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EVALUATION OF HYPOLIPIDEMIC ACTIVITY OF KALANCHOE PINNATA IN WISTAR ALBINO RATS

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Abstract:
The present study aimed to investigate the hypolipidemic effects of different doses of Kalanchoe pinnata in rats with hypercholesterolemia. Thirty albino rats weighing 180–200 g were divided into five groups. The first group (G1) served as the Normal control, while the second group (G2) was the Negative control, receiving a high fat diet (HFD) containing 2% cholesterol. The third group (G2) standard group received atorvastatin, fourth and fifth groups (G4 and G5) were also fed a 2% cholesterol diet but were supplemented with 250mg/kgbw and 500mg/kgbw, respectively, for 45 days. Hypercholesterolemic rats in G2 exhibited elevated lipid profiles, liver enzymes. Additionally, histological analysis of the heart, liver, tissues of G2 rats revealed pathological changes compared to G1. Administration of both doses of kalanchoe pinnata extracts to hypercholesterolemic rats in G4 and G5, respectively, led to improvements in lipid levels. Furthermore, histological examination of the heart and liver tissues showed restoration to nearly normal states, similar to those observed in G1.
Key Words: Kalanchoe pinnata, hydro-alcoholicextract, cholesterol, high fat diet.

1. Introduction

Hyperlipidemia, characterized by elevated levels of lipids in the blood, is a significant risk factor for cardiovascular diseases (CVDs) such as coronary artery disease and stroke. According to the World Health Organization (2021) (1), CVDs remain the leading cause of death globally, emphasizing the critical need for effective management of hyperlipidemia to mitigate cardiovascular risks. Conventional treatments for hyperlipidemia, including statins, are widely used; however, statin intolerance affects a substantial proportion of patients, limiting their therapeutic options (2).

Natural products have historically been a prolific source of new drugs, with many derived from plants, demonstrating significant pharmacological activities (3). Medicinal plants offer promising alternatives for managing hyperlipidemia. Various medicinal plants have been traditionally used to treat hyperlipidemia, leveraging their bioactive compounds to exert lipid-lowering effects.

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For instance, Kalanchoe pinnata, a plant known for its diverse medicinal properties, has been shown to contain novel compounds with potential therapeutic benefits (4). Similarly, traditional Chinese medicine employs various plants to modulate immune responses and reduce inflammation, indirectly contributing to cardiovascular health (5).

The exploration and validation of medicinal plants for hyperlipidemia management are crucial, hence the present study was undertaken to evaluate the hypolipidemic activity of Kalanchoe pinnata. This investigation seeks to determine the plant's efficacy in lowering lipid levels and improving associated blood parameters, as well as to assess its impact on the histopathology of vital organs such as the liver and heart. Through comprehensive studies and ethnopharmacological investigations, the therapeutic potential of Kalanchoe pinnata and other medicinal plants can be validated, offering safer and more accessible options for patients with hyperlipidemia (6,7). Thus, the integration of medicinal plants into hyperlipidemia treatment regimens holds promise for improving cardiovascular outcomes and enhancing patient well-being.

2. Materials and methods

2.1 Plant extraction

In this study, all the plants used were collected specifically from the Hyderabad district. To ensure accuracy and authenticity, the identification and authentication process was conducted by Dr. K. Madhava Chetty, an Assistant Professor from the Department of Botany at S.V. University in Tirupati. Voucher number 0414 was assigned to the plant sample of Kalanchoe pinnata as a reference for future verification.

To begin the extraction process, the freshly collected leaves Kalanchoe pinnata were carefully dried in the shade. Once dried, the leaves were coarsely powdered and then passed through a sieve with a mesh size of 40, resulting in a fine powder. This powdered material was carefully stored in an airtight container for later use in the study.

For the extraction of active compounds, 100g of the dried plant material powder was macerated, or soaked, in a hydro-alcoholic solution consisting of 60% ethanol. This maceration process lasted for 7 days, allowing the solvent to draw out the desired compounds from the plant material.

After the 7-day period, the macerated mixture was filtered to separate the liquid extract from the solid residue. The solvent was then evaporated from the filtered liquid, leaving behind the concentrated extract of Kalanchoe pinnata (8).

2.2 High fat diet

High fat diet was procured from National institute of nutrition (NIN) for induction of hyperlipidemia

2.3 Animals

All animal studies conducted in this research adhered to the guidelines set forth by the Organisation for Economic Co-operation and Development (OECD) for the testing of animals.

To ensure ethical treatment and compliance with animal welfare, the study received approval from the Institutional Animal Ethical Committee at KAMSRC, Hyderabad. The specific ethical project number for this study was KAMSRC/Pharm/IAEC/2020/1. Before the commencement of the experiments, the

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animals used in the study were carefully examined and allowed to acclimatize to their new environmental conditions. This acclimatization period aimed to reduce any potential stress on the animals and create a stable baseline for the study. The animal subjects in the experiment were albino rats weighing approximately 150-190 grams. Throughout the study, these rats were housed in a controlled environment with a temperature maintained at 22 ± 3° C and relative humidity ranging from 30% to 70%. The animals were subjected to a 12-hour light and dark cycle, simulating a natural day-night cycle.

2.3 Hyperlipidemia

Five groups of rats, each containing six animals, were used in this study. All the rats in these groups were fed a high-fat diet comprising specific ingredients: cholesterol (1%), cholic acid (0.5%), casein (20%), choline (0.25%), multi-vitamin mix (3.5%), and sucrose (48.4%). Alongside this high-fat diet, they were also provided with a standard pellet diet. This feeding regimen was continued for a duration of 30 days.

3. Methodolody

3.1 Experimental design:

Group I	**Control**	**Carboxy methyl cellulose**
Group II	High fat diet	High fat diet
Group III	Standard group	Atorvastatin 75mg/kgbw+HFD
Group IV	Test group I	KP 250mg/kgbw +HFD
Group V	Test group II	KP 500mg/kgbw +HFD

3.2 Collection of Blood

Under mild halothane anesthesia, blood was collected through a puncture in the retro-orbital sinus. The collected samples were then centrifuged at 2000 r.p.m. for 10 minutes, and the resulting serum samples were utilized for conducting various biochemical tests.

3.3 Estimation of Biochemical Parameters.

Lipid profile:

The lipid profile was assessed using standard diagnostic kits. It included the measurement of total cholesterol (TC), triglycerides (TG), and high-density lipoprotein cholesterol (HDL-C). Additionally, LDL-cholesterol and VLDL-cholesterol levels were calculated using the Friedwald formula.

Histopathological examination:

After the treatment period, the animals from all five groups were euthanized, and their heart, aorta, liver, and kidney were carefully removed. The collected tissues were then washed and prepared as 5 µm thick section slides. These slides were subsequently stained with haematoxylin and eosin and subjected to examination using light microscopy.

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4. Results:

Table -1 Body weight

	Control	HFD	Standard	KP 250mg/kgbw+HFD	KP 500mg/kgbw+HFD
Week 1	152 ± 0.89	156 ± 0.7	154 ± 0.84	152 ± 0.35*	157 ± 0.99
Week 2	155 ± 0.95	163 ± 0.83	162 ± 0.75	164 ± 2.07	165 ± 1.49
Week 3	161 ± 0.89	169 ± 0.92	167 ± 1.85	172 ± 1.41	169 ± 1.63
Week 4	166 ± 0.99	176 ± 1.96	179 ± 0.82	181 ± 1.92*	178 ± 1.41
Week 5	170 ± 1.88	186 ± 1.62	183 ± 1.21	189 ± 1.38	185 ± 2.26
Week 6	176 ± 1.71	194 ± 2.07	188 ± 1.91**	197 ± 1.38	195 ± 2.62
Week 7	180 ± 1.88	204 ± 2.79	194 ± 2.2**	203 ± 2.11	204 ± 2.08
Week 8	187 ± 2.09	216 ± 2.41	198 ± 2.75**	208 ± 1.59**	209 ± 2.07**
Week 9	194 ± 2.56	228 ± 2.85	203 ± 2.63**	216 ± 1.8**	213 ± 1.99**
Week 10	202 ± 1.85	238 ± 2.13	209 ± 2.5**	225 ± 1.34**	219 ± 3.09**

Mean ± SEM *p<0.05 & **p<0.001 significantly compared reduced bodyweight when compared with Group 2.

All the groups supplemented with a high-fat diet (HFD) exhibited a notable and statistically significant increase ($p<0.05$) in serum total cholesterol, triglyceride, and LDL-C levels, while there was a significant decrease ($p<0.05$) in HDL-C levels compared to the values before starting the high-fat diet. The serum levels of TC, TG, LDL-c, and HDL-c before administering the HFD, after HFD supplementation, and after treatment with Atorvastatin and extracts of kalanchoe pinnata were presented in Table-1. Both the standard drug Atorvastatin and both doses of the hydroalcoholic extracts of kalanchoe pinnata (250mg/kg, 500 mg/kg)showed a significant reduction ($p<0.05$) in total cholesterol (Figure 1), triglyceride (Figure 2), and LDL-C (Figure 3). Additionally, they exhibited a significant increase ($p<0.05$) in HDL-C levels (Figure 4) when compared to the control group.

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Table-2 Total cholesterol

	Control	HFD	Standard	KP 250mg/kgbw+HFD	KP 500mg/kgbw+HFD
Day 0	95.67 ± 1.542	92.17 ± 1.558	92.33 ± 2.512	90.0 ± 3.000	90.0 ± 2.955
Day 30	93.33 ± 2.376	133.83 ± 1.905	129.5 ± 2.527	134.67 ± 2.171	132.17 ± 3.124
Day 15 Treatment	93.67 ± 1.874	145.67 ± 3.084	120.33 ± 2.512**	131.83 ± 1.222**	127.5 ± 1.232**
Day 30 Treatment	94.67 ± 2.813	157.17 ± 4.206	116.67 ± 1.820**	128.33 ± 1.382**	122.17 ± 1.249**
Day 45 Treatment	94.67 ± 3.252	177.5 ± 4.918	107.5 ± 4.303**	126.17 ± 1.869**	119.33 ± 0.422**

Mean ± SEM **p<0.001

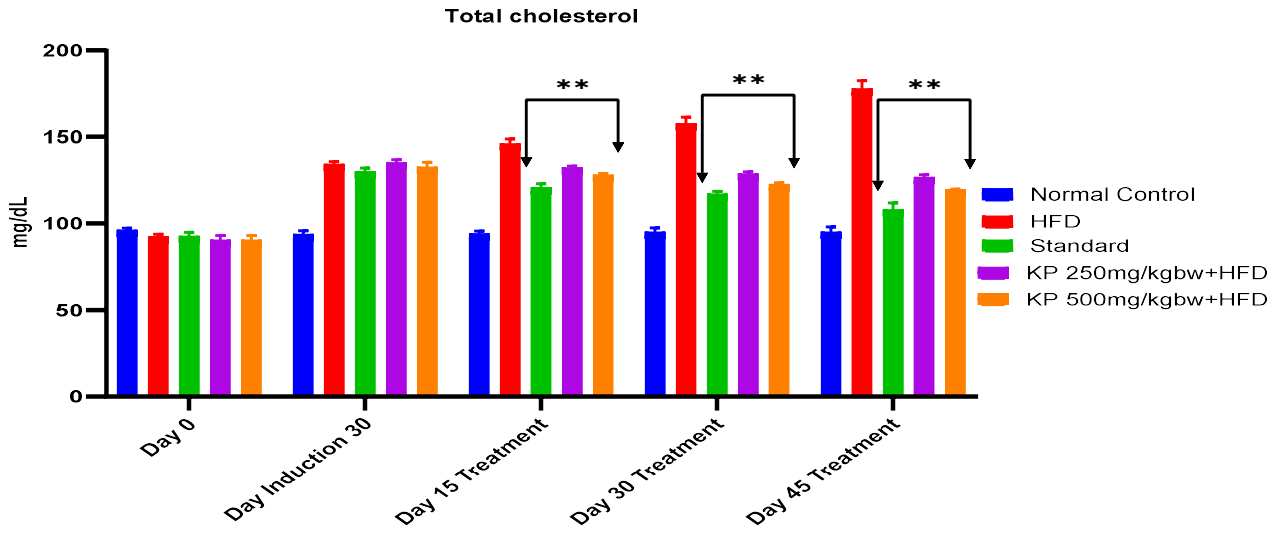

Table-3 Triglycerides

	Control	HFD	Standard	KP 250mg/kgbw+HFD	KP 500mg/kgbw+HFD
Day 0	83.17 ± 1.222	81.17 ± 1.195	79.50 ± 5.271	80.50 ± 3.836	85.00 ± 2.033
Day 30	83.83 ± 1.249	102.33 ± 5.142	100.50 ± 0.847	104.83 ± 2.372	101.5 ± 1.607
Day 15 Treatment	84.17 ± 1.447	116.5 ± 1.821	95.83 ± 1.302	100.00 ± 2.887**	97.00 ± 1.461**
Day 30 Treatment	83.17 ± 3.301	120.67 ± 2.246	90.00 ± 1.390	97.00 ± 0.894**	94.83 ± 1.537**

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Day 45 Treatment	87.83 ± 4.408	127.33 ± 2.155	82.67 ± 2.777	89.33 ± 1.856**	86.83 ± 1.662**

Mean ± SEM **p<0.001

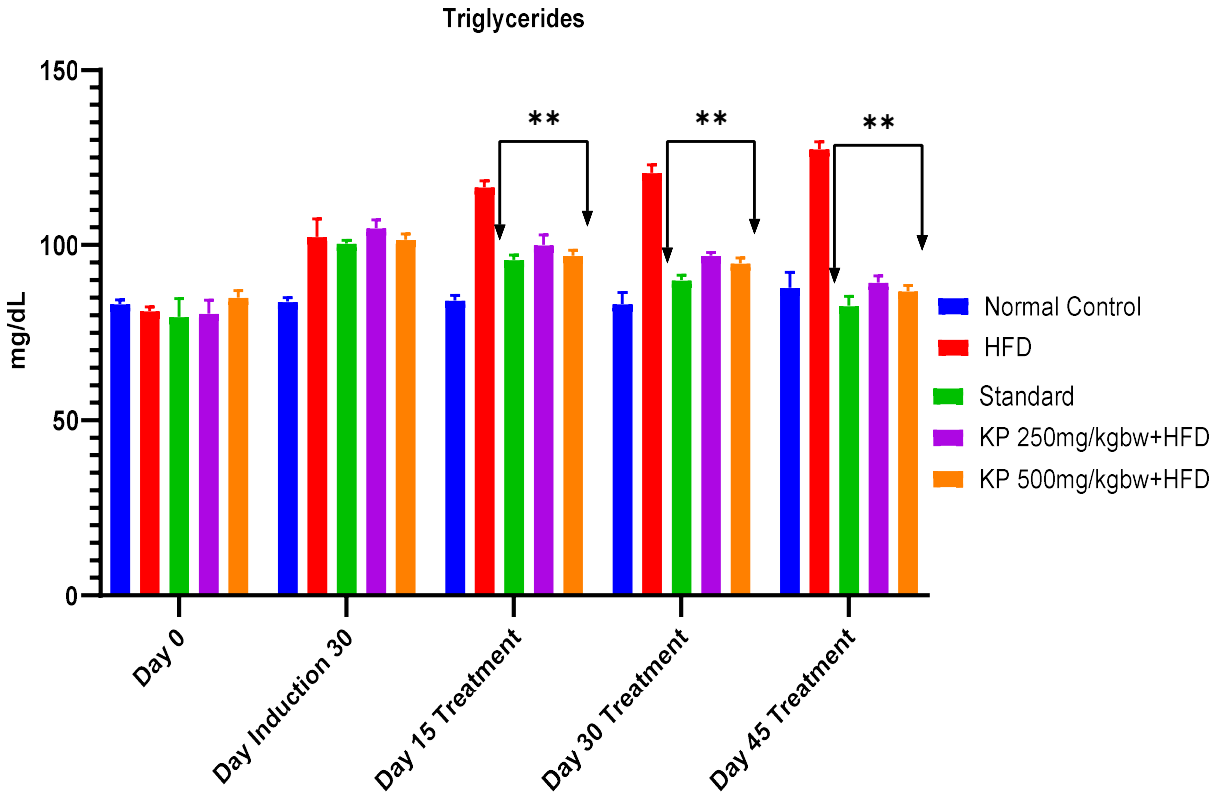

Table-4 HDL Cholesterol

	Control	HFD	Standard	KP 250mg/kgbw+HFD	KP 500mg/kgbw+HFD
Day 0	56.83 ± 1.447	57.33 ± 1.892	59.83 ± 2.798	59.83 ± 1.956	59 ± 1.483
Day 30	56.83 ± 1.558	40.33 ± 0.558	41 ± 2.352	39 ± 2.066	43.83 ± 0.872
Day 15 Treatment	57.33 ± 1.022	37 ± 2.033	46.83 ± 0.792**	38.33 ± 1.054	43 ± 1.713*
Day 30 Treatment	57.67 ± 1.687	34.17 ± 1.302	54.17 ± 1.014**	38.83 ± 0.477*	52.5 ± 1.455**
Day 45 Treatment	58.17 ± 1.905	34.17 ± 1.302	54.17 ± 1.276**	40.83 ± 1.47**	53.67 ± 1.116**

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Mean ± SEM **p<0.01

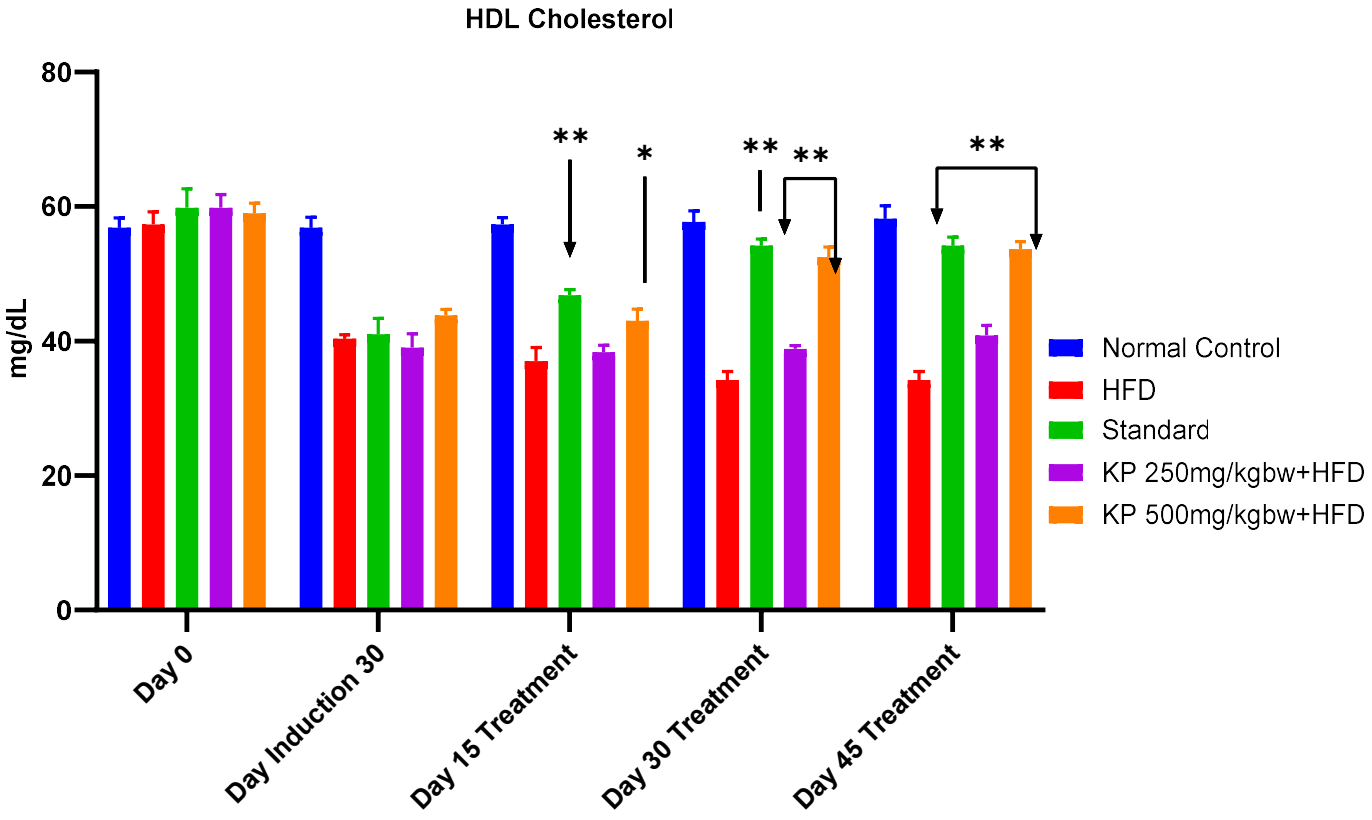

Table-5 LDL Cholesterol

	Control	HFD	Standard	KP 250mg/kgbw+HFD	KP 500mg/kgbw+HFD
Day 0	22.2 ± 2.37	18.6 ± 2.74	16.6 ± 1.711	14.07 ± 4.413	14 ± 2.779
Day 30	19.73 ± 1.183	73.03 ± 1.244	68.4 ± 3.127	74.7 ± 2.483	68.03 ± 2.933
Day 15 Treatment	19.5 ± 2.277	85.37 ± 3.687	54.33 ± 2.412**	73.5 ± 0.709**	65.1 ± 1.184**
Day 30 Treatment	20.37 ± 2.012	98.87 ± 4.199	44.5 ± 1.806**	70.1 ± 0.865**	50.7 ± 2.303**
Day 45 Treatment	18.93 ± 1.988	117.87 ± 5.696	36.8 ± 5.732**	67.47 ± 2.848**	48.3 ± 1.409**

Mean ± SEM **p≤0.001

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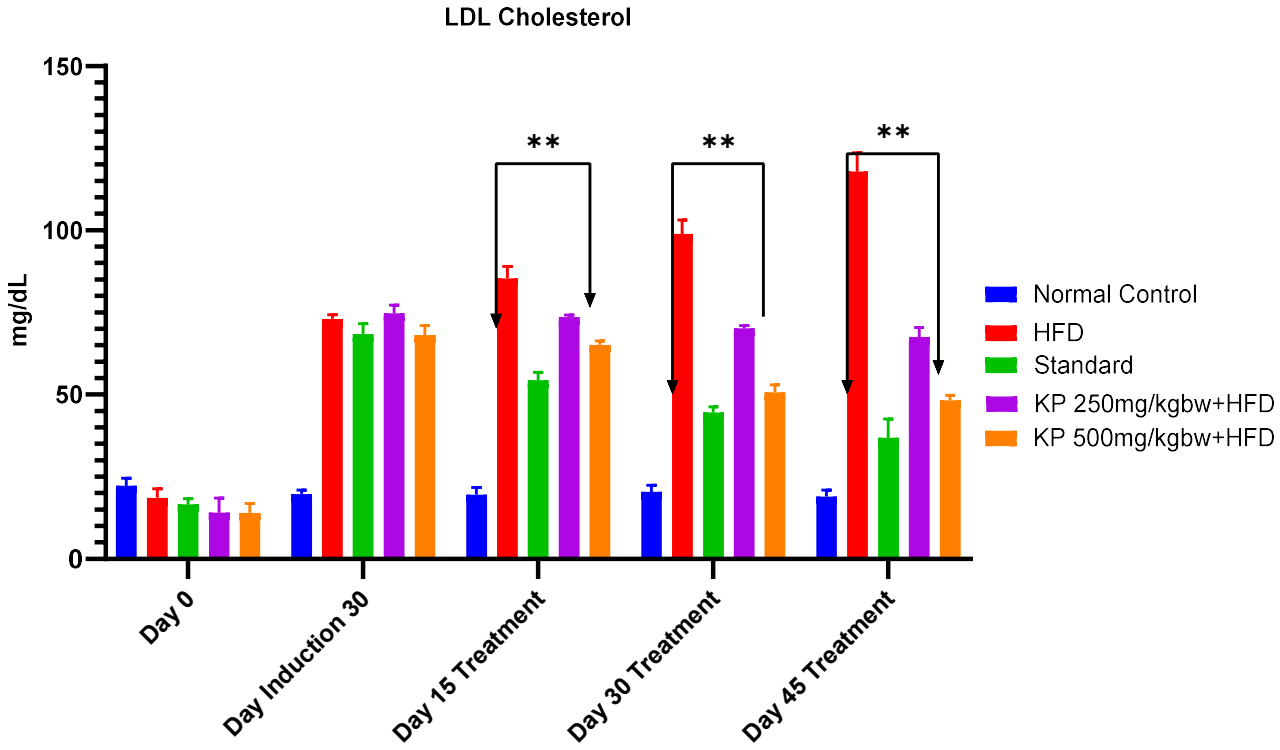

Table-6 VLDL Cholesterol

	Control	**HFD**	**Standard**	**KP 250mg/kgbw+HFD**	**KP 500mg/kgbw+HFD**
Day 0	16.63 ± 0.244	16.23 ± 0.239	15.9 ± 1.054	16.1 ± 0.767	17 ± 0.407
Day 30	16.77 ± 0.25	20.47 ± 1.028	20.1 ± 0.169	20.97 ± 0.474	20.3 ± 0.321
Day 15 Treatment	16.83 ± 0.289	23.3 ± 0.364	19.17 ± 0.26**	20 ± 0.577**	19.4 ± 0.292
Day 30 Treatment	16.63 ± 0.66	24.13 ± 0.449	18 ± 0.278**	19.4 ± 0.179**	18.97 ± 0.307
Day 45 Treatment	17.57 ± 0.882	25.47 ± 0.431	16.53 ± 0.555**	17.87 ± 0.371**	17.37 ± 0.332

Mean ± SEM **p≤0.001

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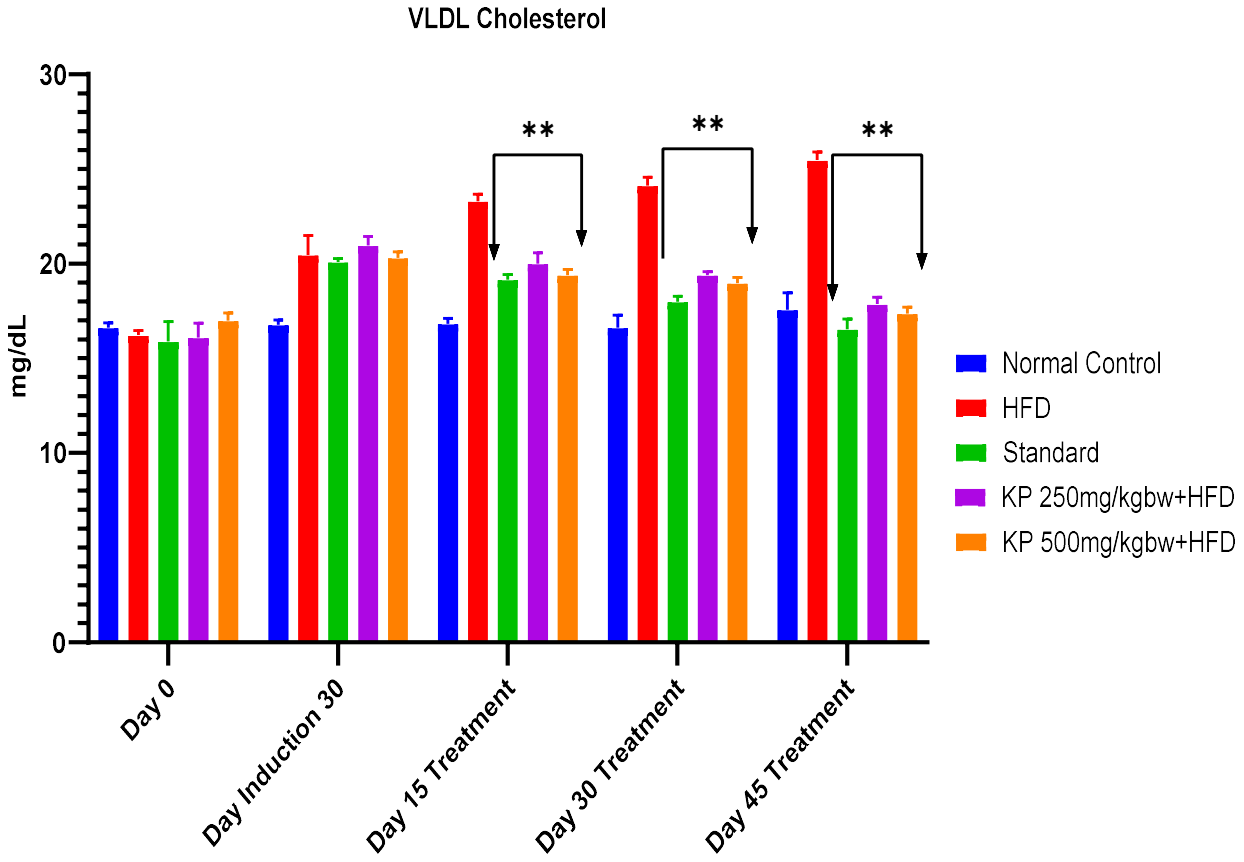

Table -7 Atherogenic Index

	Control	HFD	Standard	KP 250mg/kgbw+HFD	KP 500mg/kgbw+HFD
Day 0	1.47 ± 0.046	1.42 ± 0.056	1.35 ± 0.103	1.35 ± 0.043	1.44 ± 0.03
Day 30	1.48 ± 0.04	2.54 ± 0.14	2.5 ± 0.152	2.73 ± 0.181	2.32 ± 0.058
Day 15 Treatment	1.47 ± 0.029	3.21 ± 0.217	2.05 ± 0.05**	2.62 ± 0.117**	2.27 ± 0.087**
Day 30 Treatment	1.45 ± 0.089	3.55 ± 0.125	1.67 ± 0.055**	2.5 ± 0.033**	1.82 ± 0.079**
Day 45 Treatment	1.52 ± 0.095	3.76 ± 0.19	1.53 ± 0.052**	2.19 ± 0.069**	1.62 ± 0.038**

Mean ± SEM **p≤0.001

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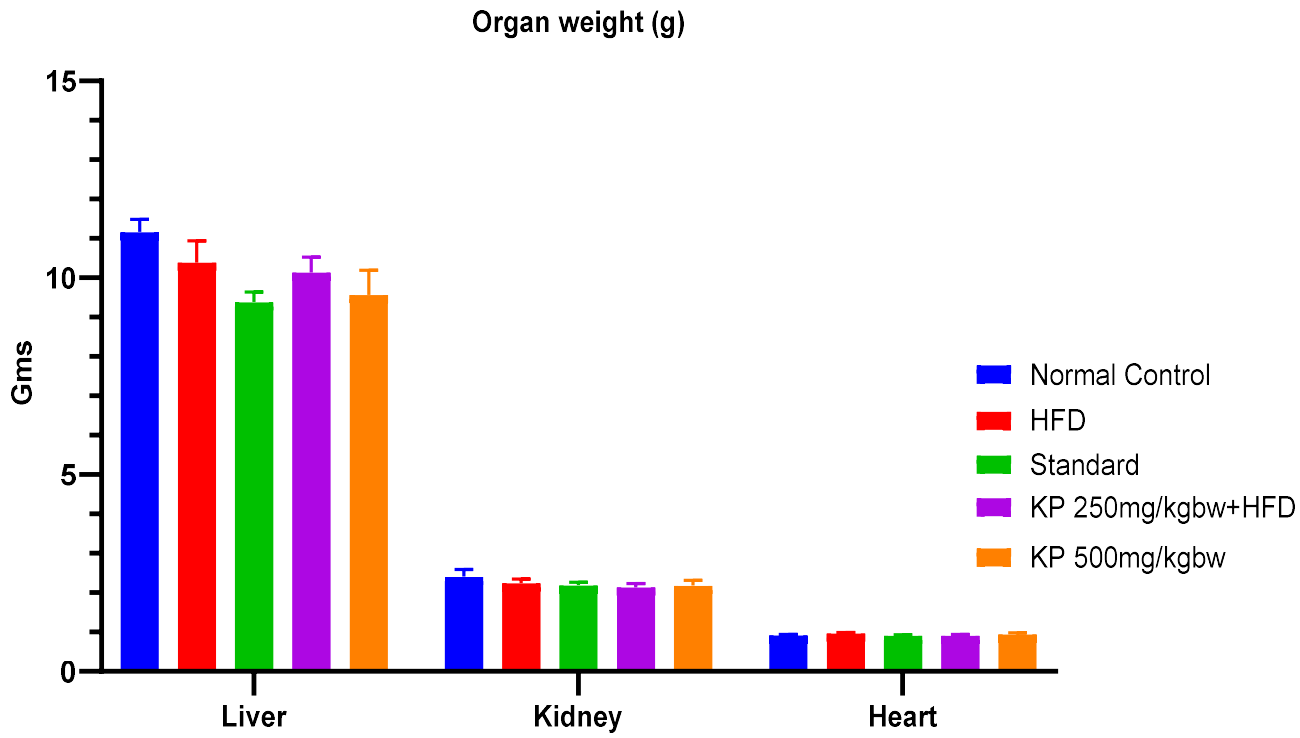
Table-8 Organ weight

	Control	HFD	Standard	KP 250mg/kgbw+HFD	KP 500mg/kgbw+HFD
Liver	11.16 ± 0.32	10.39 ± 0.555	9.38 ± 0.258	10.14 ± 0.38	9.57 ± 0.622
Kidney	2.41 ± 0.179	2.24 ± 0.104	2.19 ± 0.076	2.14 ± 0.094	2.18 ± 0.137
Heart	0.92 ± 0.018	0.97 ± 0.018	0.91 ± 0.025	0.91 ± 0.031	0.94 ± 0.04

Mean ± SEM. No significant difference found between groups $p>0.05$, when compared with Group 2



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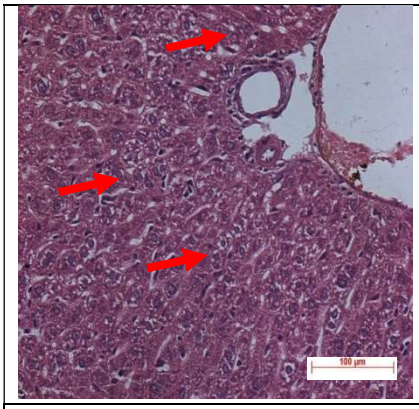
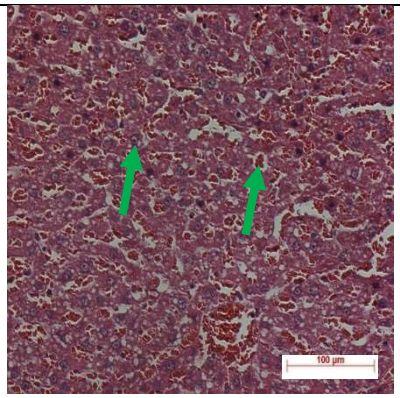
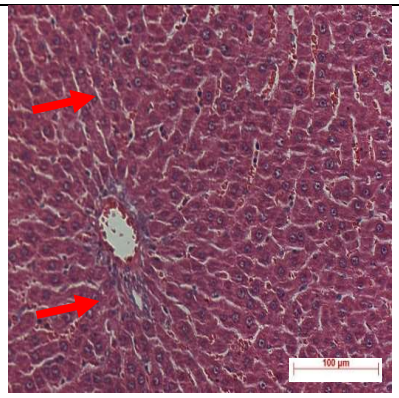
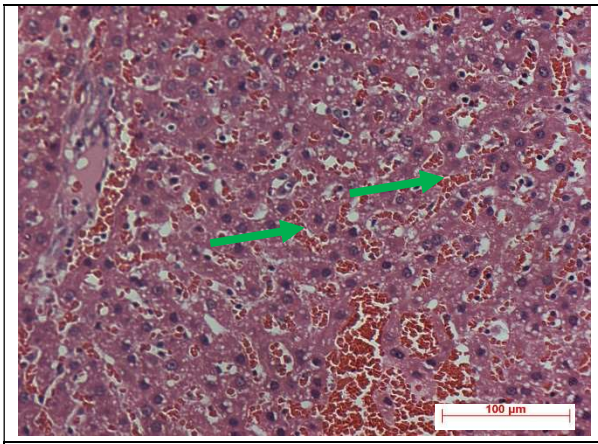
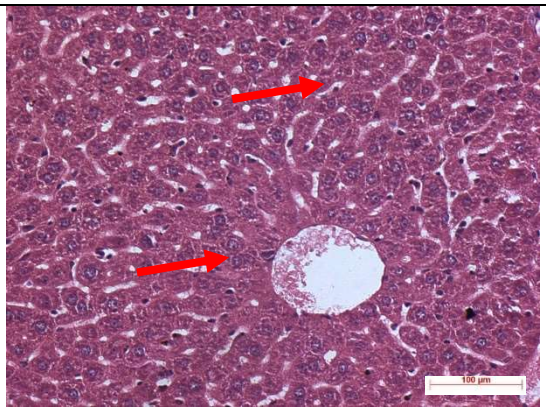
4.1 Histopathological examination

Liver

		
Control: Normal morphology of hepatocytes were observed in portal, peri portal and centri lobular region	**High fat diet:** Moderate vacuolar degeneration of hepatocytes [Red arrow] and mild sinusoidal dilatation and haemorrhages [green arrow] were noticed	**Standard:** Normal morphology of hepatocytes were observed in the portal, periportal and centri lobular region of liver - arrow

	
KP 250 mg/kgbw: Showing Moderate vacuolar degeneration of hepatocytes and mild sinusoidal dilatation and haemorrhages [green arrow] were noticed	**KP 500 mg/kgbw:** Normal morphology of hepatocytes were observed in the portal, periportal and centri lobular region of liver - arrow

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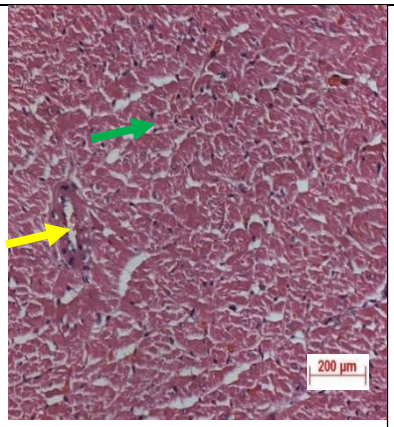
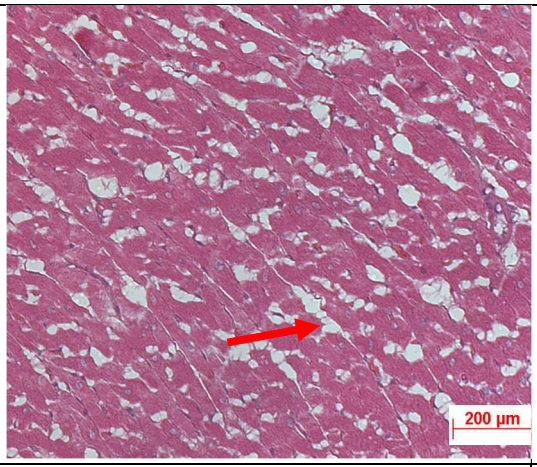
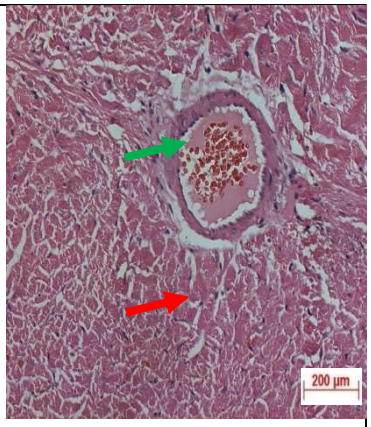
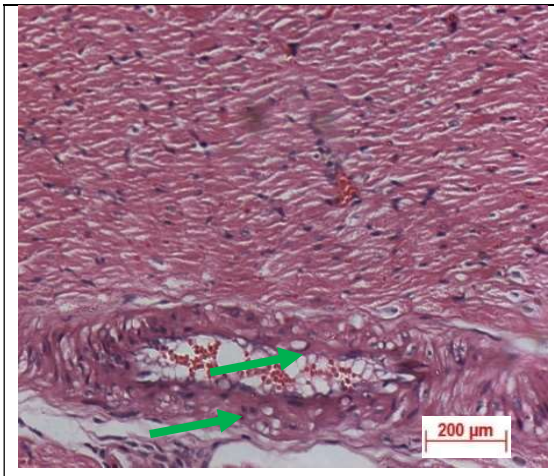
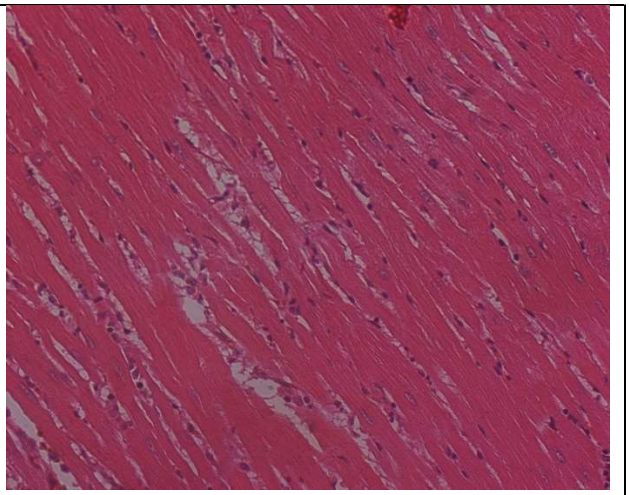
Heart

		
Control: Normal morphology of myocardium [green arrow] and coronary artery [yellow arrow] and no abnormalities were observed in heart	**High fat diet:** Multi focal vacuolar / fatty degeneration was observed in myocardium of heart – red arrow	**Standard:**Normal morphology of myocardium [Red arrow] with coronary artery of heart – green arrow; NO abnormality were observe

	
KP 250 mg/kgbw: Mild infiltration of inflammatory cells in myocardium of heart and Mild vacuolar degeneration of coronary artery of heart – green arrow	**KP 500 mg/kgbw:** no abnormalities were observed in heart

5. Discussion:

Hypercholesterolemia means having too much LDL cholesterol, which can clog arteries and up heart attack and stroke risk. Cardiovascular diseases are a major global health concern, and atherosclerosis, which causes these diseases, is a big player. Common meds like statins help, but they have drawbacks.

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So, it's important to explore other ways to manage high cholesterol. Medicinal plants, like Kalanchoe pinnata, have been used for centuries for their healing properties. This plant, also known as the Wonder plant, is rich in beneficial chemicals that could help treat various health issues, including high cholesterol.

The hypolipidemic activity of Kalanchoe pinnata may be attributed to its potent antioxidant and anti-inflammatory properties. The essential oil of Protium spruceanum exhibited significant antioxidant activities, which could be similar in other medicinal plants like Kalanchoe pinnata (9). Antioxidants play a critical role in reducing oxidative stress, which is a key factor in the pathogenesis of hyperlipidemia and atherosclerosis. Similarly, the anti-inflammatory effects of Rose geranium essential oil(10), suggest that inflammation reduction is an important therapeutic pathway for managing hyperlipidemia.

The phytochemical profile of Kalanchoe pinnata includes various bioactive compounds that contribute to its medicinal properties. Studies on other plants, such as on Ocimum gratissimum, have shown that the presence of phenolic compounds and flavonoids correlates with significant antioxidant activities (11). These compounds are known to improve lipid profiles by reducing LDL cholesterol and increasing HDL cholesterol levels.

Comparative studies have demonstrated the effectiveness of plant-based treatments in lowering lipid levels. For instance, the neem seed kernel powder had significant antihyperlipidemic effects in diabetic rabbits, comparable to standard hypolipidemic drugs (12).

The hypolipidemic effects of Kalanchoe pinnata could be linked to its influence on lipid metabolism and absorption. Saponins, which are present in many medicinal plants, including Kalanchoe pinnata can reduce cholesterol levels by inhibiting cholesterol absorption in the intestines and increasing cholesterol excretion (13).

The therapeutic potential of Kalanchoe pinnata in managing hyperlipidemia is further supported by its safety profile and minimal side effects compared to conventional drugs. Traditional use and contemporary studies highlight its role in holistic health management, encompassing antihyperlipidemic, antidiabetic, and anti-inflammatory effects (14,15).

Kalanchoe pinnata's hypolipidemic activity is underpinned by its rich phytochemical composition, antioxidant, and anti-inflammatory properties, making it a valuable candidate for managing hyperlipidemia. Further research and clinical trials are essential to fully elucidate its mechanisms and establish standardized therapeutic protocols. The integration of Kalanchoe pinnata and other medicinal plants into hyperlipidemia treatment regimens holds promise for safer, more effective cardiovascular disease management.

6. Conclusion

In conclusion, the study highlights the potential of Kalanchoe pinnata in managing

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hypercholesterolemia. Its leaf extracts showed promising effects on cholesterol levels, body weight, liver health. With its rich phytochemical profile and traditional medicinal use, Kalanchoe pinnata holds promise as a natural remedy for cardiovascular health. Further research is needed to explore its optimal use and long-term effectiveness in cholesterol management.

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