.25±0.38
5	Group V(Atherogenic Control Gum Ghatti 500mg/kg)	72.85±0.60*	78.92±0.34*	37.10±0.59
6	Group VI(Atherogenic Control Gum Ghatti 750mg/kg)	68.17±0.95*	75.93±1.05*	41.13±0.37*

Values are expressed in mg/dl,
*P<0.05 compared with control, Number of animals in each group=6.

collected and used for the assaying of serum total cholesterol, triglyceride and HDL using commercially available enzymatic kits.

Statistical analysis

Values are expressed as mean ± SEM and the statistical analysis was done using one way ANOVA.

RESULTS

The changes in serum lipid levels in the gum ghatti treated groups are summarized in Table 1. Administration of 250mg/kg of gum ghatti has shown significant (P<0.05) decrease in serum triglyceride level only (82.75±0.63) where as in case of 500 mg/kg, significant decrease has occurred both in total cholesterol (72.85±0.60) and triglyceride(78.92±0.34). However, in case of 750mg/kg, in addition to significant decrease in the total cholesterol (68.17±0.95) and triglyceride (75.93±1.05) has also shown significant elevation in the HDL (41.13±0.37) level. Thus compared to all the three concentrations 750mg/kg has shown efficient lipid lowering activity.

DISCUSSION

The article by Dr. Elmehdavi R.R. entitled "Hypolipidemia: A word of caution" has shown the multifaceted properties of cholesterol which is the most highly decorated molecule in biology (24). Hyperlipidemia is classified into a primary and secondary type, which indicates the complexities associated with the disease. The primary disease may be treated by anti-lipidemic drugs but the secondary type originating from diabetes, renal nephrosis or hypothyroidism demands the treatment of the original disease rather than hyperlipidemia (25). Consumption of much fat may lead to the production of extra VLDL, resulting in the formation of large amounts of LDL which may stick to the walls of the blood vessels if the quantity of HDL is insufficient causing blockages for the normal flow of blood. Therefore, improvement in human diet is highly recommended for disease prevention (26). Pancreatic lipase is a key enzyme for lipid breakdown and fatty acid absorption (27). Inhibitors of pancreatic lipase or HMG-CoA reductase are anti-hypercholesterolemia agents (27, 28, 29), such as orlistat and lovastatin which reduce the absorption of dietary triglycerides and inhibit cholesterol biosynthesis respectively. However, repeated use of these agents causes side effects (29, 30). Gum ghatti is a complex polysaccharide of high molecular weight. It occurs in nature as a mixed calcium, magnesium, potassium and sodium salt. Complete hydrolysis has shown that it is composed of L-arabinose, D-galactose, D-mannose, D-xylose and D-glucoronic acid in a molar ratio of 10:6:2:1:2 plus traces less than 1% of 6-deoxyhexose (31). Treatment with gum ghatti of *Anogeissus latifolia* at 750mg/kg produced a significant decrease in the serum cholesterol, triglyceride and elevation in HDL in atherogenic diet induced hyperlipidemia in rats. There was no significant effect on HDL level in 250 and 500mg/kg gum ghatti concentrations. Atherogenic diet induced hyperlipidemic model has been successfully employed for the evaluation of hypocholesterolemic effect of protein (32). Hypolipidemic effect of the gums, saponins and beta sitosterol have also been reported by several authors. Ahluwalia and Amma (33) found that feeding of oleoresin of gum guggal (*Commiphora mukul*) lowered the total cholesterol and its fractions in lipoproteins. Kotaro, et al. (34) have reported cholesterol lowering effects of *Psyllium* seed associated with urea metabolism.

CONCLUSION

Authors conclude that, atherogenic animals treated with gum ghatti of *Anogeissus latifolia* have significantly improved the lipid profile and this effect might be an additive in action with other cholesterol lowering regimes.

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