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EXEMPLIFYING THE ANTIDYSLIPIDAEMIC POTENCY OF *PTEROCARPUS MARSUPIUM* EXTRACT IN MITIGATING HIGH-FAT DIET-INDUCED DYSLIPIDAEMIA IN RODENT MODEL

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Keywords:

Dyslipidaemia, Coronary artery disease, Atorvastatin, *Pterocarpus marsupium*

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ABSTRACT: We evaluated the antidyslipidemic activity of extract of *Pterocarpus marsupium* (PM: Vijayasar) in adult Charles Foster rats of both sexes and compared this activity with that that of Atorvastatin (Atorva). 4 groups were made [Gp 1- Control group (no drug), only high fat diet (HFD); Gp 2- HFD +PM (to evaluate the role of PM in the prevention of dyslipidemia); Gps 3 & 4- only HFD]. This was the phase of disease production [for 7 weeks] and preventive role of PM was also evaluated concurrently. Then, therapy phase started for next 90 days [Gp 1- Control group (no drug). Only HFD; Gp 3- HFD+ Atorva; Gp 4- HFD+ PM]. TC (total cholesterol), TG (triglycerides), LDL (low density lipoproteins) and HDL (high density lipoproteins) levels were tested. During both the phases (prevention and therapy), PM brought significant improvements in all these parameters. Therefore, *Pterocarpus marsupium*, as an economical herbal therapeutic approach; presents a cost-effective, secure and efficacious means to address significant public health issues; such as dyslipidaemia, coronary artery disease and Atherosclerosis.

INTRODUCTION: On a global scale, the incidence of premature mortality stemming from cardiovascular diseases (CVD) has reached a pinnacle, marking an all-time high in its historical trajectory. Over the past three decades, the tally of CVD-related fatalities in the Asian region has exhibited a remarkable surge, nearly doubling from 5.6 million to a staggering 10.8 million cases. It is worth noting that the emergence and progression of dyslipidaemia engenders a twofold escalation in the susceptibility to CVD [1].

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At present, across the globe, dyslipidaemia stands culpable for approximately four million fatalities attributed to CVD. Notably, the most substantial surges in cholesterol levels in recent years have been witnessed in Asian nations, notably India, Indonesia, Thailand, Malaysia, and China. These countries have already outpaced their Western counterparts, including Europe and the United States, in this concerning epidemiological trend [2].

Dyslipidaemia may manifest as a consequence of genetic predisposition in isolation, extrinsic factors alone, or the intricate interplay of both genetic and environmental influences [3, 4]. Secondary dyslipidaemias result from the confluence of risk factors with external variables or underlying pathologies. In contrast, primary dyslipidaemias encompass a multifarious spectrum of disorders with hereditary, monogenic, or polygenic etiologies

[4, 5]. Readings of Total Cholesterol (TC), Triglycerides (TG), Low-density lipoprotein (LDL) cholesterol, and High-density lipoprotein (HDL) cholesterol are subject to fluctuations due to the presence of dyslipidaemias [6, 7].

The Third Report of the Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults, often referred to as Adult Treatment Panel III (ATP III), represents the National Cholesterol Education Program's (NCEP) contemporary and refined set of clinical guidelines concerning the evaluation and control of cholesterol levels.

Periodically, the NCEP issues ATP clinical updates in response to the evolving landscape of knowledge within the realm of cholesterol management. The third and most recent ATP report denoted as NCEP ATP-III, serves as a comprehensive overhaul of the preexisting recommendations for the clinical oversight of elevated blood cholesterol levels. Within this context, a detailed table delineates the prevailing criteria governing what constitutes normal and perturbed lipid levels, as per the dictates of NCEP ATP-III, a document of profound significance in the arena of cardiovascular health is shown below.

TABLE 1: CHOLESTEROL GUIDELINES BY NCEP ATP-III

Plasma Lipids	Optimal [mg/dL]	Borderline high [mg/dl]	High risk [mg/dL]	Very high risk for CAD [mg/dL]
Total Cholesterol	< 200	200-239	≥ 240	
TGs	< 150	150- 199	200- 499	≥ 500
LDL	< 100 (optimal)	100- 129 (> optimal)	130- 159	160- 189	> 190
HDL	≥ 60		< 40	

In the contemporary community, the prevalence of dyslipidaemia has reached exceptionally elevated levels. Lipid irregularities collaborate with metabolic and environmental elements, compounding the susceptibility to a spectrum of metabolic disorders, including diabetes, atherosclerosis, and thrombosis, among others [7, 8].

Coronary artery disease (CAD) can arise as a consequence of atherosclerosis, a condition that transcends geographical, gender, and socioeconomic distinctions. CAD may serve as a precursor to ischemic heart disease (IHD), a leading global cause of mortality [9].

A fundamental approach to the prevention and management of atherosclerotic cardiovascular disease (ASCVD) hinges upon lipid-lowering therapy, an arena characterized by its intricate nature and efficacy. Perturbations in the lipid profile constitute one of the most pervasive complications in the context of diabetes mellitus, impacting approximately 40% of the diabetic patient population [10].

Statins exhibit a notably favourable risk-to-benefit profile, representing one of the most exhaustively investigated categories of medications in the annals of medical science. Nevertheless, it is imperative not to dismiss the significant attention drawn to adverse effects, notably myalgia, and, albeit less frequently, the grave condition of rhabdomyolysis. As evidenced by the JUPITER trial, the administration of rosuvastatin medication advanced the inception of type 2 diabetes by a mere 5.5 weeks when contrasted with those individuals who received a placebo [11].

Pterocarpus marsupium (PM) is a large, deciduous plant native to India, Nepal, and Sri Lanka; where it occurs in parts of the Western Ghats and can grow up to 30 meters in height. It belongs to Fabeceae Family and is commonly known as Bijasal or Vijaysar (in Hindi), Asana (in Sanskrit), Malabar Kino or Indian Kino tree (in English) and by many other names [12].

Various portions of the bark are used as an astringent, anti-diarrheal, antacid, and antioxidant, for the treatment of toothache and the management of diabetes.

The heartwood is known to be useful in arthritis, gout, bronchitis, skin infections, asthma, diabetes, *etc*. The flavonoids *Marsupiun pterosupin*, and liquiritegenin are reported to possess antihyperglycemic and antihyperlipidaemic activities [13].

PM belongs to the following Taxonomical Classification [14]:

Class: Magnoliopsidae

Family: Fabaceae

Genus: Pterocarpus

Species: Marsupium.

Laboratory studies done so far show that gum resin of *Marsupiun pterosupin* helps to regenerate the beta cells in the pancreas. Through studies, it has been found that *Marsupiun pterosupin* is the only pure herb ever found to regenerate beta cells in the pancreas [15]. Other uses of PM as an herbal supplement include antioxidant support and skin health [16].

Constituents: Pterostilbene is one of the most active ingredients of *Marsupiun pterosupin* extract along with other significant components like epicatechin, marsupin and pterosupin reported for their anti-diabetic potential. It has been found that the active hypoglycaemic principle of the bark of this plant is (-)-epicatechin [17]. Its compounds; namely marsupsin, pterosupin, pterostilbene and liquiritigenin have shown anti-hyperlipidaemic and anti-hyperglycaemic activities [18, 19].

As demonstrated by Pratibha Singh *et al.* in a study conducted in 2019, assessment of lipid accumulation in 3T3-L1 adipocytes revealed significant attenuation of lipid content in the cells treated with extracts isolated from PM (B2), PM (BH1) as well as *Marsupiun pterosupin* (BH2). However, extract from PM (B1) was found to be toxic to cells. The results suggest that the extract from *Marsupiun pterosupin* (BH2) has certain constituents that can reduce obesity [15].

In view of the previous results described above, we have performed this research on *Marsupiun pterosupin* extract to evaluate its anti-dyslipidaemic properties depending on appropriate investigations that employ well-chosen models with adequate controls and are designed to confirm or refute its effect on lipid profile.

Aims and Objectives: The present study was conducted to evaluate the effects of anti-dyslipidaemic activities of extracts of *Pterocarpus marsupium* [PM] in the prevention and therapy phases separately in Charles foster rats fed with a high-fat diet (having 15% crude fat). The preventive role of this plant was evaluated (there was one group of rats in which PM extract was given since day 1 along with the high fat diet) in dyslipidaemia, which has not been evaluated yet.

Comparing these effects with those of the standard drug Atorvastatin in the therapy phase.

MATERIALS AND METHODS: The study was performed on experimental rats of the Charles Foster Albino species, in the Department of Pharmacology, Institute of Medical Sciences (IMS), Banaras Hindu University (BHU), Varanasi.

The Approval for the study was taken from institutional Animal Ethical Committee (IAEC), Banaras Hindu University, Varanasi, Uttar Pradesh(542/GO/ReBi/S/02/CPCSEA dated 26.5.2017) vide letter No. Dean/2022/IAEC/3250. The study procedures were performed as per CCSEA [erstwhile CPCSEA] guidelines [24].

Adult healthy Charles Foster rats of either sex, similar physical constitution (in terms of age, body weight), weighing 180-220 g were used in the study.

Tablets of Atorvastatin [Atorva] were pulverized and powder thus formed was dissolved in distilled water for oral administration. Extract of PM was provided by Swasthya Vardhak Pharmacy Pvt. Ltd, Varanasi, UP. Extract was dissolved in distilled water just before oral administration. Drugs were given orally with the help of feeding cannula (oral gavage procedure).

High fat diet [HFD] was given for the first 7 weeks [49 days] to produce the required dyslipidaemia [20]. Group 2 received PM also, besides HFD, as we were intended to observe the effect of PM in the prevention of dyslipidaemia. Groups 3 and 4 also received HFD during this phase. Thereafter, Groups 3 and 4 received Atorva and PM respectively, for next 90days, i.e. the therapy phase. HFD was continued like before in all the groups till the completion of the study. Thus, span of the study was 139 [49+90] days.

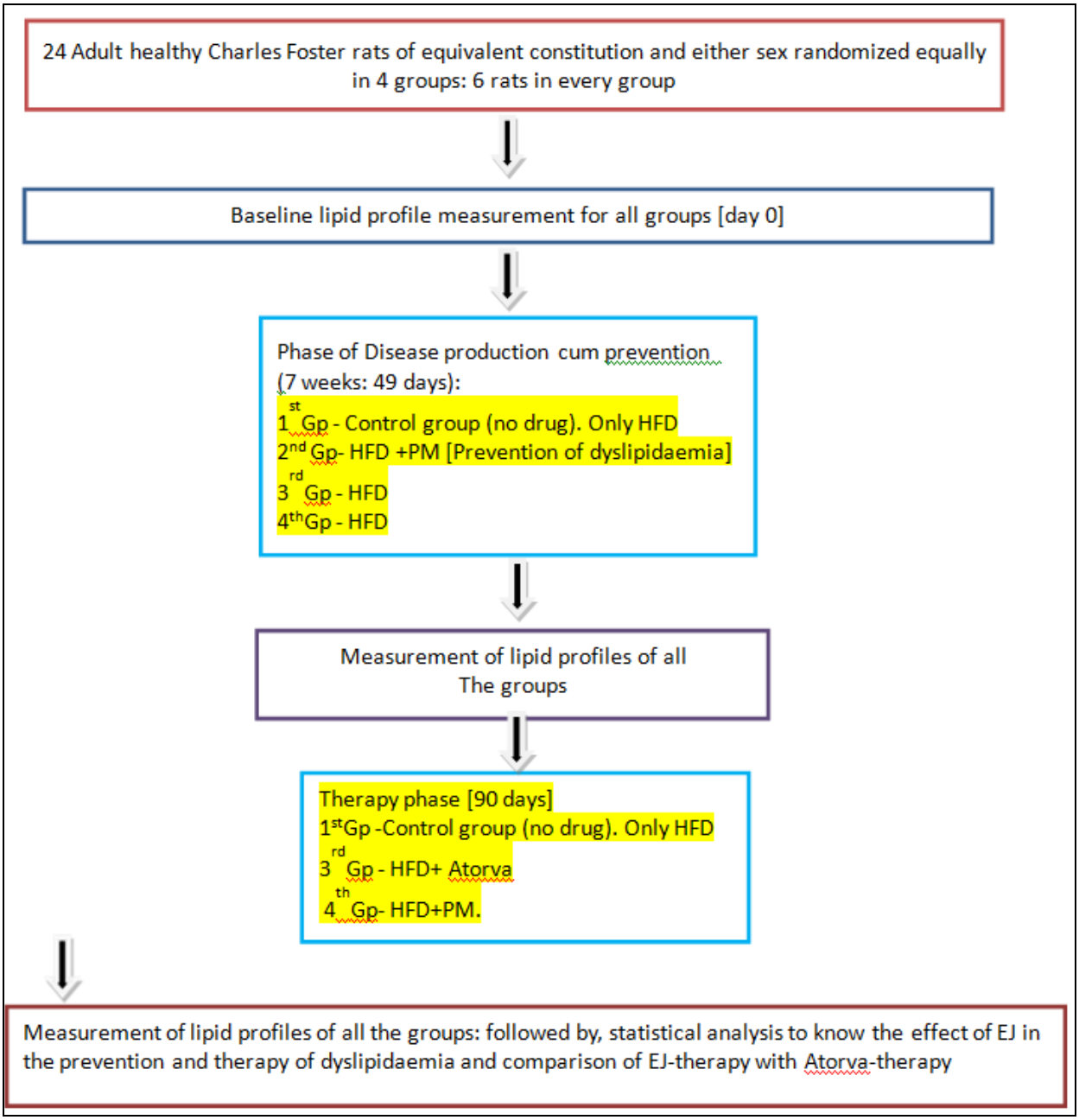

FIG. 1: LAYOUT OF EXPERIMENTAL PROTOCOL. GP: GROUP, HFD: HIGH FAT DIET, ATORVA: ATORVASTATIN, PM: *PTEROCARPUS MARSUPIUM*

Drug Doses: Atorva= 80 mg/ kg; EJ= 200 mg/ kg[21, 22, 23].

High Fat Diet (HFD): It was prepared by Dayal Industries Pvt. Ltd., Barabanki Road, Lucknow, Uttar Pradesh, India **Table 2.**

TABLE 2: COMPOSITION OF HIGH FAT DIET

Ingredients	Approximate amount
Crude Fat (Prepared from Rice Bran)	15%
Crude Protein	16%
Acid Insoluble Ash	2.30%
Moisture	8%
Vitamins and Minerals	Appropriate quantity

Measurement of Lipid Profile:

1. Blood samples of 1 ml volume each were taken from the retro-orbital plexus for chemical analysis.
2. Serum was separated with the help of centrifugation (2000 r.p.m. for 15 minutes).
3. Lipid profile was measured with the help of a semi-autoanalyzer.

Statistical Analysis: Data were summarized as mean ± SD. Groups were compared by 'two factors (groups × days) analysis of variance (ANOVA)'

and the significance of mean difference within and among the groups was done by Tukey post hoc test. $p<0.05$ was considered statistically significant. Analyses were performed on SPSS 26.0 (software).

RESULTS & DISCUSSION:

Phase of Disease Production & Prevention:

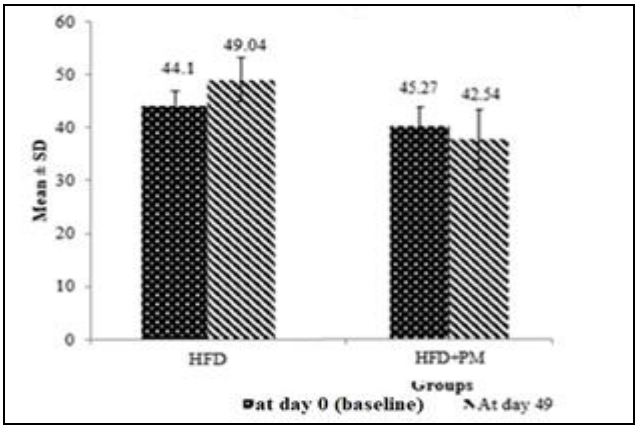

FIG. 2: BAR DIAGRAM SHOWING PRE AND POST TREATMENT MEAN (±SD) TC-LEVELS IN GROUPS 1 & 2 [CONTROL GP & HFD+PMGP] AT DAY 0 AND DAY 49 [PHASE OF DISEASE PRODUCTION & PREVENTION]

Thus, as compared to the control group, PM has caused a 13.25% decrease [statistically significant] in the TC level after 7 weeks of feeding with HFD.

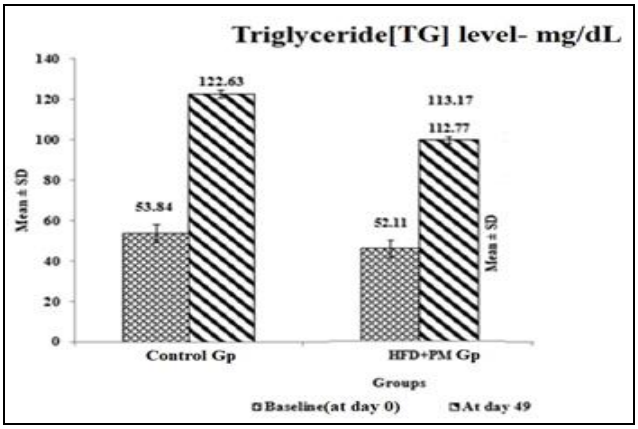

FIG. 3: BAR DIAGRAM SHOWING PRE AND POST TREATMENT MEAN (±SD) TG-LEVELS IN GROUPS 1 & 2 [CONTROL GP & HFD+PMGP] AT DAY 0 AND DAY 49 [PHASE OF DISEASE PRODUCTION & PREVENTION].

Thus, as compared to control group, EJ has caused 8.90% decrease [statistically significant] in the TG level after 7 weeks of feeding with HFD.

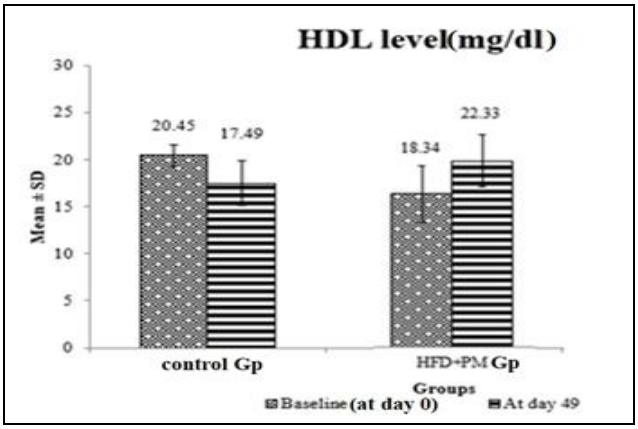

FIG. 4: BAR DIAGRAM SHOWING PRE AND POST TREATMENT MEAN (±SD) HDL-LEVELS IN GROUPS 1 & 2 [CONTROL GP & HFD+PMGP] AT DAY 0 AND DAY 49 [PHASE OF DISEASE PRODUCTION & PREVENTION]

Thus, as compared to the control group, PM has caused a 27.67% increase [statistically significant] in the HDL level after 7 weeks of feeding with HFD.

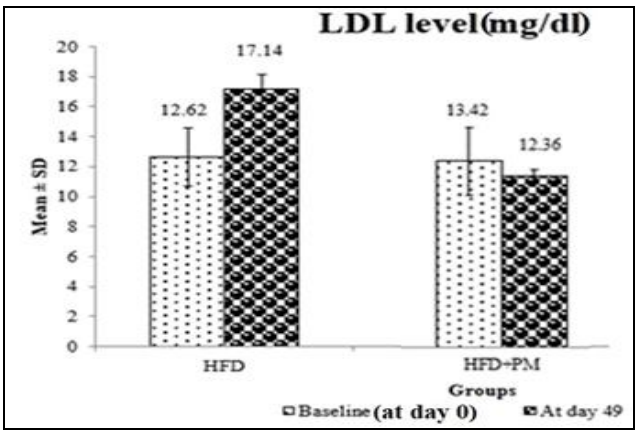

FIG. 5: BAR DIAGRAM SHOWING PRE AND POST TREATMENT MEAN (±SD) LDL-LEVELS IN GROUPS 1 & 2 [CONTROL GP & HFD+PMGP] AT DAY 0 AND DAY 49 [PHASE OF DISEASE PRODUCTION & PREVENTION]

Thus, as compared to the control group, PM has caused a 27.88% decrease [statistically significant] in the HDL level after 7 weeks of feeding with HFD.

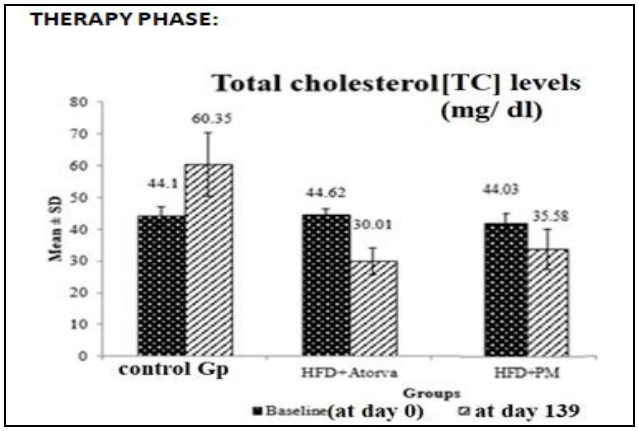

FIG. 6: BAR DIAGRAM SHOWING PRE AND POST TREATMENT MEAN (±SD) TC-LEVELS IN GROUPS 1, 3 & 4 [CONTROL GP, HFD+ ATORVA& HFD+ PM] AT DAY 0 AND DAY 139 [LATTER 90 DAYS BELONG TO THERAPY PHASE]

Thus, after completion of the therapy phase; as compared to control group, Atorva caused 50.27% and PM caused 41.04% decrease [both statistically significant] in the TC level.

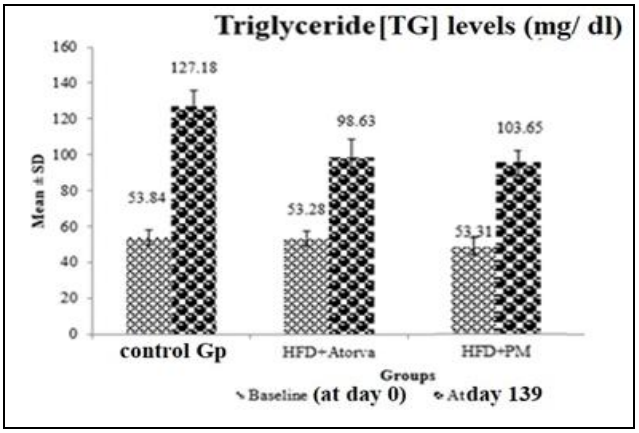

FIG. 7: BAR DIAGRAM SHOWING PRE AND POST TREATMENT MEAN (±SD) TG-LEVELS IN GROUPS 1, 3 & 4 [CONTROL GP, HFD+ ATORVA& HFD+ PM] AT DAY 0 AND DAY 139 [LATTER 90 DAYS BELONG TO THERAPY PHASE]

Thus, after completion of the therapy phase; as compared to control group, Atorva caused 22.50% and PM caused 18.50% decrease [both statistically significant] in the TG level.

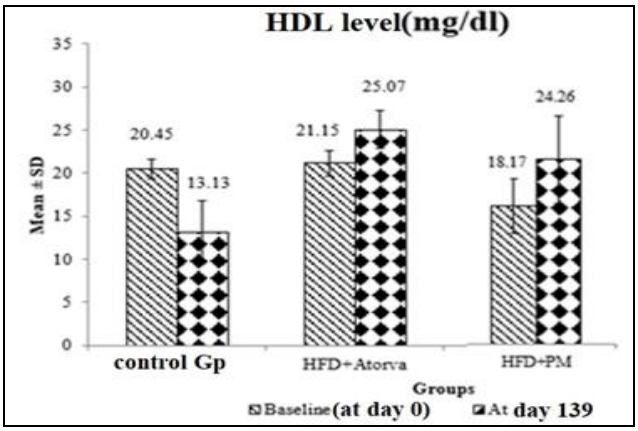

FIG. 8: BAR DIAGRAM SHOWING PRE AND POST TREATMENT MEAN (±SD) HDL-LEVELS IN GROUPS 1, 3 & 4 [CONTROL GP, HFD+ ATORVA& HFD+ PM] AT DAY 0 AND DAY 139 [LATTER 90 DAYS BELONG TO THERAPY PHASE]

Thus, after completion of the therapy phase; as compared to control group, Atorva caused 90.93% and PM caused 84.76% increase [both statistically significant] in the TG level.

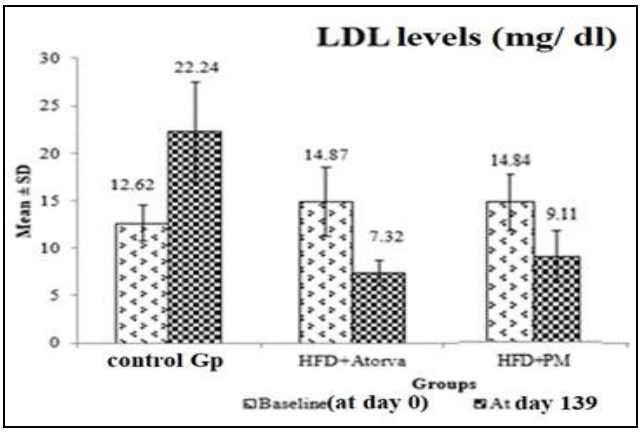

FIG. 9: BAR DIAGRAM SHOWING PRE AND POST TREATMENT MEAN (±SD) LDL-LEVELS IN GROUPS 1, 3 & 4 [CONTROL GP, HFD+ ATORVA& HFD+ PM] AT DAY 0 AND DAY 139 [LATTER 90 DAYS BELONG TO THERAPY PHASE]

Thus, after completion of the therapy phase; as compared to control group, Atorva caused 67.10% and EJ caused 50.10% decrease [both statistically significant] in the TG level.

Preclinical Safety Profile of *Pterocarpus marsupium:* In an acute toxicity in albino rats, the aqueous extract of PM heartwood was found to be safe and well tolerated even at a large dose of 5000 mg/kg [24]. According to some other earlier reports, PM was found to be non-toxic up to 8 g/kg in albino mice [25]. As the herbal treatment for diabetes is given for a longer duration, the genotoxic assessment of PM was done using both somatic and germ cells. The results indicated that the extract was not genotoxic [15].

In the present study, Atorva was found to be more efficacious than the herbal drug PM. This difference could be due to use of less-potent doses of EJ (i.e. 200 mg/kg of extract), secondly due to short duration of treatment. Though, we started our test drug PM with lower doses, but it is not so difficult to take this herbal drug in some higher dose, because it is quite free from adverse or toxic effects even at much higher doses. Longer duration is also not a major problem, because if the patient wants to compare, modern drugs are also taken for long period, sometimes lifelong; i.e. more studies with higher doses & longer durations are needed to be performed to evaluate our conclusions.

CONCLUSION: Study reveals that *Pterocarpus marsupium* [Vijayasar] is significantly effective remedy against dyslipidaemia. Extract of this herb didn't express any detrimental effects on experimental animals. Therefore, *Pterocarpus marsupium*, as a low-cost herbal therapy, offers an inexpensive, safe & effective measure to combat major public health problems *viz* dyslipidaemia/ CAD/ Atherosclerosis. The results of this study support the utilization of *Pterocarpus marsupium* as a dietary intervention strategy and functional food with potentially beneficial antidyslipidaemic effects.

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CONFLICTS OF INTEREST: Nil

REFERENCES:

1. Gebreegziabiher G, Belachew T, Mehari K and Tamiru D: Prevalence of dyslipidemia and associated risk factors among adult residents of Mekelle City, Northern Ethiopia. PLOS One 2021; 16(2): 01-18.
2. Zhao D, Liu J, Wang M, Zhang X and Zhou M: Epidemiology of cardiovascular disease in China: current features and implications. NRC 2019; 16(4): 203-12.
3. Stein R, Ferrari F and Scolari F: Genetics, Dyslipidemia, and Cardiovascular Disease: New Insights. Curr Cardiol Rep 2019; 21(8): 68. doi: 10.1007/s11886-019-1161-5. PMID: 31227920.
4. Berberich J and Hegele RA: The complex molecular genetics of familial hypercholesterolaemia. Nature Reviews Cardiology 2019; 16(1): 9–20.
5. Trinder M and Brunham LR: Polygenic scores for dyslipidemia: the emerging genomic model of plasma lipoprotein trait inheritance. Curr Opin Lipidol 2021; 32(2): 103-111.
6. Berberich AJ and Hegele RA: A Modern Approach to Dyslipidemia. Endocrine Reviews 2022; 43(4): 611-653.
7. Misra S, Lyngdoh T and Mulchandani R: Guidelines for dyslipidemia management in India: A review of the current scenario and gaps in research. Indian Heart J 2022; 74(5): 341-350.
8. Du Z and Qin Y: Dyslipidemia and cardiovascular disease: current knowledge, existing challenges, and new opportunities for management strategies. J Clin Med 2023; 12(1): 363.
9. Hwang D, Park SH and Koo BK: Ischemia with Nonobstructive Coronary Artery Disease: Concept, Assessment, and Management. JACC: Asia 2023; 3(2): 169-184.
10. Nnakenyi ID, Nnakenyi EF, Parker EJ, Uchendu NO, Anaduaka EG and Ezeanyika LU: Relationship between glycaemic control and lipid profile in type 2 diabetes mellitus patients in a low-resource setting. Pan African Medical Journal 2022; 41: 281.
11. Mahatme MS, Bargade MB, Hiware SK and Motlag MM: Effect of atorvastatin and rosuvastatin on the glycemic control in patients with type ii diabetes mellitus: a comparative, randomized, double-blind study. J of Pharmacology and Pharmacotherapeu 2021; 12(2): 54-60.
12. Ahmad A, Ahmad N, Anis M, Faisal M, Alatar AA, Salam EMA and Sivanesan I: Biotechnological Advances in Pharmacognosy and In Vitro Manipulation of *Pterocarpus marsupium* Roxb.Plants (Basel) 2022; 11(3): 247.
13. Umamaheswari A, Vijayalakshmi M, Tamilselvan N, Sowntharya S, Thirumurugan R and Prabu SL: Unravelling the Phytochemical and Pharmacognosy Contour of Traditional Medicinal Plant: *Pterocarpus Marsupium* Roxb. Qeios 2023. doi:10.32388/4MFJWG.
14. Ahmad N and Alia A: Microprapagation, Phytochemistry and Pharmacology studies on *Pterocarpus marsupium* roxb (Bijasal). An important medicinal forest tree.A Review. International Journal of Creative Research Thoughts 2021; 9(4): 2159-2176.
15. Singh P, Bajpai V, Gupta A, Gaikwad AN, Maurya R and Kumar B. Identification and quantification of secondary metabolites of *Pterocarpus marsupium* by LC–MS techniques and its *in-vitro* lipid lowering activity. Industrial Crops and Products 2019; 127: 26-35.
16. Majeed M, Majeed S, Jain R, Mundkur L, Rajalakshmi HR, Lad PS and Neupane P: An Open-Label Single-Arm, Monocentric Study Assessing the Efficacy and Safety of Natural Pterostilbene (*Pterocarpus marsupium*) for Skin Brightening and Antiaging Effects. Clin Cosmet Investig Dermatol 2020; 13: 105-116.
17. Dar MI, Rafat S, Dev K, Abass S, Khan MU, Abualsunun WA, Murshid SS, Ahmad S and Qureshi MI: Heartwood Extract of *Pterocarpus marsupium* Roxb. Offers Defense against Oxyradicals and Improves Glucose Uptake in HepG2 Cells. Metabolites 2022; 12: 947.
18. Grover B and Roy P: Effects of Pterostilbene Isolated from *Pterocarpus marsupium* on high fat diet induced diabetic rats. International Journal of Pharmaceutical Sciences and Drug Research 2021; 13(6): 705-12.
19. BagyalakshmiJ, Priya BSK and Bavya C: Evaluation of Antidiabetic Activity of Aqueous Extract of Bark of *Pterocarpus marsupium* Silver Nanoparticles against Streptozotocin and Nicotinamide Induced Type 2 Diabetes in Rats. Biomedical Journal of Scientific & Technical Research, Biomedical Research Network 2022; 43(1): 34254-34268.
20. Mishima MDV, Ladeira LCM, Da Silva BP, Toledo RCL, De Oliveira TV, Costae NMB and Martino HSD: Cardioprotective action of chia (*Salvia hispanica* L.) in ovariectomized rats fed a high fat diet. Food Funct 2021; 12(7): 3069-3082.
21. Mohamed AS, Ibrahim WM, Zaki NI, Ali SB and Soliman AM: Effectiveness of *Coelatura aegyptiaca* Extract combination with atorvastatin on experimentally induced hyperlipidemia in rats. Evid Based Complement Alternat Med 2019; 2019 (9726137): 1-9.
22. Nagabhushan C, Rao S, Satyanarayana ML, Leena G and Santosh CR: Amelioration of Streptozotocin induced hyperglycemia in rats using combination of Gymnemasylvestre and *Eugenia jambolana* plant extracts. Indian journal of veterinary pathology 2021; 45(1): 42-48.
23. Krishna DB, Rao S, Satyanarayana ML and Byregowda SM: Effects of *Eugenia jambolana* extract against streptozotocin induced acute liver damage in rats. Indian Journal of Animal Research 2023; 49(1): 81-85.
24. Koyagura N, Munge B and Vedula P: Acute toxicity study and phytochemical screening of *Pterocarpus marsupium* heartwood. Natl J Physiol Pharm Pharmacol 2022; 12(05): 707-711.

25. Goel RK, Joshi MC, Dorababu M, Prabha T and Kumar MM: Effect of *Pterocarpus marsupium* on NIDDM-induced rat gastric ulceration and mucosal offensive and defensive factors. Indian J Pharmacol 2004; 36: 296–302.

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