***Original Research Article***

# 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, $H_2O_2$, 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 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 decidous 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 *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 $CCl_4$-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 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 hebarium, 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 inceptapharmacetucals as a gift sample. Ethanol were bought from Taj Scientific store. details

**Experimental Animal Procurement, Nursing, and Grouping**

A total of 90 male rats weighing between 120and 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%)<br>Ghee (30%)<br>Mutton fat (40%)<br>Coconut oil (10%)<br>Butter (10%) |
| Carbohydrate (40%) | Boiled rice (40%)<br>Smashed potato (40%)<br>Boiled corn (20%) |
| Protein (10%) | Dry powdered prone (40%)<br>Dry boiled mutton (20%) |

| | |
|---|---|
| | Cheese (20%)<br>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+ $RV_{10}$ | Rovast10mg/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 *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.



## References:


1. Himi HZ, Rahman MM, Hasan SA, Cruze LR, Zaman TS, Chowdhury MM. An Evaluation of Anti-hyperlipidemic Activity of Ethanolic Extract of Moringa oleifera on High Fat Induced Hyperlipidemic Rat Model. International Journal of Biochemistry Research & Review. 2024 Mar 26;33(4):33-9.
2. Himi HZ, Rahman MM, Hasan SA, Cruze LR, Ishraat ST, Chowdhury MM. An Evaluation of Hepato-protective Activity of Ethanolic Extract of Solanum nigrum with Varying Doses on CCL4 Induced Hepatic Injured Rat. Asian Journal of Advanced Research and Reports. 2024 Mar 16;18(4):75-80.
3. FM SS, Juliana AB, Bornila M, Puja B, Nur-Neasha D, Rafat T. An assessment of hepato-protective activity of Psidium guajava fruit extract against hepatic injured

rodent model. Asian Journal of Medical Principles and Clinical Practice. 2023 Oct 7;6(2):240-5.

4. Baroi JA, Hossian MR, Chowdhury MM, Dolon NN, Maliha F, Rupak MA, Lima NN, Ullah MR, Tahsin R. An assessment of anti-hyperlipidemic potentialities of ethanolic extract of hemidesmus indicus in high fat induced rat model. Asian Journal of Food Research and Nutrition. 2023 Jul 9;2(4):323-30.

5. Zhang Y, Li X, Yang Q, Zhang C, Song X, Wang W, Jia L, Zhang J. Antioxidation, anti-hyperlipidaemia and hepatoprotection of polysaccharides from Auricularia auricular residue. Chemico-Biological Interactions. 2021 Jan 5;333:109323.

6. Srinivasa Rao K, Prasad T, Mohanta GP,Manna PK. An Overview of Statins asHypolipidemic Drugs. International Journalof Pharmaceutical Sciences and DrugResearch. 2011; 3(3):178-183.

7. Schachter M. Chemical, pharmacokineticand pharmacodynamic properties ofstatins: an update. Fundam ClinPharmacol. 2005;19:117-125.

8. Thompson PD, Panza G, Zaleski A, TaylorB. Statin-associated side effects. Journalof the American College of Cardiology.2016;67(20):2395-410.

9. Rupak MA, Chowdhury MM, ShuroviFS,Ferdous J, Tahsin MR, Sarif S, Hasan MM,Chowdhury JA, Kabir S, Chowdhury AA,Aktar F. An Evaluation of Analgesic andAnti-Inflammatory Activity of EthanolicExtract of CynodonDactylon on StressedRodent Model. Biomedical Journal ofScientific& Technical Research. 2022; 42(3):33550-7.

10. Islam M, Rupak AH, Nasrin N, Chowdhury MM, Sen P, Foysal AU, Uddin MJ, Ferdous J, Tahsin MR, Aktar F, Kabir S. An evaluation of potential hepato–protective properties of hylocereusundatus fruit in experimental rat model. Biomedical Journal of Scientific & Technical Research. 2022; 43(2):34405-16.

11. Mim IJ, Peya FY, Chowdhury MM, Khan TR, Mandal SK, Maliha F, Alam M, Rahman T, Tashin R. An evaluation of anti-diabetic activity of ethanolic extract of asparagus racemosus in alloxan induced rat model. International Journal of Advances in Nephrology Research. 2023; 6(1):60-8.

12. Lima NN, Dolon NN, Maliha F, Ullah MR, Humayra F, Chowdhury MM, Rupak MA, Baroi JA, Shohan FS, Tashin R. An Evaluation of Analgesic and Anti[1]Inflammatory Activity of Ficus racemosa in Rat Model.
13. Yang L, Stöckigt J. Trends for diverseproduction strategies of plant medicinalalkaloids. Natural product reports. 2010;27(10):1469-1479.
14. Saxena M, Saxena J, Nema R, Singh D,Gupta A. Phytochemistry of medicinalplants. Journal of Pharmacognosy andPhytochemistry. 2013; 1(6):168-18210
15. Lima NN, Dolon NN, Maliha F, Ullah MR, Humayra F, Chowdhury MM, Rupak MA, Baroi JA, Shohan FS, Tashin R. An Evaluation of Analgesic and Anti-Inflammatory Activity of Ficus racemosa in Rat Model.
16. Pracheta SS, Sharma V, Paliwal R, Sharma S, Yadav S, Singh L, et al. Chemoprotective activity of hydro-ethanolic extract of Euphorbia nerrifolia Linn. Leaves against DENA-induced liver carcinogenesis in mice. Biol Med. 2011; 3(2):36–44.
17. Cheng HY, Lin CC, Lin TC. Antiherpes simplex virus type 2 activity of casuarinin from the bark of *Terminalia arjuna*. *Antiviral Res.* 2002; 55:447–55.
18. Nagpal A, Meena LS, Kaur S, Grover IS, Wadhwa R, Kaul SC. Growth of suppression of human transformed cells by treatment with bark extracts from a medicinal plant *Terminalia arjuna in-vitro* cell. *Dev Biol Anim.* 2000; 36:544.
19. Chander R, Singh K, Khanna AK, Kaul SM, Puri A, Saxena R, et al. Antidyslipiddemic and antioxidant activities of different fraction of *Terminalia arjuna* bark. *Indian J Clin Biochem.* 2004; 19:141–8.
20. Manna P, Sinha M, Parames CS. Aqueous extract of *Terminalia arjuna* prevents carbon tetrachloride induced hepatic and renal disorders. *BMC Complementary and Alternative Medicine.* 2006; 6:33.
21. Mandal A, Das K, Nandi D K. In vitro bioactivity study of bark extract of Terminalia arjuna on probiotics, commercially available probiotic formulation. Int J Phytopharmacol 2010; 1(2): 109-113.
22. Das K, Chakraborty PP, Ghosh D, Nandi DK. Protective effect of aqueous extract of Terminalia arjuna against dehydrating induced oxidative stress and uremia in male rat. Iran J Pharma Res 2010; 9(2): 153-161.

23. Nema R, jain P, Khare S, Pradhan A, Gupta A, Singh D. Antibacterial and antifungal activity of Terminalia arjuna leaves extract with special reference to flavanoids. Basic Res J Med Clin Sci 2012; 1(5): 63-65.
24. Chatterjee AS. The treatise on indian medicinal plants: Council of scientific and industrial research. New Delhi: Publication and Information Directorate; 1994.
25. Biswas M, Biswas K, Karan TK, Bhattacharya S, Ghosh AK, Haldar PK. Evaluation of analgesic and anti-inflammatory activities of Terminalia arjuna leaf. J Phytol 2011; 3(1): 33-38.
26. Abdul, N. A., & Rahmat, A. (2015). jaafar Hz. Protective Effects of Tamarillo.
27. Mandal SK, Rahmat S, Sakib K, Mehjabin B, Rahman T, Rasna IJ. An Assessment of Anti-diabetic Effect of Gymnemasylvestre in Alloxan-induced Rat Model. International Research Journal of Gastroenterology and Hepatology. 2024 Feb 6;7(1):29-36.
28. Yuneldi RF, Saraswati TR, Yuniwarti EY. Profile of SGPT and SGOT on male rats (Rattus norvegicus) hyperglycemic after giving Insulin leaf extract (Tithonia diversifolia). Biosaintifika: Journal of Biology & Biology Education. 2018 Dec 19;10(3):519-25.
29. Bhowmik P, Shohan FM, Baroi JA, Pranto TI, Ullah MR, Rupak MA, Zaman TS, Rasna IJ, Tashin R. Evaluation of the Effects of Ethanolic Extract of Ficus benghalensis on the Lipid Profile and Kidney Function in Rat Model. International Research Journal of Gastroenterology and Hepatology. 2024 Feb 3;7(1):22-8.
30. Yanardağ, R., Bolkent, Ş., Özsoy□Saçan, Ö. and Karabulut□Bulan, Ö., 2002. The effects of chard (Beta vulgaris L. var. cicla) extract on the kidney tissue, serum urea and creatinine levels of diabetic rats. *Phytotherapy Research: An International Journal Devoted to Pharmacological and Toxicological Evaluation of Natural Product Derivatives*, *16*(8), pp.758-761.
31.Yousofvand N, Soltany A. Effects of hydroalcoholic extract of dill (Anethum graveolens) on the serum levels of blood lipids cholesterol, triglycerides, LDL and HDL in male NMRI mice. J Pharmaceut Chem Biol Sci. 2015 May; 3:114-21.

32. Nofianti T, Nurmayasari S, Priatna M, Ruswanto R, Nurfatwa M. The effect of the ethanolic extract of Asam Jawa leaf (Tamarindus Indica L.) in total cholesterol, triglyceride, LDL and HDL concentration on male spraguedawley rats. InJournal of Physics: Conference Series. 2019 Jul 1 (Vol. 1179, No. 1, p. 012175). IOP Publishing.