

An Evaluation of Anti-hyperlipidemic Activity of Ethanolic extract of *Terminalia arjuna* on High Fat Induced Hyperlipidemic Rat Model

Abstract:

Herbalism is the practice of using herbs and herbal remedies to enhance and maintain maximum health, as well as to prevent, treat, or cure diseases. Herbal remedies and herbal medicine may be mistakenly interchanged in some areas. This research examined the effects of a *Terminalia arjuna* extract on lipid profiles in rats that had developed hyperlipidemia due to a high-fat diet. In terms of liver function, In groups 5 and 6, at doses of 600 and 900 mg/kg, respectively, both the SGPT and SGOT levels showed statistically significant ($p < 0.05$) outcomes. During the renal function test, it was observed that groups 4, 5, and 6 had substantially increased amounts of creatinine ($p < 0.05$). The groups were given doses of 300, 600, and 900 mg/kg of a combined high-fat diet, respectively. Nevertheless, the research on urea did not provide any statistically significant results. In relation to HDL and LDL, groups 5 and 6 exhibited statistically significant outcomes ($p < 0.05$) in HDL levels when administered doses of 600 and 900 mg/kg of high fat and extract, respectively. The analysis of total cholesterol and triglycerides did not provide any statistically significant results.

Keywords: Herbal medicine, *Terminalia arjuna*, SGPT, HDL, LDL, Phytochemicals.

Introduction

The liver, which is the biggest glandular organ, is responsible for controlling the bulk of the physiological processes that occur in a person. The liver is the organ that gets the whole amount of blood from a person on several occasions during the course of a day. It plays an essential role in the metabolic processes of humans [1, 2]. Excessive alcohol consumption, drug addiction, exposure to certain hazardous substances, or infection with viruses or parasites can cause an increase in the activity of reactive oxygen species (ROS), which includes OH, H₂O₂, and O₂ [3].

This can result in cellular damage in the liver. After conducting a study with 1492 doctors who provide ambulatory care in non-government institutions, the Centres for Disease Control and Prevention discovered that hyperlipidemia is the second most common chronic ailment they see, behind only hypertension [4]. The study's findings indicate that excessive consumption of high-fat foods is the fundamental cause of hyperlipidemia [5]. The liver is responsible for the extensive metabolism of the most widely used anti-hyperlipidemic pharmaceuticals, including atorvastatin, pravastatin, fluvastatin, simvastatin, lovastatin, and rosuvastatin. As a result, these medications' bioavailability is very low [6]. It is known that statins can temporarily stop the enzyme 3-hydroxy-3-methylglutaryl-coenzyme A reductase (HMG-CoAR) from working. This enzyme lowers cholesterol levels. This allows them to reduce the production of cholesterol within the cells. This is because statins can get into hepatocytes and block HMG-CoAR, which determines their pharmacological property [7]. Muscular difficulties, often referred to as statin-associated muscle symptoms (SAMS), are the most prevalent adverse effect that restricts the use of statins. The development of diabetic mellitus (DM) and issues with the central nervous system are two additional potentially harmful outcomes [8]. Not only do these synthetic treatments have significant negative effects, but they are also quite costly, which means that the patient may have to deal with financial difficulties if they continue to take them during the whole course of therapy [9]. For this reason, it is of the utmost importance to produce potent antihyperlipidemic drugs that suffer from just a small amount of adverse effects. When it comes to the process of identifying and synthesizing new treatments, plants play an essential role [10]. They serve as a valuable and plentiful source of naturally occurring compounds for use in medicinal applications. Experts in the field suggest that certain chemical components derived from medicinal plants possess therapeutic properties. This has led researchers to constantly seek new herbal cures and other plant-derived therapies to treat a wide range of disorders [4]. On the other hand, phytotherapy has its origins in scientific study, while herbalism is largely concerned with the practical uses of medicinal plants. Plants have been of great importance to human health since the beginning of time because they contain a wide variety of substances, many of which possess medicinal capabilities [11]. Plants used for medicinal purposes include a vast variety of chemical components, which allows them to exert a wide variety of pharmacological and therapeutic effects. These compounds exemplify components such as tanning agents, glycosides, alkaloids, saponins, polysaccharides, essential oils, terpenoids, resins, and plant lipids [12-14]. Genetically

modified plants enable precise control over chemical concentrations, ultimately leading to the achievement of the desired medical effect. Reverse genetics has a number of possible applications, one of which is the enhancement of secondary metabolite synthesis, which includes the production of alkaloids [15]. Advances in scientific research on a worldwide scale have led to an increase in study on the medicinal properties of botanical species [16]. People are increasingly using plants because they are intrinsically safe, possess powerful pharmacological qualities, and offer a more cost-effective alternative to manufactured pharmaceuticals.

Terminalia arjuna, family: Combretaceae, whose medicinal value is well documented in the ayurvedic system, is an evergreen large deciduous tree. This tree is usually an evergreen tree with new leaves appearing in the hot season (February to April) before leaf fall. This tree is an exotic tree in India. It is one of the most versatile medicinal plants having a wide spectrum of biological activity. The plant has been reported in ayurvedic system of medicine for derangement of all the three humours, kafa, pitta and vayu, and all sorts of conditions of cardiac failure[17], dropsy, antinfective[18], anti-asthmatic, treatment of rheumatoid arthritis and is traditionally used to prevent kidney stone formation. Studies have also been conducting on *Terminalia arjuna* in support of its diuretic properties[19]. Aqueous extract of *Terminalia arjuna* bark is shown to protect the liver and kidney tissues against CCl₄-induced oxidative stress probably by increasing antioxidative defense activities. Its aqueous extract prevents carbon tetrachloride induced hepatic and renal disorders[20].The bark of *T. arjuna* is anti-dysentric, antipyretic, astringent, cardiogenic, lithotriptic, anticoagulant, hypolipidemi, antimicrobial[21] and antiuremic[22] agent. Many useful phytoconstituents have been isolated from *T. arjuna* which included triterpenoids for cardiovascular properties, tannins and flavonoids for its anticancer, antimicrobial properties and so on[23]. The powder of the bark acts as a diuretic in cirrhosis of liver and gives relief in symptomatic hypertension[24]. In studies in mice, its leaves have been shown to have analgesic and antiinflammatory properties[25].

The purpose of our present study is to evaluate the hepatoprotective effects of *Terminalia arjuna*.

Materials and methods

Plant Collection and Extract Preparation

Terminalia arjuna were collected from local market of Dhaka. The material was authenticated by National herbarium, Bangladesh. Firstly, *Terminalia arjuna* was cleaned properly with water and

it was then air-dried. Finally dried leaves were crushed in powder. The powder was soaked for 15 days in 70% ethanol. The solution was kept for 15 days. Vigorous shaking was also performed occasionally. Next, the solution was filtered. The collected filtrate was dried in a rotary evaporator at a low temperature and pressure. Finally, the crude residue was subjected to the required pharmacological testing.

Drugs and Chemicals

Atorvastatin drug was obtained from inceptapharmaceutucals as a gift sample. Ethanol were bought from Taj Scientific store.

Experimental Animal Procurement, Nursing, and Grouping

A total of 90 male rats weighing between 120 and 150 grams were obtained from Jahangirnagar University in Savar, Dhaka. Each of them was housed in a climate-controlled environment (temperature $25\pm 3^{\circ}\text{C}$, relative humidity $55\pm 5\%$, and a 12-h light/dark cycle) at the University of Dhaka's Institute of Nutrition & Food Science (INFS). They were given a conventional food and were permitted to drink clean water. All of the animals were maintained in this habitat for at least one week prior to the research for adaption. All experimental methods followed the recommendations of the Institutional Animals Ethics Committee (IEAC). 90 rats were randomly distributed into 9 groups where each group contains 10 rats.

Experimental design

Rats were individually weighed and then divided into nine independent groups for research on anti-hyperlipidemic action. The distribution of rodents among the groups was based on their body weight, with each group consisting of five rats. The atorvastatin control group in Table 1 shows rats that were given atorvastatin with a high-fat diet since using simply atorvastatin would result in the animals dying. N/A indicates that rats in this group did not receive any therapeutic treatment.

Table 1: Antihyperlipidemic activity analysis

Group number	Group Status	Treatment specimen & Dose	Group Abbreviation
1	Negative Control	Physiological Saline	N
2	Positive Control	High Fat Diet	P

3	High Fat Diet + RV ₁₀	High Fat Diet + RV ₁₀	HFD + RV
4	High Fat Diet + <i>T. arjuna</i>	High Fat Diet+ TA ₃₀₀	HFD + TA ₃₀₀
5	High Fat Diet + <i>T. arjuna</i>	High Fat Diet + TA ₆₀₀	HFD + TA ₆₀₀
6	High Fat Diet + <i>T. arjuna</i>	High Fat Diet + TA ₉₀₀	HFD + TA ₉₀₀
7	<i>T. arjuna</i>	TA ₃₀₀	TA ₃₀₀
8	<i>T. arjuna</i>	TA ₆₀₀	TA ₆₀₀
9	<i>T. arjuna</i>	TA ₉₀₀	TA ₉₀₀

High Fat Diet: The high-fat diet was modified based on the composition supplied by Levin and Dunn-Meynell. The high fat diet is composed of 50% lipid, 40% carbohydrate, and 10% protein. The diet's composition is shown in Table 2.

Table 2: Composition of high fat diet

Food Ingredients	Composition
Lipid (50%)	Milk powder (10%) Ghee (30%) Mutton fat (40%) Coconut oil (10%) Butter (10%)
Carbohydrate (40%)	Boiled rice (40%) Smashed potato (40%) Boiled corn (20%)
Protein (10%)	Dry powdered prone (40%) Dry boiled mutton (20%)

	Cheese (20%) Egg (20%)
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After mixing the ingredients thoroughly, the high fat diet was given to the rats to induce obesity for 10 weeks [26].

Evaluation of anti-hyperlipidemic Activity

Table 3: Application of treatment efficacy

Group Number	Group Specification	Treatment species	Dose treatment species (mg/kg)	Abbreviation of Groups
1	Negative control	Physiological saline	10 ml/kg	N
2	High Fat	N/A	N/A	HF
3	HF+ RV ₁₀	Rovast 10mg/kg	10	RV ₁₀
4	HF+TA ₃₀₀	<i>Terminalia arjuna</i>	300	TA ₃₀₀
5	HF+TA ₆₀₀	<i>Terminalia arjuna</i>	600	TA ₆₀₀
6	HF+TA ₉₀₀	<i>Terminalia arjuna</i>	900	TA ₉₀₀
7	TA ₃₀₀	<i>Terminalia arjuna</i>	300	TA ₃₀₀
8	TA ₆₀₀	<i>Terminalia arjuna</i>	600	TA ₆₀₀
9	TA ₉₀₀	<i>Terminalia arjuna</i>	900	TA ₉₀₀

For this experiment, 100 rats were randomly picked and equally divided into fourteen groups

Statistical analysis

The raw data collected was recorded and evaluated on a broadsheet using the MS Excel program. The collected data underwent descriptive statistical analysis, and the results were provided as the mean and standard deviation (SD). In order to assess statistical significance, we used the "one-way Anova test" feature of the SPSS-6 program to analyze the inter-group heterogeneity with respect to several biological parameters. The occurrences are statistically significant because the 'p' value is less than 0.05 (p<0.5).

Results and discussion

Both traditional medicine and ethnomedicine, which study the healing traditions of various ethnic groups, have been around since the dawn of human civilization. Traditional medicine has a long history of using the healing properties of the earth's own resources. Traditional medicine in many countries and cultures has its roots in the use of herbs—herbs are plants or plant products—and plant extracts as primary ingredients in medicine. People have long used traditional plant and herb extracts, along with isolated active ingredients, as medicines. Using a rat model of high-fat-induced hyperlipidemia, this study investigated how an extract from *Terminalia arjuna* affected lipid profiles.

In groups 5 and 6, where the dose was 600 and 900 mg/kg, respectively, both the SGPT and SGOT levels demonstrated statistically significant ($p < 0.05$) results. The results were the same in two other investigations [27, 28]. Groups 4, 5, and 6 were found to have significantly elevated creatinine levels ($p < 0.05$) during the renal function test. These groups were given dosages of 300, 600, and 900 mg/kg of a mixed high-fat diet, respectively. However, the urea study yielded no statistically significant findings. The results of two other investigations on the subject were similar [29, 30]. With respect to HDL and LDL, groups 5 and 6 showed statistically significant results ($p < 0.05$) in HDL levels at doses of 600 and 900 mg/kg of high fat and extract, respectively. There were no statistically significant findings from the total cholesterol and triglyceride analyses, however. Both of the other investigations came to the same conclusions [31, 32].

Table 4: Lipid profile of *Terminalia arjuna*

Groups	SGPT	SGOT	Creatinine	Urea	TC	HDL	LDL	TG
C	37.22±4.52	36.39±4.21	0.52±0.21	36.42±3.30	129.46±2.29	87.21±4.92	36.42±4.21	50.32±4.82
HF	91.83±8.93	92.43±9.63	2.83±0.83	107.53±8.93	210.46±11.26	45.53±3.24	142.21±9.32	109.63±12.21
HF+ RV ₁₀	60.27±7.39	57.51±9.19	1.46±0.74	71.84±6.29*	152.43±13.61	66.92±7.32	67.28±5.90	72.24±8.73
HF+TA ₃₀₀	88.39±6.26	88.21±8.24	2.41±0.73*	104.22±5.53	206.41±8.92	47.43±5.21	132.21±6.93*	102.46±3.16
HF+TA ₆₀₀	84.21±5.93*	83.21±7.79*	2.13±0.39*	101.63±4.93	200.23±11.32	50.59±2.93*	126.93±5.29	94.59±8.20

HF+TA ₉₀₀	80.24±6.21*	80.24±9.94*	1.82±0.78*	96.23±3.26	196.44±12.23	55.49±4.79*	118.73±6.82	88.36±5.32
TA ₃₀₀	36.21±4.90	35.57±4.82	0.63±0.30	38.20±4.50	126.46±3.39	86.82±5.63	38.20±5.19	51.20±5.30
TA ₆₀₀	39.79±2.28	38.29±5.02	0.54±0.34	30.22±4.19	132.57±5.32	84.29±6.29	35.22±3.30	48.20±4.60
TA ₉₀₀	38.46±3.21	37.16±4.29	0.73±0.14	30.21±3.31	130.57±7.32	87.29±5.50	38.21±4.21	43.20±3.19

Note: The results were expressed in Mean±SEM (standard mean error) *p< 0.05, **p< 0.01, and ***p< 0.001 were considered as statistically significant. The statistical analysis followed by one-way analysis of variance (Dunnett's test) compared to the control.

Conclusion

This investigation examined the hepatoprotective properties of *Terminalia arjuna* ethanolic extract. The results of this investigation suggest that an ethanol extract from the plant *Terminalia arjuna* may protect against excessive cholesterol, liver injury, and impaired kidney function. Consequently, additional research is required to identify the active components of the extract that are capable of reducing hyperlipidemia and diabetes. Once we identify the active chemicals, we can conduct a thorough investigation.

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