

Phytochemical Analysis and Assessment of the Antihyperlipidemic, Antihypertensive, Antidiabetic, and Anti-Inflammatory Activities of *Johrenia aromatica* in HFD-Induced Hyperlipidemic Male Albino Rats: Biochemical and Histopathological Evidence

Dr. Sachin T Jose

Assistant Professor, Department of Pharmacology, Institute of Medical Sciences and SUM Hospital,
Siksha O Anusandhan, Bhubaneswar, India

DOI: <https://doi.org/10.68050/JAMS.2026.785>

Received: 02 October 2026; Accepted: 12 October 2026; Published: 20 October 2026

ABSTRACT

Background: Hyperlipidemia is one of the most modifiable risk factors for cardiovascular disease and is often linked to obesity, hypertension, chronic inflammation, and metabolic dysfunction. While traditional lipid-lowering medications have proven effective, the incorporation of plant-based therapeutics with a favorable safety profile continues to rise.

Aim: The present study aimed to explore the phytochemical composition and pharmacologic effects of the hydroalcoholic extract of *Johrenia aromatica* (*J. aromatica*) in high-fat diet (HFD)-induced hyperlipidemic rats.

Methods: Gas chromatography–Mass Spectrometry (GC–MS) was used to characterize the extract of *J. aromatica*. Thirty male rats were randomly divided into 5 groups: the normal control group, HFD plus atorvastatin (10 mg/kg), HFD plus JA (400 mg/kg), HFD plus JA (600 mg/kg), and HFDG groups. Biomarkers of body weight, blood pressure, lipids, liver and renal function, blood glucose, C-reactive protein, and liver and kidney histopathology were assessed. Results: Sixteen phytochemical constituents were identified. *J. aromatica* treatment resulted in significantly lower serum total cholesterol, triglycerides, low-density lipoprotein, and very-low-density lipoprotein, together with lower body weight and serum C-reactive protein, than in the untreated HFD rats. The 600 mg/kg dose additionally lowered blood glucose. No treatment-related hepatic or renal injury was detected by the biochemical markers and histopathological examination performed.

Conclusion: *J. aromatica* had anti-hyperlipidemic and anti-inflammatory effects while preserving hepatic and renal safety in HFD-induced hyperlipidemic rats. These preliminary findings identify the extract as a candidate for further preclinical investigation in dyslipidemia and related metabolic disorders; its mechanism of action requires clarification before any clinical application can be considered.

Keywords: *Johrenia aromatica*, Dyslipidemia, traditional medicine, Phytochemicals, HFD-induced hyperlipidemia

INTRODUCTION

Hyperlipidemia or dyslipidemia (which can be used interchangeably) is an abnormal disorder characterized by the dysregulation of plasma lipids, including elevated plasma cholesterol, triglycerides (TG), and low-density lipoprotein (LDL), together with reduced high-density lipoprotein (HDL) (Durrington et al., 2026). The condition represents a disturbance of lipoprotein metabolism and carries a substantially increased risk of cardiovascular disease (CVD). It typically manifests as raised triglycerides, raised cholesterol, and an altered lipoprotein distribution, all of which favour atherogenesis and related lipid disorders. The clinically relevant plasma lipids are triglycerides and cholesterol, which serve as constituents of cell membranes (Nelson, 2012). According to a 2025 global systematic review and meta-analysis, the worldwide prevalence of hypercholesterolemia among adults was 24.1%, with the highest prevalence observed in Europe (37.1%),

followed by the Eastern Mediterranean (32.1%), the Americas (26.9%), the Western Pacific (22.0%), South-East Asia (18.3%), and Africa (15.9%)(Ballena-Caicedo et al., 2025).

Dyslipidemia is associated with risk factors, for example, a saturated or trans-fat diet, sedentary lifestyle, smoking, and overweight, which are causative factors in the development of dyslipidemia and exacerbate this disorder, increasing the risk for cardiovascular diseases and other lipid-related disorders. Dyslipidemia can be prevented by controlling the aforementioned risk factors (Gebreegziabiher et al., 2021). Dyslipidemia may result from changes in lipoprotein metabolism due to genetic, environmental, or other pathologic factors, thereby increasing the risk of cardiovascular disease (Ahmed et al., 2025b, Mosca et al., 2022). The common risk factors, such as insulin resistance, hypertension, obesity, and a sedentary lifestyle, play a crucial role in dyslipidemia during childhood (Sunil and Ashraf, 2020). Raised blood cholesterol is estimated to account for roughly one-third of all ischaemic heart disease, while dyslipidemia is held responsible worldwide for approximately 2.6 million deaths and 29.7 million disabilities annually, making it a considerable public health burden.

(Xing et al., 2020). According to reports, about 50–80% of hypertensives also have plasma lipid abnormalities; the combination of these two disorders increases the risk of coronary heart disease (Ayoade et al., 2020). Besides dyslipidemia, overweight is another risk factor for hypertension; therefore, an obese person with hyperlipidemia is more prone to hypertension than others (Tang et al., 2022). Obesity decreases the quality of life and increases mortality because it is a causative factor for other abnormalities such as hyperlipidemia, hypertension, diabetes, and CVD (Kim et al., 2021). According to studies, dyslipidemia not only contributes to the mentioned disorders but also exacerbates inflammation, autoimmune diseases, and atherosclerosis such as rheumatoid arthritis (Wang et al., 2020, Wilkinson and Shapiro, 2024). Inflammation may in turn accelerate the progression of arterial stiffness, so that inflammation and dyslipidemia are mutually reinforcing. Dyslipidemia itself can also trigger inflammatory responses, with C-reactive protein (CRP) considered a significant inflammatory marker in clinical practice (Aminuddin et al., 2020).

Moreover, dyslipidemia leads to complications in various organs, including the central nervous system, endocrine system, liver, and kidneys. The liver is closely involved in lipid metabolism. Abnormal lipid levels can alter liver metabolism and lead to hepatic tissue damage(Kathak et al., 2022). Controlling hyperlipidemia by both non-pharmacological and pharmacological means, using several classes of drugs, is therefore essential in order to reduce the risk factors described above (Ahmed et al., 2025a)Traditional herbal products have likewise been employed as adjuncts intended to improve therapeutic outcomes in specific diseases(Ahmed and Ahmed, 2025).

Many studies on natural products and complementary medicine have indicated that medicinal plants can reduce hyperlipidemia; on the other hand, some natural products, as adjuvant therapy, play significant roles alongside other antihyperlipidemic agents (Niknafs et al., 2021). Plants of the Apiaceae family are widely used therapeutically for a range of diseases; *Johrenia aromatica*, for example, is traditionally used to treat digestive and other disorders (Pieroni et al., 2016).

Although numerous medicinal plants have demonstrated antihyperlipidemic activity, the pharmacological effects of *J. aromatica* have not been adequately investigated in experimental hyperlipidemia. In particular, there is limited evidence regarding its effects on lipid metabolism, blood pressure, inflammatory markers, and histopathological alterations associated with hyperlipidemia. Furthermore, to the best of our knowledge, no previous study has comprehensively evaluated the antihyperlipidemic efficacy of *J. aromatica* extract using an experimental rat model while simultaneously assessing its biochemical, physiological, and histopathological effects.

J. aromatica is a plant belonging to the Apiaceae family and has been traditionally used in Kurdish and Middle Eastern folk medicine for the management of gastrointestinal disorders and other urinary tract infections. Phytochemical surveys within this family have repeatedly identified essential oils, terpenoids, flavonoids, coumarins, and phenolics among its constituents, and a considerable number of these compounds display antioxidant and anti-inflammatory activity.



Therefore, the present study was designed to investigate the antihyperlipidemic potential of *J. aromatica* hydroalcoholic extract in high-fat diet-induced hyperlipidemic rats. The study evaluated its effects on serum lipid profile, blood glucose, inflammatory biomarkers, liver and kidney function, systolic blood pressure, body weight, and histopathological changes, thereby providing new preclinical evidence supporting the therapeutic potential of this traditionally used medicinal plant.

MATERIALS AND METHODS

Plant materials:

Plant Collection and Extraction Procedure:

Fresh aerial parts of *J. aromatica* were collected between April and May of 2024 from the Sharbazhir district in the northern part of the KRG/Iraq.

After collection, the aerial parts were rinsed thoroughly to remove surface debris and left to dry in the shade at ambient temperature (25–30 °C) until a constant weight was reached; the dried material was then reduced to a coarse powder. A 1 kg portion of this powder was steeped in 1500 mL of an ethanol–water mixture (75:25, v/v) for at least 72 h with continuous agitation in a shaking incubator. The extraction procedure was performed using a conventional hydroalcoholic maceration method with minor modifications (Bharathi et al., 2025). The macerate was passed through Whatman No. 1 filter paper, and the filtration step was repeated several times. Pooled filtrates were evaporated to dryness under vacuum in a rotary evaporator, and the residue was lyophilised, yielding 93 g of dry extract that was kept in airtight containers at –20 °C until use, as illustrated in Diagram 1.

GC–MS Analysis of the Hydroalcoholic Extract

The phytochemical profile of the hydroalcoholic extract of *J. aromatica* was investigated using a Shimadzu GCMS-QP2010 Ultra gas chromatography-mass spectrometry (GC-MS) system equipped with an AOC-20i autosampler. An aliquot of the dried extract was reconstituted in HPLC-grade methanol and clarified through a 0.22 µm PTFE syringe filter before 1 µL was introduced into the instrument. Helium served as the mobile phase at a fixed flow of 1.69 mL/min, with the injection port held at 280 °C. Column temperature was programmed from 50

°C (5 min) to 100 °C at 50 °C/min (2 min hold) and finally to 280 °C at 9 °C/min, with a further 2 min hold. Detection was carried out under electron-impact ionisation, the ion source and interface being maintained at 200 °C and 280 °C, respectively, and spectra were acquired over m/z 50–800. Constituents were assigned by matching their fragmentation patterns against the NIST08 Mass Spectral Library. The relative abundance of each constituent was calculated from the percentage peak area of the total ion chromatogram. The identified compounds were considered tentative because they were assigned based on spectral library matching without confirmation using authentic reference standards. Instrumental operating conditions were those reported in the GC-MS method file, as shown in Diagram 1.

Animal experimental design:

Animal modeling:

The experimental process was conducted in accordance with the Research and Ethics Committee's animal care guidelines (Sert et al., 2020). Thirty male albino rats aged 8–10 weeks and weighing 180–250 g were allocated at random to five experimental groups ($n = 6$ per group), designated NC, ATOR-10, JA-400, JA-600, and HFDG. Owing to the nature of the experimental design, treatment administration was not blinded. The animals were accommodated in the animal research laboratory for a 5-day acclimatisation period under controlled conditions, namely a room temperature of 22–25 °C and a 12 h light / 12 h dark cycle, with food and water available ad libitum. The experiment commenced at the end of this period. Investigators responsible

for the biochemical measurements and histopathological evaluation were blinded to the group allocation to minimize assessment bias (Diagram 2).

Experimental Design

At baseline (Week 0), the blood pressure of every animal was recorded with the CODA monitor and body weight was measured. A blood sample was drawn at the same time by the retro-orbital route for baseline biochemical characterisation of the animals.

Hyperlipidemia was induced before the treatment phase by feeding the HFD to the ATOR-10, JA-400, JA-600, and HFDG groups for six weeks, while the NC group received the routine rat diet over the same period. At the end of Week 6, blood pressure and body weight were recorded and blood samples were collected again in order to confirm that hyperlipidemia and the associated biochemical changes had been established.

Following induction, the designated treatments or vehicle were administered once daily by oral gavage for 30 consecutive days. The HFD was continued in all hyperlipidemic rats, and the ATOR-10, JA-400, and JA-600 groups received their respective treatments once daily by oral gavage, whereas the HFDG continued to receive the HFD without active treatment. The normal control group received the standard laboratory diet throughout the experiment.

On the final day of the experiment the animals were deprived of food for approximately 18 h overnight while retaining free access to water. They were then anaesthetised with ketamine–xylazine, blood was withdrawn by cardiac puncture for biochemical measurement, and the animals were subsequently euthanised so that liver and kidney tissue could be harvested for histopathological examination.

Following induction, the treatment regimen was started as follows: (1) NC: Normal control group, received distilled water as vehicle daily; (2) ATOR-10: received HFD with Atorvastatin (10 mg/kg/day); (3) JA-400: HFD with *J. aromatica* (400 mg/kg/day); (4) JA-600: HFD with

J. aromatica (600 mg/kg/day); (5) HFDG: Received HFD and distilled water as vehicle daily.

The doses of *J. aromatica* extract (400 and 600 mg/kg body weight) were selected empirically based on their expected pharmacological activity and feasibility for repeated oral administration in rats. These doses fall within the range commonly used to evaluate the pharmacological activity of hydroalcoholic plant extracts in experimental rodents and were considered appropriate for repeated oral administration. This selection was guided by general recommendations for dose selection in preclinical herbal studies rather than by species-specific reports (Wojcikowski and Gobe, 2014) (Diagram 2).

Induction of Hyperlipidemia and Treatment Protocol:

All the animal groups except the normal control group were fed a high-fat diet (HFD) prepared by combining saturated fat with the routine diet (40% beef tallow, 20% casein, 25% sucrose, and 15% corn starch). The mixture was made up freshly each week to preserve its quality. (Kassab et al., 2025, Panchal and Brown, 2011)

Blood pressure measurement:

Blood pressure was recorded non-invasively by the volume–pressure recording method. Before testing, each rat was habituated to a nose-cone restrainer for 10–15 min per day on 3–5 consecutive days. On the day of measurement the animals were pre-warmed to 32–35 °C for 10–15 min so that the caudal artery dilated sufficiently. Two cuffs were then positioned at the base of the tail, a proximal occluding cuff and a distal volume–pressure sensing cuff. Using the CODA system, five habituation cycles were run before five recording cycles; any cycle affected by movement artefact, respiratory spikes, or an inadequate signal-to-noise ratio was discarded before the remaining readings were averaged (25) (Diagram 2) (Daugherty et al., 2009).

Biochemical Analysis

Serum was assayed for total cholesterol (TC), triglycerides (TG), low-density lipoprotein (LDL), high-density lipoprotein (HDL), and glucose, as well as for creatinine, urea, aspartate aminotransferase (AST), alanine aminotransferase (ALT), and alkaline phosphatase (ALP) as indicators of renal and hepatic function. All biochemical assays were performed at a controlled temperature of 37 °C to minimize error. Reagents were prepared according to the manufacturer's kit instructions. All analytes were measured with commercial rat-specific ELISA kits (Bioassay Technology Laboratory, Shanghai, China) exactly as specified by the supplier. In outline, serum and calibrators were dispensed into antibody-coated wells and incubated with the supplied detection reagents; unbound material was removed by repeated washing, colour was developed with the chromogenic substrate, and the reaction was terminated with the stop solution provided. Optical density was read at 450 nm on a microplate reader, and analyte concentrations were interpolated from the calibration curve constructed for each assay.

Histotechnique procedure and Semi-quantitative lesion scoring:

Liver and kidney specimens were immersed in 10% neutral-buffered formalin for 48 h and then transferred to cassettes labelled in solvent-resistant ink so that each sample remained identifiable throughout processing. Dehydration was achieved through an ascending ethanol series (70%, 90%, and 100%), followed by clearing in xylene and infiltration with paraffin. Embedded blocks were sectioned at 5 µm on a rotary microtome; the ribbons were floated on a 45 °C water bath, mounted on labelled slides, and held at 50 °C for 5 min to promote adhesion. Before staining, the sections were cleared of paraffin in xylene, taken down a descending ethanol series (100%, 90%, and 70%), and rinsed in distilled water.

Nuclear staining was carried out with Harris haematoxylin for 5–8 min, after which the sections were differentiated in 1% acid alcohol, blued in Scott's tap water substitute, and counterstained with 1% eosin Y. The stained sections were subsequently dehydrated in graded ethanol, cleared in xylene, and coverslipped permanently using DPX mountant. The prepared slides were air-dried before microscopic examination (Suvarna, 2024, Layton and Suvarna, 2013).

Semiquantitative histomorphometric analysis of kidney and liver tissues was performed on H&E-stained sections using a light microscope (HighTop, China) equipped with a digital microscope camera (SVPRO, China) for image acquisition. Morphometric measurements were conducted using AmScope software (USA) following prior calibration of the imaging system to ensure measurement accuracy.

For each parameter, measurements were obtained from five tissue sections per experimental group. Representative microscopic fields from each section were examined, and the mean value for each specimen was calculated. Group data were expressed as mean values and used for comparative analysis among the experimental groups (Kittel et al., 2004).

H&E-stained liver sections were examined under a light microscope at 40× magnification. Three parameters were evaluated: (1) hepatocyte nuclear count in the peripheral region of the hepatic lobule as an indicator of cellular integrity and viability; (2) hepatic steatosis, determined by measuring the area of intracellular fatty vacuoles around the central vein (µm²); and (3) hepatic inflammation, assessed by counting chronic inflammatory cells in periportal and perivascular regions. These measurements were used to quantify hepatocellular preservation, fat accumulation, and inflammatory activity, respectively.

H&E-stained kidney sections were examined under 40× magnification. Three histopathological parameters were evaluated: (1) mesangial cell proliferation, determined by counting hyperplastic mesangial cells surrounding glomerular capillary tufts as an indicator of glomerular injury; (2) tubular dilatation, assessed by measuring the area of dilated renal tubules (µm²) throughout the renal parenchyma; and (3) interstitial inflammation, quantified by counting inflammatory cells within the renal interstitium. These parameters were used to assess glomerular, tubular, and interstitial renal damage, respectively.

Statistical Analysis:

Data are presented as the mean $\pm$ standard deviation (SD). Statistical analyses were performed using IBM SPSS Statistics version 25 (IBM Corp., Armonk, NY, USA). One-way analysis of variance (ANOVA) followed by Tukey's post hoc test was used to compare differences among the experimental groups. A P-value < 0.05 was considered statistically significant.

Ethical approval:

This experimental study was approved by the ethical committee of the College of Medicine/University of Sulaimani, with reference number (No: 20; Date: 05/02/2024).

RESULTS

Phytochemical analysis:

Gas chromatography–mass spectrometry (GC–MS) analysis of the *J. aromatica* extract revealed the presence of sixteen phytochemical constituents with varying relative abundances (Table 1).

Among the detected constituents, 13-tetradecene-11-yn-1-ol was the predominant compound, accounting for 33.22% of the total peak area (retention time: 21.556 min). Other major constituents included hexadecanal (15.86%), cis-9,10-epoxyoctadecan-1-ol (14.04%), n-hexadecanoic acid (palmitic acid) (12.44%), tricyclo[20.8.0.0(7,16)]triacontane, 1(22),7(16)-diepoxy- (8.13% and 5.60%), and a second peak corresponding to 13-tetradecene-11-yn-1-ol (6.90%).

Minor constituents detected in the extract included 3,7,11,15-tetramethyl-2-hexadecen-1-ol (3.63% and 0.47%), hexadecanoic acid, 2,3-dihydroxypropyl ester (1.42%), 6,9,12-octadecatrien-1-ol (1.31%), E-2-tetradecen-1-ol (1.07%), 3 α ,5-cyclo-5 α -ergosta- derivative (0.95%), eicosanoic acid, tetradecyl ester (0.71%), 7-hexadecenoic acid, methyl ester (0.26%), and hexadecanoic acid, 15-methyl-, methyl ester (0.20%).

Overall, the GC–MS chromatogram demonstrated that the extract is rich in long-chain aliphatic compounds, including fatty acids, fatty alcohols, aldehydes, and terpenoid derivatives, with 13-tetradecene-11-yn-1-ol, hexadecanal, cis-9,10-epoxyoctadecan-1-ol, and n-hexadecanoic acid as the principal constituents.

Body weight changes

The Effect of HFD on Body Weight:

Following six weeks of HFD feeding, body weight increased in all groups, with the HFD group exhibiting the highest mean body weight (336.0 ± 21.7 g), whereas the JA-400 group showed the lowest mean body weight (280.0 ± 10.3 g) ($P = 0.002$).

At the end of 4 weeks of treatment (week 10), the rats in the HFD group continued to gain weight, reaching 345.0 ± 16.7 g, whereas those that were treated with atorvastatin (286.0 ± 24.0 g), JA-400 mg/kg (244.0 ± 10.3 g), and JA-600 mg/kg (262.0 ± 18.5 g) had comparatively lower final body weight. The body weight of the normal control group was 325.6 ± 14.7 g.

Body weight was measured at Weeks 0, 6, and 10 during the experimental period. Two-way repeated-measures ANOVA demonstrated a significant effect of time ($F = 70.482$, $P < 0.001$), a significant effect of treatment group ($F = 10.197$, $P < 0.001$), and a significant time $\times$ treatment interaction ($F = 4.328$, $P = 0.005$). Body weight increased progressively in the HFD group throughout the study, whereas rats treated with atorvastatin, *J. aromatica* 400 mg/kg, and *J. aromatica* 600 mg/kg exhibited lower body weights during the treatment period, particularly at Week 10, as shown in Table 2

Effect of HFD on biochemicals in rats at week 6:

Before initiating treatment, the biochemical parameters of the experimental animals after six weeks of HFD feeding are presented in Table 3. Significant alterations in the lipid profile were observed between the normal control and HFD-fed groups. TC, TG, HDL, LDL, and VLDL were significantly elevated in all HFD-fed groups compared with the normal control ($P < 0.05$), indicating successful induction of hyperlipidemia prior to treatment.

Regarding liver function biomarkers, serum ALT and ALP activities were significantly higher in all HFD-fed groups than in the normal control ($P < 0.05$). In contrast, no significant difference was observed in AST levels among the experimental groups ($P > 0.05$).

Renal function biomarkers, including serum urea and creatinine, showed no significant differences between the normal control and HFD-fed groups ($P > 0.05$), suggesting that six weeks of HFD feeding had not produced detectable renal dysfunction.

Similarly, fasting blood glucose levels did not differ significantly among the groups ($P > 0.05$). However, CRP concentrations were significantly higher in all HFD-fed groups than in the normal control ($P < 0.05$), indicating the development of systemic inflammation following HFD feeding.

Overall, these findings confirmed that six weeks of HFD feeding successfully established a hyperlipidemic state accompanied by elevated inflammatory and selected hepatic biomarkers before initiation of the treatment phase.

Effect of HFD on blood pressure in rats at week 6:

The effects of a six-week HFD on blood pressure and heart rate are presented in Table 4. No significant differences were observed among the experimental groups in systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial blood pressure (mABP), or heart rate (HR) ($P > 0.05$).

The mean SBP ranged from 98.4 ± 5.2 mmHg in the normal control group to 106.0 ± 5.8 mmHg in the JA-600 group. Likewise, DBP values ranged from 75.0 ± 6.4 mmHg to 79.0 ± 14.5 mmHg, while mABP ranged from 81.8 ± 2.8 mmHg to 86.0 ± 6.1 mmHg. Heart rate remained comparable among all groups, ranging from 366.2 ± 7.5 bpm in the normal control group to 381.1 ± 28.9 bpm in the JA-600 group.

Overall, six weeks of HFD feeding did not induce significant alterations in blood pressure or heart rate, indicating that hypertension had not yet developed at this stage of the experimental protocol.

Effect of the different regimens of treatment on the biochemicals at week 10:

The effects of atorvastatin and *J. aromatica* treatment on the biochemical parameters of hyperlipidemic rats after four weeks of treatment (week 10) are summarized in Table 5.

Lipid profile:

Treatment significantly improved the serum lipid profile compared with the untreated HFD group. TC was markedly reduced in the atorvastatin-, JA-400-, and JA-600-treated groups, with values comparable to those of the normal control ($P < 0.05$). Similarly, TG concentrations were markedly lower in the treatment groups than in the untreated HFD group, although greater variability was observed in the *J. aromatica*-treated groups. HDL concentrations did not differ significantly among the experimental groups ($P > 0.05$). LDL levels were significantly decreased following atorvastatin treatment and were also reduced in both JA-treated groups compared with the HFD group. Likewise, VLDL concentrations were significantly elevated in the untreated HFD group, whereas treatment with atorvastatin and *J. aromatica* reduced VLDL levels toward normal values.

Liver enzymes:

Serum AST activity remained significantly higher in the untreated HFD group than in the normal control, whereas both doses of *J. aromatica* reduced AST activity, with values comparable to those of the normal control. ALT activity was significantly elevated in the atorvastatin and HFD groups compared with the normal control, while JA-400 restored ALT to near-normal levels. Although JA-600 also reduced ALT activity, greater variability resulted in no statistically significant difference from either the normal control or HFD group. ALP activity was markedly increased in the untreated HFD and atorvastatin groups. Treatment with *J. aromatica*, particularly at 400 mg/kg, significantly reduced ALP activity compared with the untreated HFD group.

Renal function test:

Serum urea concentrations differed significantly among groups. The untreated HFD group exhibited lower urea levels than the normal control, while treatment groups showed values comparable to those of the normal control. Serum creatinine levels remained within a narrow range across all experimental groups, although the JA-400 and JA-600 groups exhibited significantly lower creatinine concentrations than the atorvastatin group.

Hypoglycemic effect:

Blood glucose concentrations were significantly reduced only in the JA-600 group compared with the other experimental groups ($P < 0.05$), indicating a pronounced antihyperglycemic effect at the higher dose. In contrast, blood glucose levels in the atorvastatin, JA-400, and untreated HFD groups remained comparable to those of the normal control.

Inflammatory biomarkers:

Serum CRP was significantly elevated in the untreated HFD group. Treatment with atorvastatin and both doses of *J. aromatica* significantly reduced CRP concentrations to levels comparable with those of the normal control.

Effect of *J. aromatica* on blood pressure at week 10:

The effects of atorvastatin and *J. aromatica* on blood pressure and heart rate are presented in Table 6.

The untreated HFD group showed a significantly greater SBP than the normal control ($P < 0.05$). JA-400 significantly reduced SBP compared with the HFD group ($P < 0.05$) and brought it close to the normal control, whereas JA-600 produced a moderate reduction ($P < 0.05$).

Atorvastatin also lowered SBP ($P < 0.05$), but the value remained significantly higher than that of the normal control ($P < 0.05$).

DBP was significantly elevated in the HFD and atorvastatin groups compared with the normal control ($P < 0.05$). JA-400 produced the greatest reduction in DBP ($P < 0.05$), while JA-600 restored DBP to values comparable with the normal control.

mABP was significantly increased in the HFD group ($P < 0.05$). Both doses of *J. aromatica* reduced mABP significantly ($P < 0.05$), with JA-400 showing the greatest improvement and values comparable with the normal control.

Heart rate was significantly higher in the HFD group than in the normal control ($P < 0.05$). Treatment with atorvastatin and *J. aromatica* reduced heart rate significantly ($P < 0.05$), with JA-600 and atorvastatin restoring values comparable with the normal control.

Histopathological results of the effect of J. aromatica:

Hepatic Tissue

Normal liver architecture was seen in the normal group with no identifiable lesions (score 0) on histopathology examination of the liver tissue. The HFD group showed significant steatosis, evidenced by a much higher number of fatty deposits in the intracellular space and a mean fatty deposit area of $2.58 \mu\text{m}^2$ (score 3). Treatment resulted in decreased lipid deposition in the liver, and the mean fatty deposit areas in the low- and high-dose groups were $1.03 \mu\text{m}^2$ and $1.63 \mu\text{m}^2$, respectively, representing mild (score 1) and moderate (score 2) steatosis. In the atorvastatin-treated group, the mean fatty deposit area was $2.00 \mu\text{m}^2$ (score 3), indicating persistent severe fatty changes. The differences among all groups were statistically significant ($P < 0.001$).

Hepatic inflammation was assessed; there was no inflammatory cell infiltration in the normal group (score 0), and severe inflammation in the HFD group with a mean value of 57.4 chronic inflammatory cells per $40\times$ field (score 3). There was a significant decrease in inflammatory infiltration in both treatment groups, with the mean number of inflammatory cells found per field being 13.2 and 18.0 for the low and high doses, respectively, which is considered mild inflammation (score 1). The atorvastatin group had a score of 2, which corresponds to moderate inflammation (22.2 cells/field). The differences among groups were highly significant ($P < 0.001$), indicating substantial reductions in hepatic inflammatory activity after treatment.

Evaluation of hepatic necrosis was carried out by the number of hepatocyte nuclei in representative microscopic fields, with more nuclei indicating more cell viability. The normal group had a mean of 32.6 nuclei per field, with no necrosis (necrosis score 0), whereas the HFD group had a significant reduction to 8.4 nuclei per field, indicative of severe necrosis (score 3). The low-dose and high-dose treatment groups had mean nuclear counts of 17.3 and 13.0 nuclei per field (mild and moderate necrotic changes, respectively). The atorvastatin group, however, had a mean of 9.2 nuclei/field (score 3), suggesting that there was still more severe necrosis. Statistical analysis revealed a highly significant difference among the groups ($P < 0.001$). In general, the treatments reduced HFD-induced histopathological changes in the liver, with the low-dose treatment providing the greatest protection. The data collected have been summarized in Table 7 with the help of the respective micrographs (1, 2, and 3).

Renal Tissue

Mesangial cell proliferation was used to assess glomerular injury. The normal group showed normal renal histology with a mean mesangial cell count of 16.20 (score 0), whereas the HFD group exhibited marked mesangial hyperplasia (42.60; score 3; $p < 0.001$). Both low- and high-dose treatments significantly reduced mesangial proliferation to 27.60 and 25.40 cells, respectively (score 2), with no significant difference between them. The atorvastatin group also showed improvement (36.40; score 2) but remained significantly different from the normal and treatment groups ($p < 0.001$).

Tubular dilatation was evaluated by measuring the tubular area. The normal group showed intact tubular morphology ($1.58 \mu\text{m}^2$; score 0), while the HFD group exhibited severe tubular injury ($4.44 \mu\text{m}^2$; score 3; $p < 0.001$). Both low- and high-dose treatments restored tubular architecture to near-normal values (1.54 and $1.53 \mu\text{m}^2$; score 0), with no significant difference between them. The atorvastatin group showed partial improvement ($2.20 \mu\text{m}^2$; score 1) but remained significantly different from the normal and treatment groups ($p < 0.001$). Interstitial inflammatory cell infiltration was absent in the normal group (score 0) but markedly increased in the HFD group (32.60 cells; score 3; $p < 0.001$). The low-dose group showed mild inflammation (4.00 cells; score 1), whereas the high-dose group demonstrated complete restoration of normal histology with no detectable inflammatory infiltration (score 0). The atorvastatin group exhibited moderate inflammation (12.80 cells; score 2), indicating partial improvement compared with the HFD group. Overall, significant differences were observed among the experimental groups ($p < 0.05$ – 0.001), demonstrating substantial renoprotective effects of the treatments. All obtained results, along with their statistically significant differences among experimental groups, are summarized in Table 8 and further demonstrated in the representative photomicrographs (Figures 4 and 5).



DISCUSSION

The present study provides the first comprehensive preclinical evaluation of the hydroalcoholic extract of *J. aromatica* in an HFD-induced hyperlipidemic rat model. To our knowledge, this is also the first study to combine phytochemical characterization using GC–MS with biochemical, physiological, and histopathological assessments to investigate the antihyperlipidemic potential of this traditionally used medicinal plant. The findings demonstrate that *J. aromatica* exerted beneficial effects on multiple metabolic abnormalities associated with HFD-induced hyperlipidemia. In particular, treatment improved serum lipid parameters, inhibited body weight gain, reduced systemic inflammation, and preserved normal blood pressure, without evidence of histopathological and biochemical hepatotoxicity or nephrotoxicity.

Several of the identified compounds have previously been associated with antioxidant and anti-inflammatory activities, which may contribute to the antihyperlipidemic effects observed in the present study. In particular, n-hexadecanoic acid (palmitic acid), 13-tetradecene-11-yn-1-ol has been reported in numerous medicinal plants and exhibits anti-inflammatory and antioxidant properties, while oxygenated fatty alcohols and epoxy derivatives have been suggested to protect against oxidative damage by reducing lipid peroxidation and preserving cellular membrane integrity (Aparna et al., 2012, Ghfil et al., 2025, Li et al., 2023, Thiviya et al., 2022). Since oxidative stress and chronic inflammation are major contributors to hyperlipidemia, the combined actions of these phytochemicals may underlie the protective effects of *J. aromatica*.

Previous phytochemical investigations of species belonging to the Apiaceae family have consistently demonstrated the presence of terpenoids, coumarins, polyacetylenes, fatty acids, and phytosterols, many of which exhibit antioxidant and lipid-lowering activities. Several studies on *Johrenia* and closely related genera such as *Ferulago*, *Ferula*, and *Hellenocarum* have reported essential oils rich in monoterpenes and sesquiterpenes (Sousa et al., 2021). In contrast, the current GC-MS analysis of the hydroalcoholic extract identified predominantly fatty acid derivatives and oxygenated long-chain hydrocarbons.

A number of these active compounds have a therapeutic value, such as 3,7,11,15-Tetramethyl-2-hexadecen-1-ol (Phytol), which has antimicrobial, anti-inflammatory, and antidiabetic properties, as well as anti-obesity, cholesterol-lowering, and anti-atherosclerotic activity (Afolayan et al., 2024, Islam et al., 2018). Hexadecanoic acid, 15-methyl-, methyl ester displays antibacterial activity against multidrug-resistant (MDR) bacteria (36). (Shaaban et al., 2021) Hexadecanal has a role in the modulation of aggression and social behavior and is a potential biomarker for preeclampsia diagnosis and risk assessment (Mishor et al., 2021, Pehlić et al., 2024). The extract also contains constituents for which no pharmacological activity has so far been reported.

Treatment with the *J. aromatica* extract produced a significant improvement in the lipid profile without any detectable adverse effect on the liver or kidneys. These results should nevertheless be interpreted with caution, since potential confounders such as the small sample size and variability in dosing compliance may have influenced the outcome.

Hyperlipidemia was successfully induced in the rats after six weeks of HFD feeding, as evidenced by increased TC, TG, and VLDL concentrations. The findings are in line with Kumar et al. (2020) (Kumar et al., 2020), who showed that chronic HFD feeding resulted in dyslipidemia by disrupting lipid metabolism in rats.

Body weight changed in all experimental groups over the four weeks of treatment; however, weight gain was significantly greater in the normal control (NC) and HFD groups than in the treated groups. The current observation is consistent with Lozano et al. (2016) (Lozano et al., 2016), who found that chronic HFD feeding leads to body weight gain, which is driven by a higher adiposity and metabolic dysfunction.

After the treatment period, the ATOR-10, JA-400, and JA-600 groups all showed a fall in body weight relative to their Week 6 values, the largest reduction occurring in the *J. aromatica*-treated groups. Based on these results, *J. aromatica* could be beneficial to body weight regulation in high-fat diet-induced hyperlipidemic rats. This observed decrease in body weight could be related to the regulation of energy homeostasis, the modulation of fat accumulation, or lipid metabolism (Chang et al., 2023). The exact mechanism of action is not



yet known, but these results suggest that *J. aromatica* could be effective in lowering blood lipids as well as a complementary treatment for body weight management. However, additional mechanistic investigations are needed to understand the routes by which these impacts occur.

The present study showed that *J. aromatica* effectively lowered the level of TC, TG, LDL, and VLDL in hyperlipidemic rats fed the HFD, and did not significantly change the level of HDL. The present results suggest that *J. aromatica* was able to improve lipid abnormalities that develop in HFD and could maintain HDL protection. The precise mechanism of antihyperlipidemic activity of *J. aromatica* is unknown, but we speculate that different chemical components of *J. aromatica* may exert these effects in different ways. This was in conformity with another study by Latifi et al. 2019(Latifi et al., 2019), which found similar hypoglycemic and hypolipidemic effects in another species of the same family of this herb, indicating a possible common action within the family.

In earlier studies, phytol has been shown to have a beneficial effect on lipid metabolism due to its antioxidant properties and ability to inhibit lipid peroxidation, as well as the modulation of lipid-regulating pathways such as peroxisome proliferator-activated receptors (PPARs), which play a major role in the regulation of cholesterol and fatty acids. Therefore, the observed drop in serum total cholesterol, triglycerides, LDL, and VLDL levels in the *J. aromatica* extract supplementation may be attributed to the phytol content in the extract(Spanoudaki et al., 2024). In terms of liver function, serum AST activity did not differ significantly after six weeks of HFD feeding, whereas ALT and ALP activities were significantly elevated. These results indicate that the duration of HFD exposure was sufficient to induce early changes in hepatic metabolism and biliary function, but not to cause significant hepatocellular damage. This has been noted by Brahmi et al (2021) in experimental models of diet-induced hyperlipidemia and hyperlipoproteinemia, when the rise in ALP is followed by significant increases in the activity of the aminotransferases(Brahmi et al., 2021).

Following the treatment period, administration of *J. aromatica*, particularly at the 400 mg/kg dose, significantly improved hepatic biochemical parameters, as evidenced by histopathological data and reductions in ALT and ALP levels toward those of the normal control group, while AST remained within the physiological range. These findings indicate that

J. aromatica exerted a hepatoprotective effect against HFD-induced hepatic dysfunction. The greater efficacy observed at the lower dose may reflect the complex pharmacodynamics of herbal extracts, in which multiple bioactive constituents interact synergistically or antagonistically, resulting in a non-linear dose–response relationship (Ashraf et al., 2020, Pasavei et al., 2020). The exact mechanism of action is unclear, but enhancement of hepatic lipid metabolism and reduction of inflammatory responses may have contributed to the normalization of liver enzyme activities observed in the treated animals (Gupta et al., 2019)

The biochemical findings were corroborated by the histopathological evaluation, which demonstrated preservation of hepatic architecture and attenuation of steatosis and inflammatory cell infiltration in the *J. aromatica*-treated groups compared with the untreated HFD group. The biochemical and histological results showed good agreement, thus highlighting the possibility that the extract was hepatoprotective rather than hepatotoxic. However, further mechanistic investigations are recommended to ascertain the main bioactive molecules responsible for these effects and to clarify the molecular pathways underlying the hepatoprotective effect of *J. aromatica*. From a renal perspective, there were no differences in urea or creatinine levels in plasma after 6 weeks of feeding with HFD, suggesting that the dietary regimen did not cause evident renal damage. The results are similar to the findings of Amin et al. (2014) (Amin et al., 2014), who also reported no notable alterations in renal function biomarkers under similar experimental conditions.

After initiation of the treatment regimen, notable changes were observed in both urea and creatinine levels in some groups, while histopathological results remained unchanged. However, renal biomarkers in all groups remained within the normal range observed in the NC group, suggesting no substantial renal impairment. The current result agrees with the findings of Moharrad, S. (2020)(Mojarrad, 2020), which showed results similar to those of other species in the same family and further supports the safety of the treatments.



Regarding blood glucose, after administration of HFD, there was no significant change that could be noted; this finding agrees with the finding of Lozano, I. et al. (2016) (Lozano et al., 2016), which reported an unchanged blood glucose level after HFD feeding under comparable conditions. With continued HFD administration, however, blood glucose rose across all groups, including the normal control group. This observation is consistent with the findings of Qi et al (2023)(Qi and Wang, 2023), who also reported elevated blood glucose levels in similar experimental conditions. Conversely, the group of rats that received a high dose of *J. aromatica* exhibited only a slight elevation in blood glucose levels compared to the other groups. This finding suggests that *J. aromatica* may also exert an antihyperglycemic effect.

Regarding inflammatory biomarkers, after six weeks of HFD feeding, CRP levels were significantly elevated in the experimental rats. This finding is consistent with the results reported by Kalsait, R. et al. (2011)(Kalsait et al., 2011), who similarly noted an increase in CRP following administration of an HFD.

After initiation of treatment, CRP levels continued to rise in the NC group, whereas reductions were observed in all hyperlipidemic groups, particularly in the group receiving atorvastatin. These results are consistent with those of Huang, C, et al. (2014)(Huang et al., 2014), who likewise reported a reduction in CRP levels following atorvastatin treatment. Notably, both doses of *J. aromatica* also significantly reduced serum CRP levels compared with the untreated HFD group, suggesting that the extract may attenuate HFD-induced systemic inflammation. This anti-inflammatory effect may be attributed to the antioxidant and anti-inflammatory phytochemicals identified by GC–MS analysis, particularly phytol, which has been reported to suppress oxidative stress and inflammatory signaling pathways(Carvalho et al., 2020). These findings indicate that *J. aromatica* may exert anti-inflammatory activity in addition to its antihyperlipidemic effects; however, further mechanistic studies are required to elucidate the underlying molecular pathways.

Regarding blood pressure, after six weeks of HFD feeding, blood pressure remained stable across all rat groups, with no significant change observed. This finding disagrees with the results reported by Islamiana, D. (2021)(Islamiana et al., 2021), who noted significant alterations in blood pressure following similar dietary interventions.

After four weeks of different treatment regimens in hyperlipidemic rats, both systolic and diastolic blood pressure increased significantly in the ATOR-10 and HFDG groups; these results align with the findings of Nemoto, T. (2020)(Nemoto et al., 2020), who suggested that hypertension in HFD-exposed rat models may be associated with elevated corticosterone levels, contributing to the observed blood pressure change. Meanwhile, systolic and diastolic blood pressure in the groups receiving either dose of *J. aromatica* remained unchanged and within the normal range, comparable with the NC group. This suggests that *J. aromatica* may inhibit the elevation of blood pressure. However, to confirm these findings, further studies are necessary.

CONCLUSION

This study is the first effort to comprehensively demonstrate the antihyperlipidemic potential of the hydroalcoholic extract of *Johrenia aromatica* in a high-fat diet-induced rat model. GC–MS profiling showed the extract to be phytochemically diverse, containing several bioactive compounds that may act collectively. Treatment with *J. aromatica* significantly improved the lipid profile and systemic inflammation, reduced body weight gain, and maintained normal blood pressure values, in addition to attenuating histopathological changes in the liver and kidney, with no evidence of hepatic or renal injury within the parameters examined; a comprehensive toxicity evaluation was not performed. The results of this study support the traditional medicinal applications of *J. aromatica* and indicate that it merits further preclinical evaluation as a source of bioactive compounds of potential relevance to dyslipidemia and related metabolic disorders. However, the active components and the molecular mechanisms have yet to be elucidated. Standardization of the extract, phytochemical profiling of the compounds, mechanistic studies, dose–response studies, pharmacokinetic profiling, and well-designed clinical trials would be useful in supporting translatability.

LIMITATION

This study has some limitations. First, the number of rats in the sample was small, and only males were used in

the study, which may restrict the generalizability of the results. Second, the doses of *J. aromatica* were selected empirically because no dose-optimisation studies are available. Third, the molecular mechanism/s of the observed antihyperlipidemic and anti-inflammatory effects were not explored. Fourth, the extract was not standardised and no comprehensive toxicity evaluation was undertaken, so the present data cannot be used to establish safety. Lastly, the short treatment period and reliance on a single animal model restrict the clinical applicability of the results. Further research is needed to evaluate the dose–response, to conduct mechanistic studies, to use standardized extracts, to explore long-term safety, and to validate the extracts in clinical studies.

RECOMMENDATION

Based on the current results, it is recommended that further studies be conducted to (1) investigate the molecular mechanisms responsible for the antihyperlipidemic and anti-inflammatory properties of *J. aromatica*, (2) conduct dose–response, pharmacokinetic and long-term toxicity studies to determine optimal therapeutic doses and safety of *J. aromatica* in humans, (3) standardise the extract by identification of and quantification of its major bioactive constituents and (4) validate the present findings in well-designed clinical trials to establish its efficacy and safety in patients with dyslipidaemia

Funding

This research received no specific grant.

Authors' contributions

F.N.A: Conceptualization, methodology, investigation, animal experimentation, data collection, formal analysis, and writing original draft. E.S.H.: Methodology, animal experimentation, and writing review and editing. H.A.S.: Phytochemical analysis, methodology, animal experimentation, and writing original draft. K.T.M.: Writing original draft, data interpretation, and methodology. M.A.S.: Histopathological investigation, Formal statistical analysis, data interpretation, and writing review and editing. All authors reviewed the manuscript carefully and approved the published version of the draft.

Conflict of interest

The authors declare that there is no conflict of interest.

Data availability

All data supporting the findings of this study are available within the manuscript.

REFERENCES

1. Afolayan, f. I. D., odayemi, r. A. & salaam, r. A. 2024. In silico and in vivo evaluations of multistage antiplasmodial potency and toxicity profiling of n-hexadecanoic acid derived from *vernonia amygdalina*. *Front pharmacol*, 15, 1445905.
2. Ahmed, f. N., jaff, s. & mohammed, g. A. 2025a. Anti-hyperlipidemic effect of statins and the role of nanomedicine in enhancing their bioactivity: a narrative review. *Journal of sulaimani medical college*, 15, 1-11.
3. Ahmed, f. N., mohammed, h. H., mohammed, g. A. & rahim, m.-o. M. 2025b. Hyperlipidemia and its systemic effects: molecular mechanisms, clinical consequences, and therapeutic approaches: a narrative review. *Journal of sulaimani medical college*, 15, 71-88.
4. Ahmed, s. F. & ahmed, f. N. 2025. Antibacterial activity of celery (*apium graveolens*) extract against urinary tract infections. *Al-mustansiriyyah journal for pharmaceutical sciences*, 25. Amin, k. A., sana'a, r. G., wala'a, g. H. & shima'a, m. R. 2014. Effects of orlistat and herbal mixture extract on renal function and oxidative stress biomarkers in a rat model of high fat diet. *International journal of biochemistry research & review*, 4, 173.



5. Aminuddin, a., lazim, m. R. M., hamid, a. A., hui, c. K., mohd yunus, m. H., kumar, j. & ugusman, a. 2020. The association between inflammation and pulse wave velocity in dyslipidemia: an evidence-based review. *Mediators of inflammation*, 2020.
6. Aparna, v., dileep, k. V., mandal, p. K., karthe, p., sadasivan, c. & haridas, m. 2012. Anti-inflammatory property of n-hexadecanoic acid: structural evidence and kinetic assessment. *Chem biol drug des*, 80, 434-9.
7. Ashraf, j., khan, m. A., minhaj, s., khatti, s., aarij, k. M., shehzad, m., khan, t. M. & khan, m. A. 2020. Statins and abnormal liver function tests: is there a correlation? *Cureus*, 12.
8. Ayoade, o. G., umoh, i. & amadi, c. 2020. Dyslipidemia and associated risk factors among nigerians with hypertension. *Dubai medical journal*, 3, 155-161.
9. Ballena-caicedo, j., zuzunaga-montoya, f. E., loayza-castro, j. A., vásquez-romero, l. E. M., tapia-limonchi, r., de carrillo, c. I. G. & vera-ponce, v. J. 2025. Global prevalence of dyslipidemias in the general adult population: a systematic review and meta-analysis. *J health popul nutr*, 44, 308.
10. Bharathi, r., prasanna, k., krishna, b. D., kariyil, b., krithiga, k. & dinesh, c. 2025. Study on the extraction yield of hydroethanolic extracts of medicinal plants using the cold maceration method. *International journal of research in agronomy*, 8, 156-162.
11. Brahmi, n., feriani, a., ben ali, m., hedfi, a., elleuch, a., ismail, i., albogami, b., saif, t., talarmin, h. & el feki, a. 2021. Potential hepatoprotective effect of *Cheatomorpha gracilis* extract against high fat diet (hfd)-induced liver damage, and its characterization by hplc. *Brazilian journal of biology*, 82.
12. Carvalho, a., heimfarth, l., pereira, e., oliveira, f., de menezes, i. R., coutinho, h., picot, l., antoniolli, a., quintans, j. & quintans-júnior, l. 2020. Phytol, a chlorophyll component, produces antihyperalgesic, anti-inflammatory, and antiarthritic effects: possible nfkb pathway involvement and reduced levels of the proinflammatory cytokines $\text{tnf-}\alpha$ and il-6 . *Journal of natural products*, 83.
13. Chang, y. B., ahn, y., seo, d., bae, s., suh, h. J., hong, y. H. & jung, e. Y. 2023. *Centella asiatica* lowers body fat accumulation via regulating cholesterol homeostasis- and lipid metabolism-related genes in mice with high-fat, high-sugar diet-induced obesity. *Applied biological chemistry*, 66, 88.
14. Daugherty, a., rateri, d., hong, l. & balakrishnan, a. 2009. Measuring blood pressure in mice using volume pressure recording, a tail-cuff method. *J vis exp*.
15. Durrington, p., bashir, b. & soran, h. 2026. Hyperlipidemia. *Metabolism of human diseases: organ physiology and pathophysiology*. Springer.
16. Gebreegziabiher, g., belachew, t., mehari, k. & tamiru, d. 2021. Prevalence of dyslipidemia and associated risk factors among adult residents of mekelle city, northern ethiopia. *Plos one*, 16, e0243103.
17. Ghfil, z., aboalhur, f. J., mshachal, m. A. & alobaidi, a. A. A. 2025. Antioxdent, antifungal activities of n-hexadecanoic acid extracted from algae. *South asian research journal of pharmaceutical sciences*, 7, 125-127.
18. Gupta, k., taj, t., thansiya, b. & kamath, j. 2019. Pre-clinical evaluation of hepatoprotective activity of phytol in wistar albino rats. *Ip international journal of comprehensive and advanced pharmacology*, 4, 17-20.
19. Huang, c., cen, c., wang, c., zhan, h. & ding, x. 2014. Synergistic effects of colchicine combined with atorvastatin in rats with hyperlipidemia. *Lipids in health and disease*, 13, 1-6.
20. Islam, m. T., ali, e. S., uddin, s. J., shaw, s., islam, m. A., ahmed, m. I., chandra shill, m., karmakar, u. K., yarla, n. S., khan, i. N., billah, m. M., pieczynska, m. D., zengin, g., malainer, c., nicoletti, f., gulei, d., berindan-neagoe, i., apostolov, a., banach, m., yeung, W. K., el-demerdash, a., xiao, j., dey, p., yele, s., jóźwik, a., strzałkowska, n., marchewka, j., rengasamy, k. R. R., horbańczuk, j., kamal, m. A., mubarak, m. S., mishra, s. K., shilpi, j. A. & atanasov, a. G. 2018. Phytol: a review of biomedical activities. *Food chem toxicol*, 121, 82-94.
21. Islamiana, d., rafsanjani, i. S., pramaningtyas, m. D. & fauziyati, a. Effect of high-fat diet on systolic blood pressure in stz-induced diabetic adolescent sprague dawley rats. 4th international conference on sustainable innovation 2020–health science and nursing (icosihsn 2020), 2021. Atlantis press, 69-74.
22. Kalsait, r., khedekar, p., saoji, a. & bhusari, k. 2011. Role of c-reactive protein in the development of atherosclerosis in diet-induced lipidemia in albino rats. *Tropical journal of pharmaceutical research*, 10, 41-45.

23. Kassab, d. Y., sheeba, d., r, g., searan, w., abdalqader, m., kayarohanam, s., jamal, i., kumar janakiraman, a., soutallu janakiram, m. K. & bhupathyraaj, m. 2025. Evaluation of antihyperlipidemic activity of leaf extracts of *rivea hypocrateriformis* (desr.) In high-fat diet-induced hyperlipidemia rat model with focus on gene expression. *International journal of nutrition, pharmacology, neurological diseases*, 15, 82-91.
24. Kathak, r. R., sumon, a. H., molla, n. H., hasan, m., miah, r., tuba, h. R., habib, a. & ali, n. 2022. The association between elevated lipid profile and liver enzymes: a study on bangladeshi adults. *Scientific reports*, 12, 1711.
25. Kim, h., lim, d. H. & kim, y. 2021. Classification and prediction on the effects of nutritional intake on overweight/obesity, dyslipidemia, hypertension and type 2 diabetes mellitus using deep learning model: 4–7th korea national health and nutrition examination survey. *International journal of environmental research and public health*, 18, 5597.
26. Kittel, b., ruehl-fehlert, c., morawietz, g., klapwijk, j., elwell, m. R., lenz, b., o'sullivan, m. G., roth, d. R. & wadsworth, p. F. 2004. Revised guides for organ sampling and trimming in rats and mice--part 2. A joint publication of the rita and nacad groups. *Exp toxicol pathol*, 55, 413-31.
27. Kumar, p., singh, s. & ahmad, m. I. 2020. Synergistic effect of *cinnamomum zeylanicum* and *murraya koenigii* formulation for antiobesity and hypolipidemic activity on wistar albino rats. *Advances in traditional medicine*, 21.
28. Latifi, e., mohammadpour, a. A., h, b. F. & nourani, h. 2019. Antidiabetic and antihyperlipidemic effects of ethanolic *ferula assa-foetida* oleo-gum-resin extract in streptozotocin-induced diabetic wistar rats. *Biomed pharmacother*, 110, 197-202.
29. Layton, c. & suvarna, k. 2013. *Bancroft's theory and practise of histological techniques* (7th edition) (co-author).
30. Li, m., li, m., wang, l., li, m. & wei, j. 2023. *Apiaceae medicinal plants: a review of traditional uses, phytochemistry, bolting and flowering, and controlling approaches*.
31. Lozano, i., van der werf, r., bietiger, w., seyfritz, e., peronet, c., pinget, m., jeandidier, n., maillard, e., marchioni, e. & sigrist, s. 2016. High-fructose and high-fat diet-induced disorders in rats: impact on diabetes risk, hepatic and vascular complications. *Nutrition & metabolism*, 13, 1-13.
32. Mishor, e., amir, d., weiss, t., honigstein, d., weissbrod, a., livne, e., gorodisky, l., karagach, s., ravia, a., snitz, k., karawani, d., zirler, r., weissgross, r., soroka, t., endevelt-shapira, y., agron, s., rozenkrantz, l., reshef, n., furman-haran, e., breer, h., strotmann, j., uebi, t., ozaki, m. & sobel, n. 2021. Sniffing the human body volatile hexadecanal blocks aggression in men but triggers aggression in women. *Sci adv*, 7, eabg1530.
33. Mojarrad, s. 2020. Responses of liver and renal function markers against arjuna tree extract in induced hyperlipidemia rats. *Issue s*, 10.
34. Mosca, s., araujo, g., costa, v., correia, j., bandeira, a., martins, e., mansilha, h., tavares, m. & coelho, m. P. 2022. Dyslipidemia diagnosis and treatment: risk stratification in children and adolescents. *Journal of nutrition and metabolism*, 2022.
35. Nelson, r. H. 2012. Hyperlipidemia as a risk factor for cardiovascular disease. *Primary care*, 40, 195.
36. Nemoto, t., nakakura, t. & kakinuma, y. 2020. Elevated blood pressure in high-fat diet-exposed low birthweight rat offspring is most likely caused by elevated glucocorticoid levels due to abnormal pituitary negative feedback. *Plos one*, 15, e0238223.
37. Niknafs, a., rezvanfar, m., kamalinejad, m., latifi, s. A., almasi-hashiani, a. & salehi, m. 2021. The effect of a persian herbal medicine compound on the lipid profiles of patients with dyslipidemia: a randomized double-blind placebo-controlled clinical trial. *Evidence-based complementary and alternative medicine*, 2021, 1-9.
38. Panchal, s. K. & brown, l. 2011. Rodent models for metabolic syndrome research. *J biomed biotechnol*, 2011, 351982.
39. Pasavei, a. G., mohebbati, r., boroumand, n., ghorbani, a., hosseini, a., jamshidi, s. T. & soukhtanloo, m. 2020. Anti-hypolipidemic and anti-oxidative effects of hydroalcoholic extract of *origanum majorana* on the hepatosteatosis induced with high-fat diet in rats. *The malaysian journal of medical sciences: mjms*, 27, 57.
40. Pehlić, m., dumančić, s., radan, m., galić, j., gruica, b., marijan, s. & vulić, m. 2024. Untargeted urinary volatilomics reveals hexadecanal as a potential biomarker for preeclampsia. *Int j mol sci*, 25.

41. Pieroni, a., ahmed, h. & hamadamin, h. 2016. The spring has arrived: traditional wild vegetables gathered by yarsanis (ahl-e haqq) and sunni muslims in western hawraman, se kurdistan (iraq). Acta societatis botanicorum poloniae, 86.
42. Qi, y. & wang, x. 2023. The role of gut microbiota in high-fat-diet-induced diabetes: lessons from animal models and humans. Nutrients, 15, 922.
43. Sert, n. P. D., ahluwalia, a., alam, s., avey, m. T., baker, m., browne, w. J., clark, a., cuthill, i. C., dirnagl, u. & emerson, m. J. P. B. 2020. Reporting animal research: explanation and elaboration for the arrive guidelines 2.0. 18, 1-65.
44. Shaaban, m. T., ghaly, m. F. & fahmi, s. M. 2021. Antibacterial activities of hexadecanoic acid methyl ester and green-synthesized silver nanoparticles against multidrug-resistant bacteria. J basic microbiol, 61, 557-568.
45. Sousa, r. M. O. F., cunha, a. C. & fernandes-ferreira, m. 2021. The potential of apiaceae species as sources of singular phytochemicals and plant-based pesticides. Phytochemistry, 187, 112714.
46. Spanoudaki, m., chrysafi, m., papadopoulou, s. K., tsourouflis, g., pritsa, a. & giaginis, c. 2024. Naturally occurring compounds targeting peroxisome proliferator receptors: potential molecular mechanisms and future perspectives for promoting human health. Applied sciences, 14, 9994.
47. Sunil, b. & ashraf, a. P. 2020. Dyslipidemia in pediatric type 2 diabetes mellitus. Current diabetes reports, 20, 1-9.
48. Suvarna, s. K. L., christopher; bancroft, john d. 2024. Bancroft's theory and practice of histological techniques, elsevier.
49. Tang, n., ma, j., tao, r., chen, z., yang, y., he, q., lv, y., lan, z. & zhou, j. 2022. The effects of the interaction between bmi and dyslipidemia on hypertension in adults. Scientific reports, 12, 927.
50. Thiviya, p., gunawardena, n., gamage, a., madhujith, t. & merah, o. 2022. Apiaceae family as a valuable source of biocidal components and their potential uses in agriculture. Horticulturae, 8, 614.
51. Wang, y., yu, h. & he, j. 2020. Role of dyslipidemia in accelerating inflammation, autoimmunity, and atherosclerosis in systemic lupus erythematosus and other autoimmune diseases. Discovery medicine, 30, 49-56.
52. Wilkinson, m. & shapiro, m. 2024. Immune-mediated inflammatory diseases, dyslipidemia, and cardiovascular risk: a complex interplay. Arteriosclerosis, thrombosis, and vascular biology, 44, 2396-2406.
53. Wojcikowski, k. & gobe, g. 2014. Animal studies on medicinal herbs: predictability, dose conversion and potential value. Phytother res, 28, 22-7.
54. Xing, l., jing, l., tian, y., yan, h., zhang, b., sun, q., dai, d., shi, l., liu, d., yang, z. & liu, s. 2020. Epidemiology of dyslipidemia and associated cardiovascular risk factors in northeast china: a cross-sectional study. Nutrition, metabolism and cardiovascular diseases, 30, 2262-2270.

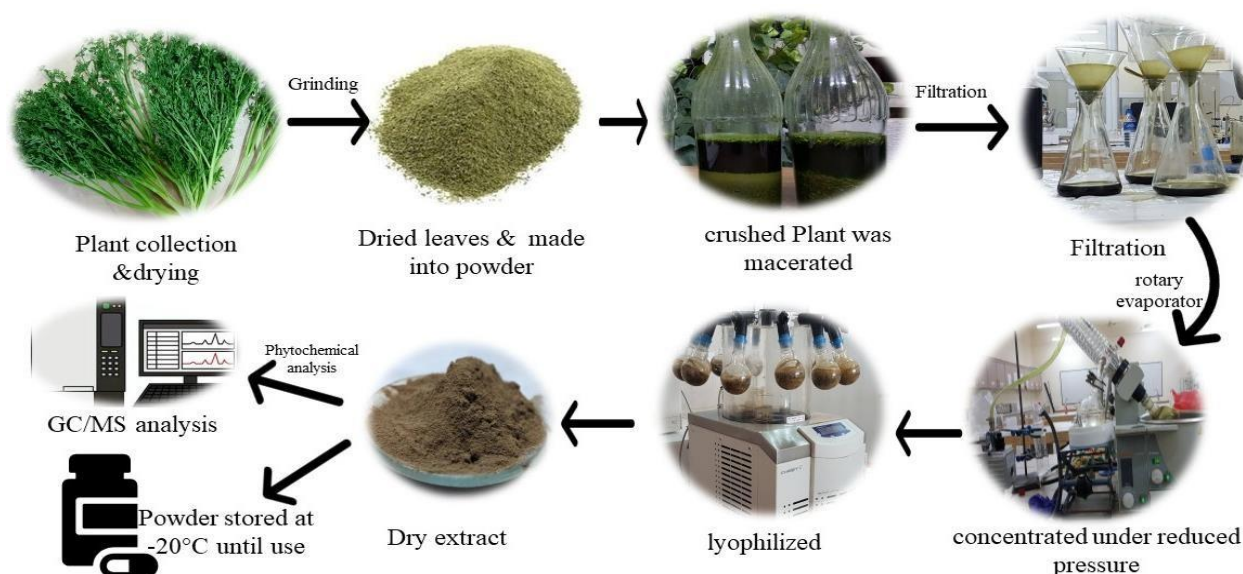


Diagram 1: J. aromatica Collection and Extraction Procedure.

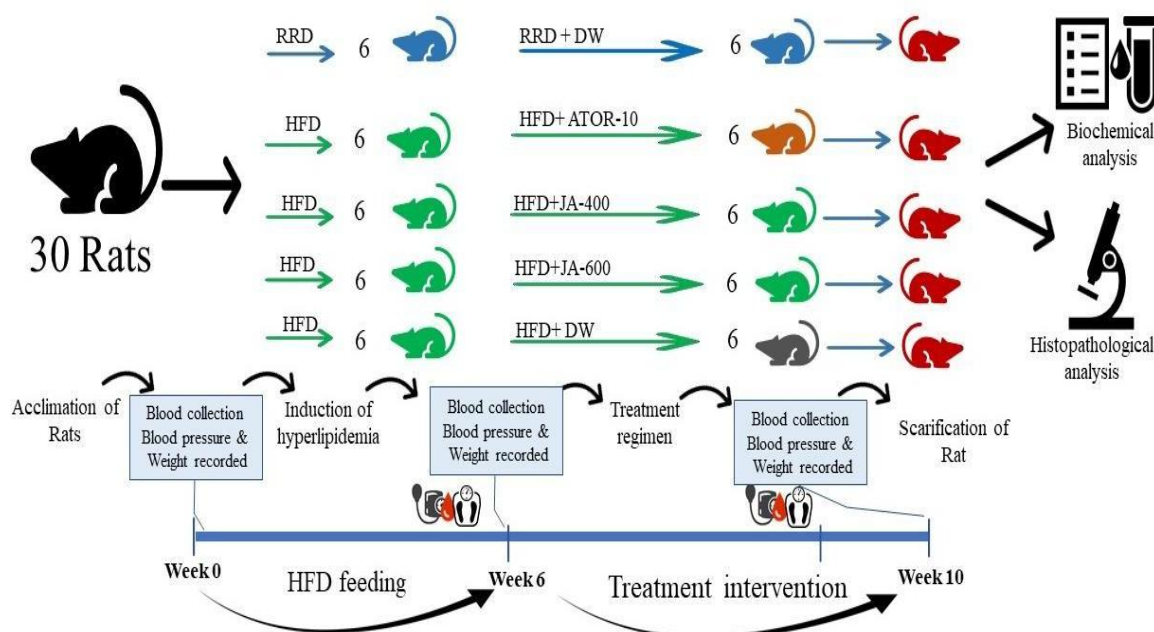


Diagram 2: Illustration of the Animal experimental design. Note: RRD: Routine Rat diet, HFD: high-fat diet, DW: distilled water, ATOR-10: received HFD with Atorvastatin (10 mg); JA-400: HFD with *J. aromatica* 400 mg, JA-600: HFD with *J. aromatica* 600 mg; HFDG: Received only HFD.

Table 1: GC/MS-Phytochemical analysis of *J. aromatica*

R.Time	Area	Area%	Name	synonyms
21.556	32717302	33.22	13-Tetradecene-11-yn-1-ol	13-tetradecynol
27.546	15620445	15.86	Hexadecanal	Palmitaldehyde
26.18	13825177	14.04	cis-9,10-Epoxyoctadecan-1-ol	Oleyl alcohol epoxide, cis-
19.73	12256388	12.44	n-Hexadecanoic acid	Palmitic acid, Hydrofol
26.3	8008278	8.13	Tricyclo[20.8.0.0(7,16)]triacontane, 1(22),7(16)-diepoxy-	
25.8	675137	6.9	13-Tetradecene-11-yn-1-ol	
27.715	5515437	5.6	Tricyclo[20.8.0.0(7,16)]triacontane, 1(22),7(16)-diepoxy-	
	3575441	3.63	3,7,11,15-Tetramethyl-2-hexadecen-1-ol	Phytene-2, Trans-phyt-2-ene
24.627	1401017	1.42	Hexadecanoic acid, 2,3-dihydroxypropyl ester	Stearin,
21.883	1289937	1.31	6,9,12-Octadecatrien-1-ol	
17.531	1054098	1.07	E-2-Tetradecen-1-ol	
28.435	940406	0.95	3.alpha.,5-Cyclo-5.alpha.-ergosta-	
28.033	700622	0.71	Eicosanoic acid, tetradecyl ester	tetradecanyl eicosanoate
17.959	463168	0.47	3,7,11,15-Tetramethyl-2-hexadecen-1-ol	Phytol (3,7,11,15-Tetramethyl-2-hexadecen-1-ol)
20.468	260164	0.26	7-Hexadecenoic acid, methyl ester, (Z)-	
18.591	197153	0.2	Hexadecanoic acid, 15-methyl-, methyl ester	Methyl isoheptadecanoate

Table 2: Body weight of the rats at different Times

Weeks	NC	ATOR-10	JA-400	JA-600	HFDG	P-Value
wk-0	237±64.7	284±33.7	200±13.6	227±24.2	248.5±48.2	0.004

wk-6	315.2±30	319±18.7	280±10.3	297±12.8	336±21.7	0.002
wk-10	325.6±14.7	286±24	244±10.3	262±18.5	345±16.7	0
Statistical analysis (Two-way repeated-measures ANOVA)						
Source		F-ratio		P-Value		
Time		70.482		<0.001		
Treatment Group		10.191		<0.001		
Time x Treatment		4.328		0.005		

Note: wk: week; NC: Normal control group; received routine diet only; ATOR-10: received HFD with Atorvastatin (10 mg); JA-400: HFD with J. aromatica 400 mg; JA-600: HFD with J. aromatica 600 mg; HFDG: Received only HFD. Data are presented as mean ±SD (n = 6 rats per group). Body weight was measured at baseline (Week 0), after six weeks of high-fat diet induction (Week 6), and after four weeks of treatment (Week 10). F-ratio= Variation explained by the model/ Random(unexplained) variation. Statistical analysis was performed using a two-way repeated-measures ANOVA, with treatment group as the between-subject factor and time as the within-subject factor. Greenhouse–Geisser correction was applied when appropriate, followed by Bonferroni-adjusted multiple comparisons. Statistical significance was considered at $P < 0.05$.

Table 3: Different biochemical parameters of the rats at week 6

Biomarkers	NC	ATOR-10	JA-400	JA-600	HFDG
Lipid profile mg/dL					
TC	90±6 ^a	389±113 ^b	389±134 ^b	394±98 ^b	350±95 ^b
TG	44.9 ± 3.7 ^a	373±65.3 ^b	370±80 ^b	374±112 ^b	354±77 ^b
HDL	15± 1.3 ^a	22.4± 2.7 ^b	23± 2.4 ^b	22± 1.5 ^b	23.8± 1.9 ^b
LDL	19.7± 1.3 ^a	28.7± 2.7 ^b	28.9± 5 ^b	27± 4.2 ^b	26.7± 6.2 ^b
VLDL	9± 0.7 ^a	74± 13 ^b	75.6± 16 ^b	73± 35 ^b	70± 15.4 ^b
Liver function biomarker IU/L					
AST	128.4±4.8 ^a	127.2±15.7 ^a	126±28.9 ^a	129±8.4 ^a	119±14.2 ^a
ALT	65.4±6.5 ^a	97±18 ^b	96±10 ^b	98±16.3 ^b	91±5.3 ^b
ALP	181±8.7 ^a	922±167 ^b	930±257 ^b	920±281 ^b	872±211 ^b
Renal function biomarker mg/dL					
Urea	27.2± 2.5 ^a	26.3± 2.3 ^a	24.2± 3.6 ^a	26.2± 7.9 ^a	27± 4 ^a
Cr.	0.44±0.5 ^a	0.5±0.02 ^a	0.52±0.04 ^a	0.5±0.03 ^a	0.52±0.07 ^a
B. Glucose mg/dL					
	119.4±5 ^a	117.2±4 ^a	116±18.8 ^a	120±13.9 ^a	119.7±20 ^a
CRP mg/dL					
	0.78±0.08 ^a	2.6±0.34 ^b	255±0.43 ^b	2.45±0.62 ^b	2.57±0.4 ^b

Note: NC: Normal control group; received routine diet only; ATOR-10: received HFD with Atorvastatin (10 mg); JA-400: HFD with J. aromatica 400 mg; JA-600: HFD with J. aromatica 600 mg; HFDG: Received only HFD; TC: Total cholesterol, TG: Triglyceride; LDL: Low-density lipoprotein; VLDL: Very low-density lipoprotein; HDL: High-density lipoprotein; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; ALP: Alkaline phosphatase; Cr.: Creatinine B. Glucose: blood glucose; CRP: C-reactive

protein. The data were analyzed using ANOVA followed by Tukey's correction and expressed as mean $\pm$ SD. Statistical comparison among groups; a-d: Mean values with different letters differ significantly ($P < 0.05$).

Table 4: The different blood pressures of the rats at week 6

Blood pressure (mm/Hg)	NC	ATOR-10	JA-400	JA-600	HFDG
Systolic BP	98.4 $\pm$ 5.2 ^a	104.2 $\pm$ 9.5 ^a	102.1 $\pm$ 11.3 ^a	106 $\pm$ 5.8 ^a	103.9 $\pm$ 16.2 ^a
Diastolic BP	78.4 $\pm$ 2.4 ^a	76 $\pm$ 5.7 ^a	75 $\pm$ 6.4 ^a	79 $\pm$ 14.5 ^a	77.8 $\pm$ 3.6 ^a
mABP	81.8 $\pm$ 2.8 ^a	85 $\pm$ 5.7 ^a	83 $\pm$ 7.3 ^a	86 $\pm$ 6.1 ^a	83 $\pm$ 11.8 ^a
Heart rate (bpm)	366.2 $\pm$ 7.5 ^a	378.6 $\pm$ 44.7 ^a	380.7 $\pm$ 36 ^a	381.1 $\pm$ 28.9 ^a	375.3 $\pm$ 48 ^a

Note: NC: Normal control group; received routine diet only; ATOR-10: received HFD with Atorvastatin (10 mg); JA-400: HFD with J. aromatica 400 mg; JA-600: HFD with J. aromatica 600 mg; HFDG: Received only HFD; BP: Blood Pressure, mABP: mean arterial blood pressure. The data were analyzed using ANOVA followed by Tukey's correction and expressed as mean $\pm$ SD. Statistical comparison among groups; a-d: Mean values with different letters differ significantly ($P < 0.05$).

Table 5: Effect of different regimens on biomarkers in hyperlipidemic rats

Biomarkers	NC	ATOR-10	JA-400	JA-600	HFDG
Lipid profile mg/dl					
TC	81 $\pm$ 4.5 ^a	87.2 $\pm$ 5.1 ^a	75 $\pm$ 6.7 ^a	71.4 $\pm$ 5.3 ^a	350.4 $\pm$ 71 ^b
TG	48.6 $\pm$ 11.6 ^a	57.8 $\pm$ 17 ^a	149.8 $\pm$ 129 ^a	138.6 $\pm$ 97 ^a	332 $\pm$ 80 ^b
HDL	16.9 $\pm$ 2.6 ^a	21.6 $\pm$ 4 ^a	23.2 $\pm$ 5 ^a	21.3 $\pm$ 1.1 ^a	20.4 $\pm$ 4.5 ^a
LDL	19.9 $\pm$ 2.9 ^a	13.4 $\pm$ 4 ^b	16.8 $\pm$ 1.1 ^{a, b}	16 $\pm$ 1.6 ^{a, b}	25 $\pm$ 3.1 ^c
VLDL	9.7 $\pm$ 2.3 ^a	11.6 $\pm$ 3.3 ^a	29.9 $\pm$ 25 ^{a, b}	27.7 $\pm$ 19.5 ^a	44.8 $\pm$ 9.3 ^b
Liver function biomarker IU/L					
AST (sGOT)	153.6 $\pm$ 21 ^a	184.2 $\pm$ 20 ^b	127.8 $\pm$ 44.5 ^a	134.6 $\pm$ 23 ^a	191 $\pm$ 60 ^b
ALT (sGPT)	87 $\pm$ 7 ^a	208 $\pm$ 63 ^b	52.2 $\pm$ 17 ^a	159.2 $\pm$ 133.4 ^{a, b}	189 $\pm$ 8.5 ^b
ALP	219 $\pm$ 27 ^a	877 $\pm$ 150.4 ^c	367.6 $\pm$ 84.4 ^a	514.2 $\pm$ 227 ^{a, b}	805 $\pm$ 267 ^{b, c}
Renal function biomarker mg/dl					
Urea	31 $\pm$ 2.5 ^a	25.2 $\pm$ 2.6 ^a	24.4 $\pm$ 2.3 ^a	25.6 $\pm$ 3 ^{a, b}	23.8 $\pm$ 4.1 ^b
Creatinine	0.54 $\pm$ 0.8 ^{a, b}	0.55 $\pm$ 0.4 ^b	0.45 $\pm$ 0.33 ^a	0.46 $\pm$ 0.01 ^a	0.53 $\pm$ 0.4 ^{a, b}
B. Glucose mg/dL	264 $\pm$ 77.2 ^a	259 $\pm$ 20 ^a	265.2 $\pm$ 36.2 ^a	166 $\pm$ 28.4 ^b	257.8 $\pm$ 27.4 ^a
CRP mg/dL	0.92 $\pm$ 0.9 ^a	0.9 $\pm$ 0.2 ^a	1.14 $\pm$ 0.6 ^a	1.1 $\pm$ 0.6 ^a	2.1 $\pm$ 0.6 ^b

Note: NC: Normal control group; received routine diet+ Distilled water; ATOR-10: received HFD with Atorvastatin (10 mg); JA-400: HFD with J. aromatica 400 mg; JA-600: HFD with J. aromatica 600 mg; HFDG: Received HFD + Distilled water; TC: Total cholesterol, TG: Triglyceride; LDL: Low-density lipoprotein; VLDL: Very low-density lipoprotein; HDL: High-density lipoprotein; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; ALP: Alkaline phosphatase; Cr.: Creatinine B. Glucose: blood glucose; CRP: C-reactive protein. The data were analyzed using ANOVA followed by Tukey's

correction and expressed as mean $\pm$ SD. Statistical comparison among groups; a-d: Mean values with different letters differ significantly ($P < 0.05$).

Table 6: Effect of different regimens on blood pressure of hyperlipidemic rats.

Biomarkers	NC	ATOR-10	JA-400	JA-600	HFDG
Systolic BP	118.8 $\pm$ 4 ^a	129 $\pm$ 8.4 ^b	112 $\pm$ 7.7 ^a	120.5 $\pm$ 4.6 ^{a, b}	140.2 $\pm$ 14 ^c
Diastolic BP	89 $\pm$ 5.3 ^a	100.2 $\pm$ 12.3 ^b	74 $\pm$ 14 ^c	88.9 $\pm$ 5.1 ^{a, b}	105.8 $\pm$ 10.6 ^b
mABP	98.2 $\pm$ 5 ^a	110 $\pm$ 10.2 ^{b, c}	87 $\pm$ 11.3 ^a	100.2 $\pm$ 4.3 ^{a, b}	117.6 $\pm$ 11 ^c
Heart rate (bpm)	353.6 $\pm$ 23.5 ^a	366.8 $\pm$ 13 ^a	390.6 $\pm$ 29.2 ^{a, b}	370 $\pm$ 11.4 ^a	419 $\pm$ 19.5 ^b

Note: NC: Normal control group; received routine diet + Distilled water; ATOR-10: received

HFD with Atorvastatin (10 mg); JA-400: HFD with J. aromatica 400 mg; JA-600: HFD with J. aromatica 600 mg; HFDG: Received HFD + distilled water; BP: Blood Pressure, mABP: mean arterial blood pressure. The data were analyzed using ANOVA followed by Tukey's correction and expressed as mean $\pm$ SD. Statistical comparison among groups; a-d: Mean values with different letters differ significantly ($P < 0.05$).

Table 7: Evaluation of Liver Sections through Histological Analysis

sections	NC	ATOR-10	JA-400	JA-600	HFDG
Fatty Deposits (μm^2)	0.00 $\mu\text{m}^2 \pm$ 0.00 ^a	2.00 $\mu\text{m}^2 \pm$ 0.04 ^e	1.03 $\mu\text{m}^2 \pm$ 0.01 ^c	1.63 $\mu\text{m}^2 \pm$ 0.04 ^d	2.58 $\mu\text{m}^2 \pm$ 0.05 ^b
Inflammation	0.00 $\pm$ 0.00 ^a	22.2 $\pm$ 1.30 ^e	13.2 $\pm$ 1.30 ^c	18.0 $\pm$ 1.00 ^d	57.4 $\pm$ 1.51 ^b
Remaining hepatocyte (N/HPF)	32.6 $\pm$ 1.14 ^a	9.20 $\pm$ 1.30 ^d	17.8 $\pm$ 0.83 ^c	13.0 $\pm$ 0.70 ^d	8.4 $\pm$ 0.89 ^b

Note: N/HPF: nuclei per high-power field; NC: Normal control group; received routine diet + Distilled water; ATOR-10: received HFD with Atorvastatin (10 mg); JA-400: HFD with J. aromatica 400 mg; JA-600: HFD with J. aromatica 600 mg; HFDG: Received HFD + distilled water; BP: Blood Pressure, mABP: mean arterial blood pressure. The data were analyzed using ANOVA followed by Tukey's correction and expressed as mean $\pm$ SD. Statistical comparison among groups; a-d: Mean values with different letters differ significantly ($P < 0.05$).

Table 8: Evaluation of Kidney Sections through Histological Analysis

Kidney	NC	ATOR-10	JA-400	JA-600	HFDG
Proliferation	16.20 $\pm$ 1.92 ^a	36.40 $\pm$ 1.14 ^d	27.60 $\pm$ 1.14 ^c	25.40 $\pm$ 1.14 ^c	42.60 $\pm$ 1.14 ^b
Tubular Dilatation (μm^2)	1.58 $\mu\text{m}^2 \pm$ 0.02 ^d	2.20 $\mu\text{m}^2 \pm$ 0.02 ^b	1.54 $\mu\text{m}^2 \pm$ 1.01 ^c	1.53 $\mu\text{m}^2 \pm$ 1.01 ^c	4.44 $\mu\text{m}^2 \pm$ 0.03 ^a
Inflammation	0.00 $\pm$ 0.00 ^d	12.80 $\pm$ 0.83 ^b	4.00 $\pm$ 0.70 ^c	0.00 $\pm$ 0.00 ^d	32.6 $\pm$ 1.14 ^a

Note: NC: Normal control group; received routine diet + Distilled water; ATOR-10: received HFD with Atorvastatin (10 mg); JA-400: HFD with J. aromatica 400 mg; JA-600: HFD with J. aromatica 600 mg; HFDG: Received HFD + distilled water; BP: Blood Pressure, mABP: mean arterial blood pressure. The data were analyzed using ANOVA followed by Tukey's correction and expressed as mean $\pm$ SD. Statistical comparison among groups; a-d Mean values with different letters differ significantly ($P < 0.05$).

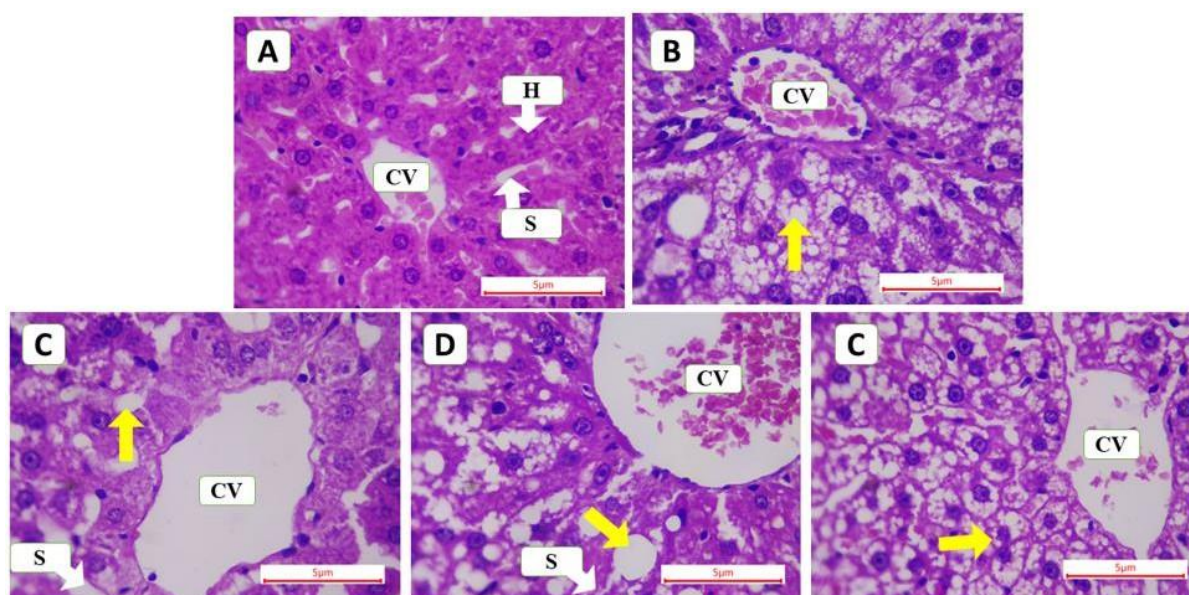


Figure (1): Representative photomicrographs of liver tissue sections from the normal, model, and treatment groups, stained with hematoxylin and eosin (H&E) and examined at $\times 40$ magnification (scale bar = $5\ \mu\text{m}$). Panel A (NC) shows normal hepatic architecture with a central vein (CV) surrounded by radiating hepatic sinusoids (S) lined by cords of hepatocytes (H), with no significant histopathological alterations. Panel B (HFDG group) demonstrates severe hepatic steatosis (score 3), characterized by extensive cytoplasmic lipid vacuolation within hepatocytes (yellow arrows), resulting in peripheral displacement of nuclei and a characteristic signet-ring appearance. Marked hepatocellular swelling and distortion of the hepatic cords are also evident, accompanied by compression and partial obliteration of the sinusoidal spaces. Panel C (JA-400 group) reveals noticeable histological improvement, with preservation of the central vein and surrounding sinusoids and only mild fatty change (score 1) in hepatocytes (yellow arrows). Panel D (JA-600 group) shows moderate fatty degeneration (score 2) within hepatocytes (yellow arrows), with slight distortion of the hepatic sinusoids surrounding the central vein. Panel E (ATOR-10 group) exhibits persistent severe steatosis (score 3), characterized by marked intracellular lipid accumulation, peripheral nuclear displacement producing signet-ring hepatocytes, and pronounced loss of normal sinusoidal architecture.

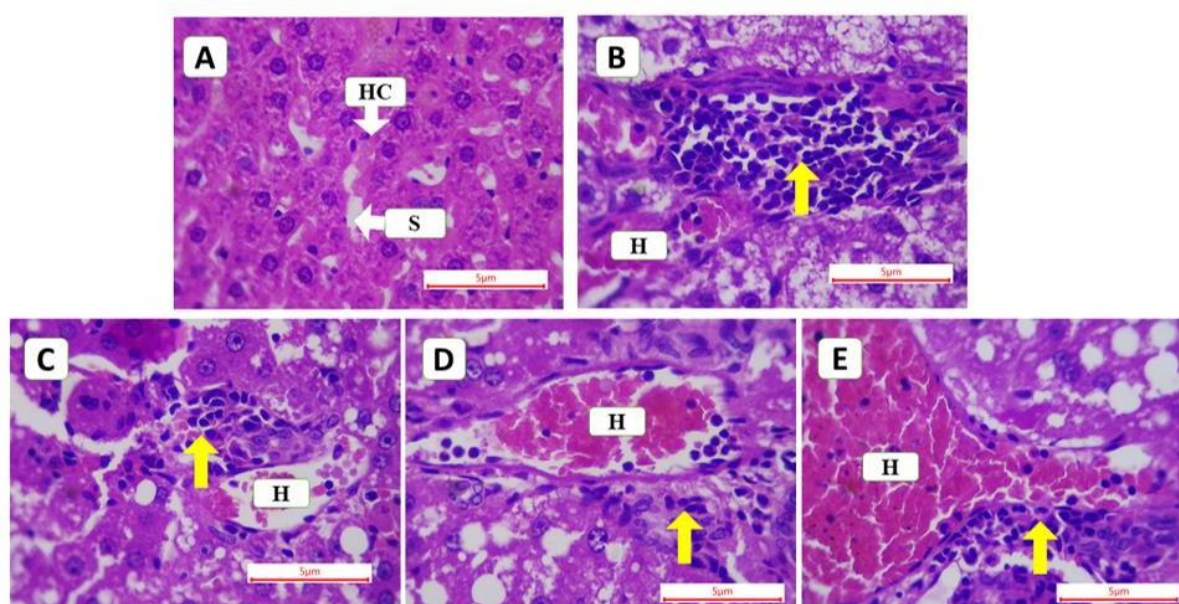


Figure (2): Representative photomicrographs of liver tissue sections stained with hematoxylin and eosin (H&E) and examined at $\times 40$ magnification (scale bar = $5\ \mu\text{m}$). Panel A (NC) shows normal hepatic parenchyma composed of hepatocytes (HC) arranged around patent hepatic sinusoids (S), with no significant histopathological alterations. Panel B (HFDG) demonstrates marked hepatic injury characterized by

hyperemic blood vessels (H) associated with severe chronic inflammatory cell infiltration (score 3) throughout the examined sections (yellow arrows). Panels C and D (JA 400 and JA 600, respectively) reveal hyperemic blood vessels (H) surrounded by only mild chronic inflammatory cell infiltration (score 1), indicating a significant reduction in inflammatory changes compared with the model group. Panel E (A TOR 10) shows hyperemic blood vessels (H) accompanied by moderate chronic inflammatory cell infiltration (score 2), reflecting partial improvement relative to the model group but greater inflammatory activity than that observed in the low and high dose treatment groups.

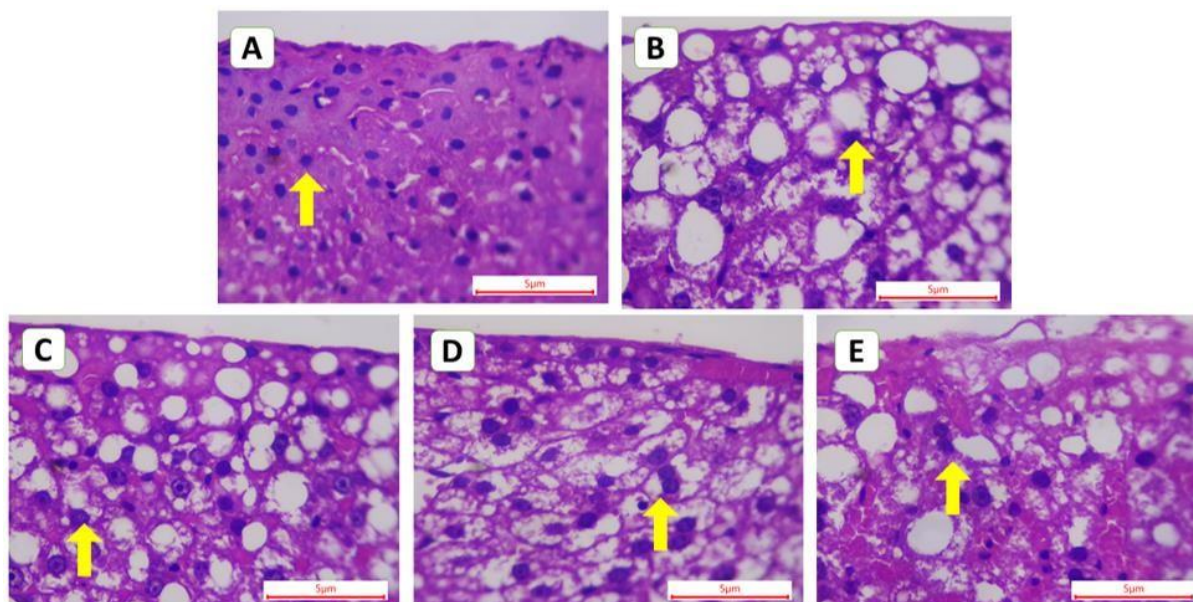


Figure (3): Representative photomicrographs of liver tissue sections from the normal, model, and treatment groups stained with hematoxylin and eosin (H&E) and examined at $\times 40$ magnification (scale bar = 5 μm). Panel A (NC) demonstrates normal hepatic architecture with well-preserved hepatocytes containing centrally located nuclei and no significant histopathological abnormalities. Panel B (HFDG) exhibits a marked reduction in the number of hepatocytic nuclei, with many nuclei showing pyknosis (yellow arrows), indicative of severe hepatocellular necrosis (score 3). Panel C (JA-400) reveals partial preservation of hepatocytic nuclei, corresponding to a mild degree of necrosis (score 1). Panel D (JA-600) shows a greater degree of nuclear preservation, with moderate necrotic changes observed (score 2), indicating substantial improvement compared with the model group. Panel E (ATOR-10) demonstrates a pronounced reduction in the number of hepatocytic nuclei (score 3), with numerous pyknotic nuclei (yellow arrows), consistent with severe hepatocellular necrosis and marked tissue injury.

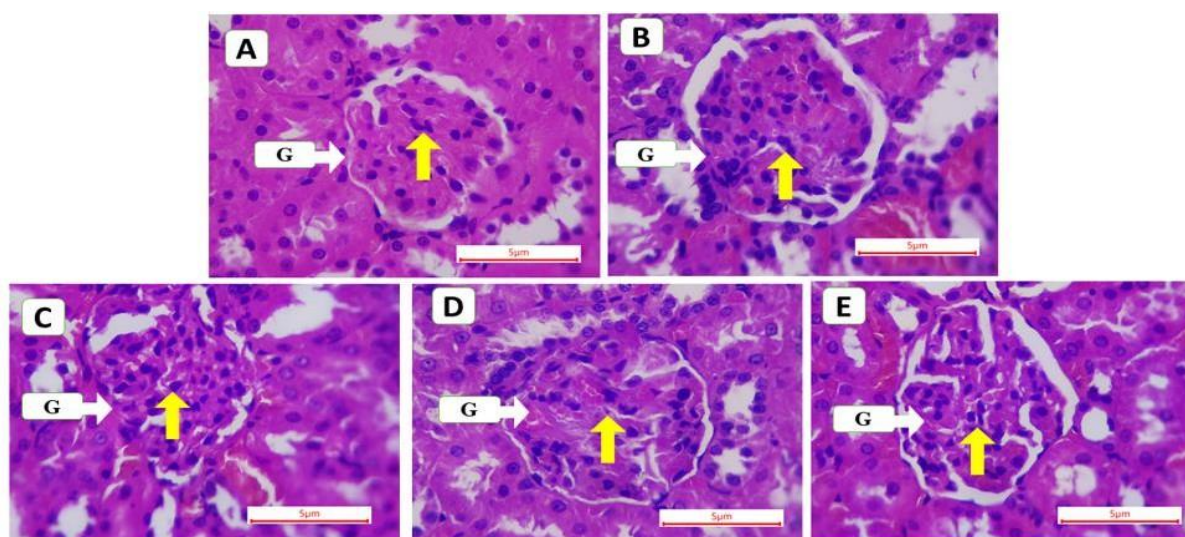


Figure (4): Hematoxylin and eosin (H&E)-stained renal cortex sections of experimental groups at $\times 40$ mag-

nification (scale bar = 5 μ m). The photomicrographs demonstrate glomeruli (G) within the renal cortex across all experimental groups. Panel (A) shows the renal cortex of the normal control group with intact glomerular architecture and normal mesangial cellularity within the capillary tuft (yellow arrow), with no detectable pathological changes, corresponding to score 0 (normal grade). Panel (B) illustrates the HFDG group, demonstrating marked mesangial cell hypercellularity within the glomerular tuft (yellow arrow), indicative of severe mesangial hyperplasia corresponding to score 3. Panels (C) and (D) represent the low-dose and high-dose treatment groups, respectively, both showing a reduction in mesangial cellularity compared with the HFD group (yellow arrows), corresponding to score 1 (mild mesangial hyperplasia). Panel (E) illustrates the atorvastatin-treated group, which shows persistent moderate mesangial hyperplasia with increased cellularity within the glomerular tuft (yellow arrow), corresponding to score 2.

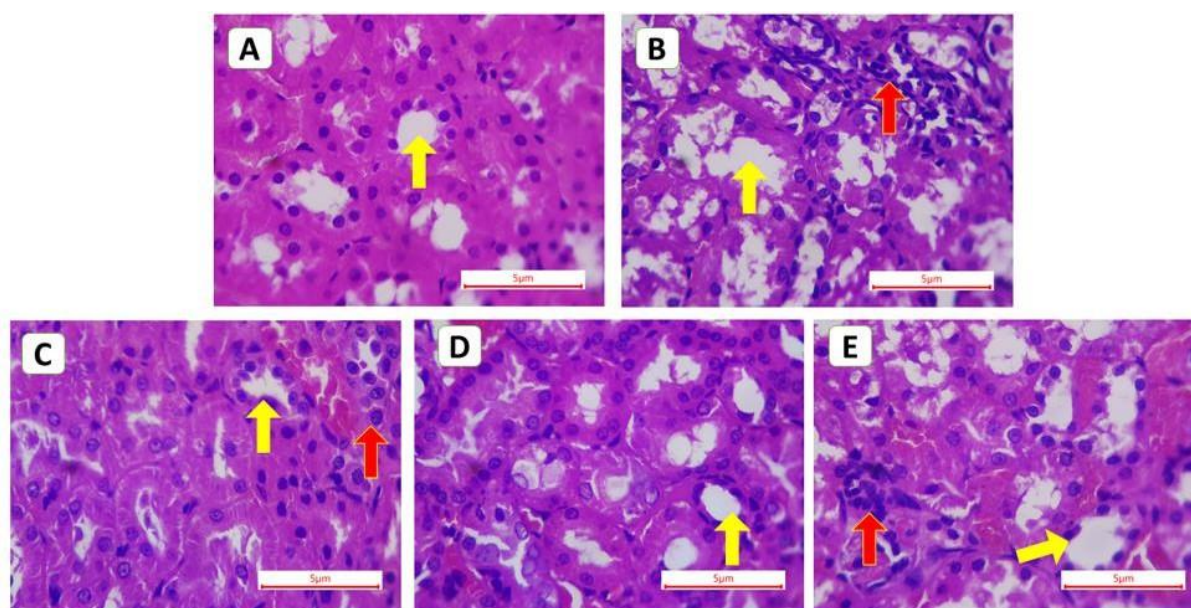


Figure (5): Hematoxylin and eosin (H&E)-stained sections of renal cortex from different experimental groups at $\times 40$ magnification (scale bar = 5 μ m). The photomicrographs demonstrate renal cortical architecture, including renal tubules, across all experimental groups. In panel (A), the normal control group shows preserved tubular structure with normal tubular spaces and no histopathological alterations, corresponding to score 0 (normal grade) for both tubular dilation and inflammatory cell infiltration. In panel (B), the HFD group exhibits severe tubular dilation and marked chronic inflammatory cell infiltration within the interstitium, corresponding to score 3 (severe grade) for both parameters. In panels (C) and (D), the low-dose and high-dose treatment groups demonstrate restoration of near-normal tubular architecture, with preserved tubular spaces and score 0 (normal grade) for tubular dilation; however, mild inflammatory cell infiltration is observed in the low-dose group, whereas the high-dose group shows normal inflammatory status. In panel (E), the atorvastatin-treated group shows mild tubular dilation (score 1) and moderate chronic inflammatory cell infiltration (score 2). In all panels, yellow arrows indicate tubular spaces, while red arrows indicate inflammatory cell infiltration within the renal interstitium.