Journal of Pharmaceutical Research International

Volume 36, Issue 9, Page 81-89, 2024; Article no.JPRI.122221
ISSN: 2456-9119, NLM ID: 101716968
(Past name: British Journal of Pharmaceutical Research, Past ISSN: 2231-2919, NLM ID: 101631759)

Experimental Study of Hypolipidemic Effect of *Manjal Noiku Kudineer*

K. Aiswarya [a++*] and G. Essakky Pandian [a#]

[a] Department of Gunapadam, GSMC, Palayamkottai, India.

Authors' contributions

This work was carried out in collaboration between both authors. Author KA Performed the study and prepared the manuscript. Author GEP guided the study. Both authors read and approved the final manuscript.

Article Information

DOI: https://doi.org/10.9734/jpri/2024/v36i97579

Open Peer Review History:
This journal follows the Advanced Open Peer Review policy. Identity of the Reviewers, Editor(s) and additional Reviewers, peer review comments, different versions of the manuscript, comments of the editors, etc are available here: https://www.sdiarticle5.com/review-history/122221

Original Research Article

Received: 27/06/2024
Accepted: 03/09/2024
Published: 10/09/2024

ABSTRACT

Hyperlipidemia, is a major stake for the development of serious diseases like atherosclerosis, Coronary Artery Diseases, Stroke. Siddha system of Medicine with the numerous combination of medicines has *Manjal Noiku Kudineer*(MNK), a Siddha poly herbal formulation indicated for *Manjal Noi*. This study deals with the Hypolipidemic activity of *Manjal Noiku Kudineer* on atherogenic diet induced hyperlipidemia in experimental Wistar Albino Rats

Place of Study: The study was conducted at Arulmigu Kalasalingam College of Pharmacy, Virudhunagar.

Methodology: The study protocol for MNK was reviewed and approved by Institutional Animal Ethics Committee (IAEC), Arulmigu Kalasalingam College of Pharmacy, Virudhunagar, with the IAEC number AKCP/IAEC/10/24-25. The experimental hyperlipidemic diet consists of well-pulverized 400 mg/kg cholesterol, 50 mg/kg cholic acid, and coconut oil. All groups other than the control group were fed the prepared atherogenic meal in lieu of the regular pellet diet. Group I

[++] PG Scholar;
[#] Professor & HOD;
**Corresponding author: E-mail: draiswaryabsms1996@gmail.com;*

Cite as: *Aiswarya, K., and G. Essakky Pandian. 2024. "Experimental Study of Hypolipidemic Effect of Manjal Noiku Kudineer". Journal of Pharmaceutical Research International 36 (9):81-89. https://doi.org/10.9734/jpri/2024/v36i97579.*

served as normal control, Group II represented hyperlipidemic control rats given an atherogenic diet, Group III and IV represented test groups given MNK 200 mg/kg and MNK 400 mg/kg, respectively, and Group V represented standard-administered atorvastatin (10 mg/kg/day). All groups were compared, observations were noted and the observations were statistically evaluated.
Results: The study shows the results of reduction in body weight, blood lipid profile, liver lipid profile of hyperlipidemic rats on treating with the study medicine, which possess hypolipidemic activity. Histopathologic images of rat liver also shown normal parenchyma and parenchyma with minimal necrosis and minimal inflammatory changes on treating with the study medicine MNK.
Conclusion: The results stands as a support for MNK hypolipidemic activity, which in turn can be used as a antihyperlipidemic therapeutic agent from the Siddha System of Medicine.

Keywords: Manjal Noi; siddha; atorvastatin; karisalai; keezhanelli; hyperlipidemia.

1. INTRODUCTION

Siddha system of medicine has numerous medicinal preparations in the literature for treating various ailments in the human body. Apparently it heals the body but it also heals the soul to attain longevity and eternity [1]. Liver is the largest organ that plays a major role in the bodily metabolisms. However, Liver is injured by various toxic chemicals, infections and unhealthy diet and alcohol consumption. Herbs and herbal medicines were widely used in the treatment of liver injury by rejuvenating its cellular pathology [2]. Deaths due to liver diseases accounts for about 2 million annually, which is 1 out of every 25 deaths, and among which Non alcoholic fatty liver disease is the second leading cause of end stage liver disease evident by global burden of liver disease: 2023 update [3]. Liver regulates cholesterol metabolism. Abnormality in the lipid level can alter liver metabolism and hepatic tissues. Hyperlipidemia is the most important cause for the risk of coronary heart disease and atherosclerosis [4]. Atorvastatin is the commonly used drug to lower cholesterol levels. In Siddha system of Medicine, liver disease comes under *Manjal Noi(Kaamalai)* with its yellowish discoloration of skin and mucous membrane [5]. *Manjal Noiku Kudineer* (MNK) is one among the Siddha Medicines which is indicated for *Manjal Noi, Velluppu Noi, Oodhal Noi* [6,7]. MNK is a six ingredients based Siddha poly herbal formulation comprises of *Phyllanthus Amarus (Keezhanelli), Eclipta prostrata (Karisalai), Trichosanthes Cucumerina (Peipudal), Piper nigrum (Ven milagu), Foeniculum vulgare (Sombu), Aegle marmelos (Vilvam)* [6,8]. Analysing hypolipidemic activity of*Manjal Noiku Kudineer* would be greatest significance in the scientific world among hyperlipidemia. The present study deals with the Hypolipidemic activity of Siddha medicine *Manjal Noiku Kudineer* against atherogenic diet induced Hyperlipidemia in experimental animals, compared with atorvastatin, which will contribute to strengthen the efficacy of MNK and also further research.

2. MATERIALS AND METHODS

2.1 Drug Authentication

The herbal raw drugs of MNK were procured from a reputed raw drug store. Herbs were authenticated by the faculties of Department of PG Gunapadam and the Botanist, Department of Botany, Government Siddha Medical College, Palayamkottai.

2.2 Medicine Preparation

The herbal raw drugs were cleaned and purified as mentioned in Siddha literature *Sikitcha Rathna Deepam in Vaithiya Nool* [9]. Purified ingredients of MNK was chopped and coarsely powdered. The MNK decoction was prepared by adding 650ml of water to the coarse powder, boiled, reduced to 85ml of its volume and filtered. It is indicated for *Manjal Noi* with the dosage of 85ml, thrice a day, for three days.

2.3 Animal Care and Husbandry

The study protocol for MNK was reviewed and approved by Institutional Animal Ethics Committee (IAEC), Arulmigu Kalasalingam College of Pharmacy, Virudhunagar, with the IAEC number AKCP/IAEC/10/24-25. Male adult Wistar albino rats, weighing between 150 and 200 grams, were kept in polypropylene cages with a temperature control of 27°C ±1°C and a 12-hour light and dark cycle at the animal housing facility of Vels University. For a period of seven days, the animals were given a regular pellet meal (Sai Durga foods, Bangalore) and unlimited water to help them adjust to their new surroundings. The following chemicals were

utilised in the study: Atorvastatin, which was purchased from the neighbourhood pharmacy in Tamil Nadu (periyandavar medicals). Anaesthesia ether, ethyl acetate, and ethanol (SD Fine Chemicals, Mumbai) were bought as diagnostic kits for estimate from Merck Diagnostics India Ltd.

2.3.1 Atherogenic diet

A well-pulverized combination of 400 mg/kg of cholesterol, 50 mg/kg of cholic acid, and coconut oil makes up the experimental hyperlipidemic diet. The rats are given this combination in the form of paste-like moulds. All groups other than the control group were fed the prepared atherogenic meal in lieu of the regular pellet diet. The impact of MNK on experimental hyperlipidaemia was investigated in rats that were fed an atherogenic diet and had unlimited access to water for 20 days.

2.4 Pharmacological Evaluation

Prior to the trial, every animal was given unlimited access to water and fasted for eighteen hours. Five groups of six rats each were created from the animals. Group I served as normal control administered with 2% CMC only,Group II represented hyperlipidemic control rats given an atherogenic diet, Group III and IV represented test groups given MNK 200 mg/kg and MNK 400 mg/kg, respectively, and Group V represented standard-administered atorvastatin (10 mg/kg/day). All groups were given an atherogenic diet for two days, with the exception of the normal control group and compared. The same medication was administered for seven days after the hyperlipidaemia was induced. The animals received a normal pellet diet and unlimited access to water. After the experiment was completed, the next day, the rats' blood was drawn while they were under a light anaesthesia.

2.5 Histopathology

Following the collection of a blood sample, all rats were killed. The rats' livers were removed in order to visually identify any large lesions. The livers were then weighed to ascertain weight Changes and kept in 10% neutral formalin for histopathologic examination. After the tissue was fixed in paraffin, it was sectioned, stained with eosin and haematoxylin, and looked over under a microscope.

2.6 Statistical Evaluation

The observations were statistically evaluated. All the values were expressed as mean ± standard error of mean. The data were statistically analyzed by one-way ANOVA followed by Dunnett's t-test, and value $P < 0.05$ was considered to be significant. *p<0.001;**p<0.01 vs control.

3. RESULTS

3.1 Body Weight

According to the results of the effect of MNK on body weight of atherogenic- induced hyperlipidemic rats, the total body weight of the hyperlipidemia-induced group has considerably risen in comparison to normal rats. Values for Group I (normal rat group) ranged from 161.18±3.28 mg/dl, whereas the current values are 281.36±1.15 mg/dl from which Hypercholesterolaemia is indicated by this. The readings are lowered by 188.34±2.19 ($P < 0.001$) and 176.23±0.66 mg/dl ($P < 0.01$), respectively, in the treatment group that received MNK (200 mg/kg) and MNK (400 mg/kg). However, as seen by Table 1, atorvastatin also dramatically lowered blood total cholesterol levels to 164.95±0.78 mg/dl ($P < 0.001$).

3.2 Blood Lipid Profile

When compared to normal rats, the group with hyperlipidemia-induced rats, total cholesterol levels were considerably higher. Compared to Group I (normal rat group), whose values range from 70.85 to 1.27 mg/dl, the levels have increased to 175.14 ± 1.35 mg/dl. This suggests

Table 1. Effect on body weight

S.no	Groups	Body weight
1	Normal control	161.18±3.28
2	Hyperlipidemic Control	281.36±1.15
3	MNK 200mg/kg	188.34±2.19*
4	MNK 400mg/kg	176.23 ±0.66*
5	Atorvastatin(10mg/kg/day)	164.95±0.78**

p<0.001;p<0.01 vs control*

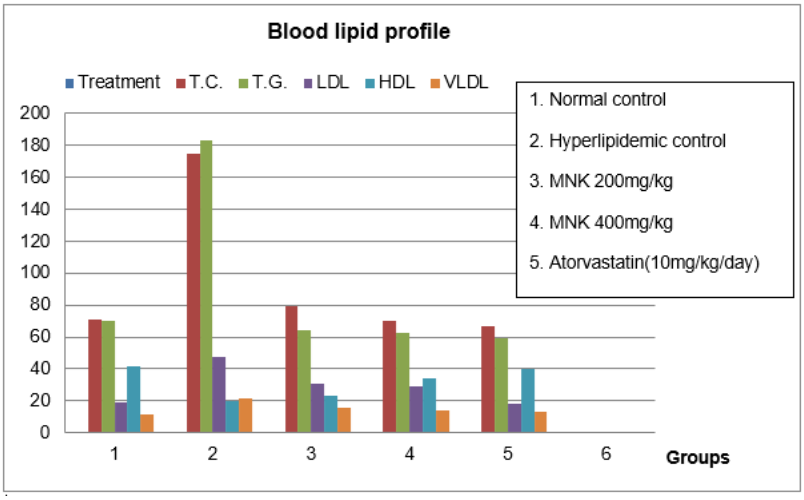

Fig. 1. Effect on Blood lipid profile

elevated cholesterol levels. Values are decreased to 79.31 ± 1.26 ($P < 0.001$) and 70.53 ± 1.42 mg/dl ($P < 0.01$) in the treatment group treated with MNK (200 mg/kg) and MNK (400 mg/kg), respectively. The MNK treatment group's total cholesterol readings have significantly decreased. However, as Fig. 1 demonstrate, atorvastatin also lowered blood total cholesterol levels to 66.5 ± 1.11 mg/dl ($P < 0.001$).

In the group of rats with hyperlipedemia, the TG levels were 183.17±1.53 mg/dl, whereas in the normal group, the values were 70.14±1.52 mg/dl. Triglyceridemia is indicated by this. The results in the MNK treatment group (200 mg/kg and 400 mg/kg) are substantially lower, at 64.65±1.05* mg/dl ($P < 0.01$) and 62.81±0.58 mg/dl ($P < 0.01$), respectively. The results are lower in the atorvastatin-treated group, at 58.85±1.76 mg/dl ($P < 0.001$). [Tabel 2] [Fig. 1].

In the atherogenic-induced group, LDL-cholesterol was 18.87±1.36 mg/dl, show a substantial increase from the normal rat group's 47.15±1.29 mg/dl. The MNK treatment group received 200 mg/kg and 400 mg/kg, respectively, resulting in decreased levels of 31.19±1.52 and 29.31±1.05 mg/dl ($P < 0.001$). The MNK treatment group's LDL-cholesterol readings have significantly decreased. The LDL-cholesterol level has been greatly lowered by atorvastatin to 18.65±1.28 mg/dl ($P < 0.001$). [Table 2] [Section 2].

When compared to normal rats, the atherogenic-induced group's HDL cholesterol has significantly reduced. Compared to the normal rat group's results of 20.13±1.12 mg/dl, the values have decreased to 41.34±1.49 mg/dl. The results in the MNK treatment group were 23.21±0.93 ($P < 0.01$) and 34.17±1.20 mg/dl ($P < 0.01$), respectively, at 200 mg/kg and 400 mg/kg. The results in the group treated with atorvastatin were 40.23±1.45 mg/dl ($P < 0.001$). [Fig. 1] [Table 2].

Compared to the normal rat group's VLDL-cholesterol of 11.34±1.05 mg/dl, the atherogenic-induced group's VLDL-cholesterol has greatly raised to 21.81±1.57 mg/dl. The results in the MNK treatment group (200 mg/kg) and the control group (400 mg/kg) are 15.39±0.40 ($P < 0.01$) and 14.11±1.61 mg/dl ($P < 0.01$), respectively. There is a notable decrease in the MNK treatment group. The level of VLDL cholesterol has been significantly decreased by atorvastatin to 13.62±1.91 mg/dl ($P < 0.001$). [Tables 2] [Section 2].

3.3 Liver Lipid Profile

When compared to normal rats, the group with hyperlipidemia-induced rats, total cholesterol levels have been significantly increased. Compared to Group I (normal rat group), whose values range from 73.17±0.91 mg/dl, the levels have increased to 154.17±1.12 mg/dl. This suggests elevated cholesterol levels. MNK (200 mg/kg) and MNK (400 mg/kg) treatment groups showed a reduction in values of 80.15±0.96 ($P < 0.001$) and 73.3±0.89 mg/dl ($P < 0.01$), respectively. The MNK treatment group's total cholesterol readings have significantly decreased. However, as Fig. 2 demonstrate, atorvastatin also significantly reduced blood total cholesterol levels to 71.05±1.01 mg/dl ($P < 0.001$).

Table 2. Effect of MNK on Blood lipid profile of hyperlipidemic rats

Group	Treatment	T.C.	T.G.	LDL	HDL	VLDL
I	Normal Control	70.85±1.27	70.14±1.52	18.87±1.36	41.34±1.49	11.34±1.05
II	Hyper lipidimic Control	175.14±1.34	183.19±1.42	47.15±1.29	20.13±1.12	21.81±1.57
III	MNK 200mg/kg	79.31±1.26*	64.65±1.05*	31.19±1.52*	23.21±0.93*	15.39±0.40*
IV	MNK 400mg/kg	70.53±1.42*	62.81±0.58*	29.31±1.05*	34.17±1.20*	14.11±1.61*
V	Atorvastatin 10Mg/kg	66.5±1.11**	58.85±1.76**	18.65±1.28*	40.23±1.45*	13.62±1.91**

Table 3. Effect of MNK on liver lipid profile of hyperlipidemic rats

Group	Treatment	TC	T.G.	LDL	HDL	VLDL
I	Normal Control	73.17±0.91	68.75±1.97	18.17±1.74	34.27±0.85	17.69±1.38
II	Hypo lipidemic Control	154.17±1.12	156.82±1.50	43.32±2.57	21.25±1.17	33.1±1.07
III	MNK 200mg/kg	80.15±0.96*	82.15±1.07*	31.22±1.15*	28.96±0.98*	25.32±0.39*
IV	MNK 400mg/kg	73.3±0.89*	72.12±1.01*	20.7±1.22*	311.15±1.54*	18.98±1.26*
V	Atorvastatin 10mg/kg/day	71.05±1.01*	65.25±1.19*	18.98±1.45*	28.4±1.13*	16.5±0.98*

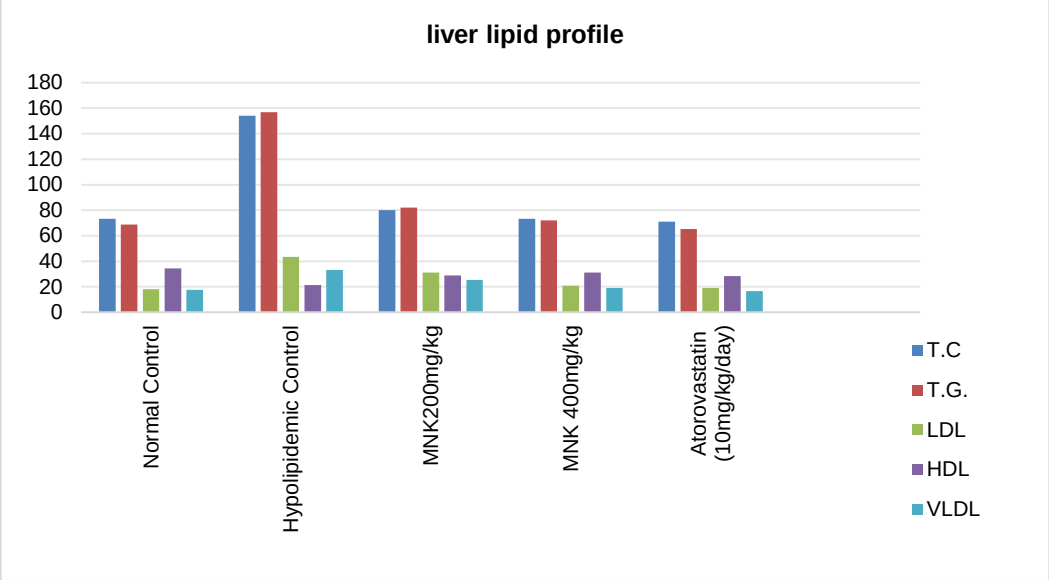

Fig. 2. Effect on Liver lipid profile

In the group of rats with hyperlipedemia, the TG levels were 156.82±1.50 mg/dl, whereas in the normal group, the values were 68.75±1.97 mg/dl. This indicates triglyceridemia. The readings are much lower in the MNK treatment group (200 mg/kg and 400 mg/kg) to 82.15±1.07 mg/dl (P < 0.01) and 72.12±1.01/dl (P < 0.01), respectively. The results in the group treated with atorvastatin are decreased to 65.25±1.19 mg/dl (P < 0.001). [Table 3] [Fig. 2].

Compared to the normal rat group's LDL-cholesterol of 18.17±1.74 mg/dl, the atherogenic-induced group's LDL-cholesterol has considerably increased to 43.32±2.57 mg/dl. Values decreased to 31.22±1.15 and 20.7±1.22 mg/dl (P < 0.001) in the MNK treatment group (200 mg/kg and 400 mg/kg, respectively). The MNK treatment group's LDL-cholesterol readings have significantly decreased. LDL-cholesterol level has been considerably lowered with atorvastatin to 18.98±1.45 mg/dl (P < 0.001). [Table 3] [Fig. 2].

When compared to normal rats, the atherogenic-induced group's HDL cholesterol has significantly lowered. Compared to the normal rat group's readings of 34.27±0.85 mg/dl, the levels have decreased to 21.25±1.17 mg/dl. The results in the MNK treatment group were 28.96±0.98 (P < 0.01) and 31.15±1.54/dl (P < 0.01), respectively, at 200 mg/kg and 400 mg/kg. The results in the group treated with atorvastin were 28.4±1.13 mg/dl (P < 0.001). [Table 3] [Fig. 2].

The atherogenic-induced group's VLDL cholesterol increased to 33.1±1.07 mg/dl, which is substantially higher than the normal rat group's 17.69±1.38 mg/dl. The levels are lowered to 25.32±0.39 (P <0.01) and 18.98±1.26 mg/dl (P <0.01) in the group treated with MNK (200 mg/kg) and (400 mg/kg), respectively. There is a notable decrease in the MNK treatment group. The level of VLDL cholesterol has been significantly reduced by atorvastatin to 16.5±0.98 mg/dl (P < 0.001). [Tables 3] [Fig. 2].

3.4 Histopathology

The liver section of normal control rats shown parenchyma with normal hepatocyte and central vein, portal tract were also normal. Hyperlipedemic Control rat liver sections shown hepatocyte parenchyma with scattered focal area of necrosis. The liver section of positive control shown normal parenchyma. Treatment group IV rats shown parenchyma with minimal necrosis, and minimal inflammation. Treatment group V shown parenchyma with normal hepatocyte, central vein and portal tract. The following histopathologic images in the Fig. 3 shows the above results of MNK on rat groups.

4. DISCUSSION

According to the current study, hyperlipidemic rats fed an atherogenic diet had higher body weights, indicating hypercholestrolemia, while the MNK-treated group's body weight decreased. Additionally, every rat treated with an

atherogenic diet had hyperlipidaemia, as demonstrated by elevated levels of triglycerides, liver and blood cholesterol levels, VLDL, and LDL, together with a reduction in HDL. A lower risk of ischaemic heart disease has been linked to higher HDL cholesterol and lower levels of TC, LDL cholesterol, and TG, according to earlier studies and research. Increased VLDL leads to the development of the maximum amount of LDL, which can adhere to blood vessel walls and impede normal blood flow. The reduction in cholesterol might mean that the oxidation of fatty acids has been increased by lipolysis or inhibition [10]. Elevated levels of low-density lipoprotein (LDL-C) have been linked to an increased risk of coronary artery disease (CAD), while low levels of high-density lipoprotein (HDL-C) have also been linked to this association [11].

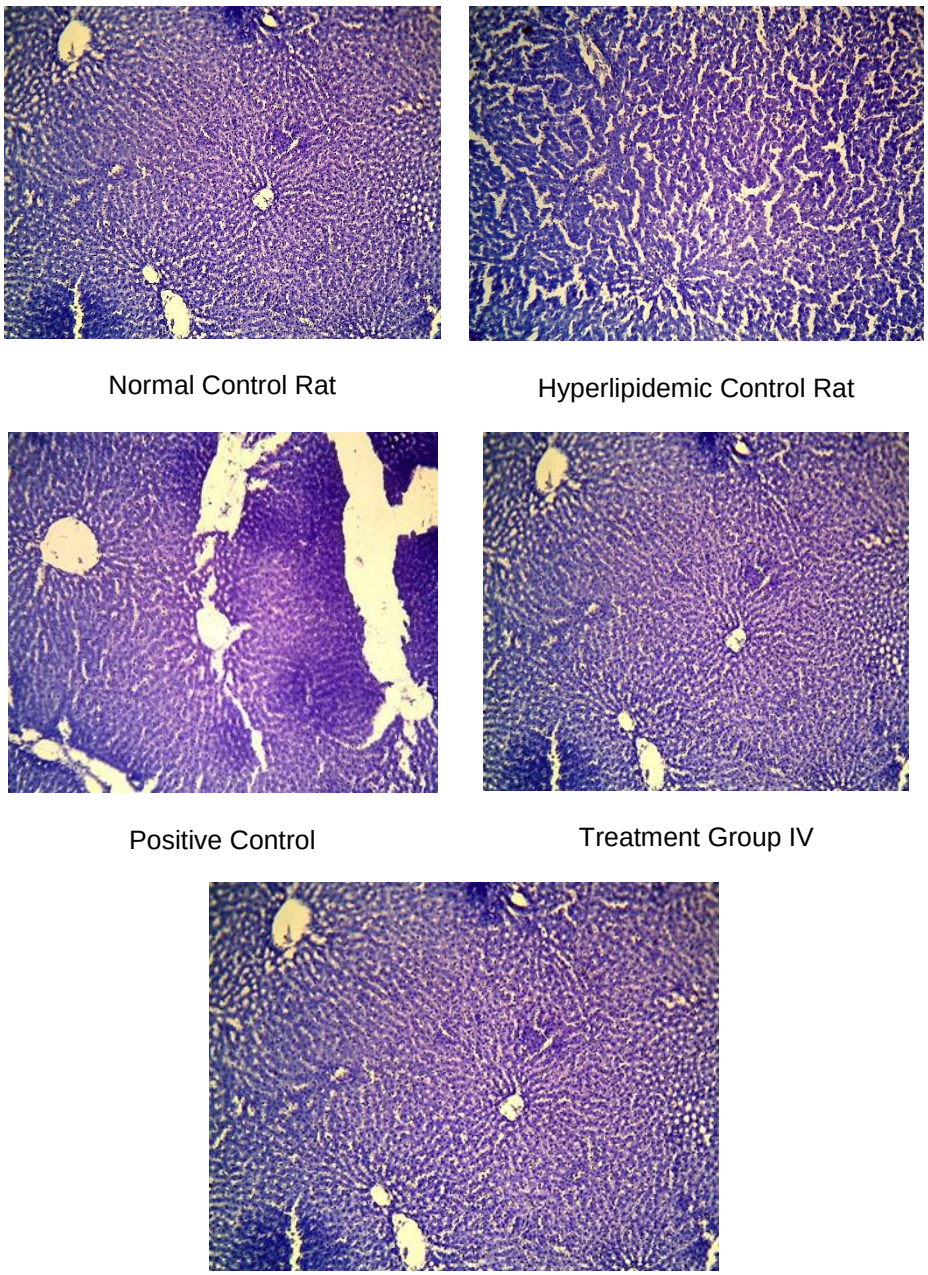

Fig. 3. Histopathologic images of rat liver

In order to test natural or synthetic hypolipidemic medications, atherogenic diets that cause acute hyperlipidaemia, especially in rats, have been employed. Based on the results, MNK significantly decreased the level of cholesterol in the rats and reversed the hyperlipidemic impact caused by atherogenic factors. MNK demonstrated a major decrease in plasma triglyceride and cholesterol levels when administered at 200 mg/kg and 400 mg/kg. Lowering LDL is the ultimate goal of many hypolipidemic medications, and it may be linked to the reduction in total cholesterol caused by the MNK at dosage levels of 200 mg/kg and 400 mg/kg.

Also, other research evidence include that there is hypolipidemic activity, hepatoprotective activity, nephroprotective activity in *Phyllanthus Amarus (Keezhanelli)* [12], and there is hypolipidemic activity, anti inflammatory activity, hepatoprotective activity, rejuvenative property in *Eclipta prostrata (Karisalai)* [13] which are all the ingredients of MNK which also supports the results of the present study. Another previous study related to MNK reveals the anti viral potential of MNK against Hepatitis C Viral RNA using insilico docking technique [14]. The study of hypolipidemic activity of MNK, which is lowering cholesterol levels, may increase the fecal bile excretion with the consequent reduction of hepatic cholesterol because of its metabolism. This demonstrates how the rate of diffusion across the intestinal mucosa has slowed down, lowering the amount of cholesterol and triglycerides that are absorbed.

5. CONCLUSION

The results obtained from the pharmacological screening have led to the conclusion that the study medicine *Manjal Noiku Kudineer* (MNK) has significant hypolipidemic activity. Hence it can be exploited as an antihyperlipidemic therapeutic agent or adjuvant in existing therapy for the treatment of hyperlipidemia. Further study by measurement of heparin-releasable plasma LPL activity and LCAT activity on MNK can be done to strengthen the above results and thereby can be implemented in clinical trials.

DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc) and text-to-image generators have been used during writing or editing of manuscripts.

ETHICAL APPROVAL

Animal Ethic committee approval has been collected and preserved by the author(s)

CONSENT

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Christian G, Ponnappan Shanmugapriya, Elansekaran S, Thangamani, Subathra Meenakumari R. Acute and Sub-acute toxicity studies of a siddha medicine ganthaga mezhugu by oral administration in sprague dawley rats. Journal of Natural Remedies. 2023;937-947.
   DOI:10.18311/jnr/2023/31703
2. Rane J, Jadhao R, Bakal RL. Liver diseases and herbal drugs: A review. J Innov Pharm Biol Sci.. 2016;3(2):24-36.
3. Harshad Devarbhavi, Sumeet K. Asrani, Juan Pablo Arab, Yvonne Ayerki Nartey, Elisa Pose, Patrick S. Kamath,Global burden of liver disease: 2023 update, Journal of Hepatology. 2023;79(2): 516-537.
   ISSN 0168-8278.
   Available:https://doi.org/10.1016/j.jhep.2023.03.017
4. KK, ST, PP, GV, JS. Anti-hyperlipidemic herbs in siddha system of medicine; 2014.
5. KN Kuppusamy Mudhaliyar, HBIM. Siddha Maruthuvam Pothu (2022nd ed.) [Tamil]. Department of Indian Medicine and Homeopathy; 1936.
6. Ministry of Ayush, Govt. of India. Siddha Formulary of India Part II Tamil. Ministry of Ayush, Govt. of India; 2011.
7. Ministry of Ayush, Govt. of India. Siddha Formulary of India Part II Tamil. Ministry of Ayush, Govt. of India; 2011.
8. Visweswaran S, Iyswarya S, Muthukumar NJ. Revealing anti-viral potential of siddha formulation manjal noiku kudineer against hepatitis C Viral - RNA Dependent RNA Polymerases.
9. Pillai C Kannusamy. Sikitcha rathna deepam ennum vaidhiya nool. Chennai: B Rathna Nayakkar & Sons; 2018.

10. Pourush Badal, Rajendra Mani Badal. Hypolipidemic activity of *Perosolinum cripsum* plant in Triton WR-1339 induced rats. Herbal Tech Industry; 89.
11. Priya F, Velpandian V, Ayyasamy S, Pitchiahkumar M. Hypolipidemic activity of Kadukkai Chooranam (*Terminalia chebula*) in Triton WR-1339 induced hyperlipidemic rats. Journal of Pharmacy and Biological Sciences (IOSR-JPBS). 2013; 5(5):77-84.
12. Jay Ram Patel, Priyanka Tripathi, Vikas Sharma, Nagendra Singh Chauhan, Vinod Kumar Dixit, Phyllanthus amarus: Ethnomedicinal uses, phytochemistry and pharmacology: A review. Journal of Ethnopharmacology. 2011;138:2.
13. Li Feng, Yuan-Yuan Zhai, Jia Xu, Wei-Feng Yao, Yu-Dan Cao, Fang-Fang Cheng, Bei-Hua Bao, Li Zhang, A review on traditional uses, phytochemistry and pharmacology of *Eclipta prostrata (L.)* L. Journal of Ethnopharmacology. 2019;245: 112109.
ISSN 0378-8741.
Available:https://doi.org/10.1016/j.jep.2019.112109
14. Visweswaran S, Iyswarya S, Muthukumar NJ. Revealing anti-viral potential of siddha formulation manjal noi kudineer against hepatitis C viral-rna dependent rna polymerase using in-silico docking technique. Pharmacognosy Research. 2022;14(3).

Peer-review history:
The peer review history for this paper can be accessed here:
https://www.sdiarticle5.com/review-history/122221