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ORIGINAL ARTICLE

Efficacy of Herbal Coded Traditional Medicine Formulation "Lipitame" for Primary Hyperlipidemia

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All the authors contributed significantly to the research that resulted in the submitted manuscript.

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ABSTRACT

Objective: The intention of the study was to find out the efficacy of selected herbal medicine (Lipitame) for Primary Hyperlipidemia in comparison with allopathic drug (Simvastatin).

Method: Herbal coded traditional medicine 'Lipitame' was tested for its efficacy in comparison with 'Simvastatin' to control Primary Hyperlipidemia through a randomized controlled prospective study at Shifa-ul-Mulk Memorial Hospital for Eastern Medicine, Hamdard University, Karachi. The test group (n=50) was administered Lipitame 500 mg b.d and the control group (n=50) to Simvastatin 20 mg at bed time. The test drug 'Lipitame' comprises of whole dried powder of Terminalia arjuna, Commiphora mukul, Phyllanthus emblica and Terminalia chebula.

Results: Lipitame reduced mean total cholesterol from 276.80+32.65 to 184.98+41.71mg%, mean triglyceride from 189.68+24.51 to 153.24+30.80 mg%, mean LDL from 185.46+23.79 to 129.62+24.83 mg% while increase in mean HDL from 34.22+0.84 to 34.92+0.72 mg% in comparison to Simvastatin which reduced mean total cholesterol from 271.46+38.63 to 193.10+46.17 mg%, mean triglycerides from 205.08+4.812 to 143.88+4.10 mg%, mean LDL from 176.30+23.81 to 131.34+22.44 mg% while increase in mean HDL from 33.82+0.77 to 35.00+0.78 mg%. The level with 'p-value' less than 0.05 in Paired Samples t-test was defined as statistically significant.

Conclusion: It was concluded that Lipitame is effective for the treatment of Primary Hyperlipidemia after 16 weeks' trial. There were no untoward or significant side effects associated with the use of Lipitame that proved its good acceptability by the patients. Results of the study suggest 'Lipitame' as an effective alternative herbal drug for Primary Hyperlipidemia.

INTRODUCTION

Primary Hyperlipidemia has become increasingly evident that hyperlipidemia and atherosclerosis are very much related to each other and the major cause for the coronary artery diseases (CAD). However, atherosclerosis has been reported to start from infancy but it progresses extensively in middle and late ages. Moreover, the risk factors like smoking, alcoholism, diabetes mellitus, sedentary lifestyle, stress, lack of exercise also play their role in the contribution towards the atherosclerosis phenomenon. Hyperlipidemia refers to elevated Total Cholesterol and Low Density Lipoprotein Cholesterol and lower levels of High Density Lipoproteins <35 mg/ dL. The plasma lipid levels recommended by

National Cholesterol Education Program, USA should be LDL-Cholesterol (mg/dL) <100 optimal, 100-129 near optimal/ above optimal, 139-159 borderline high, 160-189 high, >190 very high. HDL-Cholesterol <40 low, >60 high. Triglycerides <150 normal, 159199 borderlines high, 200-499 high, >500 very high. Total Cholesterol <200 desirable, 200-239 borderline high, >240 high [1]. Atherosclerosis starts from the development of macrophage into the foam cells that are deposited within the layers of arteries, i.e. tunica intima and media from the first week of life and convert into a fibrous atheroma from 30 years of age onwards as degree of endothelial injury progresses [2]. The oxidized phospholipids of lipoproteins are very important in the development of atherosclerosis which is vulnerable to free radical activity or enzymatic oxidation by myeloperoxidase, lipoxygenase, and other enzymes that are present in the vascular wall. The phospholipids after being oxidized become charged and bind covalently to proteins thus making them dysfunctional and enhancing the process of atherosclerosis. Both the in vivo and in vitro studies have shown the presence of oxidized phospholipids in atherogenic plaques [3]. The conventional medicine has provided the medicinal solution for this clinical problem in the form of cholesterol lowering drugs like statins, fibrates, nicotinic acid etc. But due to their side effects, cost and affordability, the new alternatives are required. Keeping all these relations in mind this study was conducted at Shifa-ul-Mulk Memorial Hospital for Eastern Medicine, Hamdard University, Karachi to find out alternative herbal medicines for primary hyperlipidemia.

METHODOLOGY

A randomized control study conducted on total 100 Hyperlipidemic patients attending the OPD of Shifa-ul-Mulk Memorial Hospital for Eastern Medicine, Hamdard University, Karachi. The study was conducted from 1st September 2008 to 31st November 2009 for the testing of the efficacy of herbal coded test drug 'Lipitame' and compared with the control drug 'Simvastatin'. Test group n=50 was treated with Lipitame 500mg which comprises of whole dried powders of Terminalia arjuna, Commiphora mukul, Phyllanthus emblica and Terminalia chebula) twice daily for 16 weeks following monthly follow ups for lipid profile and liver function tests. Similarly, control group n=50 was treat with Simvastatin 20 mg once daily for 16 weeks following monthly follow ups for lipid profile and liver function tests. After administration of test and control drug the lipid profiles of the cases were tested after 4, 8, 12, and 16 weeks and analyzed through T-test using SPSS version 12.0.

Study unit

Patients ranging from 30 to 70 years comprised of both sexes with abnormal lipid profiles and on treatment for primary hyperlipidemia were enrolled in the study. Subjects having history of myocardial infarction, severe ischemic heart diseases, valvular heart disease, coagulation disorders, diabetes mellitus type I and II both, suffering from hepatitis and liver cirrhosis, malnutrition, hypothyroidism and hyperthyroidism, alcoholics, pregnancy, medications such as progesterone, cyclosporine, thiazide diuretics, beta blockers and anabolic steroids were excluded from the study as these have been found to be potential confounding factors.

Sampling unit

Patients were registered and selected using randomized sampling. On average 2-3 respondents were registered per clinic day following screening test like fasting lipid profile and fasting blood sugar.

Total 100 patients were enrolled in the clinical trial. Both test and control groups had 50 patients each (test n=50, control n=50) after meeting the inclusion and exclusion criteria.

The major data analysis based on a statistical parameter e.g. reduction in blood LDL, VLDL, and TG and if any rise in HDL. It was a randomized controlled trial and the conclusion based on the prospective randomized clinical trial. The criteria of inclusion and exclusion were followed to find out the effect on size and level of evidence in relevant patient population.

RESULTS

After 16 week clinical trial herbal coded medicine, Lipitame reduced mean total cholesterol from 276.80±32.65 to 184.98±41.71mg%, mean triglyceride from 189.68±24.51 to 153.24±30.80 mg%, mean LDL from 185.46±23.79 to 129.62±24.83 mg% while increase in mean HDL from 34.22±0.84 to 34.92±0.72 mg% in comparison to Simvastatin which reduced mean total cholesterol from 271.46±38.63 to 193.10±46.17 mg%, mean triglycerides from

205.08±143.88 mg%, mean LDL from 176.30±23.81 to 131.34+22.44 mg% while increase in mean HDL from 33.82+0.77 to 35.00+0.78 mg%.

Patient characteristics

The mean age of 30 males in the test group was 47.06±9.09 years and of 27 males in control group was 46.62±9.73 years while the age of 20 females in test group was 50.95±9.81 years and of 23 females in control group was 48.17±10.69 years shown in Figure **1** and Table **1**.

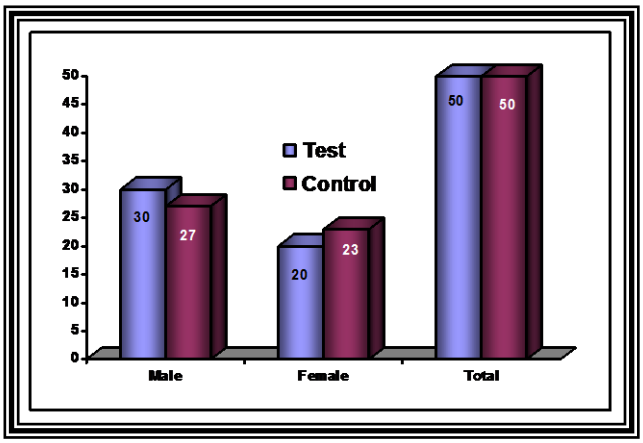

Figure 1. Total number of patients.

Table 1. Age distribution by treatment group.

Sex	Treatment Group	Mean	Number (n)	Std. Deviation
Control	Male	46.62	27	9.73
	Female	48.17	23	10.69
	Total	47.34	50	10.11
Test	Male	47.06	30	9.09
	Female	50.95	20	9.81
	Total	48.62	50	9.48
Total	Male	46.85	57	9.32
	Female	49.46	43	10.26
	Total	47.98	100	9.77

The mean age of 50 patients (both males and females) in test group was 48.62±9.48 and the mean age of 50 patients (both males and females) in control group was 47.34±10.11. The distribution of patients was classified in different class interval ranging from 35 to 70 years. The age of 100 patients recorded having 8 class intervals accordingly, 35-40, 41-45, 45-50, 51-55, 56-60, 61-65, and 66-70. There were three patients between 30-35 years, seven in between 36-40 years, fifteen in between 41-45 years, twenty-three in between 46-50 years, twenty-three in between 51-55 years, twelve in between 56-60 years, thirteen in between 61-65 years and four in between 66-70 years shown in Table **2**.

Table 2. Distribution of age group in total patients.

Age Group	Treatment Group		Total (n)
	Test (n)	Control (n)	
30 -35 Years	1	2	3
36 -40 Years	4	3	7
41 -45 Years	8	7	15
46-50 Years	11	12	23
51-55 years	10	13	23
56-60 years	8	4	12
61-65 years	7	6	13
66-70	1	3	4
Total	50	50	100

Response of Test and Control drug in total cholesterol levels

The test drug was administered to 50 cases whose mean cholesterol level was 276.80±32.65 mg% at the base line and control drug was administered to 50 cases whose mean cholesterol level was 271.46±38.63 mg%. After 16 weeks of drug administration total cholesterol levels were reduced to 184.98±41.71 mg % from the base line in test group and 193.10±46.10 mg% in control group as shown in Figure **2**.

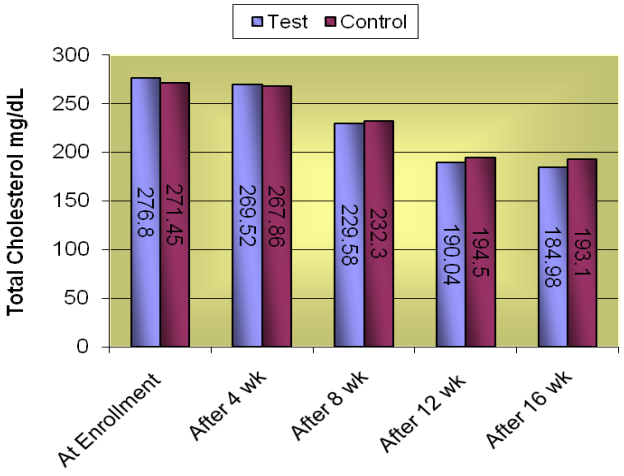

Figure 2. Response of test and control drug on total cholesterol levels.

Response of Test and Control drug in triglycerides levels

The test drug was administered to 50 cases whose mean Triglycerides level was 189.68 ±24.51 mg% at the baseline and control drug was administered to 50 cases whose mean cholesterol level was 205.08±34.03 mg%. After 16-week drug administration, total Triglycerides levels were reduced to 153.24±30.80 mg % from the baseline in test group and 143.88±29.00 mg% in control group as shown in Figure **3**.

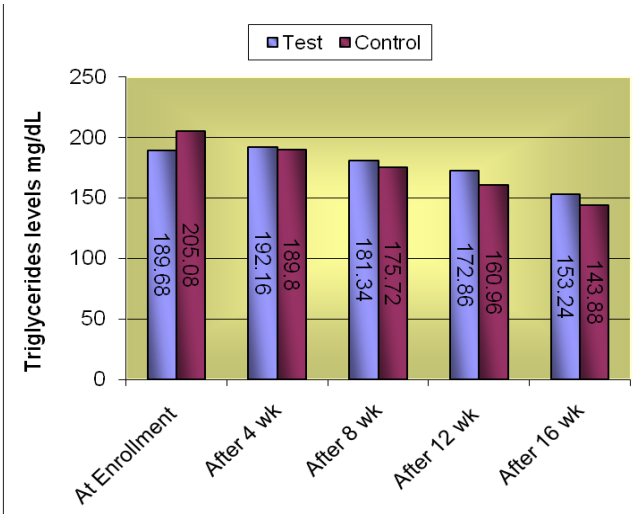

Figure 3. Response of test and control drug on triglycerides levels.

Response of Test and Control Drug in HDL-cholesterol levels

The test drug was administered to 50 cases whose mean HDL-Cholesterol level was 34.22±0.84 mg% at the baseline and control drug was administered to 50 cases whose mean cholesterol level was 33.82±0.77 mg%. After 16-week drug administration, HDL-Cholesterol levels were increased to 34.92±0.72 mg% from the baseline in test group and 35.00±0.78 mg% in control group as shown in Figure **4**.

Response of Test and Control drug in LDL-cholesterol levels

The test drug was administered to 50 cases whose mean LDL-Cholesterol level was 185.46±23.79 mg% at the baseline and control drug was administered to 50 cases whose mean cholesterol level was 176.30±23.81 mg%. After 16-week drug administration LDL-Cholesterol levels were reduced to 129.62±24.83 mg% from the baseline in the test group and 131.34±22.44 mg% in control group as shown in Figure **5**.

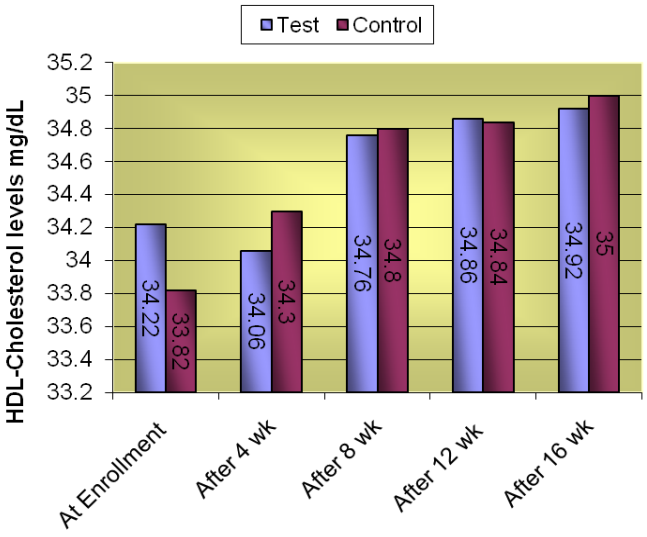

Figure 4. Response of test and control drug on HDL-Cholesterol levels.

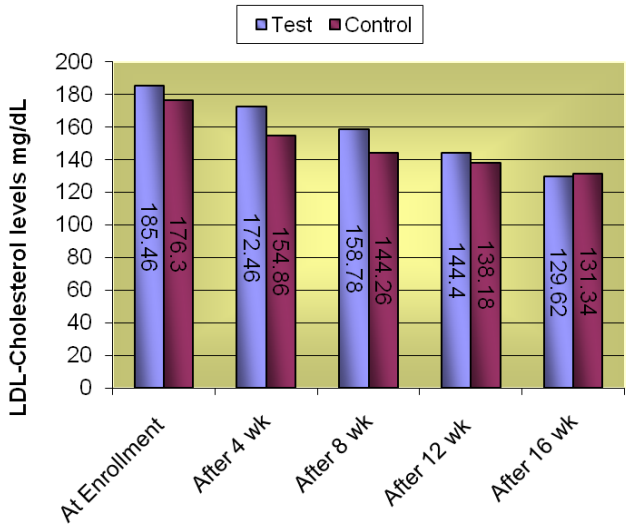

Figure 5. Response of test and control drug on LDL-cholesterol levels.

DISCUSSION

In this study the efficacy of herbal coded drug 'Lipitame" was tested in comparison with the conventional drug "Simvastatin" in terms of the reduction of total mean cholesterol, triglyceride, low-density lipoprotein while an increase in high-density lipoprotein.

Lipitame characteristics

The test drug "Lipitame" comprised of whole powders drug of *Terminalia arjuna, Commiphora mukul, Phyllanthus emblica and Terminalia chebula.* Among these four drugs *Terminalia arjuna* and *Commiphora mukul* possess significant hypolipidemic activity while *Phyllanthus emblica* and *Terminalia chebula* have good antioxidant activity. Research work on *Terminalia arjuna* supports its role as a hypolipidemic herbal drug. *Terminalia arjuna* has got very powerful antioxidant property along with hypolipidemic in comparison with Vitamin E that has been demonstrated in a randomized trial decreasing total cholesterol 12.7% and LDL cholesterol 25.6% respectively [4]. *Terminalia arjuna* has got mild diuretic effect thus helping in regulation of blood pressure along with its protective antithrombotic activity due to prostaglandin E_2 enrichment [5]. *Terminalia arjuna* posses endogenous antioxidant activities that were observed when its alcoholic extract was administered in dose of 6.75mg/kg to rat heart that was ischemically injured induced by isoproterenol [11]**.** Similarly, *Commiphora mukul* also possesses hypolipidemic effects. The compounds isolated from *Commiphora mukul* like cembrenoids, a bicyclic diterpene, guggulsterone derivatives, myrrhanonol derivatives, myrrhanol derivatives, and a lignan, individually or combined together inhibit the lipid peroxidation by 79%, 57% and 58% respectively [12]. *Commiphora mukul* has been proved for its hypolipidemic effects in a randomized double blind trial where it reduced total cholesterol 11.7%, the LDL cholesterol 12.5%, triglycerides 12% and 11.1% improvement in total cholesterol/ HDL ratio in comparison with the placebo [13]. *Commiphora mukul* has been studied in six clinical trials five in India and one in the United States also confirmed the hypolipidemic effects in which it was compared with two reference compounds and reduced total cholesterol from 10% to 27% and a significant decrease in lipid peroxide levels [14]. Serum cholesterol and triglyceride were reduced by the utilization of purified gum of *Commiphora mukul* given twice gm daily upto 4^{th} and 8^{th} weeks in twenty subjects of hyperlipidemia [6]. *Phyllanthus emblica* has shown its hypocholesterolemic and antiatherogenic properties in a study done in Department of Food and Nutrition, Lady Irwin College, University of Delhi. It was used as a supplementary diet in hypercholesterolemic and control mal subjects and reduced the cholesterol levels from 265 mg/dL to 240 mg/dL, LDL cholesterol from 175 mg/dL to 150 mg/dL, triglyceride from 220 mg/dL to 190 mg/dL and increased HDL from 40 mg/dL to 50 mg/dL [7]. Its fresh juice has also been tested for hypolipidemic effects by giving in dose of 5ml/Kg body weight per rabbit per day for 60 days. It showed the reduction in serum cholesterol 82%, triglycerides 77%, phospholipids 77% and LDL 90% [8]. Similarly, the ethanol extract of *Phyllanthus emblica* at a dose of 10 to 20 mg/Kg body weight / day for 20 days to rats fed 1% cholesterol diet, significantly reduced total, free and LDL-Cholesterol levels in a dose-dependent manner [9]. Like statins its flavonoid extract from the fresh fruit inhibits HMG-CoA reductase and increases degradation of cholesterol [10]. Hypolipidemic effects of dried powder of *Phyllanthus emblica* fruit has been confirmed in a study in which it reduced total cholesterol 42%, triglyceride 29% and LDL 31% and increased HDL 33% along with reduction of plaque areas 38% in different body vessels [15]. Similarly, the alloxan-induced diabetic rats also shown the reduction in serum cholesterol when they were given the aqueous extract of *Phyllanthus emblica* [16]. *Terminalia chebula* has been tested for antioxidant properties at different magnitudes of strengths [17]. Chebulinin has greater antioxidant and anti lipid peroxidation effects along with its inhibitory action on the production of superoxide radicals [18]. Its extract has been proved for hypocholesterolemic effects in rabbits that were fed on high cholesterol diet. Further, it slowed atherosclerosis in vessels of these animals that were experimentally induced atherosclerosis [18].

Chemical constituents

Terminalia arjuna

Terminalia arjuna renders different types of chemical compounds such as Tannin, Friedlin, Cerasidin, Co-enzume Q10, Arjuna glycosides- Arjunine, Arjunetein, Arjunetosides, Saponins-Arjunolic acid, Arjunic acid, Arjungenin, Beta-sitosterol, Oligomeric Proanthocyanidins, Ellagic acid, Oleanolinic acid, Gallic acid, Arjunone, Arjunolone, Luteolin are the natural antioxidants. Bark water extract contains 23% calcium salts and 16% tannins [19].

Commiphora mukul

Commiphora mukul contains Z-guggulsterone, E-guggulsterone, Z-guggulsterol, 16-α hydroxy-4-pregnen-3-one, 20α-hydorxy-4-pregnen-3-one, 20 β-hydorxy-4-pregnen-3-one, guggulsterol –I, guggulsterol-II, guggulsterol-III, 3.5, 6-cholestanetriol,

5-hydroxycholestane-3, 6-dione, 16, 20-dihydroxycholest-4, 24-dien-3-one, mukulol, Cembrene-A, Myrcene, Myrcenol, D-xylo-guggultetrol-18, 4, 5 dihydro: 8, 12 epoxy-1(10)4, 7, 11-germacratetaen-6-one and ferulic acid [20].

Phyllanthus emblica

Phyllanthus emblica pulp contains moisture, protein, fat, minerals, fiber, carbohydrates, nicotinic acid and vitamin C. It contains 720 mg/100 gm Vitamin C which is approximately 20 times more than available in one or two oranges. Fresh and dry fruit retains its Vitamin C contents due to its tannin comprise of gallic acid, ellagic acid and glucose that slow down the degradation of ascorbic acid. Fruit contains tannin about 28%, twig bark 21%, stem bark 8-9%, and leaves 22% respectively. Overall two types of tannins are found in fruit [21].

Terminalia chebula

30% of chebulinic acid, tannic acid about 20 to 40%, gallic acid, resin and some purgative principle of the nature of anthraquinone are found in its fruit [22].

Lipitame pharmaceutical characteristics

Lipitame is a thin film coated tablet having 8 mm thickness, 16 mm length, and 10 mm width in an oval shape. Its hardness is 5 kg, dissolution 90% after 30 minutes, friability 3%, and viscosity e15cps. The binding agents used are liquid glucose, talc and magnesium stearate.

CONCLUSION

Paired sample t-test was applied by using SPSS version 12.0 to analyze the statistical significance. From the statistical results obtained out of clinical response, it was concluded that Lipitame is effective for the treatment of Primary Hyperlipidemia. The significant result with 'p-value' less than 0.05 was defined as statistically significant. There were no untoward or significant side effects associated with the use of Lipitame that proved its good acceptability by the patients. Moreover there was subjective feeling of wellbeing regarding breathlessness and chest tightness or pressure among the patients taking Lipitame. This makes an interesting point to focus for further research work on this effective alternative drug for Primary Hyperlipidemia.

Adverse Effects Profile

All patients enrolled in the study were evaluated for safety. Side effects were defined among the sign and symptoms that fist occurred or become more severe during the course of study. The adverse events were assessed as mild in severity and self limiting in nature. Three patients treated with the test drug experienced the dryness of mouth, bloating of abdomen and mild sweating which disappeared within two to three days. While two patients in the control group reported lethargy and mild pain in legs but was not consistent. They all continued the control drug. Therefore, none of the patients withdrew from the study due to these adverse events in test and control group.

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REFERENCES

1. W Robert. Mahley, P Thomas. Bersot, National Cholesterol Education Program Guidelines for Treatment: Managing Patients with Dyslipidemia, *Goodman and Gilman's, the pharmacological basis of therapeutics* (Joel G. Hardman, Lee E. Limbird, Alfred Goodman Gilman), 10th edition, International edition, McGraw Hill, New York, 2001: 979.
2. John S, Drobnik W, Lackner K, Schmieder RE. Soluble thrombomodulin and endothelial dysfunction in early atherosclerosis. Lancet. 1999; 354(9190):1647.

3. Berliner JA, Watson AD. A role for oxidized phospholipids in atherosclerosis. N Engl J Med. 2005; 353(1):9-11.
4. Gupta R, Singhal S, Goyle A, Sharma VN. Antioxidant and hypercholesterolemic effects of Terminalia arjuna tree-bark powder: a randomized placebo controlled trial. J Assoc Physicians India, 2001; 49: 231-5.
5. Dwivedi S. Terminalia arjuna Wight & Arn. a useful drug for cardiovascular disorders. J Ethnopharmacol. 2007; 114(2):114-29.
6. Verma SK, Bordia A. Herbal monograph, Commiphora mukul. Indian J Med Sci, 1988; 87:356-60.
7. Jacob A, Pandey M, Kapoor S, Saroja R. Effect of the Indian gooseberry (amla) on serum cholesterol levels in men aged 35-55 years. Eur J Clin Nutr. 1988; 42(11):939-44.
8. Mathur R, Sharma A, Dixit VP, Varma M. Hypolipidaemic effect of fruit juice of Emblica officinalis in cholesterol-fed rabbits. J Ethnopharmacol. 1996 ;50(2):61-8.
9. Kim HJ, Yokozawa T, Kim HY, TOHDA C, RAO TP, JUNEJA LR. Influence of amla (Emblica officinalis Gaertn.) on hypercholesterolemia and lipid peroxidation in cholesterol-fed rats. J Nutr Sci Vitaminol. 2005; 51(6):413-8.
10. Anila L, Vijayalakshmi N. Flavonoids from Emblica officinalis and Mangifera indica—effectiveness for dyslipidemia. J Ethnopharmacol. 2002; 79(1):81-7.
11. Karthikeyan K, Bai BS, Gauthaman K, Sathish KS, Devaraj SN. Cardioprotective effect of the alcoholic extract of Terminalia arjuna bark in an in vivo model of myocardial ischemic reperfusion injury. Life sciences. 2003; 73(21):2727-39.
12. Francis JA, Raja SN, Nair MG. Bioactive Terpenoids and Guggulusteroids from Commiphora mukul Gum Resin of Potential Anti-Inflammatory Interest. Chem Biodivers. 2004; 1(11):1842-53.
13. Singh RB, Niaz MA, Ghosh S. Hypolipidemic and antioxidant effects of Commiphora mukul as an adjunct to dietary therapy in patients with hypercholesterolemia. Cardiovasc Drugs Ther. 1994; 8(4):659-64.
14. Joanna S, Thompson Coon, Edzard Ernst. A systematic review Herbs for serum cholesterol reduction. *J Fam Pract*, 2003; 52-6.
15. TsingHua. Effect of Emblica officinalis on Formation of Atherosclerotic Plaque in Hypercholesterolemia Rabbits. *Applied Journal of General Practice*. 2005.
16. Qureshi SA, Warda A, Viqar S. The Effect of Phyllanthus emblica Linn on Type-II Diabetes, Triglycerides and Liver-Specific Enzyme. *P J Nutr.* 2009; 8:2:125-8.
17. Cheng HY, Lin TC, Yu KH, Yang CM, Lin CC. Antioxidant and free radical scavenging activities of Terminalia chebula. Biol Pharm Bull. 2003; 26(9):1331-5.
18. Chattopadhyay RR, Bhattacharyya SK. Terminalia chebula: An update. Pharmacogn Rev. 2007; 1(1):151.
19. Kapoor LD. CRC handbook of Ayurvedic plants. CSIR, USA. 1990;183.
20. Abbasi MA. Bioactive Chemical Constituents of Symplcos Racemosa and Commiphora Mukul (Doctoral dissertation, HEJ Research Institute of Chemistry, ICCBS, University of Karachi).
21. Said MH. Emblica officinalis, *Hamdard Pharmacopoeia of Eastern Medicine*, The Times Press, Karachi, p. 383.
22. Kapoor LD. CRC Handbook of Ayurvedic Plants. CSIR, USA. 1990;183.