

Hypolipidemic Action of Leaf Extracts of *Raphanus sativus* var. *Longipinnatus* in High Fat Diet Induced Rats

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Abstract This study aims to investigate the hypolipidemic effects of an aqueous extract from the leaves of *Raphanus sativus* var. *longipinnatus* using rat models. Hyperlipidaemia, a condition caused by a high-fat diet, was produced in Wistar albino rats through the continuous administration of such food. During this period, weight growth and changes to the serum lipid profile were observed. It specifically indicated a reduction in high-density lipoprotein levels and an increase in total cholesterol (185 ± 0.96), triglycerides (281 ± 1.2), low-density lipoprotein (123 ± 2.0), and very low-density lipoprotein (57 ± 1.4). Atorvastatin administered at a dosage of 10 mg/kg served as the reference medication for the standardisation process. Following a 14-day testing period, rats administered 300 mg/kg of leaf extract exhibited a significant alteration in their weight. A significant increase ($P<0.001$) was observed in total cholesterol, triglycerides, low-density lipoprotein, and very low-density lipoprotein after the administration of the 300 mg/kg dosage. The quantity of high-density lipoprotein significantly increased ($P<0.001$) with the 200 mg/kg dosage. Microscopic examination of the liver elucidates the alterations that transpire in hepatic cells throughout the course of treatment. The leaf extract exhibited a notable reduction in oxidative stress markers, along with decreased SGOT and SGPT levels. Comprehensive studies demonstrate that the use of the leaf extract resulted in weight gain and an improved lipid profile in the blood stream.

Keywords *Raphanus sativus*, Extract, Hyperlipidemia, Atorvastatin, Lipoprotein

1. Introduction

Steroid cholesterol offers significant advantages to human physiology. It primarily contributes to the stabilisation of cell membranes, influencing fluidity and permeability. As a sterol molecule, it serves as a crucial precursor for the manufacture of steroid hormones, Vitamin D, and bile acids. Conversely, research indicates that both excessive and insufficient levels can adversely affect the body, one consequence being an elevation in cholesterol levels. For lipids to be anticipated, there must be an adequate equilibrium between antioxidative enzymes and reactive oxygen species. Excessive cholesterol levels contribute to atherosclerosis, elevating the risk of heart attacks and strokes [1]. Elevated cholesterol levels account for around 33% of global cases of ischaemic heart disease and stroke. A variety of conditions termed "hyperlipidaemia" are characterised by elevated lipid levels in the body and may be either hereditary or acquired. The World Health Organisation reported that excessively high cholesterol accounts for 29.7 million disability-adjusted life years (DALYs; 2% of total DALYs) and 2.6 million deaths (4.5% of total fatalities) [2]. This includes the decrease in very low-density lipoprotein (VLDL), triglycerides (TG), high-density lipoprotein (HDL), and low-density lipoprotein (LDL), total cholesterol (TC) [3].

The researchers' diligence and commitment have yielded a hypolipidemic medication that has proven effective in preventing hyperlipidaemia. Nonetheless, prolonged usage also leads to some detrimental effects on the body. Numerous prior studies have indicated the efficacy of Atorvastatin in the management of dyslipidaemia and cardiovascular diseases (CVDs) [4, 5]. Moreover, owing to its potent capacity to reduce cholesterol levels, Atorvastatin was first chosen over other statins [6, 7]. Nonetheless, several recent studies have emerged, including a substantial meta-analysis of clinical trial data indicating deleterious consequences associated with statins [4, 6, 8–10]. Currently, no medicine exists that provides a durable hypolipidemic effect with minimal adverse effects [11–13]. Consequently, a pharmacological intervention with few ramifications has been employed to reduce blood cholesterol levels. Numerous research studies have demonstrated that ancient natural therapies derived from plants have been effectively utilised for human therapy [14]. It is asserted that several eastern medicinal plants possess biological properties [15].

Recent research on plants has garnered significant attention from scientists globally. Numerous studies have emphasised the therapeutic advantages of various medicinal plants in a range of traditional uses. Leaves, stems, roots, fruits, and seeds are diverse botanical elements recognised for their ability to improve human health and nutrition by supplying bioactive chemicals for dietary intake [16]. Controlling dyslipidaemia can largely be achieved through dietary adjustments, physical exercise, and weight reduction using a balanced nutritional strategy [17]. The plant is scientifically designated as *Raphanus sativus* L. Numerous phylogenetic studies indicate that the radish plant belongs to the Rapa/Oleacera clade within the Brassicaceae family. The radish plant has an outer colour variety, ranging from white in Asia to red in Europe, and purple-green to black elsewhere [18]. Depending on their chemical make-up, they contribute to a wide range of scents and flavours [19]. Researchers and pharmaceutical companies are increasingly interested in radish as a potential source of bioactive phytochemicals with important potential health and therapeutic applications [20]. In turn, these phytochemicals can be employed in the fight against oxidative stress, bacterial infections, hypertension, and cardio metabolic disorders [21, 22].

Research in the field of pharmacology has shown that *Raphanus sativus* has many beneficial effects, such as regulating metabolism, improving digestion, protecting the central nervous system, and fighting tumours and osteoporosis. It also has anti-inflammatory, anti-hypertensive, anti-tussive, anti-asthmatic, and detoxifying properties. Reportedly, *Coptidis rhizoma* and *Evodia rutaecarpa*, two medicinal herbs, can effectively lower lipid levels. As a hypolipidemic agent, *Coptidis rhizoma* is a traditional Chinese medication. When coupled with Berberine, *Evodia rutaecarpa* also acts as a

hypolipidemic agent. A large number of plants, including *Ampelopsis grossedentata*, *Glycyrrhiza glabra*, *Moringa oleifera*, *Psidium guajava* Linn, *Terminalia arjuna*, *Zingiber officinale*, *Allium sativum*, and many more, have demonstrated activities that lower cholesterol levels [23]. Furthermore, research has demonstrated that the leaves of the *Raphanus sativus* plant species contain a higher quality of nutrients compared to the root [24]. Further components of the leaves that may help lower lipid levels include alkaloids, flavonoids, amino acids, fatty components, and phenolic components. Since no one has previously documented the hypolipidemic action of *Raphanus sativus* leaf extract, this study intends to fill that void.

2. Materials and Methods

2.1. Experimental Animals

We purchased both male and female Wistar albino rats from Chakraborty Enterprises, which is located at 3/1D Girish Vidyaratna Lane, Narkeldanga, Kolkata-700011. The range of their weight was 100–150 grams. For our experiments, we employed the GGV, Bilaspur animal facility to keep the rats. The next step was an entirely arbitrary seven-day acclimatisation period for the animals. Items were placed into roomy polypropylene containers covered with husk as part of the process. In a carefully controlled setting, the animals spent 12 hours in the light and 12 hours in the dark, at a temperature of $23^{\circ}\text{C} \pm 3^{\circ}\text{C}$ and a relative humidity of $55\% \pm 10\%$. We utilised professional rat chow (Kapila Posuahar), kept the cages spotless, and made sure the rats had water available at all times. The experiments used a variety of animal types. To ensure that the animals were comfortable and acclimated to their normal husbandry circumstances before the research began, we gave them a week to settle in. Both the Institutional Animal Ethics Committee of the Department of Pharmacy at Guru Ghasidas Vishwavidyalaya in Bilaspur (994/GO/Re/S/06/CPCSEA) and the Committee for Control and Supervision of Experimental Animals (CPCSEA) authorised the experiment to go ahead.

2.2. Drugs and Chemicals

The drug atorvastatin was sourced from the Gujarat, India-based Alkem Laboratories. Both cholesterol and citric acid came from the same Indian company, Himedia. C.G., Bilaspur, which is home to the Department of Pharmacy's central pharmacy, and is the source for all of the other chemicals and reagents. We obtained the HDL, LDL, TG, cholesterol, and serum glutamic oxaloacetic transaminase (SGOT) testing kits from the Navsari, India-based Beacon Diagnostics Pvt. Ltd. Viola Diagnostic Systems of Pantnagar, India, which provides a Serum glutamic pyruvic transaminase (SGPT) kit that was used to evaluate the biochemical parameter.

2.3. Collection and Preparation of Plant Extract

In January 2023, plants were acquired in a local market in Koni, Bilaspur, Chhattisgarh. The leaves were thereafter permitted to air-dry at an ambient temperature following a rinse with tap water. Dr. A.K. Dixit, a specialist in plant science from Guru Ghasidas Vishwavidyalaya in Koni, Bilaspur, Chhattisgarh, verified the authenticity of the specimen. The specimen voucher, identified by the number (Bot/GGV/2023/71), was submitted to the department. The therapeutic material was ground using a hand grinder following its desiccation. The recently developed leaves of *Raphanus sativus* were meticulously washed with tap water. It was subsequently dehydrated and converted into a granulated form. For a duration of two to three days, the raw powder was subjected to temperatures ranging from 60 to 70°C in a Soxhlet apparatus to extract its components utilizing distilled water. The extract acquired a greenish-brown hue during concentration with a rotary evaporator at 40°C. An extraction yield of 11.18% was attained.

2.4. Preliminary Phytochemical Screening

The chemical components included in the resultant extracts were identified by a battery of analytical procedures [25]. Carbohydrates, phenols, phytosterols, glycosides, flavonoids, and alkaloids, were among the phytochemicals identified in a study of *Raphanus sativus* leaf extract.

2.5. Analysis using Gas Chromatography-Mass Spectrometry

A QP-2010 Ultra auto sampler-equipped GC-MS was utilized. The column Rtx-5MS, with its 30 m × 0.25 mm diameter and 0.25 µm film thickness, was directly injected with the given solution. Helium was used as the carrier gas for the injection, which was done using the spitless mode. We set the injector temperature to 280.00 °C and the ion source temperature to 200.00 °C. A value of 1.32 kilovolts was detected. The mass spectra were obtained using 0.50 scans per second in full-scan mode, covering a range of 40 to 850 m/z. After a 5-minute initialization, the temperature of the column oven was programmed to 70.0 °C. After that, the temperature was maintained at 310 °C for 12 minutes. A search similarity criterion larger than 70 was used to search the NIST 2008 mass spectra library in order to identify peaks. Peak area normalization was used to quantify chemicals as percentages of relative areas.

2.6. Dose Selection

A combination of distilled water and Tween-20 was employed to homogenize the *Raphanus sativus* leaf extract, while Atorvastatin was utilized as the reference medication. Individual body weight was used to determine the dosage

of Atorvastatin. Over the course of 14 days, each patient was given one dose orally by oral gavage. Doses of 100 mg/kg, 200 mg/kg, and 300 mg/kg of body weight are recommended for the extract of *Raphanus sativus* leaves [26, 27].

2.7. High-Fat Diet Formula

A combination of distilled water and Tween-20 was employed to homogenize the *Raphanus sativus* leaf extract, while Atorvastatin was utilized as the reference medication. Individual body weight was used to determine the dosage of Atorvastatin. Over the course of 14 days, each patient was given one dose orally by oral gavage. Doses of 100 mg/kg, 200 mg/kg, and 300 mg/kg of body weight are recommended for the extract of *Raphanus sativus* leaves [28, 29]. Various rodent models of diet-induced hyperlipidemia have been developed, yielding important insights into the causes and treatments for this condition. Two to four weeks of a high-fat, high-sugar diet allowed the rats to develop into HFD models.

2.8. Methodology and Treatment Plan

The hyperlipidemia model mice were administered treatments in accordance with the protocol. Six rats made up each of the six groups into which the animals were placed (Table 1).

Table 1. Treatment Groups

Groups	Treatment (mg/kg body weight)
I	Normal
II	Hyperlipidemia Control
III	HFD + Standard (Atorvastatin-3 mg/kg, p.o)
IV	HFD + extract (100 mg/kg, p.o)
V	HFD + extract (200 mg/kg, p.o)
VI	HFD + extract (300 mg/kg, p.o)

Group I- Normal group: For 42 days, the rats consumed a typical rodent diet. Beginning on day 29, they continued for an additional 14 days (days 29-42) by ingesting 10 milliliters of distilled water per kilogram of body weight through oral gavage.

Group II- Hyperlipidemia control: After 28 days of being given a high-fat diet, the rats in the experiment developed hyperlipidemia. After 29–42 days, or 14 days of HFD treatment, the vehicle dose is 10 milliliters per kilogram for another 14 days.

Group III – Standard (10 mg/kg): Experimental rats were fed a high-fat diet for 28 days followed by 14 days of dietary restriction to cause hyperlipidemia (29-42 days). Take 14 mg of atorvastatin orally once a day as prescribed.

Group IV- Test – 1 (100 mg/kg): The rats who were part of the study developed hyperlipidemia after being fed

a high-fat diet for 28 days. For an additional 14 days, beginning on day 29, the high-fat diet was continued until day 42. The extract was administered orally to the rats for a period of fourteen days.

Group V- Test – 2 (200 mg/kg): The rats who were part of the study developed hyperlipidemia after being fed a high-fat diet for 28 days. Participants continued to consume a high-fat diet for the following 14 days (ranging from 29 to 42 days) while taking an oral extract for the same duration.

Group VI- Test – 3 (300 mg/kg): The experimental rats were subjected to a high-fat diet for 28 days to bring about hyperlipidemia. Participants continued to consume a high-fat diet for the following 14 days (ranging from 29 to 42 days) while taking an oral extract for the same duration. After the experiment was finished, the animals were killed via cervical dislocation. Drawing blood samples by cardiac puncture was the next stage in assessing the biochemical levels and lipid profile. Furthermore, the liver had to be removed for the histological analysis.

2.9. *In vivo* Pharmacological Evaluation

2.9.1. Body Weight

The weight of the animals was measured every week for 42 days. To measure weight, a digital weighing equipment was employed.

2.9.2. Biochemical Estimations

Using the physical method of neck dislocation, the animals were euthanized after 42 days. The cardiac puncture blood samples were transferred to a sterile centrifuge tube and spun at 2500 rpm for 10 minutes. Lipid markers, such as total cholesterol (TC), triglycerides (TG), low-density lipoprotein (LDL), and high-density lipoprotein (HDL), were subsequently assessed in the serum that had been collected. A mathematical procedure was used to obtain the VLDL quantity. The TG value was divided by 5. The Friedewald et al. (1972) approach was used to estimate the LDL value. This method takes the total cholesterol (TC) value and subtracts the total HDL and VLDL values to get the LDL value in mg/dl. The Elico Bio Chemistry instrument, a semi-automatic device, was used to measure the levels of SGOT and SGPT in the liver function test. After the animals were sacrificed, researchers took two samples of their livers: one for histological study and one for antioxidant parameter assessment. It was necessary to treat the liver slices with formaldehyde so that

they would stay intact. Similarly, the liver slices were homogenized by treating them with a buffer solution so they were uniform in appearance.

2.10. Statistical Analysis

The results were shown as the average plus or minus the standard error of the mean (SEM). We used Graph Pad Instat® to run the statistical analyses. Next, a Newman-Keuls post-test was administered after a one-way analysis of variance (ANOVA) was used to compare the various groups. An analysis of variance (ANOVA) with two-way effects and Bonferroni's post hoc test were performed on the data. At * $P < 0.05$, ** $P < 0.01$, and *** $P < 0.001$, the levels of statistical significance were set. Graph Pad Prism (Version 5) was used to create the visual representation.

3. Results

3.1. Initial Examination of the Chemical Composition of Plants

Glycosides, alkaloids, tannins, phenols, carbohydrates, and amino acids were all found in the *Raphanus sativus* leaf extract. There were no steroid or glycoside chemicals found in the crude extracts, though. The amounts of phenolic compounds in substances can be swiftly and easily determined using Folin-Ciocalteu's assay. The anhydrous extract showed 1.631 mg GAE/g of total phenolic content when diluted to 1 mg/ml. The amount of flavonoids in the extracts was determined by measuring how well the flavonoids and aluminium formed a complex. At a concentration of 1 mg/ml, the total flavonoid content in the water extract was found to be 23.687 mg QE/g.

3.2. GC-MS

The chemical components in various crude extracts were identified and described using gas chromatography (GC) measurements of retention time. The computational comparison was made with the mass spectra of standards that were located in mass spectrum libraries. Using gas chromatography-mass spectrometry (GC-MS), twenty-five different chemical compounds were effectively extracted and identified (Figure 1 and Table 2).

3.3. Effects on Body Weight

The experimental rats' weight changes were recorded weekly using a weighing scale (MRC Ltd.). In Table 3, you can see the computed weekly weight changes. A significant increase in body weight was noted in all five groups after the high-fat diet (HFD) treatment for four weeks (28 days). During weeks five and six of treatment, the experimental medication began to be administered. Compared to the Normal group on day 0, the HFD group did not show any noticeable weight gain until day 14. Despite this, there was a significant increase in weight ($P < 0.01$) on days 21 and 28. On the 42nd day of the final week of observation, a notable increase in weight was observed ($P < 0.001$). If you compare

T1, T2, and T3 every day (or week), you won't see any weight increase until day 14. However, there was a significant increase in weight on days 21 and 28 ($P < 0.001$). On the 42nd day of the 14-day treatment period, T3 showed a significant decrease ($P < 0.001$) in weight, while T1 and T2 showed no significant change. When comparing the HFD group with the test groups daily on the 42nd day, there is a notable drop ($P < 0.001$) in weight for all groups.

Shown as mean \pm SEM are the values ($n = 6$). The data was analyzed using a two-way ANOVA, followed by Bonferroni's post hoc test. From the normal group, we can see that $aP < 0.05$, $bP < 0.01$, and $cP < 0.001$. When comparing to the HFD control group, we find that $dP < 0.05$, $eP < 0.01$, and $fP < 0.001$, respectively.

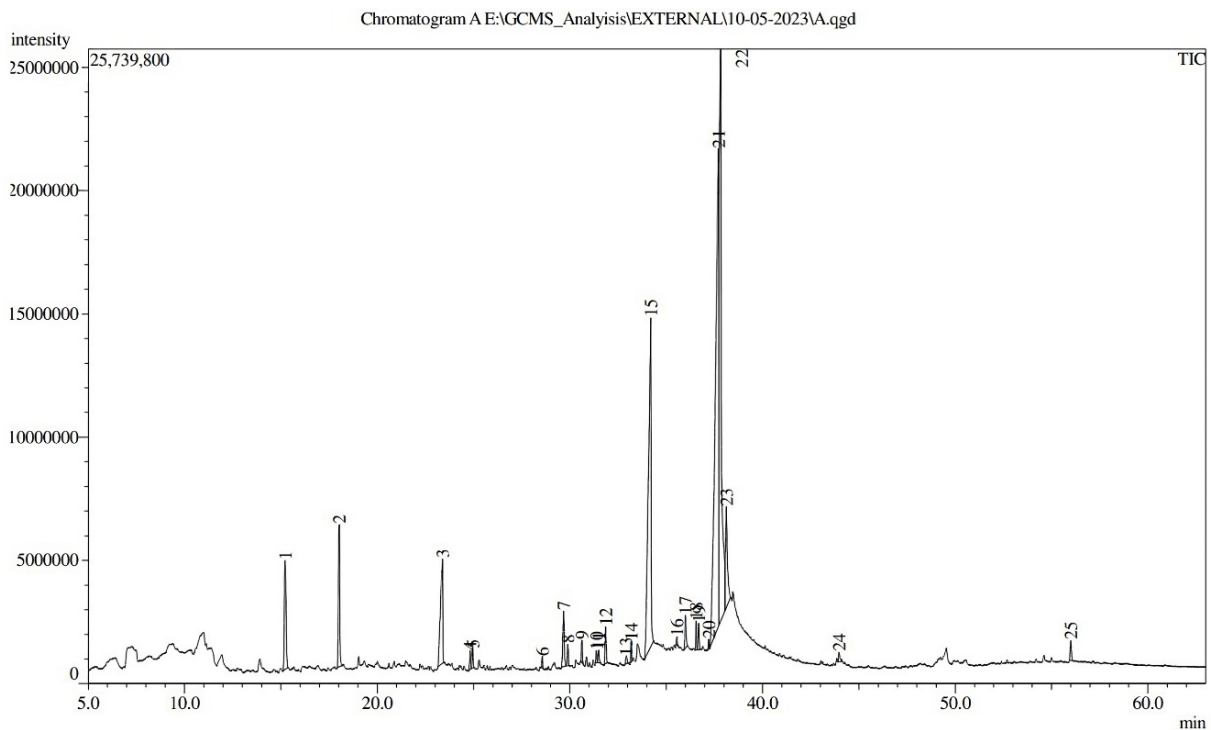


Figure 1. GC-MS qualitative analysis report of leaves extract of *R. sativus*

Table 2. GC–MS Qualitative Analysis Report of Leaves Extract of *R. sativus*

Peak Report TIC										
Peak	R.Time	L.Time	F.Time	Area	Area%	Height	Height%	A/H	Mark	Name
1	15.214	15.117	15.367	28675974	3.91	4420624	4.93	6.49		4-Vinylphenol
2	18.024	17.925	18.158	25343704	3.45	5767932	6.43	4.39		2-Methoxy-4-vinylphenol
3	23.393	23.150	23.450	36968116	5.04	4230100	4.72	8.74		3-(Methylthio)pent-4-yn-1-ol
4	24.821	24.758	24.875	2880432	0.39	766745	0.85	3.76		Hexahydropyrrolizm-3-one
5	24.952	24.875	25.017	3280713	0.45	787914	0.88	4.16	V	Dodecanoic acid
6	28.562	28.508	28.625	1612008	0.22	455445	0.51	3.54		3-Methyl-2,3,6,7,8,8a-hexahydropyrr
7	29.678	29.567	29.792	11243511	1.53	2254295	2.51	4.99		Tetradecanoic acid
8	29.890	29.792	29.958	3246702	0.44	874205	0.97	3.71	V	Loliodide
9	30.621	30.558	30.708	3409223	0.46	910465	1.01	3.74		1H-Indole-3-acetonitrile
10	31.371	31.325	31.443	1568094	0.21	487374	0.54	3.22		Cyclopentadecanone, 2-hydroxy-
11	31.492	31.443	31.575	1908727	0.26	522743	0.58	3.65	V	6-Octadecenoic acid. (Z)
12	31.859	31.775	31.942	5750938	0.78	1491054	1.66	3.86		Pentadecanoic acid
13	32.917	32.875	33.133	1033762	0.14	292348	0.33	3.54		Pyrrlo[1,2-a]pyrazine-1,4-drone, hex
14	33.181	33.133	33.233	2342276	0.32	834472	0.93	2.81		Hexadecanoic acid, methyl ester
15	34.196	33.875	34.342	130558847	17.79	13346203	14.88	9.78		n-Hexadecanoic acid
16	35.553	35.508	35.625	1117443	0.15	338051	0.38	3.31		Oleic Acid
17	35.996	35.925	36.100	5592153	0.76	1332943	1.49	4.20		Octadecanoic acid
18	36.556	36.500	36.617	3506280	0.48	1180297	1.32	2.97		9,12-Octadecadienoic acid (Z,Z)-. me
19	36.687	36.617	36.758	3930875	0.54	1072422	1.20	3.67	V	9-Octadecenoic acid (Z)-, methyl este
20	37.198	37.150	37.250	1108287	0.15	406488	0.45	2.73		Methyl stearate
21	37.711	37.528	37.733	238919829	32.56	19410556	21.64	12.31		10E, 12Z-Octadecadienoic acid
22	37.818	37.733	38.042	185541246	25.28	23222604	25.89	7.99	V	Oleic Acid
23	38.124	38.042	38.325	28626533	3.90	4089242	4.56	7.00	V	Octadecanoic acid
24	43.965	43.892	44.075	1994982	0.27	401634	0.45	4.97	MI	Hexadecanoic acid. 2-hydroxy-1-(hyd
25	55.999	55.092	56.092	3705764	0.50	812680	0.91	4.56		gamma-Sitosterol
				733866419	100.00	89708836	100.00			

Table 3. Effect on Average body weight

Groups	Average weight (grams)						
	0 day	7 th day	14 th day	21 st day	28 th day	35 th day	42 nd day
Normal	120 ± 00	121 ± 50	125 ± 50	125 ± 67	126 ± 33	126 ± 50	127 ± 33
Hyperlipidemia Control	124 ± 67	125 ± 50	131 ± 50 ^a	137 ± 83 ^c	141 ± 33 ^c	145 ± 33 ^c	148 ± 83 ^c
Standard	123 ± 50	120 ± 83	127 ± 33	132 ± 67 ^a	138 ± 50 ^c	145 ± 17 ^c	151 ± 33 ^c
Test -1	120 ± 83	115 ± 00 ^{af}	122 ± 33 ^f	129 ± 83 ^c	134 ± 17 ^{bc}	136 ± 00 ^{cfi}	140 ± 67 ^{cei}
Test -2	120 ± 17	115 ± 50 ^{af}	118 ± 83 ^{afi}	122 ± 00 ^{fi}	129 ± 33 ^{fi}	131 ± 83 ^{fi}	132 ± 67 ^{fi}
Test -3	121 ± 17	118 ± 67 ^d	126 ± 00	134 ± 83 ^c	146 ± 33 ^{ch}	154 ± 67 ^{ch}	146 ± 67 ^c

3.4. Effect on Serum Lipid Parameters

3.4.1. Estimation of Serum TC (Total Cholesterol)

The hyperlipidemia control group had significantly elevated total cholesterol (TC) values compared to the normal group ($p < 0.001$). The standard group's total cholesterol (TC) levels were significantly lower ($p < 0.001$) compared to the normal and hyperlipidemia control groups. Initially, we compared TC levels in four groups: TC, Normal, Hyperlipidemia Control, and Standard. There was a substantial decrease in the TC level ($p < 0.001$). In the second test, an analysis was conducted to compare TC levels among the normal, hyperlipidemia control, and standard groups. The total cholesterol (TC) levels dropped significantly in every group ($p < 0.001$, $p < 0.05$). In the third and final test, the TC group was compared to the normal, hyperlipidemia control, and standard groups using TC level as the endpoint. The substantial decline in TC level ($p < 0.001$) was observed. For Test 3, a p-value below 0.001 indicates statistical significance.

3.4.2. Estimation of Serum TG (Triglyceride)

In comparison to the normal group, the hyperlipidemia control group had considerably higher TG levels ($p < 0.001$). There were substantial reductions in TG levels ($p < 0.05$ and $p < 0.001$, respectively) in the control groups with normal and hyperlipidemia when compared to the standard group. The initial step in the testing technique involved comparing TG to three distinct groups: normal, hyperlipidemia control, and standard. It is statistically significant that the amount of TG reduced ($p < 0.001$). Test-2 looked at normal TG levels as well as hyperlipidemia control and standard levels. Remarkably, TG levels decreased ($p < 0.001$). Test-3 contrasted the Normal, hyperlipidemia Control, and standard groups to assess TG levels. A statistically significant decrease ($p < 0.001$) was observed in the levels

of TG. A far more pronounced result ($p < 0.001$) is shown in the third test.

3.4.3. Estimation of Serum HDL (High Density Lipoprotein)

It was statistically observed ($p < 0.05$) that the normal group had significantly greater HDL levels than the hyperlipidemia control group. The standard group's HDL values were significantly lower ($p < 0.01$) compared to the control group's hyperlipidemia. Hyperlipidemia Control, Normal, and Ordinary HDL values were compared in Test-1. All three groups showed a statistically significant rise in HDL values ($p < 0.05$, $p < 0.001$, $p < 0.001$). In comparison to the Normal, hyperlipidemia Control, and standard groups, Test 2 had noticeably elevated HDL values ($p < 0.001$). The third group showed significantly lower HDL levels compared to the hyperlipidemia control, normal, and test groups ($p < 0.05$, $p < 0.001$). Observing the outcomes of Test 2 is considerably less difficult ($p < 0.001$).

3.4.4. Estimation of Serum LDL (Low Density Lipoprotein)

Lipid levels were significantly higher in the hyperlipidemia control group compared to the normal group ($p < 0.001$). The standard group showed significantly lower levels of LDL compared to the hyperlipidemia control group ($p < 0.001$). One part of test-1 was looking at LDL levels in the control group for hyperlipidemia and the standard group. In that sequence, LDL levels decreased significantly in all three groups ($p < 0.05$, $p < 0.001$, $p < 0.001$). In Test-2, compared to the Normal, hyperlipidemia Control, and standard groups, there was a notable decrease in LDL levels ($p < 0.001$). Furthermore, when compared to the control, normal, and hyperlipidemia groups, the third test showed a notable decline in LDL levels ($p < 0.001$). The third test reveals a markedly more significant result ($p < 0.001$) (Table 4).

Table 4. Effect on serum lipid parameters

Groups	Lipid profile of rat serum (mg/dl of Hb)				
	TC	TG	HDL	LDL	VLDL
Normal	78 ± 2.4	119 ± 1.0	52 ± 1.8	92 ± 2.3	25 ± 1.3
Hyperlipidemia control	185 ± 0.96 ^c	281 ± 1.2 ^c	45 ± 1.1 ^a	123 ± 2.0 ^c	57 ± 1.4 ^c
Standard	88 ± 1.2 ^{ef}	125 ± 1.6 ^{af}	55 ± 1.9 ^{bc}	112 ± 0.95 ^{cf}	25 ± 0.83 ^f
Test-1	102 ± 1.7 ^{efi}	155 ± 1.9 ^{efi}	59 ± 2.8 ^{afi}	102 ± 1.7 ^{afi}	32 ± 1.4 ^{efi}
Test-2	82 ± 1.7 ^{fg}	108 ± 2.4 ^{efi}	85 ± 2.5 ^{efi}	121 ± 1.2 ^{ci}	21 ± 1.2 ^f
Test-3	58 ± 0.99 ^{efi}	103 ± 1.8 ^{efi}	61 ± 1.6 ^{af}	98 ± 1.4 ^{afi}	20 ± 1.3 ^f

3.4.5. Estimation of Serum VLDL (Very Low-Density Lipoprotein)

In comparison to the normal group, the hyperlipidemia control group exhibited greatly elevated levels of very low-density lipoprotein (VLDL) ($p < 0.001$). Low levels of very low-density lipoprotein (VLDL) were seen in the control group with hyperlipidemia as compared to the standard group ($p < 0.001$). Hypolipidemia (low density lipoprotein) concentrations were lower in test-1 compared to normal, control, and hyperlipidemia groups. Statistical analysis revealed that the decline was noteworthy ($p < 0.001$). Normal, hyperlipidemia control, and standard groups were utilized to ascertain VLDL levels in the second portion of the test. The level of VLDL dropped significantly ($fp < 0.001$) in this study. The LDL level was shown to be considerably reduced ($fp < 0.001$) in Test-3 in the Normal, hyperlipidemia Control, and standard groups. Examining Test 3, we find a substantially higher level of significance ($p < 0.001$).

Displayed as mean ± SD ($n = 6$), the data are accurate. Researchers used a one-way analysis of variance (ANOVA) and the Newman-Keuls multiple comparison test to examine the data. When compared to the Normal, Hyperlipidemia control, and Standard groups, the following results were reported: aP < 0.05, bP < 0.01, cP < 0.001, dP < 0.05, eP < 0.01, fP < 0.001, and gP < 0.05, hP < 0.01, iP < 0.001, respectively.

3.5. Effect on Liver Enzymes

3.5.1. SGOT (AST)

In terms of SGOT levels, there was a notable disparity ($p < 0.001$) between the normal group and the control group with hyperlipidemia. The hyperlipidemia control group displayed significantly higher SGOT levels compared to the standard group, which had a significant decline ($p < 0.001$). In comparison to the control group with hyperlipidemia, Test-1 showed a significantly lower SGOT level ($p < 0.001$). The SGOT level was found to be significantly lower ($p < 0.01$) in the Test-2 group compared to the hyperlipidemia control group. There was a marked decrease in SGOT levels when comparing Test-3 results to

the normal range. The significance level of Test-1's results is quite high ($p < 0.001$).

3.5.2. SGPT (ALT)

The hyperlipidemia group's SGPT levels were substantially greater than those of the normal group. This result is statistically significant if the p-value is less than 0.001. There was a significant difference ($p < 0.001$) in the SGPT levels between the normal and standard groups. In test-1, there was a substantial decrease in SGPT levels in both the control group with hyperlipidemia ($p < 0.001$) and the standard group ($p < 0.05$). In comparison to the initial level, the SGPT levels in Test 2 were significantly lower in the hyperlipidemia Control and standard groups ($p < 0.001$). The third test showed that SGPT levels were significantly higher in the experimental group than in the control group ($p < 0.05$ and $p < 0.01$). In addition, the level of SGPT decreased significantly ($p < 0.01$) when contrasted with the control group that had hyperlipidemia (Table 5).

Table 5. Effect on Liver Enzymes

Groups	SGOT (U/L of Hb)	SGPT (U/L of Hb)
Normal	25 ± 1.7	41 ± 2.0
Hyperlipidemia control	45 ± 1.6 ^c	58 ± 1.6 ^c
Standard	26 ± 1.9 ^f	53 ± 1.3 ^c
Test-1	28 ± 1.7 ^f	45 ± 2.5 ^{fg}
Test-2	34 ± 1.6 ^{bf}	38 ± 2.0 ^{fi}
Test-3	41 ± 2.3 ^{ci}	49 ± 1.9 ^{ac}

The data is shown as the mean ± standard deviation ($n = 6$). By utilising the one-way ANOVA and the Newman-Keuls multiple comparison test, the data were compared to the Normal, Hyperlipidemia control, and Standard groups, in that order. The obtained results were presented as follows: aP < 0.05, bP < 0.01, cP < 0.001, dP < 0.05, eP < 0.01, fP < 0.001, and gP < 0.05, hP < 0.01, and iP < 0.001.

3.5.3. Effects on Antioxidant Parameters

The outcomes of the biochemical analysis of the liver's

antioxidants are shown in Table 6.

The hyperlipidemia control group showed significantly lower levels of superoxide dismutase compared to the normal group ($p < 0.001$). The control group showed no change, but the standard group showed a significant decrease ($p < 0.001$). However, a significant increase in SOD levels was seen ($p < 0.001$) when comparing the control group with hyperlipidemia to the standard group. The first experiment compared the SOD levels of the normal group with those of the hyperlipidemia control group. There was a noticeable increase in SOD levels that was statistically significant ($p < 0.001$). Compared to the Normal group, Test-2 had a considerably decreased quantity of superoxide dismutase (SOD) ($p < 0.001$). In contrast, the hyperlipidemia control group showed no such difference. The control group likewise had a considerably lower SOD level ($p < 0.001$). The levels of superoxide dismutase (SOD) were noticeably lower in Test-3 than in the normal group ($p < 0.001$). In any case, compared to both the control group for hyperlipidemia and the standard group, the SOD level was considerably higher ($p < 0.001$). Compared to the hyperlipidemia control group, the normal group had significantly higher GPx levels ($p < 0.001$). The hyperlipidemia control group had a significantly lower concentration of GPx ($p < 0.001$) in comparison to the standard group. With $p < 0.05$ and $p < 0.001$, respectively, the GPx levels in the hyperlipidemia control group were significantly higher than those in the normal control group in test-1. In Test 2, the GPx level decreased significantly ($p < 0.001$) in comparison to the control groups. In the hyperlipidemia control group, the GPx level in Test-3 was noticeably lower ($p < 0.001$). The hyperlipidemia control group showed significantly decreased GSH levels ($p < 0.001$) in comparison to the normal group. By comparing the normal group to the standard group, a notable decrease was seen. Unlike the control group without hyperlipidemia, the hyperlipidemia control group exhibited a statistically significant rise in GSH levels ($p < 0.001$). In test-1, GSH levels were higher compared to the hyperlipidemia control group ($p < 0.001$). A control group with hyperlipidemia was used to compare GSH in Test-2. We observed a considerable increase in the GSH

level ($p < 0.001$). The final piece of evidence was a comparison of GSH levels between the control and normal groups. The GSH levels were discovered to be lower ($p < 0.001$).

The normal group showed significantly lower levels of malondialdehyde (MDA) compared to the hyperlipidemia control group ($p < 0.001$). The comparison between the normal and standard groups revealed a notable rise ($p < 0.001$). However, contrasted with the ordinary group, the control group with hyperlipidemia showed a significant reduction in MDA levels ($p < 0.001$). When compared to normal, the first test showed a significantly higher MDA level ($p < 0.001$). A significant decrease in MDA levels ($p < 0.001$) was observed in both the control and standard groups for hyperlipidemia. Researchers used MDA levels to compare the Test-2 and Normal groups. The results showed that MDA levels were considerably higher ($p < 0.001$) in the Test-2 group and considerably lower ($p < 0.001$) in the control group. Researchers compared the control groups and the test-3 group's MDA levels while the study was running. The levels of MDA were substantially greater in the test-3 group compared to the normal group ($p < 0.001$). Furthermore, the MDA levels of the test-3 group were contrasted with those of the control group for hyperlipidemia and the standard group. The test-3 group demonstrated a significant decrease in MDA levels ($p < 0.001$) when compared to the control group with hyperlipidemia and the standard group.

The results indicated that Test-1 showed the most antioxidant activity for SOD, GPx and MDA parameters, but showing the most significant result for GSH.

The data is presented as the average plus or minus the standard deviation ($n=6$). A one-way analysis of variance (ANOVA) and the Newman-Keuls multiple comparison test were used to analyse the data. $P < 0.05$, $P < 0.01$, and $P < 0.001$ were the representations used to illustrate the data. More specifically, in comparison to the Normal group, $dP < 0.05$, $eP < 0.01$ and $fP < 0.001$ were observed. Similar to the Hyperlipidemia control and Standard groups, we found $gP < 0.05$, $hP < 0.01$ and $iP < 0.001$ in comparison.

Table 6. Effect on antioxidant levels on liver tissue of Hyperlipidemic rats

Groups	SOD ($\mu\text{moles/mg}$ liver tissue)	GPx ($\mu\text{moles of GSH oxidized/min/mg liver tissue}$)	GSH ($\mu\text{moles/mg}$ liver tissue)	MDA ($\mu\text{moles/mg}$ liver tissue)
Normal	318 \pm 7.9	0.65 \pm 0.0069	0.63 \pm 0.019	24 \pm 1.5
Hyperlipidemia Control	203 \pm 5.6 ^c	0.55 \pm 0.020 ^c	0.35 \pm 0.026 ^c	97 \pm 2.0 ^c
Standard	242 \pm 3.8 ^{cf}	0.70 \pm 0.011 ^f	0.55 \pm 0.024 ^f	115 \pm 1.6 ^{cf}
Test-1	283 \pm 4.4 ^{cfi}	0.73 \pm 0.030 ^{af}	0.46 \pm 0.027 ^{ceg}	59 \pm 1.8 ^{cfi}
Test-2	208 \pm 4.5 ^{ci}	0.68 \pm 0.010 ^f	0.55 \pm 0.033 ^{bf}	94 \pm 1.5 ^{ci}
Test-3	264 \pm 3.3 ^{efi}	0.66 \pm 0.013 ^f	0.32 \pm 0.015 ^{ci}	66 \pm 1.7 ^{efi}

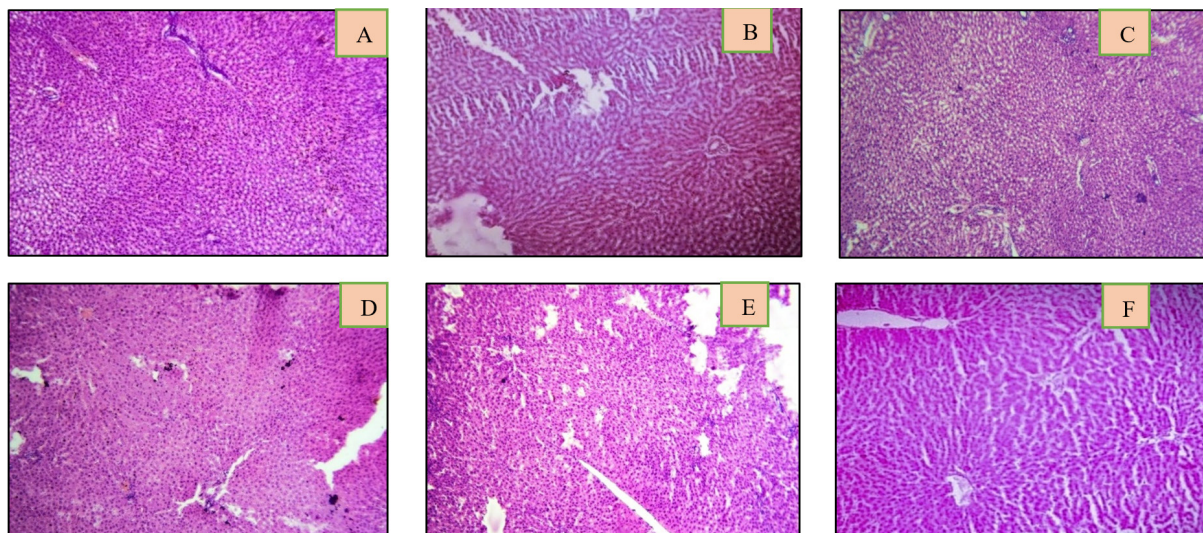


Figure 2. Effect of Leaves Extract of *R. sativus* in HFD Induced Experimental Rat's liver. [A] Effect of Leaves Extract of *R. sativus* on Liver of Normal Group. [B] Effect of Leaves Extract of *R. sativus* on Liver of Hyperlipidemia Control Group. [C] Effect of Leaves Extract of *R. sativus* on Liver of Standard Group. [D] Effect of Leaves Extract of *R. sativus* on Liver of Test-1 Group. [E] Effect of Leaves Extract of *R. sativus* on Liver of Test-2 Group. [F] Effect of Leaves Extract of *R. sativus* on Liver of Test-3 Group

3.6. Histological Studies

Figure 2 shows the results showing the effect of *Raphanus sativus* leaf extract on experimental rat livers caused by a high-fat diet. Pathological evaluation of liver tissue: The normal animal group does not have any anomalies in the structure of its liver cells, and it does not have any inflammatory cells that would indicate degeneration or inflammation.

Hepatic cell organization is more flexible in the hyperlipidemia control group compared to the normal group. There is also proof of infiltration and swollen degeneration. The standard group's liver cell organization is very similar to the control groups. Comparing the test-1 and test-2 groups, it seems that the cellular organization is normal. Nonetheless, when contrasted with the control group, the test-3 group has lower cell density. This could be a sign of inflammation or hepatocytic degeneration.

4. Discussion

The *R. sativus* (radish) leaf extract's LD50 result indicates that it is non-toxic and safe for up to 5000 mg/kg of ingestion [18]. Its pharmacological characteristics include antihypertensive effects in spontaneously hypertensive rats, generation of spasms in the ileum and colon of guinea pigs, and antioxidant and cytoprotective activities. Additionally, these leaves have certain advantageous medicinal qualities that could be applied as a useful anticancer drug that targets breast cancer in particular [13, 22, 25, 28]. In contrast, the earlier animal study demonstrated that *R. raphanistrum*, or *Raphanus sativus* var. *longipinnatus*, crude leaf extract, avoided obesity in rats [29]. The antihyperlipidemic qualities of *R.*

sativus leaves have not yet been demonstrated across the board in terms of antihyperlipidemic activity. Nonetheless, the preliminary phytochemical analysis conducted in this study provided insights into the chemical components present, such as amino acid compounds, phenols, and flavonoids, which have demonstrated effectiveness in hepatoprotective, antioxidant, and antihyperlipidemic effects [30-32]. Thus, the purpose of this study is to demonstrate the antihyperlipidemic effects of *Raphanus sativus* leaf extract in a high-fat situation that induces hyperlipidemia.

Because the HFD model is widely used and accepted for examining the effectiveness of antihyperlipidemic actions, it was selected for this purpose among the available models. It depicts the typical course of hyperlipidemia development in humans [35]. A secondary form of hyperlipidemia is brought on by HFD. Secondary hyperlipidemia subtype is a result of a metabolic disorder, an unbalanced diet, inadequate physical activity in daily life, and side effects from some medications.

Studies reveal that blood levels of low-density lipoprotein (LDL), very low-density lipoprotein (VLDL), triglycerides (TG), and total cholesterol (TC) increased significantly over the 28-day induction phase. Nonetheless, there was a significant drop in blood levels of high-density lipoprotein (HDL) [36]. In addition to elevated levels of serum lipid profile markers, hyperlipidemia is marked by elevated levels of SGOT, SGPT, and ROS, which are indications of liver function. In general, hyperlipidemia is characterized by elevated levels of total cholesterol [37, 38]. When levels of reactive oxygen species (ROS) increase, lipid peroxidation also increases. This indicates that antioxidant markers such as superoxide dismutase (SOD), glutathione (GSH), and glutathione peroxidase (GPx) are decreasing, while the lipid peroxidation

biomarker MDA is growing. Both glutathione (GSH) and superoxide dismutase (SOD) are examples of naturally occurring antioxidant enzymes that play a role in the detoxification process of potentially harmful oxygen radicals. The enzyme known as superoxide dismutase is responsible for the transformation of the radical superoxide (O_2^-) into two distinct forms: hydrogen peroxide (H_2O_2) and more conventional molecular oxygen (O_2) [39]. In addition to being able to neutralize free radicals such as alkoxy, hydrogen peroxide, and superoxide, glutathione is an essential biological antioxidant that does not require enzymes to function. Unscavenging free radicals is one of the functions that it performs. The accumulation of reactive oxygen species (ROS) to an excessive degree is the root cause of the cellular damage that is brought on by oxidation [40].

Degeneration of liver cells, also known as hepatocytic cells, has been demonstrated in a literature review as a consequence of any hyperlipidemic condition or the delivery of a high-fat diet for an extended period of time [41]. Through extended consumption of fructose, a condition known as macrovesicular and microvesicular steatosis can occur [42]. The current study found that when animals were given a high-fat diet for the first week, there was a significant decrease in their weight [43]. However, after that, there was a significant increase in their weight compared to the beginning of the study. The first test (100 mg/kg orally) and the second test (200 mg/kg orally) did not result in any weight loss during the course of the treatment period. However, during test 3, which was administered orally at a dosage of 300 milligrams per kilogram, a remarkable reduction in weight was observed as early as the 35th day of the experiment. As the dosage is increased, the effectiveness of the *R. sativus* leaf extract in causing weight loss remains the same.

Blood testing revealed that rats who were fed a diet lacking in fat had high blood lipids and low levels of HDL cholesterol. In a mouse with a high-fat diet, the administration of *R. sativus* leaf extract orally at a dose of 300 mg/kg resulted in a reduction in total cholesterol, total fat, LDL, and VLDL levels. At a dose of 200 milligrams per kilogram, the consumption of *R. sativus* leaf extract led to an increase in HDL levels. The oral administration of atorvastatin at a dose of 10 mg/kg was also a part of this study. The purpose of this was to analyse the effectiveness of the study extract in comparison to the effectiveness of conventional medication. The findings demonstrated that the presence of SGOT and SGPT in the blood of mice that were given fat was elevated. Following the oral administration of 100 mg/kg leaf extract in test-1 and 200 mg/kg leaf extract in test-2, respectively, there was a substantial reduction in the levels of SGOT and SGPT. Increased levels of SGOT and SGPT, on the other hand,

were shown to be connected with the negative effects of large dosages of crude extract. This suggests that these levels may be toxic or suggestive of hepatocyte degeneration or inflammation.

A high-fat diet was fed to rats, and the results showed that SOD, GPx, and Glutathione were all decreasing [44]. This suggests that the antioxidant defenses of the rats may have been less effective. A considerable increase in the levels of SOD and GPx, which are antioxidant markers, was observed in test-1 when 100 mg/kg of the leaf extract was supplied orally. This was the case when the leaf extract was delivered. Furthermore, in the instance of test-2, it was discovered that the levels of GSH were greatly enhanced (200 mg/kg orally). In the most effective manner, MDA levels were dramatically reduced when oral test-1 was administered at a dose of 100 mg/kg. Histopathology was used to examine samples of liver tissue, and the results showed that the animals in the control group did not exhibit any symptoms of cellular abnormalities or inflammatory cell infiltration into their liver tissues.

The hyperlipidemia control group exhibits less compact cell packing, infiltration, and ballooning degeneration than the normal group does. This is in comparison to the normal group. The normal group and the standard group are very similar in terms of their cellular organization, and there is very little difference between the two groups. This would suggest that the levels of cellular organization in both the test-1 and test-2 groups are within the usual range. In contrast to the group that served as the control, the test-3 group possesses a reduced cell density. Inflammation or hepatocytic degeneration could be the cause of this condition.

5. Conclusions

The leaf extract of *Raphanus sativus* was found to have hypolipidemic effects, as evidenced by the observation of hyperlipidemia in rats that were fed a diet high in fat. In order to obtain the desired results, it is necessary to decrease levels of low-density lipoprotein (LDL), total cholesterol, triglycerides, and very low-density lipoprotein (VLDL), while simultaneously boosting levels of high-density lipoprotein (HDL) cholesterol.

Conflict of Interest

We pronounce that we have no conflict of interest.

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