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Effect of *Terminalia chebula* fruits on lipid profiles of rats

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Abstract

Objective: To study the effect of *Terminalia chebula* on serum lipids in hyperlipidemic rats. Methods: The hypolipidemic action of *T. chebula* has been studied in normal rats and in atherogenic (cholesterol containing) diet induced hyperlipidemic albino rats. Results: In atherogenic diet induced hyperlipidemic model, the rats receiving alcoholic extract of immature (IMF), mature (MF) fruits and ethyl acetate soluble fraction (immature fruits) of *T. chebula* treatment showed marked reduction in total cholesterol (TC) ($p<0.05$), total triglyceride (TG) ($p<0.001$), total protein (TP) ($p<0.001$) and elevation in high density lipoprotein cholesterol (HDL-C) ($p<0.001$). In normocholesterolemic model, the feeding of ethanolic extract (immature fruits) lowered the levels of TC, TG, TP and increased level of HDL-C. Conclusions: The ethanolic extract and ethyl acetate fraction were found to possess significant hypolipidemic activity. The most active extract of *T. chebula* is ethyl acetate fraction of immature fruits, which was able to bring high serum lipid to normal level. The present study brings forth the efficacy of *T. chebula* as a hypolipidemic agent.

Key words: *Terminalia chebula*, Hypolipidemic activity, Cholesterol, Triglyceride.

1. Introduction

T. chebula (Combretaceae) is ascribed with many therapeutic effects and has great reputation in Ayurveda. The fruits, leaves and bark of *T. chebula* has been used since Vedic periods and recommended in many diseases. *T. chebula* (regional name "Harda" is recognised as the large ripe mature fruits (MF) called Haritaki and the small unripe immature fruits (IMF) called jani-haritiki or Himaj [4,5]. Charak Samhita states the importance of Haritaki, which mentions it as a panacea for all disease. In Ayurveda hypolipidemia is mentioned by the name of Medoroga (fat disease) [6].The hypolipidemic activities of *T. chebula* in leaves extract are reported by Khanna *et al* [1]. This plant has been investigated for its chemical constituents and

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found to contain a large amount of pentacyclic triterpenes [2]. Naturally occurring triterpenoids and some of their derivatives are known to have hypolipidemic activity [3]. The present paper is an attempt to assess the effect of fruits (mature and immature) of *T. chebula* on TC, TG, TP and HDL-C.

2. Material and methods

2.1 Preparation of extracts

The fruits of *T. chebula* were procured from State Forest Research Institute, Jabalpur (M.P). Both mature and immature fruits were cleaned, air dried and reduced to coarse powder. The powdered fruits were extracted with ethanol in a Soxhlet extractor. Evaporation of solvent under reduced pressure yielded 10% gummy material. About 50g of this material, taken in a beaker and extracted with ethyl acetate yielded about 51% of ethyl acetate fraction. Weighed quantity (2g each) of ethanolic extract of mature fruits, immature fruits and ethyl acetate fraction were triturated with 0.2% gum acacia and final volume made up to 250 ml.

2.2 Animal

Male adult albino rats [200-250gms] were used for the present study. Animals were divided in groups of 6 rats each. The rats were divided in 2 sets. Set A animals were fed with normocholesterolemic diet (normal animal feed) whereas Set B animals were fed with high cholesterol diet (atherogenic diet). The composition of diet used during the study was as follows. (Table 1)

2.3 Treatment

With a view to evaluate hypolipidemic activity of the extracts, the animals of normocholes-trolemic model were given the following treatment by oral route.

Set-A (normocholesterolemic model) – The animals were divided in 3 groups. Group I received normal diet, group II animals were given atherogenic diet containing 1% cholesterol and group III animals were treated with 100mg/kg/day ethanolic extract of immature fruits. The treatment was undertaken for 45 days.

Set-B (In atherogenic diet induced hyperlipidemic model) – The animals were divided into 5 groups and received following treatment for 45 days orally.

Group IA : Normal diet

Group IIA : Atherogenic diet containing 1% cholesterol.

Group IIIA : Ethanolic extract of mature fruits (100mg/kg/day) + atherogenic diet.

Group IVA : Ethanolic extract of immature fruits (100mg/kg/day) + atherogenic diet.

Group VA : Ethyl acetate fraction of immature fruits (100mg/kg/day) + atherogenic diet.

At the end of the treatment the rats were fasted overnight, blood was drawn from retro orbital plexus, serum was separated and stored in refrigerator until assay. The serum concentration of total cholesterol, total triglyceride, total protein and total HDL cholesterol were estimated by using autopak

Table 1.
Composition of Atherogenic diet

Composition	Atherogenic diet (%)	Normal diet (%)
Proteins	10	12
Carbohydrates	61	70
Sugar	05	05
Fat	15	05
Vitamins	01	01
Fibers	02	02
Cholesterol	01	-
Total weight	100	100

kit method and Statistically analysed using student's *t* - test. The atherogenic index was calculated by using the following formula:

$$\text{Atherogenic Index} = \frac{\text{Total serum triglyceride}}{\text{Total serum HDL-C}}$$

3. Results

The administration of cholesterol diet (1%) to rats brought a 1.3 - fold increase in serum cholesterol level as compared to normal. The serum triglyceride level exhibited 4.17-fold increase together with high protein level by this treatment. In normocholesterolemic model (Set-A) the ethanolic extract of immature fruits reduced the serum total cholesterol, triglyceride and total protein, and increased high-density lipoprotein cholesterol as compared to normal rats [TC 13%, TG 7.3%, TP 17%].

In atherogenic diet induced model (Set-B), the administration of ethanolic extract of IMF, its ethyl acetate fraction and ethanolic extract of mature fruit decreased the serum total cholesterol, triglyceride and total protein. Increase in the beneficial HDL-C was observed. In atherogenic diet induced model, the ethanolic extract of IMF decreased the serum TC, TG and TP level by 33.5%, 58% and 51% respectively. The decrease in serum level observed by its ethyl acetate fraction was TC =42%, TG = 82%, TP = 49%. Ethanolic extract of mature fruit reduced the level of TC by 42%, TG by 78%, and TP by 44%.

In atherogenic diet induced model, the ethanolic extract of mature fruit and ethyl acetate fraction of immature fruit was found more effective. There was significant difference between control-ethyl acetate fraction (IMF) and control-ethanolic extract (MF). The maximum reduction of serum triglyceride was observed in ethyl acetate fraction(IMF), which was able to bring it to normal level.

The most active part of *T. chebula* extract is ethyl acetate fraction of IMF. It decreased elevated serum cholesterol, triglyceride and protein level by 42%, 82% and 49% respectively. The serum HDL-C level increased significantly. Another beneficial effect of the drug was that it decreased the atherogenic index in all treated groups (Table 4).

4. Discussion

Present investigation shows that *T. chebula* caused a significant decrease in the serum level of cholesterol in atherogenic diet induced hyperlipidemia in rats. Atherogenic diet induced hyperlipidemic model has been successfully employed for the evaluation of hypocholesterolemic effect of protein and the essential oil

Table 2.
Set-A Estimation of Serum biochemical parameters in normocholesterolemic animals.

Groups	Total Cholesterol (mg/dl)	Triglyceride (mg/dl)	Total protein (g/dl)	HDL-C (mg/dl)
Group I (normal)	0.153 ± 0.228	41.78 ± 1.095	4.51 ± 0.072	47.31 ± 2.694
Group II(control)	0.2 ± 0.0232	171.48 ± 1.948	11.33 ± 0.086	85.81 ± 0.561
Group III (ethanolic ext., IMF)	0.133 ± 0.0191[a]	38.06 ± 0.686[b]	3.76 ± 0.0559[b]	78.23 ± 1.283[b]

Each value is the mean of 6 rats ± SD, in statistical analysis group-III is compared with group-II, [a] $p<0.05$; [b] $p<0.001$

Table 3.
Set-B Estimation of Serum biochemical parameters in diet induced hyperlipidemic animals

Groups	Total Cholesterol (mg/dl)	Triglyceride (mg/dl)	Total protein (g/dl)	HDL-C (mg/dl)
Group IA (normal)	0.153 ± 0.0228[a]	41.78 ± 1.095[b]	4.51 ± 0.072[b]	47.31 ± 2.694[b]
Group IIA (control)	0.2 ± 0.0232	171.48 ± 1.948	11.33 ± 0.086	85.81 ± 0.561
Group IIIA (ethanolic ext. MF)	0.116 ± 0.0151[a]	37.23 ± 0.738[b]	6.56 ± 0.0730[b]	76.23 ± 1.532[b]
Group IV A (ethanolic ext. IMF)	0.133 ± 0.019[a]	71.71 ± 0.981[b]	5.53 ± 0.076[b]	67.88 ± 1.037[b]
Group VA (ethyl acetate ext. IMF)	0.116 ± 0.015[a]	30.55 ± 1.318[b]	5.75 ± 0.039[b]	93.7 ± 0.387[b]

Each value is the mean of 6 rats ± SD, [a] $p<0.05$, [b] $p<0.001$, statistical significance in comparison to group-IIIA, IVA, VA with group-IIA.

Table 4.
Atherogenic index in various groups

Groups	Atherogenic Index*	% protection
Group IA(normal)	0.883	-
GroupIIA(control)	1.998	-
GroupIIIA (ethanolic ext. MF)	0.488	75.57
GroupIVA (ethanolic ext.,IMF)	1.056	47.14
GroupVA (ethyl acetate ext., IMF)	0.326	83.68

*Atherogenic Index =Total Serum Triglyceride / Total Serum HDL-C

$$\%\text{Protection} = \frac{\text{Atherogenic index of control} - \text{Atherogenic index of treated group}}{\text{Atherogenic index of control}} \times 100$$

of garlic in albino rats. [7] Faulty diet is a very common cause of heart disease. Particularly, with an increase in inclination towards fast foods, which are rich in saturated fats, an increase in coronary heart disorder (CHD) is being observed in the developing countries since past few decades.

A number of studies also indicate that feeding of diet rich in cholesterol increases the risk of CHD and hypercholesterolemia [8]. In our study also male albino rats were fed with atherogenic diet containing 1% cholesterol (Table 1). The lipid profile was found to be raised significantly. The increase in serum total cholesterol level was 1.3 times and serum triglyceride level was increased 4.17 times as compared to normocholesterolemic rats.

Dietary therapy plays a pivotal role in the management of hyperlipidemia. The aim of dietary therapy is to achieve a balanced healthy diet with just the right amount of caloric intake [9]. Dietary therapy progressively lowers

hyperlipidemia resulting in about 10-20% decrease in total cholesterol and 30-40% in triglyceride level [10].

In our study also it was observed that the withdrawal of atherogenic diet and its replacement with normal diet lowered total cholesterol and triglyceride level significantly as is evident from the Table-2 Set-A. High-density cholesterol is considered good cholesterol since it ferries cholesterol away from the heart to the liver for biosynthesis, thus decreasing plasma cholesterol level.

A 1% decrease in HDL-cholesterol is associated with a 3-4% increase in risk of heart disease. For male and females, concentration of HDL cholesterol below 1.0 and 1.2 mmol/L (39, 46, mg/dl) and especially below 0.8 and 1.0 mmol/L (31, 39 mg/dl), confer an increased risk of CHD, whereas concentration exceeding 1.5 and 1.7 mmol/L (58, 66 mg/dl) diminish the influence of other risk factors (11). In our study also an increase in plasma HDL cholesterol level was observed (Table 3).

The lipid lowering effect of *T. chebula* was earlier reported by Khanna *et al* (1). In our present study, the reduction in serum lipid level was observed by the ethanolic extract (IMF) its ethyl acetate fraction and ethanolic extract (MF) of *T. chebula* fruits.

Our findings were found to be consistent with the above. The decrease in plasma cholesterol level, by *T. chebula* could be due to inhibition of cholesterol biosynthesis, decreased absorption of dietary cholesterol, reduced levels of serum cholesterol and to increased faecal bile acid excretion [1]. The present studies bring forth the efficacy of *T. chebula* as a hypolipidemic agent.

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