

Most commonly natural and synthetic antihyperlipidemic agents available and distracted in Erbil city

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Abstract

Background and objective: Hyperlipidemia refers to elevated levels of lipids and cholesterol in the blood, and is also identified as dyslipidemia, to describe the manifestations of different disorders of lipoprotein metabolism. The aim of this study was to investigate the available and commonly distracted natural and synthetic antihyperlipidemic agents in herbal shops, pharmacies and prescribed by physicians in Erbil city, and to determine physicians' response for the use of natural products.

Methods: Between November 2013 to February 2014; 20 herbal shops and 40 pharmacies in Erbil city were visited randomly for asking on available and most commonly distracted natural and synthetic antihyperlipidemic agents. Forty doctors at private clinics were asked about the most frequently prescribed natural and synthetic antihyperlipidemic agents in Erbil city.

Results: Of eight synthetic drugs available in pharmacies, statins were considered the first line agents as antihyperlipidemic drugs particularly atorvastatin and rosuvastatin. Of 16 natural products available in Erbil herbal shops and pharmacies, garlic and omega 3 give positive response by patients and highly distracted by pharmacist and herbalist. Of 40 physicians, 27 (68%) prescribe both natural and synthetic agents while only 13 (32%) prescribe synthetic drugs as antihyperlipidemic agents for patients.

Conclusion: Statins used in first order as antihyperlipidemic drugs and uses of natural products, as lipid lowering agents in Erbil, is getting larger interest by people, herbalists, pharmacists and doctors. Of 40 doctors, 68% prescribe natural products along with synthetic drugs but also there is a need to educate the people on how to use these natural agents and choice suitable products for them.

Keywords: Hyperlipidemia, Natural products, Synthetic drugs, Erbil city.

Introduction

Hyperlipidemia is a disorder of lipid metabolism manifested by increase of plasma concentrations of the various lipid and lipoprotein fractions such as increase of serum total cholesterol (TC), low-density lipoprotein (LDL), triglyceride (TG) concentrations, and a decrease in the high-density lipoprotein (HDL) concentration.^{1,2} Hyperlipidemia is the key risk factor for cardiovascular disorders and has been reported as the most common cause of death in developed as well as developing nations.³⁻⁵ Hyperlipidemia may be caused by specific genetic abnormalities called primary hyperlipidemia⁶ or may be idiopathic

caused by lifestyle habits or medical diseases such as diabetes, kidney disease, pregnancy, hypothyroidism and heart disease. One has a greater chance of developing hyperlipidemia is a man (>45 years) or a woman (>55) or having familial history of hyperlipidemia.⁷ Lipid-lowering agents are a diverse group of pharmaceuticals that are used in the treatment of hyperlipidemia such as statins, fibrates, niacin, bile acids, ezetimibe, etc. These reduce cholesterol level with different mechanisms; some may lower "bad cholesterol" (LDL) more than others, while others may prudentially increase HDL, "the good cholesterol". Since the different

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medications act differently to reduce cholesterol and triglyceride levels, most physicians may prescribe a combination therapy of two medications.⁸ Statins are the drugs of choice where the major dyslipidaemia is high-baseline LDL-cholesterol and that fibrates are particularly effective in the case of hypertriglyceridaemia.⁹ Statins lower LDL-cholesterol by 20-60% and TG by 10-20%,¹⁰ and raise HDL cholesterol by competitively inhibiting 3-hydroxy-3-methylglutaryl-coenzyme A, reductase, the rate-limiting enzyme in the cholesterol biosynthesis pathway in the liver. Rosuvastatin is a new member of the statin family with higher efficacy in reducing LDL cholesterol, possesses a relatively long half-life and a high degree of selectivity for liver cells (the main site of cholesterol synthesis) compared with non-hepatic cells than other statins at comparable doses.¹¹ Fibrates typically lower triglycerides by 40% to 60%, LDL by 10-20% and increase level of the good cholesterol HDL.¹⁰ The dissatisfaction with high costs and potentially hazardous side-effects of synthetic hypolipidemic drugs, the potential of natural products for treating hyperlipidemia is under exploration. This may be an excellent alternative strategy for developing future effective and safe hypolipidemic drugs. A variety of natural products, including crude extracts and isolated compounds from plants can reduce body cholesterol and prevent hyperlipidemia. A wealth of information indicates numerous bioactive components from nature are potentially useful in hyperlipidemia and/or hypercholesterolemia treatments. A good example of such is the polyphenols as apigenin, genistein, and catechins that show strong antihypercholesterolemic activity. Saponin, sterols, stanols polyunsaturated fatty acids, mucilage, and carbohydrates also have potent hypocholesterolemic activity.⁷ In Erbil city, different kinds of antihyperlipidemic agents of synthetic and natural products are available in pharmacies and herbal shops and are used by patients. Some of these

natural products are used traditionally and some of them are prescribed by physician. Hence, this study was planned to investigate the natural and synthetic antihyperlipidemic agents available, distracted in herbal shops, pharmacies and prescribed by physicians in Erbil city and to determine physicians' response for the use of natural products.

Methods

A study was carried out at Bazaar, Brayati and Medical street in Erbil city during the period from November 2013 to February 2014. The study population consisted of physicians, pharmacists and herbalists. Three groups of structured questionnaire forms were designed. The first questionnaire was administered to 20 randomly selected traditional medicine practitioners or herbalists on available and most commonly distracted natural antihyperlipidemic products in Erbil market herbal shops. The second questionnaire was administered to 40 randomly selected pharmacists on available and most commonly distracted natural and synthetic antihyperlipidemic agents in Erbil pharmacies. The third questionnaire was administered to 40 randomly selected physicians on most commonly natural and synthetic antihyperlipidemic agents they prescribe. The time taken to complete each questionnaire ranged from 15 to 20 minutes. Microsoft Excel 2010 was used for statistical analysis of the data that included calculation of frequencies and percentages.

Results

Of 20 herbal shops included in this study, 10 natural products were used as antihyperlipidemic agents in Erbil city. Black seed oil and fenugreek were available in all of the 20 herbal shops (100%), while artichoke was available in only two herbal shops (10%) (Table 1). The most commonly distracted natural antihyperlipidemic agents from the 20 herbal shops was flaxseed oil (55%) followed by black seed (50%), and

only 10% distracted sesame oil and parsley oil were less requested by patients ginger root. Fenugreek, artichoke and (Figure 1).

Table 1: Available natural antihyperlipidemic products in Erbil herbal shops (n=20).

Available natural product	Botanical name	Available form	No.	%
Omega 3	Fish oil supplementation	Capsule	4	20
Garlic oil	Allium sativum	Capsule	16	80
Black seed oil	Nigella sativa	Oil, seed & capsule	20	100
Fenugreek oil	Trigonella foenum-graecum	Oil, seed & capsule	20	100
Flax seed oil	Linum usitatissimum	Oil, seed & capsule	14	70
Sesame oil	Sesamum indicum	Oil & seed	16	80
Olive oil	Olea europaea	Oil & fruit	9	45
Artichoke leaf	Cynara scolymus	Leaf & capsule	2	10
Parsley oil	Petroselinum crispum	Oil, seed & capsule	7	35
Ginger root	Zingiber officinale	Root & capsule	4	20

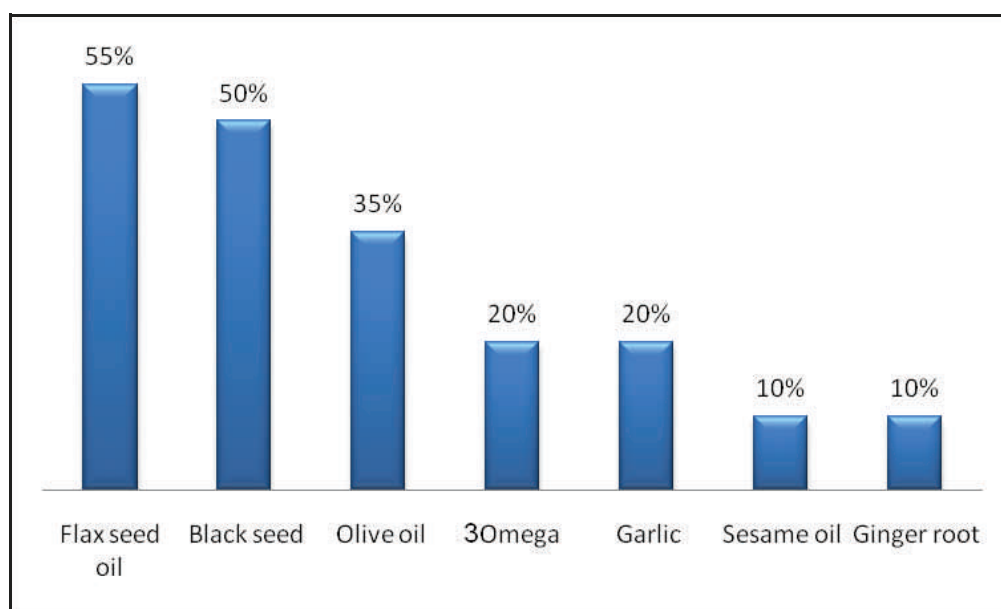


Figure 1: Most commonly distracted natural antihyperlipidemic products in Erbil herbal shops

Eight drugs were available as synthetic and nine natural antihyperlipidemic agents in Erbil pharmacy (Table 2). Atorvastatin was available in 38 pharmacies (95%), Omega 3 in 32 (80%), while ezetimibe and apple cidar vinager were available in only two (5%) pharmacies. The most commonly

distracted synthetic antihyperlipidemic drugs distracted in pharmacies were atorvastatin (85%), rosuvastatin (50%), simvastatin (25%) and fluvastatin (3%). Ezetimibe was available but not commonly distracted in pharmacies (Figure 2).

Table 2: Available synthetic and natural antihyperlipidemic agents in Erbil pharmacies (n=40)

Available synthetic drugs	Dosage form	No.	%	Available natural products	Botanical name	Dosage form	No.	%
Atorvastatin	Tablet	38	95	Omega 3	Fish oil supplementation	Capsule	32	80
Rosuvastatin	Tablet	34	85	Garlic oil	Allium sativum	Capsule	12	30
Simvastatin	Tablet	36	90	ketone raspberry	Rubus idaeus	Capsule	10	25
Fenofibrate	Tablet	4	10	Green coffee	Coffea arabica	Sachets	8	20
Gemfibrozil	Tablet	24	60	Green tea leave	Camellia sinensis	Sachets	8	20
Fluvastatin	Capsule	4	10	Pineapple	Ananas comosus	Tablet	4	10
Ezetimibe	Tablet	2	5	Acaiberry	Euterpe oleracea	Capsule	12	30
Orlistat	Capsule	20	50	Apple cidar vinager	Malus domestica Borkh	Capsule	2	5
				Ginger root	Zingiber officinale	Capsule	4	10

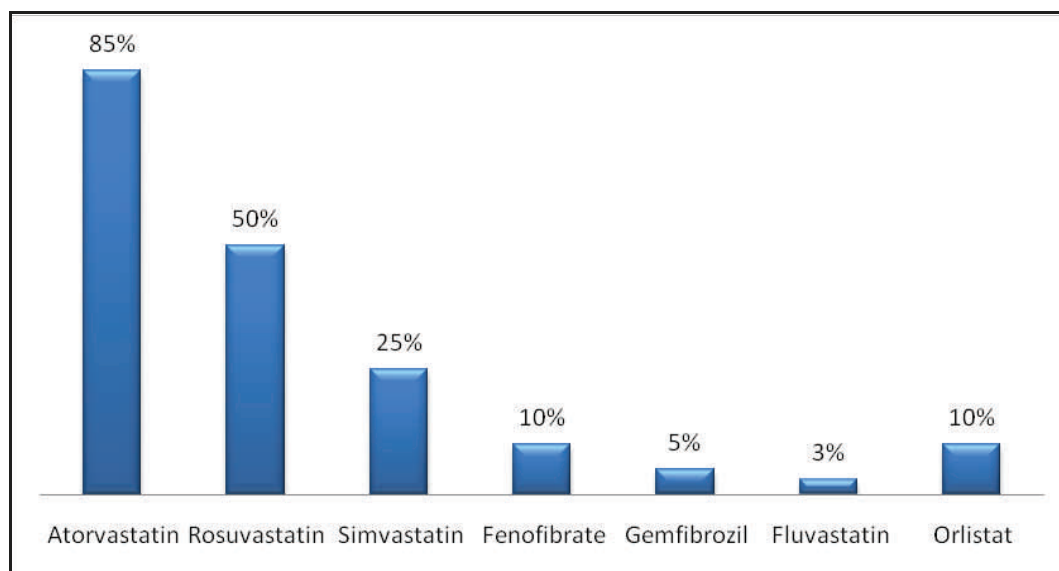


Figure 2: Most commonly distracted synthetic antihyperlipidemic drugs in Erbil Pharmacies

Figure 3 shows the commonly distracted natural antihyperlipidemic drugs in Erbil pharmacies in which high percent of omega 3 (75%), and low percentage of pineapple, keton raspberry and acaiberry (5%). The most commonly prescribed synthetic antihyperlipidemic drugs by physicians were atorvastatin (75%), rosuvastatin (50%), simvastatin (35%), fenofibrate (15%), gemfibrozil (10%), fluvastatin (10%) and orlistat (5%) as shown in Figure 4.

For natural products, most physicians preferred omega 3 to reduce lipid (50%), followed by green tea (20%), olive oil (15%), garlic (15%) and pineapple (10%) as shown in Figure 5. Of 40 physicians, 27 (68%) prescribe both natural and synthetic agents together, while only 13 (32%) prescribe synthetic drugs alone as antihyperlipidemic agents for patients (Figure 6).

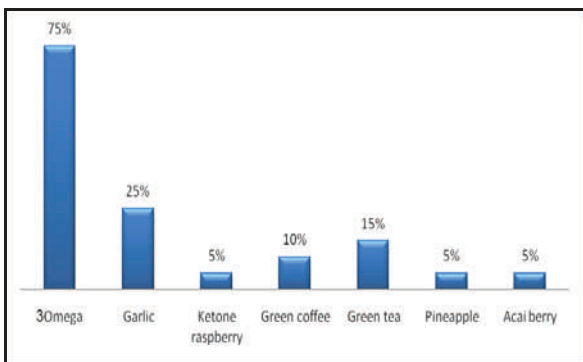


Figure 3: Most commonly distracted natural antihyperlipidemic products in Erbil Pharmacies

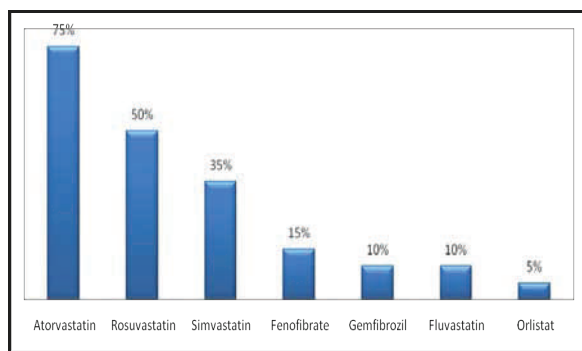


Figure 4: Most commonly synthetic antihyperlipidemic drugs prescribed by physicians.

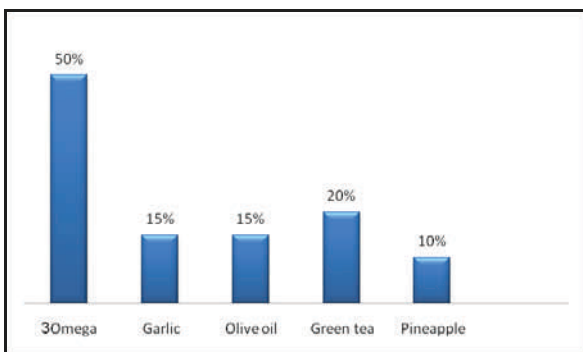


Figure 5: Most common natural antihyperlipidemic products prescribed by Physicians

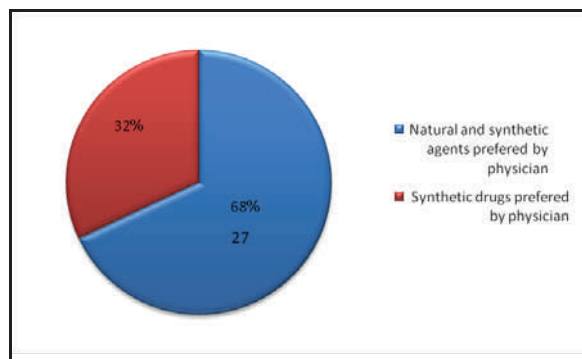


Figure 6: Physicians response for natural and synthetic antihyperlipidemic agents (n=40)

Discussion

Increased level of different kinds of lipids have been implicated in the production of atherosclerosis which is considered the primary cause of cardiovascular disease such as myocardial infarction, stroke and peripheral vascular diseases which account for significant mortality in developed and developing countries.¹² In the present study on available and mostly distracted antihyperlipidemic agents in Erbil city showed that omega 3, garlic, black seed oil, fenugreek, flax seed oil, sesame oil, olive oil, artichoke, parsley oil, ginger root, ketone raspberry, green coffee, green tea leave, pineapple, acaiberry and apple cidar vinager are the commonly available natural products while atorvastatin, rosuvastatin, simvastatin, fenofibrate, gemfibrozil, fluvastatin, ezetimibe and orlistat are the available synthetic drugs in Erbil city. Among the synthetic drugs, statins which include atorvastatin, rosuvastatin and simvastatin are highly prescribed by doctors because of its positive response by patients. In Erbil among statins group atorvastatin is dispensed more and this may be related to its cost which is cheaper than rosuvastatin and patients are not familiar with it. Fibrates (Fenofibrate and gemfibrozil) are distracted in Erbil only in 5-15%. These results are in agreement with the study reported by Moser and Segars who concluded that in the United States among the lipid lowering agents, statins were the most commonly used class of medications; these accounted for 76.1% of all prescribed treatments. The second most frequently cited drug class was fibric acid derivatives (10%) closely followed by the cholesterol absorption inhibitor ezetimibe (7.2%) and niacin (6.3%).¹³ We noticed that orlistat listed by the pharmacist as an antihyperlipidemic drug and only prescribed by 5% of physicians. We know that it is used in sever obese patient but also have antihyperlipidemic effect and is a derivative of the naturally-occurring lipase inhibitor produced by *Streptomyces toxytricini*. It inhibits pancreatic lipase

through a covalent bond to the lipase's active site serine so it reduces TG absorption.¹⁴ The World Health Organisation has estimated that perhaps 80% of earth's six billion inhabitants relies upon traditional medicine for their primary health care needs, and a major part of this therapy involves the use of plant extracts or their active principles. Nearly all 'wonder drugs' in use today are derived from natural products. Of about 120 plant derived drugs commonly in use in one or more countries, 74% were discovered as a result of chemical studies directed at the isolation of the active constituents of plants used in traditional medicine.¹⁵ Omega 3 and garlic showed the highest percent in natural products distracted in pharmacies, herbal shops and 50% of doctors prescribe it and this is supported by the presence of many studies that support its effectiveness as antihyperlipidemic natural supplement. A study by Ibraheem concluded that omega 3 reduced total cholesterol and LDL as compared with control.¹⁶ Lipid lowering effect of garlic demonstrated on human and animals due to organosulfur compounds, especially S-allylcysteine, are potent inhibitors of cholesterol synthesis, and hence may be the major principles of garlic responsible for the reduction of plasma cholesterol level.¹⁷ Flax seed and black seed distracted in highest percent as a natural products in Erbil herbal shops as antihyperlipidemic agent. According to Vijaimohan et al flaxseed oil supplementation lowered the increase in plasma cholesterol, TG, phospholipids, free fatty acids, HDL, LDL, VLDL, LDL/HDL and TC/HDL ratio in rats.¹⁸ However, patients ingested 2 g/day black seed displayed a significant decline in TC, TG, and LDL-c, and a significant elevation in HDL/LDL.¹⁹ Department of Physiology, College of Medicine, University of Dammam, Dammam, Saudi Arabia¹ Department of Internal Medicine, College of Medicine, University of Dammam, Dammam, Saudi Arabia Address for correspondence: Dr. Abdullah O. Bamosa, Department of

Physiology, College of Medicine, University of Dammam, P.O. Box 2114, Dammam 31451, Saudi Arabia. E-mail: aosbamosa@gmail.com Sesame oil and ginger root got the lowest percent their lipid lowering effect confirmed only on animal^{20,21} and no herbalist selected neither fenugreek nor artichoke and parsley oil as the commonly requested by patients. The other natural products selected by herbalist and pharmacist as lipid lowering agents have been confirmed to help in managing hyperlipidemia on animal such as olive oil,²² green coffee,²³ green tea leaves,²⁴ pineapple,²⁵ apple cidar vinager,²⁶ ketone raspberry,²⁷ while acai berry²⁸ and artichoke²⁹ on human. In this study we can notice the difference in the presence of natural agents in herbal shops from that of pharmacies, because pharmacies only bring the agents that are common and those which doctors prescribe. Many natural agents that are present in the herbal shops did not exist in the pharmacies and only the proved and tested ones are brought. In herbal shops peoples come and buy what they think traditionally is better for them and little of them take natural products on recommendation of herbalist. From 40 doctors, 27 (68%) prescribe natural products along with synthetic drugs. During this study, a lower percent was expected. This high percent shows that doctors nowadays are more interested in natural agents and their benefits and their role in completing the action of the synthetic drugs. The results of this study indicated that antihyperlipidemic products could be easily purchased in Erbil city with and without a prescription.

Conclusion

Different kinds of antihyperlipidemic agents are used in Erbil. Among synthetic drugs statins is in the first order give positive response by patients. The use of natural products as lipid lowering agents in Erbil is getting larger interest by people, herbalists, pharmacists and doctors. A high percent of doctors prescribe natural products along

with synthetic drugs but there is still a need for doing more research about the natural agents that have possibility to aid in lipid lowering and their role in using them in combination with synthetic agents as a booster and to decrease the needed dose for synthetic drugs, thereby, a possibility for minimizing their unwanted side effects. There is also a need to educate people of how to use these natural agents and choose suitable products and getting these agents under the control of health care providers because although they are natural, not all of them fit everybody's condition. In Erbil city antihyperlipidemic products could be easily purchased with and without a prescription.

Conflicts of interest

The author reports no conflicts of interest.

References

1. Mahmood ZA, Ahmed SW, Sualeh M, Mahmood SBZ. Hyperlipidemia development and consequences. *Med Channel* 2009; 5:14-17.
2. Ducharme N, Radhamma R. Hyperlipidemia in the elderly. *Clin Geriatr Med* 2008; 24:471-87.
3. Reiner Z, Tedeschi-Reiner E. Atherosclerosis – a paradox of Eastern European countries. *Atherosclerosis* 2006; 7:461.
4. Simons LA. Additive effect of plant sterol-ester margarine and cerivastatin in lowering low density lipoprotein cholesterol in primary hypercholesterolemia. *Am J Cardiol* 2002; 90:737.
5. Yokozawa T, Ishida A, Cho E J, Nakagawa T. The effects of *Coptidis rhizoma* extract on a hypercholesterolemic animal model. *Phytomedicine* 2003; 10:17.
6. Soutar AK, Naoumova RP. Mechanisms of disease: genetic causes of familial hypercholesterolemia. *Nat Clin Pract Cardiovasc Med* 2007; 4:214-25.
7. Ibrahim SRM, Mohamed GA, Banjar ZM, Kamal HKM. Natural antihyperlipidemic agents: Current status and future perspectives. *Phytopharmacology* 2013; 4(3):492-531.
8. Durrington P. Dyslipidaemia. *Lancet* 2003; 362:717-31.
9. Farnier M. Cerivastatin in the treatment of mixed hyperlipidemia: the right study. The Cerivastatin Study Group. Cerivastatin, Gemfibrozil, Hyperlipidemia Treatment. *Am J Cardiol* 1998; 82:47-51.
10. Trevor AJ, Katzung BG, Clipstone N. Drugs used to treat Hyperlipidemia I & II. *Pharmacology: Examination and Board Review*. 9ed. Anthony J 2012; 605-17.

11. Naples M, Federico LM, Xu E, Nelken J, Adeli K. Effect of rosuvastatin on insulin sensitivity in an animal model of insulin resistance: evidence for statin-induced hepatic insulin sensitization. *Atherosclerosis* 2008; 198(1):94-103.
12. Souza TD, Mengi SA, Hassarajani S, Chattopadhyay S. Efficacy study of the bioactive fraction (F-3) of *Acorus calamus* in hyperlipidemia. *Indian J Pharmacol* 2007; 39(4):196-200.
13. Moser A, Segars LW: Assessment of antihyperlipidemic therapy in US patients with coronary heart disease. *J Am Osteopath Assoc* 2010; 110(6):331-39.
14. Tsujita T, Takaichi H, Takaku T, Aoyama S, Hiraki J. Antiobesity action of -polylysine, a potent inhibitor of pancreatic lipase. *J Lipid Res* 2006; 47:1852-58.
15. Farnsworth NR, Akerels O, Bingel AS, Soejarto DD, Guo Bull Z. Medicinal plants in therapy. *Bull World Health Organ* 1985; 63:965.
16. Ibraheem DA. Comparative study between plant and animal sources of Omega-3 fatty acid in their potential role of regulating blood glucose and lipid profile in healthy volunteers. *Yemeni J Med Sci* 2011; 5:7-14.
17. Yeh Y, Liu L. Cholesterol-lowering effect of garlic extracts and organosulfur compounds: Human and animal studies. *The Am Soc Nutr Sci* 2001; 131(3):9895-935.
18. Vijaimohan K, Jainu M, Sabitha KE, Subramaniyam S, Anandhan C, Shyamala Devi CS. Beneficial effects of alpha linolenic acid rich flaxseed oil on growth performance and hepatic cholesterol metabolism in high fat diet fed rats. *Life Sci* 2006; 79(5):448-54.
19. Kaatabi H, Bamosa AO, Lebda FM, Abdulmohsen H, Al-Sultan AI. Favorable impact of *Nigella sativa* seeds on lipid profile in type 2 diabetic patients. *J Fam Commun Med* 2012; 19(3):155-61.
20. Asgary S, Rafieian-Kopaei M, Najafi S, Heidarian E, Sahebkar A. Antihyperlipidemic effects of *Sesamum indicum* L. in Rabbits Fed a High-Fat Diet. *The Sci World J* 2013; 5.
21. Fuhrman B, Rosenblat M, Hayek T, Coleman R, Aviram M. Ginger extract consumption reduces plasma cholesterol, inhibits LDL oxidation and attenuates development of atherosclerosis in atherosclerotic, apolipoprotein e-deficient mice. *J Nutr* 2000; 130(5):1124-31.
22. Yousaf MJ, Naveed AK, Ahmed T, Khan S, Azeem Z. Hypolipidemic effect of extra virgin olive oil in diabetic rats. *J Rawal Med Col* 2012; 16(1):70-72.
23. Jäger S, Trojan H, Kopp T, Laszczyk M, Scheffler A. Pentacyclic triterpene distribution in various plants - rich sources for a new group of multi-potent plant extracts. *Molecules* 2009; 14: 2016-31
24. Suriyamoorthy P, Mary MRF, Subrhamanian H, Kanagasapabathy D. Anti hyperlipidemic effect of aqueous extract of *Aegle marmelos* and *camellia sinensis* in oil fed hyperlipidemic rats. *Int J Pharm Sci*, 2014; 6(2):338-41.
25. Vuyyuru A, Kotagiri S, Vrushabendra Swamy BM, Archana Swamy P. Antihyperlipidemic activity of *Ananas Comosus* L. leaves extract in Albino rats. *Res J Pharma Biol Chem Sci* 2012; 3(3):1229.
26. Leontowicz H, Leontowicz M, Gorinstein S, Martin-belloso O, trakhtenberg S. apple peels and pulp as a source of bioactive compounds and their influence on digestibility and lipid profile in normal and atherogenic rats. *J Med weter* 2007; 63(11):1434-6.
27. Qin Y, Xia M, Ma J, Hao YT, Liu J, Mou HY et al. Anthocyanin supplementation improves serum LDL- and HDL-cholesterol concentrations associated with the inhibition of cholesteryl ester transfer protein in dyslipidemic subjects. *Am J Clin Nutr* 2009; 90:485-92.
28. Udani JK, Singh BB, Singh VJ, Barrett ML. Effects of Açai (*Euterpe oleracea* Mart.) berry preparation on metabolic parameters in a healthy overweight population: a pilot study. *Nutr J* 2011; 10:45.
29. Englisch W, Beckers C, Unkauf M, Ruepp M, Zinserling V. Efficacy of Artichoke dry extract in patients with hyperlipoproteinemia. *Arzneimittelforschung* 2000; 50:260-65.