doi.org/10.36721/PJPS.2024.37.5.REG.1033-1041.1

Comparative and combination study of simvastatin alone and in combination with *Beta vulgaris* in hyperlipidemia patients

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Abstract: Phytomedicine is gaining acceptance as well preference in health care management for various diseases. Drug combinations are mostly used clinically for hyperlipidemia, as single-agent therapy is insufficient. Statins remain the cornerstone of hyperlipidemia. The objective of the present research is to manage hyperlipidemia with the least amount of medicine effective clinically, thereby limiting its side effects. Study was carried out with 140 registered hyperlipidemia patients, divided into two groups. Group-A received simvastatin 20mg oral daily & Group B received a combination of simvastatin and *beta-valgaris* capsules twice a day for 90 days. Pre and post treatment values were compared within the groups and between the groups. Group B shows statistically significant decrease ($p<0.05$) in serum total cholesterol, low density lipoprotein (LDL), triglycerides (TG) and CRP levels. Also significant improvement ($p<0.05$) was noted for high density lipoprotein (HDL) levels (20.1% to 57.4%) in group B after completion of study. On the basis of our study results, we can conclude that statins remained to be the mainstay treatment for patients with elevated cholesterol levels. However, the combination has a synergistic effect and reduces oxidative stress (OS) as well.

Keywords: Simvastatin, cap *Beta-vulgaris*, lipid fraction, C reactive protein, CRP.

Submitted on 06-05-2024 – Revised on 13-8-2024 – Accepted on 13-8-2024

INTRODUCTION

Since long ago, human society has utilized plants in their diet and used them to treat many kinds of diseases. These plants have been essential for preserving human body functions and metabolism, as well as in the treatment of many diseases. Numerous of research investigations have shown that using organic food in everyday meal can significantly improve human wellbeing and slow the onset of diseases and illnesses (Amin *et al.,* 2020). The consumption of organic compounds as medicinal or protective agents has attracted a lot of attention from around world over the past decade. Red beetroot and its active ingredients, betalains, have been associated with a number of health advantages in the past few years, including blood pressure reduction, lipid lowering, anti-oxidative, anti-inflammatory, anti-cancer and anti-obesity effects (Hadipour *et al.,* 2020).

Dyslipidemia, one of the most prevalent diseases in the world, is characterized by abnormal blood levels of lipids and lipoproteins. Many of the treatments for these conditions have been the focus of extensive research over the years, with traditional medicine serving as a major inspiration. More recently, there has been advocacy for the prevention and control of dyslipidemia as a major risk factor and its prognostic significance in reducing the incidence of myocardial infarction and stroke (Kim *et al.,* 2017).

Food is considered functional if it has ingredients that can assist in preventing or treating specific disorders in addition to being digested to meet regular nutritional demands. Presently, many people turn to traditional medicine, especially when more contemporary medical procedures fail to resolve a patient's health issue. Studies on the effectiveness and safety of these plant-based remedies have resulted in their integration into traditional medicine as adjunctive or alternative treatments (Ikram, *et al.,* 2015).

Red beetroot, or *Beta vulgaris*, is a root vegetable that has observed a significant surge in popularity recently due to its reputation as a functional diet that supports overall health. Reports of beetroot's use as a natural treatment date back to the Roman era, although the fact that it has only recently attracted greater scientific attention (Ninfali & Angelino 2013). However, a variety of additional bioactive substances found in beetroot may have health benefits, particularly in situations marked by chronic inflammation. Thus, the motive of this study is to accomplish the following pair of objectives to highlight

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the results from recent studies that provide a reason for the physiological and biochemical advantages of beetroot. There are still a lot of undiscovered areas where beetroot supplementation may have a positive impact on health because of its high biological activity (Chowdhury *et al.*, 2014).

Although estimations in Central Asian nations are far lower than those in affluent nations. The prevalence of hyperlipidemia, according to the World Health Organization (WHO), is 30.3% in South East Asia, 36.7% in the Western Pacific, 53.7% in Europe and 47.7% in America (Lin *et al.,* 2018).

The incidence and prevalence of hyperlipidemia are rising in Pakistan as a result of changes in the national lifestyle. Due to their sedentary lifestyles and lack of exercise, people in upper class society have high levels of hyperlipidemia (Meng-Shiuan *et al.,* 2017).

Statins are the most preferred agents for the treatment of dyslipidemia. Although different types of statins ought to have similar efficacy treating dyslipidemia (Bhattarai *et al.,* 2020). Statins have demonstrated a positive risk-benefit ratio when it comes to lowering low density lipoprotein (LDL) levels and lowering the risk of CVD because of their capacity to modify endothelial redox status and have anti-inflammatory actions. Statins were considered to be the pillars of anti-LDL treatments in the 2019 ESC/EAS (European society of cardiology and the European Atherosclerosis Society) guidelines (Mach, *et al.,* 2020).

The potential health advantages of nutraceuticals, which include dietary supplements and bioactive ingredients in foods, are being researched. Assessing these compounds' effects on numerous health indicators, such as serum lipid profiles and inflammation (Williamson *et al.,* 2020). *Beta vulgaris* (beetroot) is a member of Chenopodiaceae family of plants. Its secondary metabolites betalains, betaine and nitrites are functionally the most key phytochemicals, providing health benefits including hyperlipidemia. (Thiruvengadam et al., 2024).

A large percentage of individuals with hyperlipidemia pose a serious risk to their health. One of the key objectives of therapy for all individuals with hyperlipidemia is still lowering LDL. A variety of management strategies are available to suppress LDL.

The goal of treatment modalities is to lower LDL levels in order to control and manage hyperlipidemia (Ezeh & Ezeudemba, 2021). The primary objective of present study was to summarize the biological activities of red beetroot and its active compounds betalains. Secondary objectives were to note any Improvement in quality of life & symptoms in hyperlipidemia patients.

MATERIALS AND METHODS

Clinical interventional trial carried out with approval from the ERB and the BASAR University of Karachi.at Pharmacology Department BMSI, JPMC Karachi' Patients in this study were split into two groups:

Group-A received daily oral treatment with simvastatin (20mg).
Group-B received daily combination therapy (650mg of beet root capsules and simvastatin). 120 hyperlipidemia patients were registered out of the 137 reported cases, after providing consent and meeting the inclusion and exclusion criteria.

Treatment is administered as directed to divided groups, and the lipid fraction (cholesterol, LDL, high density lipoprotein (HDL) and triglyceride) and CRP findings are compared with the record symptoms card of the clinical questionnaire to estimate the improvement and compliance of the drugs.

Sample size: Sample size of investigational study using https://www.openepi.com, was determined using a 95% confidence level, 80% power, and an odd ratio of 4.46 (Najafipour *et al.,* 2021 & Lim, 2023). Research study groups are treated as per protocol and compares the results of lipid fraction (Cholesterol, LDL, HDL, Triglyceride) & CRP along with diary symptoms card of clinical questionnaire, to estimate the improvement and compliance of the drugs.

STATISTICAL ANALYSIS

Statistical analysis was done by using SPSS–22 software. The results were analyzed by applying One-way ANOVA and the Tukey test. Data were presented as mean ±SD and $p<0.05$ considered as level of significance.

RESULTS

Simvastatin treated groups change of lipid parameters from baseline (Day-0) to Day-90 i.e. serum Cholesterol decreased from (241.47±29.06) to (184.58±13.86) mg/dl i.e.-23.6%, HDL increased from (29.95±4.97) to (35.98±4.84) mg/dl, i.e. 20.1%, LDL decreased from (137.08±18.75) to (114.63±17.18) mg/dl, i.e. -16.4% Triglyceride decreased from (231.67±26.15) to (192.55±17.38) mg/dl i.e. -16.9% & CRP reduced from (28.50±12.23) to (17.72±8.22) -37.5% at day-90 and p-values statistically highly significant <0.001.

Group-B study, where combination of Simvastatin 20mg daily with capsule beet root 650 mg twice daily for the duration of 90-days. In study group male 96.7%, smokers 95%, history of hypertension & Diabetes 60% & 70% respectively. Mean age 56.36±6.26 years with hyperlipidemia duration of 5.75±1.17 years.

Lipid fraction change from day-0 to day 90 of the study period, Cholesterol change from mean 249.1667±38.18 to 169.33±23.44 mg/dl, i.e., -32.1%. LDL from 139.45±17.36 to 89.57±12.422 mg/dl, i.e., -35.8%.

Triglyceride from 234.32±23.05 to 174.72±12.41mg/dl, i.e., -25.5%, HDL from 29.75±5.85 to 46.83±7.96mg/dl i.e., 57.4% & CRP change from baseline 27.62±8.91 to 15.80±4.68mg/dl i.e 42.8%, showed statistically significant with p-value <0.001.

Comparative study of Group-A & Group-B on lipid profile & CRP of Hyperlipidemia Patients

Group-A patients treated with Simvastatin 20mg/daily & Group-B patients treated with combination of Tab simvastatin 20mg/d plus Capsule beet root 650 mg twice/d for 90-days.

Thus, post hoc analysis revealed that Group A significantly decrease serum CPR levels (Mean=17.72 SD=8.22) than Beet root (Mean=19.00 SD=10.04) therapy.

Post hoc cholesterol analysis with pairwise comparison of treated groups with each other showed that at day 90, there were statistically significant differences found between: Group A vs B (mean difference = 15.25, p = 0.001).

Thus, post hoc cholesterol analysis revealed that Group A (Simvastatin Therapy) decrease serum cholesterol levels significantly decrease from 241.47±29.06 mg/dl day-0 to 184.58±13.86 mg/dl at Day-90 than combination therapy from 249.1667±38.18 mg/dl to 169.33±23.44mg/dl at 90-days therapy with p-value <0.001.

Post hoc HDL analysis with pair wise comparison of treated groups with each other showed that at day 90, there were statistically significant differences found between: Group A vs B (mean difference = -10.85, p = 0.000).

Thus, post hoc HDL analysis revealed that Group-A (Simvastatin Therapy) significantly increased serum HDL from baseline 29.95±4.97 mg/dl to 35.98±4.84 mg/dl than combination (Simvastatin + beetroot) therapy from 29.75±5.85 mg/dl to 46.83±7.96 mg/dl Day-90.

Post hoc LDL analysis with pair wise comparison of treated groups with each other showed that at day 90, there were no statistically significant differences found between: Group A vs B (mean difference = 25.066, p = <0.001).

Thus, post hoc LDL analysis revealed that Group-A (Simvastatin Therapy) significantly decrease serum LDL levels from 137.08±18.75mg/dl day-0 to 114.63±17.18 mg/dl Day-90 than combination therapy from 139.45±17.36mg/dl to 89.57±12.422mg/dl at 90-days with p-value <0.001.

Post hoc Triglyceride analysis with pair wise comparison of treated groups with each other showed that at day 90, there were statistically significant differences found between: Group A vs B (mean difference = 17.833, p = <0.001).

Thus, post hoc triglyceride analysis revealed that Group-A (Simvastatin Therapy) significantly decrease serum triglyceride levels from 231.67±26.15mg/dl day-0 to 192.55±17.38mg/dl Day-90 than combination therapy from 234.32±23.05mg/dl to 174.72±12.41mg/dl at 90-days with p-value <0.001.

Post hoc CRP analysis with pair wise comparison of treated groups with each other showed that at day 90, there were no statistically significant differences found between: Group A vs B (mean difference = 1.916, p=0.387) (table 1).

Symptoms severity of daily intake of drug in groups A&B

Side effects of group-A compare with Group-B on day 90. Severity of muscle aches improved in both group on day-90. While the severity of lack of energy and severity of joint pain remain high in both groups. Patients not stops taking drug in both groups (tables 2-3).

Post hoc analysis with pairwise comparison of treated groups with each other showed that at day-90, there were statistically no significant differences between: Group A vs Group B (mean difference = -1.400, p = 0.775), Thus, post hoc analysis revealed that Group B not significantly change serum SGPT levels (Mean=32.650 SD=4.34) than alone therapy (table 4).

Post hoc analysis with pair wise comparison of treated groups with each other showed that at day-90, statistically no significant differences found between: Group A vs Group B (mean difference = 1.416, p = 0.880), Thus, post hoc analysis revealed that Group B not significantly change Serum alkaline phosphatase levels (Mean=144.98 SD=17.97) than alone therapy.

Post hoc analysis with pair wise comparison of treated groups with each other showed that at day-90, statistically no significant differences found between: Group A vs B (mean difference = -0.019, p=0.791), Thus, post hoc analysis revealed that Group C (Combination Therapy) no significant change serum creatinine levels (Mean=0.996 SD=0.153)) than alone therapy (table 5).

DISCUSSION

Hyperlipidemia is one of the most common disorders worldwide. Many of the new and existing treatments for hyperlipidemia that have been studied over the years. Pakistani people's changing lifestyles are contributing to

Table 1: Post hoc multiple comparisons of lipid fraction & CRP in Group-A & Group-B

Variables	Day	Group (I)	Group (J)	Mean Difference (I-J)	P value.	95% Confidence Interval	
						Lower Bound	Upper Bound
Cholesterol	0	A	B	-7.70	0.402	-21.794	6.394
Cholesterol	90	A	B	15.25	0.001	5.827	24.672
HDL	0	A	B	0.20	0.979	-2.234	2.634
HDL	90	A	B	-10.85	0.000	-13.582	-8.118
LDL	0	A	B	-2.366	0.698	-9.281	4.548
LDL	90	A	B	25.066	<0.001	19.071	31.061
Triglyceride	0	A	B	-2.650	0.832	-13.496	8.196
Triglyceride	90	A	B	17.833	<0.001	10.446	25.220
CRP	0	A	B	0.883	0.917	-4.387	6.154
CRP	90	A	B	1.916	0.387	-1.519	5.352

Group-A: Patients on Tab Simvastatin 20 mg daily, Group-B: Patients on Cap Beet root 650 mg twice+ Tab Simvastatin 20 mg daily

Table 2: (Symptoms evaluation day-90 Group-A & B)

Group	Group-A					Group-B				
Score	0	1	2	3	4	0	1	2	3	4
In general, do you feel tired?										
Day-0	7 (11.7)	35 (58.3)	18 (30)	------	--	8(13.3)	45(75.0)	7 (11.7)	---	--
Day-90	23 (38.3)	37 (61.7)	-------	------	--	28(46.7)	32(53.3)	------	-----	--
p-value	0.008	0.705	--	---	-	0.001	0.018			
Do you experience shortness of breath?										
Day-0	------	41 (68.3)	16 (26.7)	3(5)	--	------	40(66.7)	16 (26.7)	4(6.7)	--
Day-90	30 (50.0)	29 (48.3)	1 (1.7)	-----	--	31 (51.7)	27(45.0)	2 (3.30)	-------	
p-value		0.027	0.001	-	-	-	0.022	0.001		
Do you feel difficulty in doing strenuous activities										
Day-0	------	14 (23.3)	37 (61.7)	9(15)	--	-----	23(38.3)	30 (40.0)	7 (11.7)	--
Day-90	8 (13.3)	40 (66.7)	12 (20.0)	------	--	7(11.7)	42(70.0)	11 (18.3)	----	--
p-value		0.001	0.001	-	-	-	0.001	0.002	-	-
Do you notice any mood impairment (depressed)										
Day-0	46 (76.7)	14 (23.3)	------	------	--	38(63.3)	22(36.7)	-----	-----	--
Day-90	55 (91.7)	5(8.3)	-------	------	--	51(85.0)	9(15.0)	------	------	--
p-value	0.025	0.025				0.011	0.001			
Is your sleep impaired?										
Day-0	-	12 (20)	35 (58.3)	13(21.7)	--	-----	22(36.7)	34 (56.7)	4(6.7)	--
Day-90	4 (6.7)	31 (51.7)	22 (36.7)	3(5.0)		9(15.0)	44(73.3)	7(11.7)	-----	--
p-value		0.001	0.018	0.007		-	0.0001	0.0001		
Do you feel lightheaded?										
Day-0	-	45 (75)	15 (25)	-----	--	4(6.7)	40(66.7)	16(26.7)	------	--
Day-90	12 (20.0)	46 (76.7)	2(3.3)	------	--	22 (36.7)	37(61.7)	1(1.7)	----	--
p-value		0.828	0.0007			0.0001	0.589	0.0001		
Did you experience palpitation?										
Day-0	-	21(35)	32(53.3)	7(11.7)	--	-----	20(33.3)	34 (56.7)	6 (10.0)	--
Day-90	6 (10.0)	41 (68.3)	13 (21.7)	------	--	9(15.0)	36(60.0)	15 (25.0)	---	--
p-value	-	0.0003	0.0004	-	-	-	0.005	0.0006	-	-
Do you suffer from muscle cramps/spasm?										
Day-0	-	13(21.7)	41(68.3)	6(10.0)	--	9(15.0)	42(70.0)	9(15.0)	-----	--
Day-90	2 (3.3)	43 (71.7)	15 (25.0)	------	--	3(5.0)	37(61.7)	20(33.3)	-----	--
p-value	-	0.0001	0.0001	-	-	0.073	0.364	0.023		
Do you have digestive/ GI problems?										
Day-0	12 (20.0)	26 (43.3)	20 (33.3)	2 (3.3)	--	4(6.7)	38(63.3)	16 (26.7)	2(3.3)	--
Day-90	20 (33.3)	36 (60.0)	4(6.7)	------	--	28(46.7)	30(50.0)	2(3.3)	-----	--
p-value	0.101	0.068	0.0003	-	-	0.0001	0.157	0.0005	-	-

Group-A Simvastatin 20 mg /day Group-B Combination of Simvastatin + Cap Beet root treated for 90 Days. Symptom of tiredness, shortness of breath, strenuous activities, mood impairment, sleep disturbance markedly improved, palpitation decreased, muscle cramps improved, no digestive disturbances, in both study group. Result are highly significant statistically on day-90.

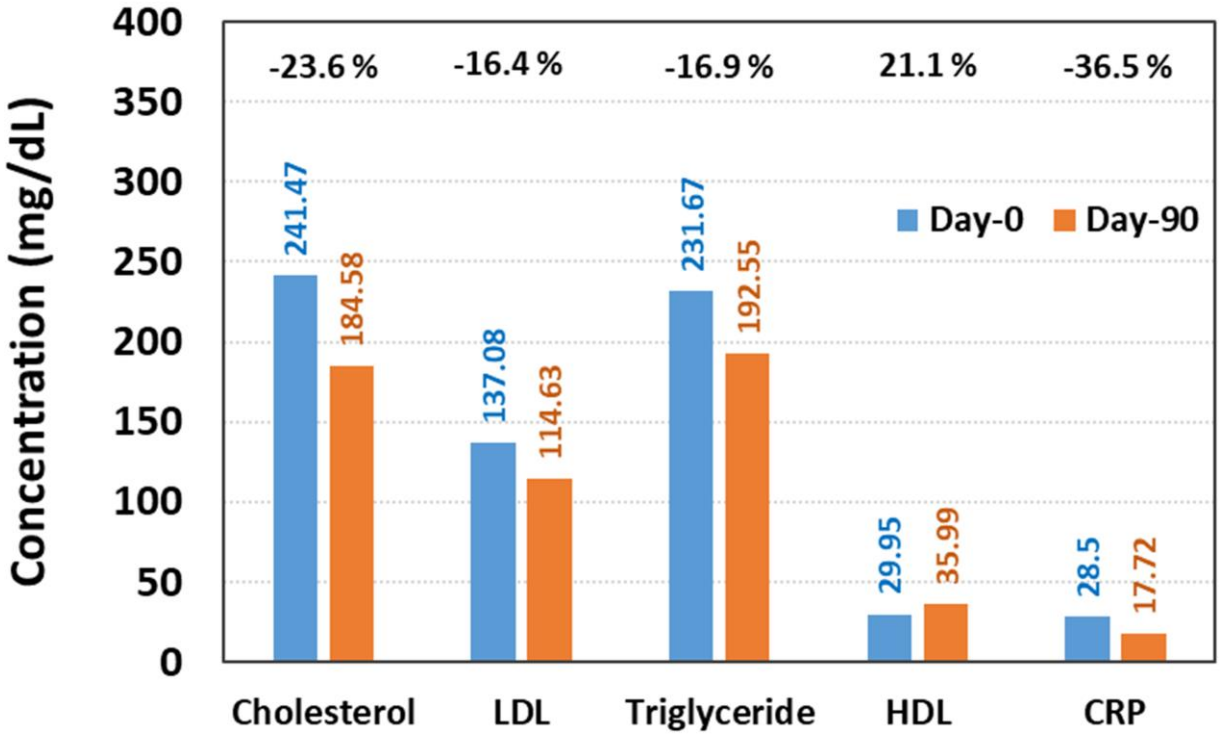

Fig. 1: Group-A Treatment Simvastatin 20mg daily in Hyperlipidemia Patients

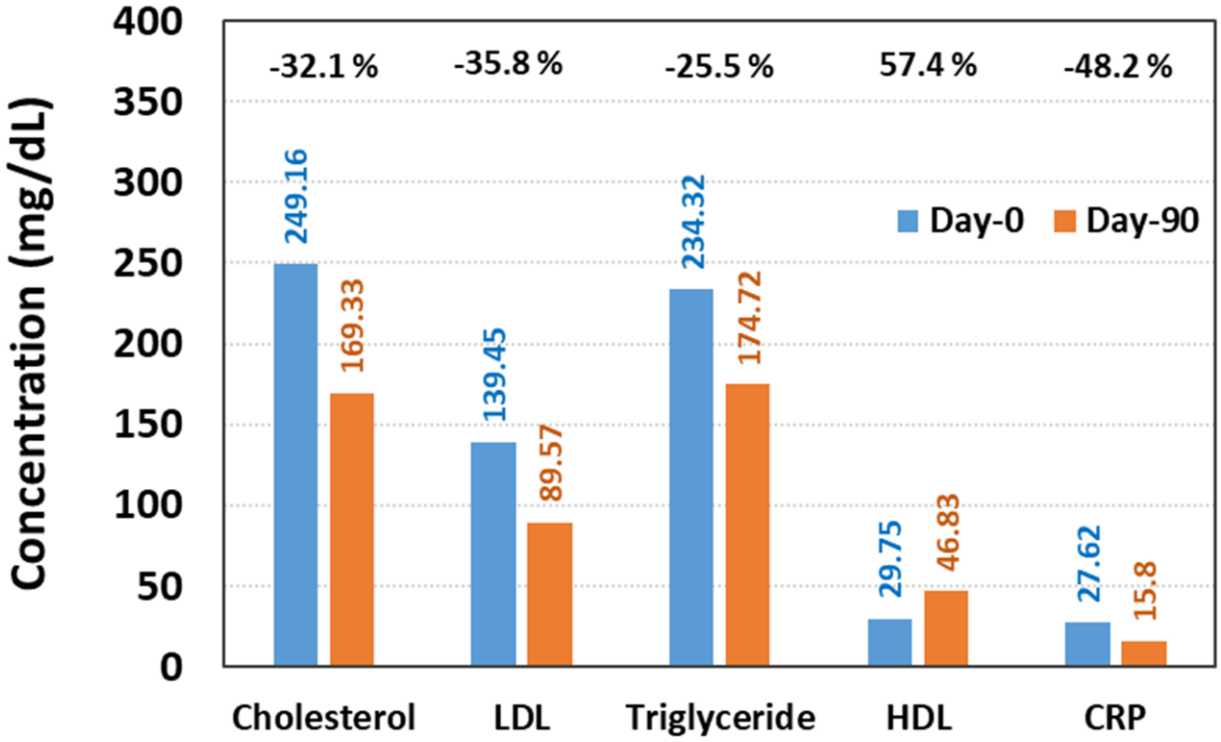

Fig. 2: Group-B (Combination simvastatin + Beetroot) from day-0 to day-90 in Hyperlipidemia Patients

Table 3: Side effects of group-A compare with Group-B on day 90

Groups	A				B			
Scores	0	1	2	3	0	2	2	3
Rate the severity of your muscle aches (e.g., muscles feeling sore, strained or stiff)								
Day-0	-------	21 (35.0)	39(65)	------	-----	18 (30.0)	42 (70)	---
Day-90	11 (18.3)	37 (61.7)	12 (20.0)	--------	16 (26.7)	40(66.7)	4(6.7)	------
P value	-	0.004	0.0001	-	0.001	0.0001	0.0001	-
Rate the severity of your muscle cramps.								
Day-0	32 (53.3)	27 (45.0)	1(1.7)	-------	51(85.0)	9(15)	------	-----
Day-90	1(1.7)	49 (81.7)	10 (16.7)	-------	46 (76.7)	14 (23.3)	-----	----
P value	0.0001	0.0001	0.005	-	0.249	0.249	--	-
Rate the severity of lack of energy.								
Day-0	11 (18.3)	33(55)	16 (26.7)	------	1(1.7)	37 (61.7)	22(36.7)	----
Day-90	27 (45.0)	33 (55.0)	--------	-------	29 (48.3)	31 (51.7)	----	------
P value	0.002	1.00	-	-	0.0001-	0.271	-	-
Rate the severity of your joint pain.								
Day-0	2(3.3)	32 (53.3)	26 (43.3)	-------	--	24 (40)	36(60)	-----
Day-90	-------	15 (25.0)	45 (75.0)	--------	10(16.7)	42 (70)	8(13.7)	------
P value	-	0.002	0.0004	-	--	0.001	0.0001	--
Have you stopped taking drug as prescribed because of symptoms?								
Day-0	21 (35.0)	30 (50.0)	9(15)	--------	19 (31.7)	39(65)	2(3.3)	--------
Day-90	35 (58.3)	25 (41.7)	---------	----------	45 (75.0)	15 (25.0)	----------	---------
P value	0.011	0.364	-	-	0.0001	0.0001	-	-
Overall, how likely to stop taking your medication because of the symptoms								
Day-0	40 (66.7)	20 (33.3)	-------	-------	33 (55.0)	27(25)	--------	--------
Day-90	51(85)	9(15)	---------	----------	49 (81.7)	11 (18.3)	---------	--------
P value	0.020	0.020	-	-	0.002	0.375	-	-

0 = Not at all, 1 = A little, 2 = somewhat, 3 = Quite a bit, 4 = Very, Group-A: Patients on Tab Simvastatin 20 mg daily, Group-B: Patients on Cap Beet root 650 mg twice+ Tab Simvastatin 20 mg daily

Table 4: Safety profile of group A & B

Variables	Day	Group A Mean ±SD N= 60	Group B Mean ±SD N= 60	P value
SGPT	0	30.26±5.25	31.03±4.51	0.071
	90	31.25±4.47	32.650±4.34	0.057
Alkaline Phosphatase	0	144.00±18.02	143.15±17.94	0.644
	90	146.40±16.13	144.98±17.97	0.759
CRP	0	28.50±12.23	27.62±8.91	0.769
	90	17.72±8.22	15.80±4.68	0.089
Serum Creatinine	0	0.99±0.022	1.003±0.17	0.835
	90	0.97±0.159	0.996±0.153	0.770
Blood Sugar	0	204.41±30.90	202.65±29.44	0.929
	90	202.58±30.43	197.88±30.13	0.666

Group-A: Patients on Tab Simvastatin 20mg daily, Group-B: Patients on Cap Beet root 650 mg twice +Tab Simvastatin 20 mg/d, Day-0 Start of treatment & Day-90 completion of therapy

Table 5: Safety profile Post hoc multiple comparison in Group-A & B

Variables	Day	Group (I)	Group (J)	Mean Difference (I-J)	P value.	95% Confidence Interval	
						Lower Bound	Upper Bound
SGPT	0	A	B	-0.766	0.929	-5.721	4.187
SGPT	90	A	B	-1.400	0.775	-6.265	3.465
S. Alkaline Phosphatase	0	A	B	0.850	0.959	-6.422	8.122
S. Alkaline Phosphatase	90	A	B	1.416	0.880	-5.534	8.367
S. Creatinine	0	A	B	-0.011	0.938	-0.085	0.064
S. Creatinine	90	A	B	-0.019	0.791	-0.087	0.049

Group-A: Patients on Tab Simvastatin 20mg daily, Group-B: Patients on Cap Beet root 650mg twice+ Tab Simvastatin 20mg daily

an increase in the incidence and prevalence of hyperlipidemia in the country. Because of their sedentary lifestyles and lack of exercise, upper-class society has a high prevalence of hyperlipidemia.

The first objective of therapy in lowering plasma cholesterol has traditionally been the use of three main classes of cholesterol-lowering medications, including HMG-CoA reductase inhibitors, anion-exchange resins and fibrates, in addition to a nutritionally balanced diet that lowers cholesterol and saturated fat intake. Hyperlipidemia aggravates the condition by causing oxidative stress (OS), which is caused by the inhibition of enzymes that are beneficial for avoiding tissue oxidation.

Even though statins were discovered more than 25 years ago, they continue to be the mainstay of treatment for hypercholesterolemia. However, questions remain about their long-term safety, effect on all-cause mortality and cost-effectiveness of use, particularly with regard to primary prevention. Since statins successfully lower both LDL and triglycerides (TG), they are a good first line of treatment for patients with moderate hypertriglyceridemia (James, 2001).

Simvastatin was utilized by at doses of 40 mg/d in patients with heterozygous familial hypercholesterolemia, drug dramatically lowers LDL cholesterol (35-45%) and total cholesterol (>30%) and it also tends to increase HDL cholesterol and decrease TG (Mauro, 1993). Statins have an outstanding risk-benefit profile and are among the pharmacological classes that have been thoroughly and intensely examined throughout the period (Sidney *et al.*, 2016).

As a nutrient with potential medicinal uses, the *Beta vulgaris* has received significant scientific attention in recent years. Betalainic and taxanthropic compounds are the major chemical components found in beetroot (Khan, 2016). *Beta vulgaris*, containing large concentrations of both bioactive and nutritional components. The macronutrients, micronutrients, phenolic compounds, betalains, carotenoids, alkaloids, terpenoids, coumarins, volatile components and tannins in beetroot are among the necessary nutrients and phytochemicals (Hadipour *et al.*, 2020).

Betalains can be found in a plant's fruits, seeds, leaves, flowers, roots, and beehives (Ge Li, *et al.*, 2019). Although red beetroot also contains effective antioxidants like rutin, epicatechin, caffeic acid, betanin's and its high electron donor characteristic accounts for its antioxidant capacity. Hadipour *et al.*, 2020 used of betalains as an active treatment for disorders linked to excess OS may be justified by red beetroot/betalains clinical evaluation of short-term OS situations, such as athletic activities. The antioxidant capacity of beetroot has been improved in both animal and human situations, Betalains may reduce LDL cholesterol and preserve DNA from damage (Chen *et al.*, 2021).

Our study investigated into the potential anti-hyperlipidemia effects of beetroot, suggests that lipid-lowering and cardio-protective qualities since beetroot treatment increased HDL levels, decreased cholestrol and TG. The beetroot's hypolipidemia influence is caused by the flavonoid and saponin contents. Our study led us to the conclusion that beetroot lowered the lipid profile.

In our study Simvastatin 20mg significantly altered cholesterol, LDL, TG and low HDL in hyperlipidemia patients. Moreover, red beets contain phytosterols, which are plant chemicals with molecular structures similar to cholesterol that may lower cholesterol levels in the body by promoting cholesterol excretion and reducing the risk of cardiovascular disease. In order to lower dangerous low-density lipoprotein (LDL) cholesterol and the amount of cholesterol absorbed, phytosterols compete with cholesterol in the body Sarfaraz *et al.*, 2021. Singh, *et al.*, 2015 study in individuals with high levels of physical activity who used red beetroot juice for 15 days, observed increases in HDL and decreases in OS.

Williamson, 2020 conducted a clinical studies meta-analysis and assessed the impact of beetroot consumption on the lipid profile in humans. According to our findings, taking beetroot significantly improved the levels of cholestrol, TG, LDL-C, and HDL-C among the beetroot group, as compared to the simvastatin group. Rahimi, *et al.*, 2019 in a randomized crossover trial study, found a significant reduction in glucose, cholestrol, TG, and LDL-C levels after two weeks of red beetroot supplementation; however, the LDL-C reduction was very small. De Castro, *et al.*, 2019 reported significant differences of pre & post beetroot consumption on LDL-C levels within the study group.

Holy, *et al.*, 2017 examined the effects of beetroot consumption for one session on lipid profiles in people who appeared to be in good health, consistent with the findings of Brown's *et al.*, 2017 study, their investigation revealed noteworthy changes in TG, T and LDL, but no significant change in HDL. Though few research has been done on the antioxidant qualities of beetroot juice, revealed that long-term consumption of the juice can boost antioxidant capacity in both human and animal events (Roth, 2015).

Combination therapy, lipid fraction change from baseline to day 90, cholesterol from mean 249.1667±38.18 to 169.33±23.44mg/dl, LDL mean 139.45±17.36 to 89.57±12.422mg/dl, triglyceride mean 234.32±23.05 to 174.72±12.41mg/dl, HDL from 29.75±5.85 to 46.83±7.96 mg/dl exhibited statistically significant changes with p-

value <0.001. While CPR modify from baseline 27.62±8.91 to 15.80±4.68mg/dl at the completion of study.

Nicola & Alberto 2020 concluded that most frequent causes of statin non-adherence, statin switching, and statin discontinuation can occur up to 75% of the time due to muscle soreness and its impact on glucose metabolism. While beetroot's hypolipidemic impact is brought on by the presence of flavonoids and saponins. Compared to when either drug is given alone, this dual method of inhibition significantly boosts the ability to raise high-density lipoprotein and lower serum levels of atherogenic low-density lipoproteins. For patients with dyslipidemia, this combination increases the chance of a successful course of treatment.

Current research has demonstrated that beet root and its active ingredient, betalains (betanin), offer numerous health benefits. These benefits include strong antioxidant effects on the lipid peroxidation of membranes, prevention of LDL oxidation, anti-inflammatory, anti-cancer, blood pressure-lowering, and lipid-lowering properties.

CONCLUSION

Significant antioxidant and anti-hypercholesterolemic effects were observed in beetroots (Moftah *et al.,* 2023). The present study provides an important evidence base for the hypolipidemic properties of beetroot, which when combined with statins the most recommended agent have a synergistic impact. A suitable sample size must be obtained for a multi-centric investigation to yield more conclusive and convincing results. Further elaboration on the research modalities is necessary.

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