Original Research Article

Hepatoprotective and Anti-Hyperlipidemic Effects of Ethanolic Extract of *Terminaliaarjuna* in a High-Fat-Induced Hyperlipidemic Rat Model

Abstract

Herbalism is the use of herbs and herbal medicines to improve and preserve health, ward off illness, or cure existing conditions. It is possible to hear the terms "herbal remedy" and "herbal medicine" used interchangeably. This study examined the effects of an extract from *Terminaliaarjuna* on the lipid profiles of rats suffering from hyperlipidemia due to a high-fat diet. In terms of liver function, the SGPT and SGOT levels were statistically significant ($p<0.05$) in groups 5 and 6, when the doses were 600 mg/kg and 900 mg/kg, respectively. Groups 4, 5, and 6 showed significantly higher levels of creatinine ($p<0.05$) during the renal function test. A mixed high-fat diet was administered to the groups at dosages of 300, 600, and 900 mg/kg, respectively. However, there were no statistically significant outcomes from the urea investigation. The levels of HDL were shown to be significantly affected ($p<0.05$) by the dosages of high fat and extract given to groups 5 and 6, respectively, when it came to HDL and LDL. The examination of total cholesterol and triglycerides yielded no statistically significant results. The main goal of this study is to find out what happens to the lipid profile of hyperlipidemic albino rats when they are given an ethanolic*T. arjuna* extract. In rat models, the present investigation demonstrated that T. arjuna exerted a hyperlipidemic effect by substantially raising cholesterol levels. The plant's ability to protect the heart is due to its bioactive components, which include tannins, flavonoids, and phenolics. We need to do further processing on the ethanolicextract of *T. arjuna* to understand how certain biologically active principles function.

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, H_2O_2, and O_2 [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 Centre 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.

Terminaliaarjuna, belonging to family Combretaceae, which 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-asthamatic, treatment of rheumatoid arthritis and is traditionally used to prevent kidney stone formation. Studies have also been conducting on *T.arjuna* in support of its diuretic properties [19]. Aqueous extract of *T.arjuna* bark is shown to protect the liver and kidney tissues against CCl_4-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, cardiotonic, 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 [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 anti-inflammatory properties [25].

The purpose of our present study is to evaluate the hepatoprotective effects of *T.arjuna*.This discovery provides a cost-effective alternative to statins, which are more expensive and have certain adverse effects. The anti-hyperlipidemic feature of the *T. arjuna* tree may be used to create medicine that is acceptable and very effective for treating cardiovascular disorders and other related conditions.

Materials and methods

Plant Collection and Extract Preparation

*T. arjuna*were collected from local market of Dhaka. The material was authenticated by National herbarium, Bangladesh. Firstly,*T.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

Sigma-Aldrich in Germany supplied the ethanol. Healthcare Pharmaceutical Limited sent a free sample of rosuvastatin, a frequently prescribed medication for lowering elevated cholesterol levels in the bloodstream. We used the Humalyzer 3000, a partially automated clinical chemistry analyzer, to assess the biochemical parameters. We purchased the components for the high-fat diet from a grocery 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±3°C, relative humidity 55±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 were each groups contain 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 + *T. arjuna*	High Fat Diet+ TA_{300}	HFD + TA_{300}
5	High Fat Diet + *T. arjuna*	High Fat Diet + TA_{600}	HFD + TA_{600}
6	High Fat Diet + *T. arjuna*	High Fat Diet + TA_{900}	HFD + TA_{900}
7	*T. arjuna*	TA_{300}	TA_{300}
8	*T. arjuna*	TA_{600}	TA_{600}
9	*T. arjuna*	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%)

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}	*Terminalia arjuna*	300	TA_{300}
5	HF+TA_{600}	*Terminalia arjuna*	600	TA_{600}
6	HF+TA_{900}	*Terminalia arjuna*	900	TA_{900}
7	TA_{300}	*Terminalia arjuna*	300	TA_{300}
8	TA_{600}	*Terminalia arjuna*	600	TA_{600}
9	TA_{900}	*Terminalia arjuna*	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 *T.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].This plant is rich in phytochemical compounds, including saponins, alkaloids, flavonoids, and triterpenoids. These compounds possess antioxidant

characteristics, may eliminate harmful free radicals, and can inhibit lipid peroxidation activity [29].

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 [30, 31].The antioxidant capabilities of *T. arjuna* may be responsible for its preventative action by reducing oxidative damage in the renal tubular cell membrane [32].

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 [33, 34].Indoles, flavonoids, lignans, and phytosterols have the capacity to decrease LDL, cholesterol, and triglyceride levels [35].

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[a]	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[a]	104.22±5.53	206.41±8.92	47.43±5.21	132.21±6.93[a]	102.46±3.16
HF+TA_{600}	84.21±5.93[a]	83.21±7.79[a]	2.13±0.39[a]	101.63±4.93	200.23±11.32	50.59±2.93[a]	126.93±5.29	94.59±8.20
HF+TA_{900}	80.24±6.21[a]	80.24±9.94[a]	1.82±0.78[a]	96.23±3.26	196.44±12.23	55.49±4.79[a]	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) $^{a}p< 0.05$,$^{b}p< 0.01$, and $^{c}p< 0.001$ were considered as statistically significant. The statistical analysis followed by one-way analysis of variance (Dunnett's test) compared to the control. HF= High Fat, TA= *TerminaliaArjuna*, RV= Rosuvastatin.

Conclusion

The ethanolic extract of *Terminaliaarjuna* was tested for its hepatoprotective effects. This study's findings provide support for the hypothesis that an ethanol extract of *Terminaliaarjuna* may provide protection against high cholesterol, liver damage, and kidney dysfunction. Hence, further study is needed to determine which parts of the extract are effective in lowering blood sugar and cholesterol levels, as well as those associated with diabetes. A comprehensive study may be undertaken after the active compounds have been identified.Potentially lowering LDL, cholesterol, and triglyceride levels include indoles, flavonoids, lignans, and phytosterols.

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