Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/6b7xhd56

TO STUDY THE EFFECTS OF ZINC, OMEGA 3 AND DAPAGLIFLOZIN ON LIPID PROFILE OF DIABETIC ALBINO RATS

Muhammad Sair[1*], Syeda Afroz[2], Shahnaz Usman[3], Sana Imran[4], Sumaira Khadim[5], Nabeela Sikander.[6]

[1*,2,4,5,6]Department of Pharmacology, Faculty of Pharmacy and Pharmaceutical Sciences, University of Karachi ,
[3]Professor, Department of Pharmaceutics, RAK College of Pharmacy, RAK Medical & Health Sciences University, Ra's Al khaimah, UAE

***Corresponding Author:** Muhammad Sair
*Department of Pharmacology, Faculty of Pharmacy and Pharmaceutical Sciences, University of Karachi

ABSTRACT

Introduction: Diabetes Mellitus (DM) is a chronic condition characterized by chronic hyperglycemia, poly urea, polydipsia and disturbances in primarily in carbohydrate metabolism but also fat and protein metabolism abnormalities been observed Different studies also indicates that omega 3 fatty acids obtained from fish and fish oil are protective against atherosclerosis and ischemic heart disease . In diabetic patient's hyperlipidemia is one of dangerous feature and leads to IHD. Zinc is required for structural and functional integrity of more than 2000 transcription factors and 300 enzymes; almost all metabolic pathways require zinc.

Material and Method: We took 40 albino rats and made 4 groups Streptozotocin were given to group 2,3, and 4 to produce diabetes and they were kept at high fat diet. Each group contains 10 rats. Group 1 were control group, group 2 Dapagliflozin group. Group 3 was given zinc and group 4 was given omega 3 for 2 months.

Objectives :

To observe the effects of zinc on lipid profile
To observe the effects of Omega 3 on lipid profile

Results: At the end of study all data were analyzed by SPSS vision 20. Zinc and omega 3 showed beneficial effects on dyslipidemia, they reduce total cholesterol and triglyceride and on the other hand slightly decreases level of LDL.

Conclusion: Omega 3 and zinc can be used in diabetic and patients with ischemic heart disease for dyslipidemia.

1. INTRODUCTION

Diabetes Mellitus (DM) is a chronic condition characterized by chronic hyperglycemia, poly urea, polydipsia and disturbances in mainly in carbohydrate metabolism and also fat and protein metabolism, Diabetes develop due to deficiency of insulin in human body [1]. Two types of diabetes are common, Type I DM which is insulin dependent and Type II which is noninsulin dependent, Type II diabetes is more common and it is associated with other disorders such as obesity, dyslipidemia, and increase in blood pressure [2].

Objectives:

- To observe the effects of zinc on lipid profile
- To observe the effects of Omaga 3 on lipid profile
- To observe the effects of Dapagliflozin on lipid profile

Framingham Heart Study showed that there is strong association between coronary artery disease (CAD) in diabetic patients and also in patients with dyslipidemia. In Diabetic patients increased triglycerides and decreased HDL are common in dyslipidemia.[3] In fish and some vegetable Omega-3 fatty acids are present in large quantity. Omega 3 is necessary for normal growth and development. Omega-3 fatty acids reduce plasma triglycerides, and increase HDL. [4]Dyslipidemia is a major risk factor of cardio vascular diseases.[5] Studies in human also showed that CLA and omega have beneficial effects on plasma lipids levels.[6] It is found in different studies that omega 3 fatty acids are essential fatty acid and human body need it for different body metabolic function.[7] Different studies also indicates that omega 3 fatty acids obtained from fish and fish oil are protective against atherosclerosis and ischemic heart disease.[8,9]

Fish oil and omega-3 fatty acids are very important in prevention of CVD. Studies also showed that Omega-3 fatty acids are important in regulating of genes critical for controlling lipid homeostasis.[10] Omega 3 fatty acids are present in fish, fish oils, canola oil, flaxseed, and certain vegetables.[11] In diabetes production of oxygen free radicals increases, they have toxic effects. Theses free radicals are super oxide (O2 o-), hydrogen peroxide (H2O2) and hydroxide (OHo). In diabetic patients' oxygen free radicles are formed due to Auto-oxidation and nonenzymatic glycation.[12,13]

In diabetic patient's hyperlipidemia is one of the causative factors for increased lipid peroxidation.[14,15] Omega-3 fatty acids and Omega-6 fatty acids are the essential fatty acids needed in the structure and function of cell membrane.[16.17] Fish oil and its derivatives such as omega-3 are very effective in prevention of cardiovascular adverse consequences of diabetes by inhibiting coronary atherosclerosis. [18,19] Omega 3 supplementations are effective in prevention of coronary artery diseases progression and lipid diseases disturbances [20,21]. Hypertriglyceridemia, is prevalent diseases, and significant public health problem worldwide.

Complications of hypertriglyceridemia are eroding people's health. Hypertriglyceridemia is a risk factor for atherosclerotic cardiovascular disease (ASCVD)[22,23]. Zinc plays a vital role in many human biological processes, such as enzyme action, cell membrane stabilization, gene expression and cell signaling[24]. Zinc is required for structural and functional integrity of more than 2000 transcription factors and 300 enzymes; almost all metabolic pathways require zinc[25,26]. SGLT2 inhibition using empagliflozin or canagliflozin showed improvement in cardiovascular outcomes in diabetic patients. SGLT2 inhibitors have additional effects on some cardiometabolic parameters such as body weight and blood pressure by effecting a decrease in them[27,28]. SGLT2 inhibitors increases HDL [29]. Omega -3 fatty acids helps in the treatment of hypertriglyceridemia and in the enhancement of HDL-cholesterol (HDL-C) levels in diabetic patients.[30]

2. MATERIAL AND METHODS

This study conducted in the department of pharmacology M Islam medical college Gujranwala. Duration of study was 10 weeks. In this study 4 groups were made and each group contain 10 albino rats. Group 1 control group, Group 2 dapagliflozin, group 3 zinc group, and omega 3 group 4. Sample collected from each animal at day 1 and at the end of study to perform lipid profile test.

- Group 1 control group
- Group 2 Dapagliflozin group

- Group 3 Zinc group
- Group 4 Omega 3

Male albino rats weighing approximately 240-250 g (10 weeks old). All group were fed high fat diet, with lipids (22%) carbohydrate (10%) and protein (12%). The rats were kept in cages in an environmentally controlled room (light from 6 AM to 6 PM, 30 0c) and had free access to food and water.

The body weight, water intake, and food intake of each rat were recorded daily. Glycaemia was measured every week with the help of test strips (Accu-Chek). a single dose of STZ was administered intraperitoneally (40 mg/ kg body weight) to animals fasted for 12 hours. The control animals were given vehicle (0.01 M citrate buffer, pH 4.5). After 3 days animals were given STZ, and blood glucose was measured to confirm the establishment of diabetes. They were considered diabetic if they had postprandial glycemic values greater than or equal to 288 mg/dL. The study was approved by the Ethics Committee of M. Islam medical college. Lipid profile was tested at the start and the end of the study.

3. RESULTS

Table 1. Comparison of Serum Cholesterol in different groups at day 1,day 30 and day 60

Groups	DAY 1	DAY 30	DAY 60
Group 1	126	230	300
Group 2	140	188	220
Group 3	118	110	206
Group 4	137	80	70

Figure 1. Comparison of Serum Cholesterol in different groups at day 1,day 30 and day 60

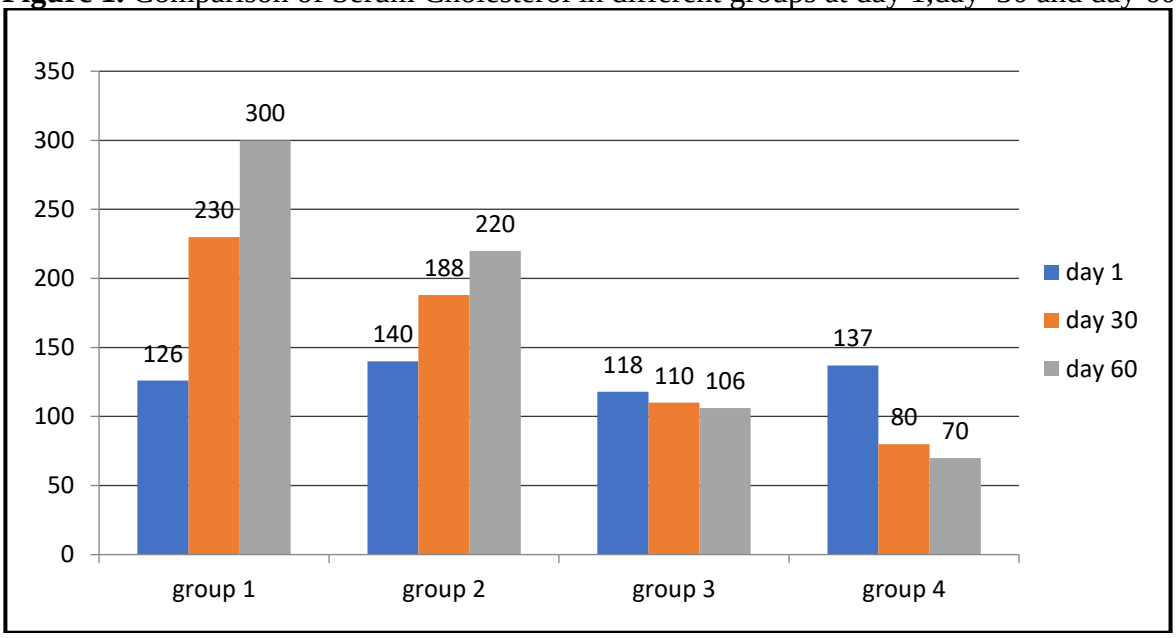


Table 2. Comparison of triglyceride in different groups at different days

Groups	DAY 1	DAY 30	DAY 60
Group 1	80	160	250
Group 2	82	90	98
Group 3	82	72	68
Group 4	78	66	56

Figure 2. Comparison of triglyceride in different groups at different days

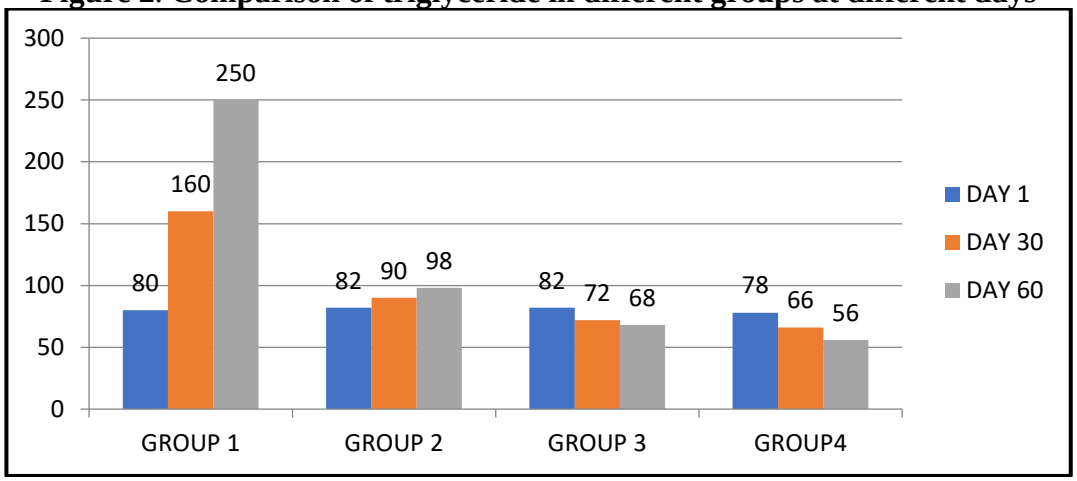


Table 3. Comparison of HDL in different groups at different days

Groups	DAY 1	DAY 30	DAY 60
Group 1	42	38	30
Group 2	38	38	36
Group 3	40	42	45
Group 4	36	42	48

Figure 3. Comparison of HDL in different groups at different days

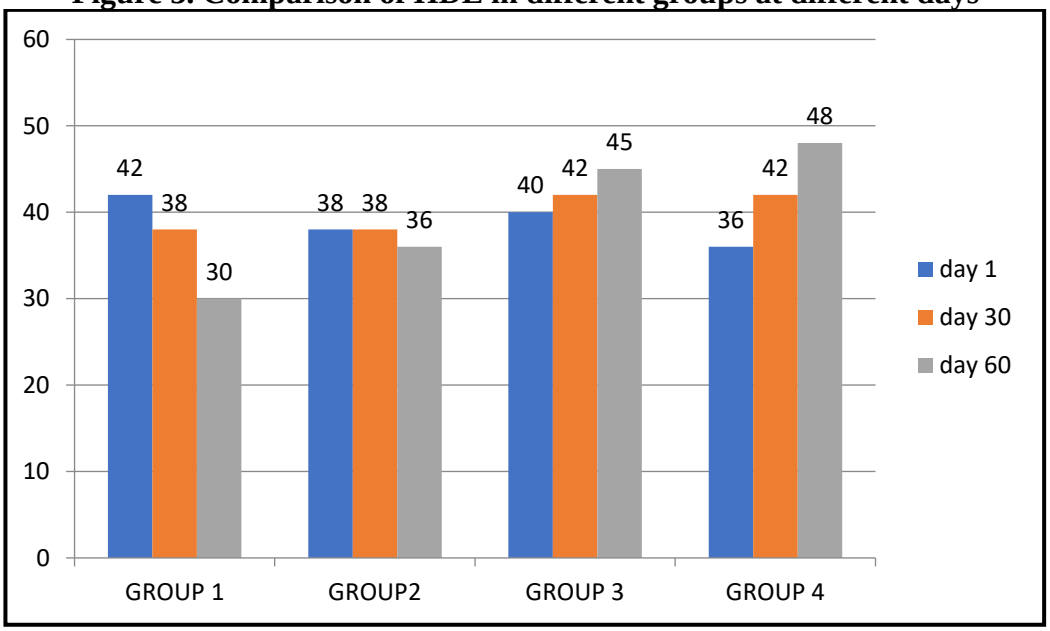


Table 4. Comparison of LDL in different groups at different days

Groups	DAY 1	DAY 30	DAY 60
Group 1	36	56	98
Group 2	30	35	40
Group 3	34	32	30
Group 4	32	28	22

Figure4. Comparison of LDL in different groups at different days

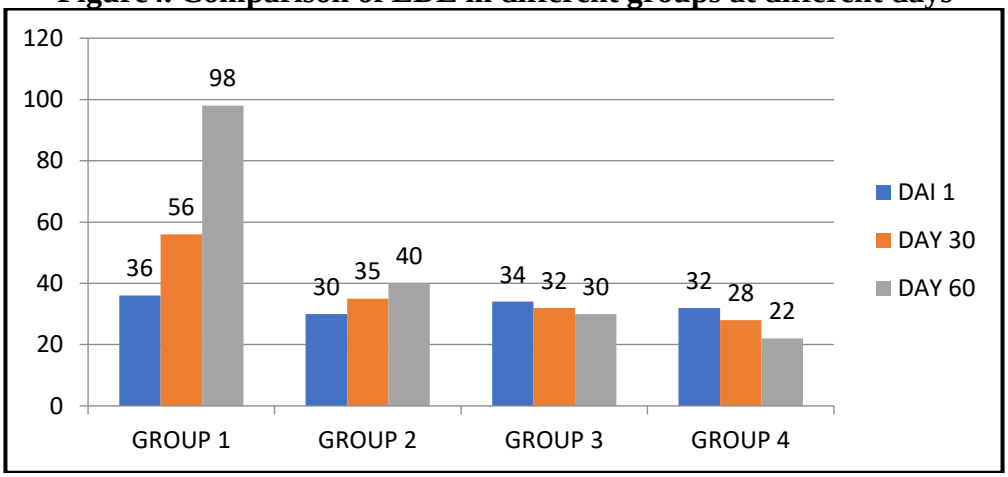
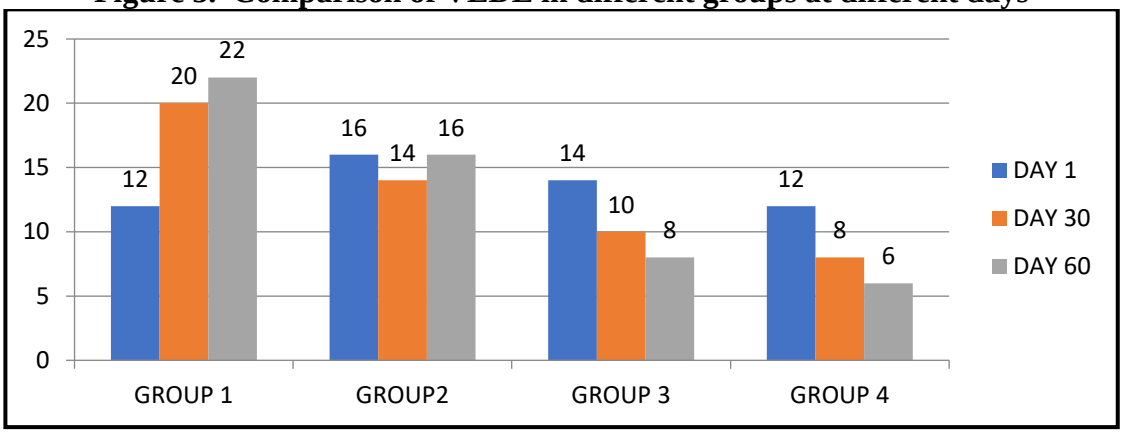


Table5. Comparison of VLDL in different groups at different days

Groups	DAY 1	DAY 30	DAY 60
Group 1	12	20	22
Group 2	16	14	16
Group 3	14	10	8
Group 4	12	8	6

Figure 5. Comparison of VLDL in different groups at different days



Control Group 1

All reading of cholesterol, triglyceride, LDL, HDL and VLDL are with in normal limits on day 1 and all values are high at day 30 and day 60.

Group 2 Dapagliflozin group

Introduction of streptozotocin and high fat diet causes dyslipidemia in this group. Values of lipid profile are high in this group but Dapagliflozin showed some good results as compared to control group in preventing the rise of all lipid profile.

Group 3

Introduction of zinc in this group showed good response in controlling serum cholesterol, serum triglyceride, also showed decrees in LDL and VLDL. Also slightly increases in HDL level (good fat) seen in this group. So, zinc is beneficial in dyslipidemia

Group 4

Introduction of fish liver oil (omega 3) showed good response in dyslipidemia. That is reduces s. cholesterol, triglyceride, LDL, VLDL level seen in this group and also increase good fat HDL is seen.

4. DISCUSSION

In past studies have showed that zinc is beneficial in reducing total cholesterol, LDL cholesterol and triglycerides, and also increases HDL cholesterol levels in humans. [31-34] In our study same results also observed, in group 3 we used zinc sulphate, it reduced cholesterol, triglyceride, LDL, and VLDL. Zinc also increases good fat (HDL) in albino rats. Zinc plays important role in our study and it showed beneficial effects in lipid profile it is consistent with the study conducted by zhang et all in his study.[35] Zinc was capable of decreasing the levels of blood glucose, HbA1c, and lipid profiles accompanied by increased AKT activity in diabetic murine model[15]. In the study conducted by Zak et al., and Mc Manus et al. have shown no change in LDL-C levels after the treatment with omega -3 fatty acids, while Haban et al. have reported increase in LDL-C levels after omega 3 fatty acid treatment, but in our study we found only mild decrees in LDL. Big scientific research has shown that OM3-FA can reduce triglyceride levels. Two meta-analyses of OM3-FA on antiretroviral. Therapy (HAART) association hypertriglyceridemia in HIV/AIDS patients discover that OM3- FA significantly reduced triglyceride levels [36]

5. CONCLUSION

Zinc and omega 3 are good alternatives to statins in the treatment of dyslipidemia and zinc as well as omega 3 can be used in patients of ischemic heart disease and patients with dyslipidemia.

REFERENCES

1. Bennet P. Definition, diagnosis and classification of diabetes mellitus and impaired glucose tolerance in Kahn JR. Joslin's Diabetes Mellitus 3th ed, USA. 1994:193-200.
2. Genuth S. Classification and diagnosis of diabetes mellitus. Medical Clinics of North America. 1982;66(6):1191-207.
3. Bersot TP. Drug therapy for hypercholesterolemia and dyslipidemia. Goodman and Gilman's, The Pharmacological Basis of Therapeutics McGraw-Hill. 2011:877-908.
4. Raghu B, Venkatesan P. Effect of n-3 fatty acid supplementation on blood glucose, lipid profile and cytokines in humans: a pilot study. Indian Journal of Clinical Biochemistry. 2008;23:85-8.
5. Jawalekar SL, Kulkarni UJ, Surve VT, Deshmukh Y. Status of lipid profile, MDA and protein carbonyl in patients with cardiovascular diseases. Arch Appl Sci Res. 2010;2(6):8-14.
6. McLeod RS, LeBlanc AM, Langille MA, Mitchell PL, Currie DL. Conjugated linoleic acids, atherosclerosis, and hepatic very-low-density lipoprotein metabolism. The American journal of clinical nutrition. 2004;79(6):1169S-74S.
7. Manjula B, Shivalinge GK, Ahamed SM, Nagarjan T, Gaurav G. Role of omega fatty acids in human body. Asian Journal of Research in Chemistry. 2009;2(2):93-9.
8. Kris-Etherton PM, Harris WS, Appel LJ. Fish consumption, fish oil, omega-3 fatty acids, and cardiovascular disease. Arteriosclerosis, thrombosis, and vascular biology. 2003;23(2):e20-e30.
9. Connor SL, Connor WE. Are fish oils beneficial in the prevention and treatment of coronary artery disease? The American journal of clinical nutrition. 1997;66(4):1020S-31S.
10. Kromhout D, Yasuda S, Geleijnse JM, Shimokawa H. Fish oil and omega-3 fatty acids in cardiovascular disease: do they really work? European heart journal. 2012;33(4):436-43.
11. Harper CR, Jacobson TA. The fats of life: the role of omega-3 fatty acids in the prevention of coronary heart disease. Archives of internal Medicine. 2001;161(18):2185-92.
12. Gillery P, Monboisse J-C, Maquart F-X, Borel J-P. Does oxygen free radical increased formation explain long term complications of diabetes mellitus? Medical Hypotheses. 1989;29(1):47-50.
13. Hunt JV, Smith CC, Wolff SP. Autoxidative glycosylation and possible involvement of peroxides and free radicals in LDL modification by glucose. Diabetes. 1990;39(11):1420-4.
14. Nacítarhan S, Özben T. Serum and urine malondialdehyde levels in NIDDM patients with and without hyperlipidemia. Free Radical Biology and Medicine. 1995;19(6):893-6.
15. Losada M, Alio J. Malondialdehyde serum concentration in type 1 diabetic with and without retinopaty. Documenta ophthalmologica. 1997;93:223-9.

16. Morris MC, Sacks F, Rosner B. Does fish oil lower blood pressure? A meta-analysis of controlled trials. Circulation. 1993;88(2):523-33.
17. Shimizu H, Ohtani K-i, Tanaka Y, Sato N, Mori M, Shimomura Y. Long-term effect of eicosapentaenoic acid ethyl (EPA-E) on albuminuria of non-insulin dependent diabetic patients. Diabetes research and clinical practice. 1995;28(1):35-40.
18. Eritsland J, Arnesen H, Grønseth K, Fjeld NB, Abdelnoor M. Effect of dietary supplementation with n-3 fatty acids on coronary artery bypass graft patency. The American journal of cardiology. 1996;77(1):31-6.
19. Thies F, Garry JM, Yaqoob P, Rerkasem K, Williams J, Shearman CP, et al. Association of n-3 polyunsaturated fatty acids with stability of atherosclerotic plaques: a randomised controlled trial. The Lancet. 2003;361(9356):477-85.
20. Friedman AN, Moe SM, Perkins SM, Li Y, Watkins BA. Fish consumption and omega-3 fatty acid status and determinants in long-term hemodialysis. American journal of kidney diseases. 2006;47(6):1064-71.
21. Friedman AN, Siddiqui R, Watkins BA. Acute rise of omega-3 polyunsaturated fatty acids during hemodialysis treatment. Journal of Renal Nutrition. 2008;18(3):301-3.
22. Simha V. Management of hypertriglyceridemia. bmj. 2020;371.
23. Nichols GA, Philip S, Reynolds K, Granowitz CB, Fazio S. Increased cardiovascular risk in hypertriglyceridemic patients with statin-controlled LDL cholesterol. The Journal of Clinical Endocrinology & Metabolism. 2018;103(8):3019-27.
24. Ross AC, Caballero B, Cousins RJ, Tucker KL. Modern nutrition in health and disease: Jones & Bartlett Learning; 2020.
25. Coleman JE. Zinc proteins: enzymes, storage proteins, transcription factors, and replication proteins. Annual review of biochemistry. 1992;61:897-946.
26. Vallee BL, Falchuk KH. The biochemical basis of zinc physiology. Physiological reviews. 1993;73(1):79-118.
27. Zinman B, Wanner C, Lachin JM, Fitchett D, Bluhmki E, Hantel S, et al. Empagliflozin, cardiovascular outcomes, and mortality in type 2 diabetes. New england journal of medicine. 2015;373(22):2117-28.
28. Neal B, Perkovic V, Mahaffey KW, De Zeeuw D, Fulcher G, Erondu N, et al. Canagliflozin and cardiovascular and renal events in type 2 diabetes. New england journal of medicine. 2017;377(7):644-57.
29. Liu J, Sempos C, Donahue RP, Dorn J, Trevisan M, Grundy SM. Joint distribution of non-HDL and LDL cholesterol and coronary heart disease risk prediction among individuals with and without diabetes. Diabetes care. 2005;28(8):1916-21.
30. Zak A, Zeman M, Tvrzicka E, Stolba P. The effect of fish oil on metabolic parameters in patients with type 2 diabetes mellitus associated with dyslipidemia. Casopis Lekaru Ceskych. 1996;135(11):354-9.
31. Hashemipour M, Kelishadi R, Shapouri J, Sarrafzadegan N, Amini M, Tavakoli N, et al. Effect of zinc supplementation on insulin resistance and components of the metabolic syndrome in prepubertal obese children. Hormones. 2009;8:279-85.
32. Afkhami-Ardekani M, Karimi M, Mohammadi SM, Nourani F. Effect of zinc sulfate supplementation on lipid and glucose in type 2 diabetic patients. Pak J Nutr. 2008;7(4):550-3.
33. Partida-Hernández G, Arreola F, Fenton B, Cabeza M, Román-Ramos R, Revilla-Monsalve M. Effect of zinc replacement on lipids and lipoproteins in type 2-diabetic patients. Biomedicine & pharmacotherapy. 2006;60(4):161-8.
34. Kadhim HM, Ismail SH, Hussein KI, Bakir IH, Sahib AS, Khalaf BH, et al. Effects of melatonin and zinc on lipid profile and renal function in type 2 diabetic patients poorly controlled with metformin. Journal of pineal research. 2006;41(2):189-93.
35. Zhang C, Lu X, Tan Y, Li B, Miao X, Jin L, et al. Diabetes-induced hepatic pathogenic damage, inflammation, oxidative stress, and insulin resistance was exacerbated in zinc deficient mouse model. PloS one. 2012;7(12):e49257.

36. McManus RM, Jumpson J, Finegood DT, Clandinin MT, Ryan EA. A comparison of the effects of n-3 fatty acids from linseed oil and fish oil in well-controlled type II diabetes. Diabetes care. 1996;19(5):463-7.