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Research Article

A Comparative Research between Pharmacological and Non-Pharmacological Profile of Anti-Hyperlipidemic Activity on Rodents

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Abstract

The condition of hyperlipidemia is found to be a great establisher for all the negative health consequences which may lead to cardiac complications. Continuous usage of medication alone is not permanent remedy but also need physical exercise. The same situation was established in animals to assess the performance of pharmacological and non-pharmacological profile by standardized screening using *In-vivo* methods. The high-cholesterol diet caused a significant increase in total lipids, total cholesterol (TC), total triglycerides (TG), low-density lipoprotein cholesterol (LDL-C), and the atherogenic index, whereas the level of high-density lipoprotein cholesterol (HDL-C) was significantly decreased for the treatment groups intended for physical exercise. This article enables the importance of health benefited by physical performance by depicting the biochemical parameters.

Keywords: Hyperlipidemia, Triglycerides, low-density lipoprotein, activity wheel, Physical exercise, Cardiac performance.

INTRODUCTION

Hyperlipidemia means that high levels of fats (or lipids) are in the blood. These fats include cholesterol and triglycerides. They are important for our bodies to function but when they are too high, they can put people at risk for heart disease and stroke¹. Fats do not dissolve in water. For them to be carried in the blood (which is mostly water) they combine with another substance called a protein to create a lipoprotein (LDL, HDL and VLDL). Too much LDL, or "bad" cholesterol, can build up in the arteries (the blood vessels that carry blood throughout the body) and, over time, cause heart disease or stroke. On the other hand, having too much HDL, or "good" cholesterol, protects the heart by helping to remove the buildup of LDL from the arteries². Low levels of HDL and high triglycerides can also increase fat build up in the arteries and cause heart disease, especially in people who are obese or have diabetes.

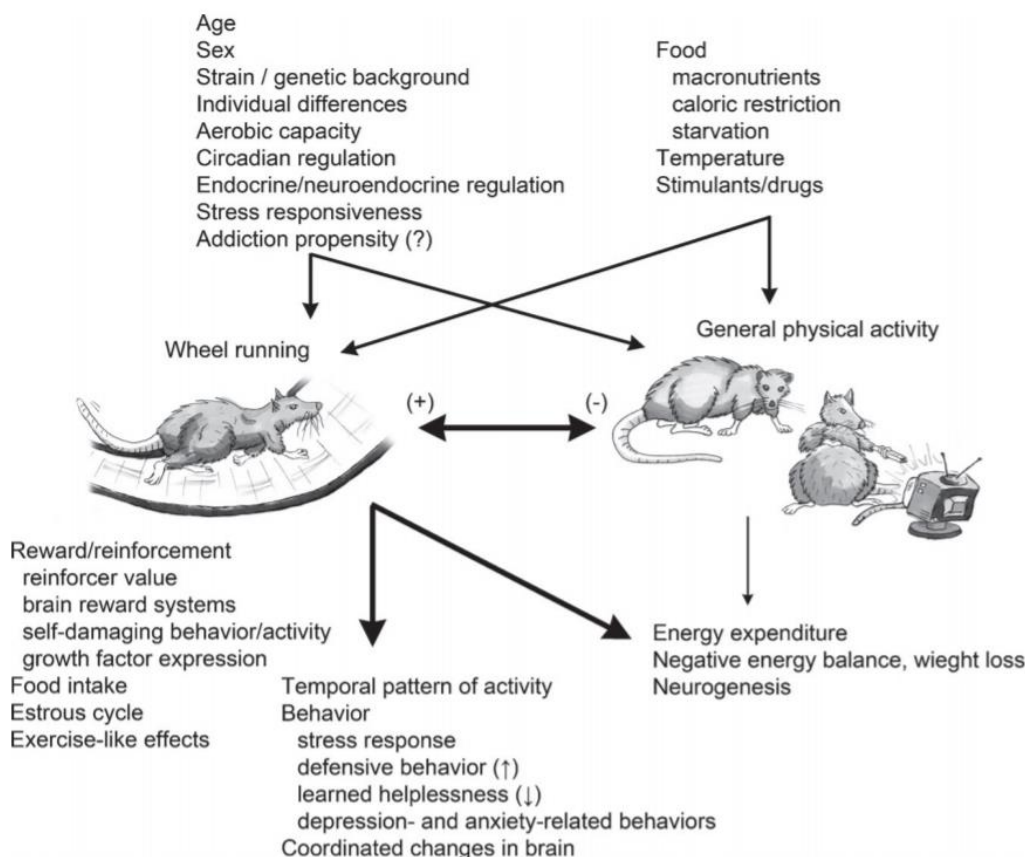
Being overweight or obese, not getting enough exercise, and a diet high in saturated fat and cholesterol and low in fruits,

vegetables and fiber can play a role in the development of hyperlipidemia³. Beyond diet, however, there are other factors that can lead to this condition. Hyperlipidemia generally has no symptoms. Screening is done with a simple blood test to measure levels of cholesterol and triglycerides. According to the National Cholesterol Education Program Guidelines, healthy adults should be screened once every five years starting at age 20. If you have a family history of high cholesterol or other risk factors you may need earlier or more frequent screening⁴.

Hyperlipidemia is treated with changes in diet, weight loss and exercise. If necessary, your doctor will also prescribe medication. The type and dose of the medication will depend on your specific blood fat levels (rather than total cholesterol) and if you have heart disease, diabetes, or other risk factors for heart disease⁵⁻⁷.

Table: 1 Normal level for a lipid profile

Lipids	Desirable Value	Border line	High risk
Cholesterol	<200 mg/dl	200 -239 mg/dl	240 mg/dl
Triglycerides	<140 mg/dl	150 -199 mg/dl	200 -499 mg/dl
HDL Cholesterol	60 mg/dl	40 – 50 mg/dl	< 40 mg/dl
LDL Cholesterol	60 -130 mg/dl	130 – 159 mg/dl	160 -189 mg/dl
Cholesterol/HDL Ratio	4.0	5.0	6.0



Prevention of Hyperlipidemia⁸⁻⁹

- A low-fat, low-cholesterol diet is recommended.
- Consume soluble fiber-rich foods such as oats, beans, and some fruits.
- Maintaining a healthy weight requires frequent exercise.

The greatest strategy to combat hyperlipidemia is to make small, manageable lifestyle adjustments. However, if lifestyle measures fail to control the illness, cholesterol-lowering medicines must be used.

Treatment of Hyperlipidemia

The National Cholesterol Education Program (NCEP) was established in 1987 by the National Institute of Health (NIH) under the direction of the Adult Treatment Panel (ATP) for the purpose of disseminating information to health professionals and the general public about hyperlipidemia testing, evaluation, monitoring, and treatment.

(a) Therapeutic lifestyle changes

Dietary changes, regular physical activity, quitting smoking, and losing weight should be tried first, especially in

moderate cases of hyperlipidemia and in people who do not have CHD or CHD risk equivalent and 2 risk factors. It's important to remember that when you're dieting, you're lowering your cholesterol consumption. At the same time, cholesterol production, particularly in the liver, rises. It is recommended that cholesterol intake be limited to 25 percent to 35 percent of total energy intake, with saturated fatty acids accounting for less than 7% of total energy intake and cholesterol intake being less than 200 mg per day. It is recommended that you consume plant sterol esters and soluble fiber. A good diet can lower cholesterol levels by ten to fifteen percent in the blood¹⁰.

(b) Drug Therapy

If you have high LDL, risk factors, or documentation of CHD, you should consider starting pharmacological therapy in addition to TLC. Although monotherapy has been found to be successful in the treatment of hyperlipidemia, a comprehensive approach may necessitate the use of combination medication. Statins, ezetimibe, and bile acid sequestrants are some of the current lipid-lowering medications¹¹.

When dietary changes are insufficient, medication tailored to lower blood cholesterol levels may be administered. Repeated evacuation of blood plasma may be indicated to decrease blood cholesterol levels in rare people with exceedingly high cholesterol levels¹². Most people need to treat hyperlipidemia for the rest of their lives, which includes both lifestyle changes and medicines.

(c) Pharmacological Treatment

For the treatment of hyperlipidemia, a variety of hypolipidemic medications are available on the market. The results of the Coronary Drug Project, published in 1975, showed that the medications are unsuccessful in preventing myocardial infarction in patients with pre-existing CHD.

Table: 2 Antihyperlipidemic Drugs

Class	Drug	Major effect	Dose (mg/dl)
HMG Co –A Reductase inhibitors	Mevastatin	Lowers LDL concentration	20-40
	Lovastatin	Lowers LDL concentration	40
	Pravastatin	Lowers LDL concentration	30
	Simvastatin	Lowers LDL concentration	5-10
Fibrates	Clofibrate	Lowers serum TG concentration	2 gm/day
	Gemfibrozil	Lowers Plasma TG	1.2 gm
	Fenofibrate	Lowers plasma LDL concentration and rise HDL concentration	2-5 gm/day
	Simfibrate	Lowers chol and TG concentration	1.5 gm/day
	Etofibrate	Lowers VLDL and LDL concentration	900mg/day
Antioxidant	Probuocol	Lowers plasma chol by 10 – 15 %	250-500mg/day
Other lipid lowering drugs	Nicotinic acid	Lowers LDL concentration	2-6 gm
	Neomycin	Lowers LDL concentration	0.5-2 gm
	Tiademol	Lowers plasma chol level	1600mg
Bile acid binding resins	Cholestyramin	Binds bile acid resulting chol catabolism	12-16 mg/day
	Colestipol	Lowers plasma LDL levels	15-30 mg/day

METHODS

Selection of Animals

Sprague Dawley rats of either sex (250g-300g) were maintained for 7 days in the animal house of Chalapathi Institute of Pharmaceutical Sciences, Guntur under standard conditions temperature (24 ± 10 C), relative humidity (45-55%) and 12:12 light: dark cycle. The animals were fed with standard rat pellet and water ad libitum. The animals could acclimatize to laboratory conditions 48 h before the start of the experiment. 5 mice/group were used in all sets of experiments. All the experiments were conducted after obtaining permission from the Institutional Animal Ethics Committee (IAEC) Chalapathi Institute of Pharmaceutical Sciences, Guntur (08/IAEC/CLPT/2020-21 (Dt:05-12-2020)).

- GROUP 1 - Control
- GROUP 2 – Negative Control - Diet induced Hyperlipidemia
- GROUP 3 – Standard (Atorvastatin 40mg/kg)
- GROUP 4 – Activity Wheel (Overall Body Performance)
- GROUP 5 – Muscular Strength Maze (Cardio Performance)

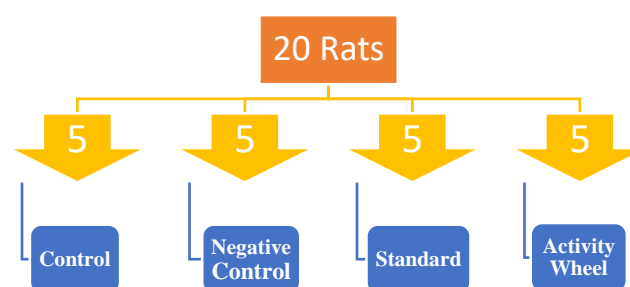


Figure 1: Treatment groups for Anti-hyperlipidemic activity

Hyperlipidemic Diet

Mixing vanaspati Ghee + coconut oil (3:1 v/v Ration). The Diet was given orally (3mg/kg/day).

Preparation of Standard Drug

Standard Atorvastatin at a dose of 40 mg/kg was prepared by suspending bulk atorvastatin in aqueous 1% Carboxy Methyl Cellulose was given orally.

Diet induced hyperlipidemic model

The Animals were selected, weighed then marked for individual identification. In this model, rats were made hyperlipidemic by the oral administration of high fat diet for 14 days by mixing with regular pellet diet. and rats were

then given with standard Atorvastatin at a dose of 40 mg/kg orally suspended in in aqueous 1% Carboxy Methyl Cellulose once daily in the morning for 14 days. During these days, all the groups were given the same dose of high fat diet as before. The hyperlipidemic food and vehicle were given to the control animals¹³. The animals were utilized to analyze several biochemical indicators at the end of the treatment period. Blood was drawn from the rat's orbital plexus under ether anesthesia and spun at 2000 rpm for 30 minutes to obtain serum.

Biochemical Analysis

The serum samples were analyzed for Total serum Cholesterol (TC), Triglyceride (TG), High Density Lipoprotein

(HDL), Low Density Lipoprotein (LDL), Very Low-Density Lipoprotein (VLDL).

Pharmacological evaluation

Activity Wheel

The activity wheel is applicable to assess the overall body performance of the rat/mice. The assessment and evaluation of the wheel is based on the rotating speed of the wheel. More the speed of wheel represents high activeness of animal as it possesses lighter weight¹⁴. The speed of the activity wheel is observed and recorded using tachometer. The average speed of all treatment groups is assessed and compared for anti-hyperlipidemic activity.

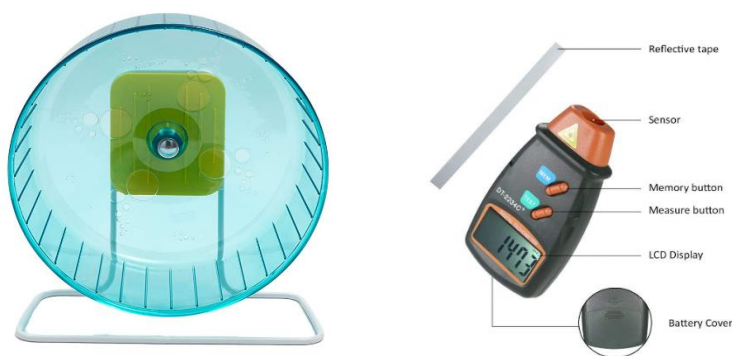


Figure 2: Activity Wheel with tachometer

RESULTS

The body weights of different treatment groups were assessed at Day 0, Day 7 and Day 14.

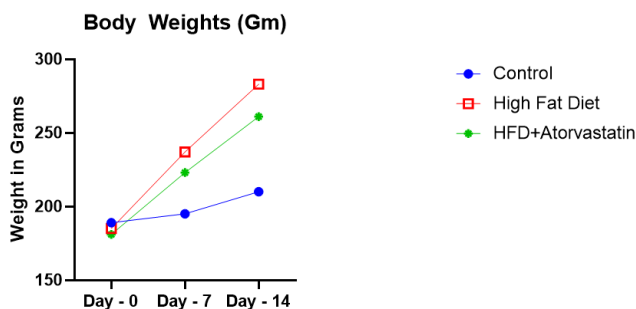


Figure 3: Comparison of Body weights for 14 Days

The serum lipid profiles were assessed for week 1 and week 2 by collecting blood sample from retro orbital puncture.

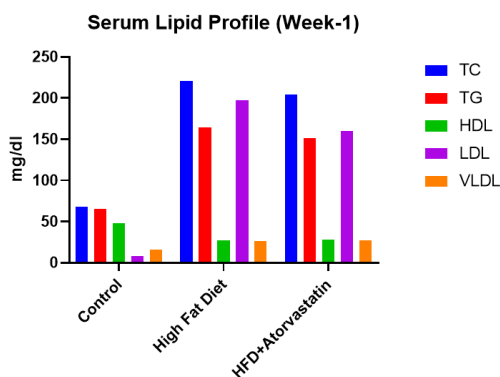


Figure 4: Lipid profile (week 1)

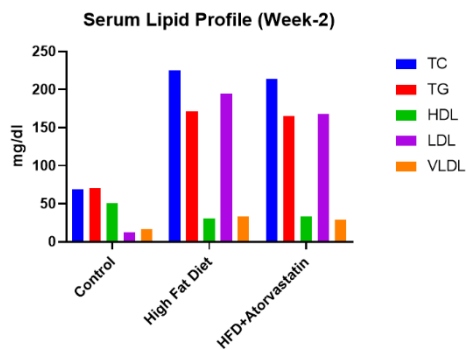


Figure 5: Lipid profile (week 2)

The performance of animals of all treatment groups on activity wheel was assessed for all weeks. After exposing the treatment groups to physical exercise, the lipid profiles were assessed for week 3 and week 4.

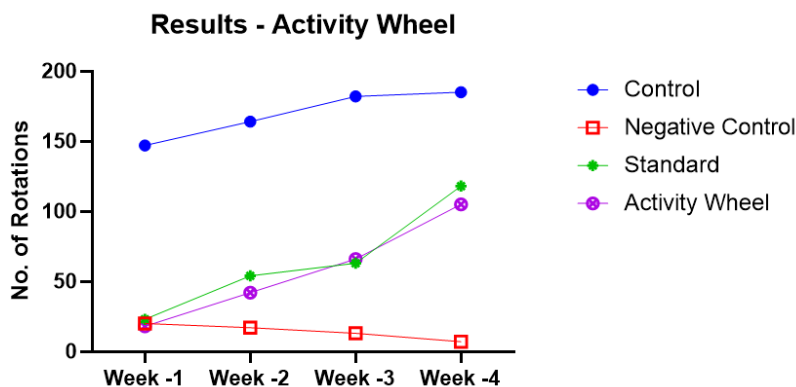


Figure 6: Rotations of Activity wheel for all treatment groups

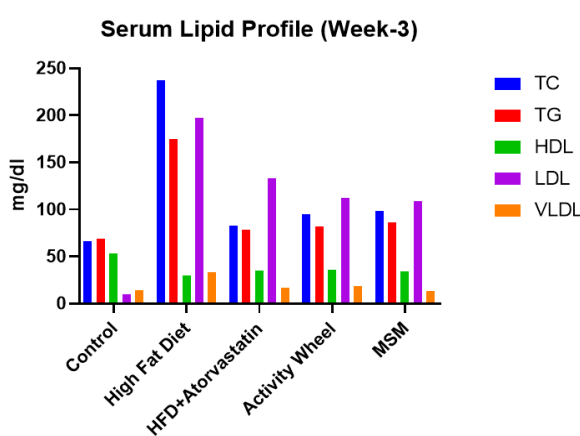


Figure 6: Lipid profile (week 3)

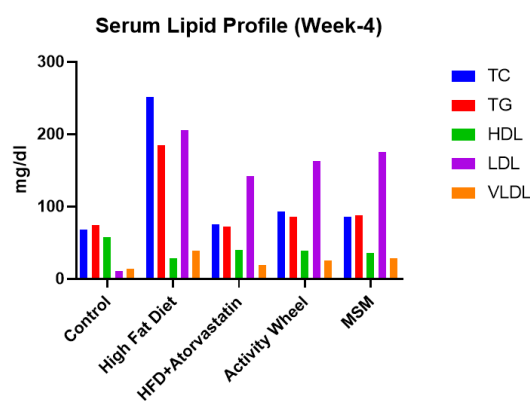


Figure 7: Lipid profile (week 4)

DISCUSSION

The high fat diet initiated for all treatment groups except control makes the animals to gain weight. The differences in the body weight of various groups is depicted in Table:4. The difference in weight gain was found to be 30-40 gms at the end of first week and 60-70 gms at the end of 14 days.

After analysing the biochemical parameters for week 1 and week 2, slight variance is found in case of HDL, TC and TG levels, but the variation increases positively following week 3 and 4.

The levels of HDL gradually enhanced during the fourth week in treatment groups related to activity wheel and MSM, which clearly defines the potency of physical exercise than any other pharmacological treatments.

CONCLUSION

Screening models to evaluate anti-hyperlipidemic activity were standardized using activity wheel and muscle strength maze. The biochemical parameters were evaluated for all treatment groups and the animals which undergone with physical performance found to be active and have controlled TG, TC, HDL and LDL levels.

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CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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