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Effect of Silver Nanoparticles and Rosuvastatin on Lipid Profile in Rats Induced By High Fat- Diet.

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ABSTRACT

Hyperlipidemia is excessive amounts of fatty substance in the blood. In the present study, the effects of silver nanoparticles and rosuvastatin on serum lipid profile in high cholesterol diet-induced hyperlipidemia in rats have been evaluated. This study was carried out on 60 male rats. They were randomly divided in to 11 groups. The first group served as a control group (negative group) fed on standard diet. The second group fed on high cholesterol diet referred to positive group. The other groups that fed on high cholesterol diet and treated with silver nanoparticles subdivided in to four groups according to concentration (5, 10) mg/kg and periods of treatment (8, 12) weeks. The remaining four groups fed on atherogenic diet and treated with rosuvastatin .This group also subdivided according to concentration (5, 10) mg/kg and periods of treatment (8, 12) weeks. The obtained results showed that, significant increase ($p < 0.05$) in TC, TG, HDL, LDL and VLDL in rats fed on atherogenic diet in compared with the control group. While TC, TG, HDL and VLDL were statistically significant decline ($p < 0.05$) after treated with silver nanoparticles and rosuvastatin in compared with atherogenic group. There was no important or statistically significant difference in mean serum LDL-C between a group of atherogenic and groups which treated with silver nanoparticles and rosuvastatin drug. The present study concluded that silver nanoparticles and rosuvastatin have the beneficial effect on hyperlipidemia by improving the lipid profile in the male rats fed on high fat diet.

Keywords: silver nanoparticles, rosuvastatin, lipid profile

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INTRODUCTION

Hyperlipidemia is a condition refers to elevated in the level of lipid in blood and it consists of hypercholesterolemia and hypertriglyceridemia [1]. Hyperlipidemias may be classified into two types, familial (primary hyperlipidemia) that resulting from particular abnormality in genetic, or acquired (known secondary hyperlipidemia) caused by another underlying condition that leads to changes in the level of lipid and lipoprotein in blood [2].

Hyperlipidemia is a major cause of multiple diseases such as atherosclerotic and cardiovascular diseases (CVD) [3, 4].

Rosuvastatin drugs are a new type of statins with medical and pharmacological properties which differentiate it from other statins. Rosuvastatin have very effective ability in improving the lipid profile of a person with dyslipidemia [5]. Rosuvastatin can be reduced in plasma cholesterol, LDL and VLDL and increases HDL level in patient with Hyperlipidimia [6]. Besides its ability to decrease the cholesterol in blood, rosuvastatin can increase the formation of NO in vascular endothelial [7].

Nanotechnology is a most promising field for generating new applications in medicine [8]. The most important NPs, which have an interest for a variety of biomedical applications is silver NPs (AgNPs) [9, 10]. Now a day's, silver nanoparticles (AgNPs) having a particle size less than 100 nm comes into focus due to its anti-bacterial activity [11, 12, 13], anti-viral and anti-tumor activity [14]. Silver nano-particles are able to peroxidation of fat in the body [15]. So that, the administration of silver nano-particle was effective in decreasing triglyceride amount of blood [16]. These properties fundamentally referred to elevation in the surface area to volume ratio that possibly caused increase the ability of reaction [17]. Aim of present study is showed the effect of silver nanoparticle and rosuvastatin on lipid profile in rat fed high fat diet.

MATERIALLS AND METHODS

Experimental animals

Male albino rats are (55) in number. Their weight ranged between (145-255) g and aged between (12-17) weeks were obtained from higher institutes of fertility and university of Babylon and the study begin from (1/7/2015) to (1/1/2016).Animals were housed in the animal house University of Al Kufa /Faculty of Science under control condition (light for12-h and dark for 12-h cycle) at room temperature (21-24) °C and give a standard and atherogenic diet.

Silver nanoparticle and Rosuvastatin

The silver nanoparticles were obtained from (Nanjing Nano Technology co, Itd) with average size 50 nm and purity 99.9 were examined by scanning electron microscope to confirm primary particle size image (3-1). 2mg of $AgNO_3$ were diluted in 10 ml of deionized water a stock solution for preparation of 5 and 10 mg/ml concentration of silver nanoparticles.

Rosuvastatin drug with 5 and 10 mg/kg concentration was obtained from (RANBAXY).

Blood samples

The blood was drawn by heart puncture by using a disposable syringe (same in volume) and then left at room temperature for coagulating, after that the clotted blood centrifuged for 15 minutes at 3000 rpm, then the serum was isolated at storied at deep freeze in Al- Sadder Teaching City in Al-Najaf Al-Ashraf province until using for measurement of biomarkers and lipid profile.

Biomarker measurement

Measurements serum cholesterol rat estimation kit

This was done by a method based on enzymatic colorimetric test, executed with rats specific kit for test, supplied by BIOLABO.

Measurements serum triglyceride rat estimation kit

This was done by a method based on enzymatic colorimetric test, executed with rats specific kit for test, supplied by BIOLABO.

Measurements serum HDL-cholesterol rat estimation kit

This was done by a method based on phosphotungstic precipitation test, executed with rat specific kit for test, supplied by BIOLABO.

Calculation of LDL-cholesterol

LDL-cholesterol, (mg/dl) was calculated according to the following formula:

LDL Chol=Total Chol. – (Triglycerides/5) HDL Chol.

Calculation VLDL-cholesterol

VLDL-cholesterol, (mg/dl) was calculated according to the following formula:

VLDL Chol = (Triglycerides / 5)

Statistical analysis

Statistical analyses were performed using social sciences (SPSS). Data were expressed as mean ± SEM. The least difference (LSD) test was performed to determine the significant variances. P< 0.05 was used as statistically significant.

RESULTS

The result of table (1) show the mean total serum cholesterol was statistically significant decrease ($p < 0.05$) in control group 138.75mg/dl in compared with group fed on atherogenic diet 187.75mg/dl. There was statistically significant decline ($p < 0.05$) in mean total serum cholesterol in groups treated with silver nanoparticles and rosuvastatin in compared with atherogenic group.

Also, serum triglyceride statistically significant decrease ($p < 0.05$) in control group 217.5 mg/dl in compared with group fed on atherogenic diet (283 mg/dl). There was statistically significant decrease ($p < 0.05$) in mean serum triglyceride in groups treated with silver nanoparticles and rosuvastatin in compared with atherogenic group.

The mean serum LDL-C was statistically significant decrease ($p < 0.05$) in control group 55.75mg/dl in compared with group fed on atherogenic diet 71.65 mg/dl. There was no important or statistically significant difference in mean serum LDL-C among group of atherogenic, group treated with silver nanoparticles and group which treated with rosuvastatin drug and the VLDL-C was lowest in control animals on standard diet 43.5 mg/dl and highest in positive control group on atherogenic diet 56.6 mg/dl. The VLDL-C values were statistically significant decrease ($p < 0.05$) in group treated with silver nanoparticles and rosuvastatin when compared with atherogenic group. There was no important or statistically significant difference in mean serum TC, TG, LDL, HDL, VLDL between group treated with silver nanoparticles and group which treated with rosuvastatin drug.

In present study, the more effective period for treating the rats with hyperlipidemia is three month as show in table (2). So, group treated with silver nanoparticles in concentration 10 mg/kg was highly significant decrease ($p < 0.05$) in lipid profile in compared with other study groups.

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Table 1: The difference in mean of the serum lipid profile among study groups.

Parameters / Groups	Mean ± SE				
	Cholesterol mg/dl	TG mg/dl	LDL mg/dl	HDL mg/dl	VLDL mg/dl
C (g)	138.75±1.49	217.5±1.04	55.75±1.96	39.5±2.10	43.5±0.21
AD	187.75±2.95*	283±3.63 *	71.65±2.26*	59.5±2.63 *	56.6±0.73 *
S5	168.75±4.27*	246.75±2.14	70.65±3.40	48.75±1.49	49.35±0.43*
S10	150±2.04	231.25±1.49	61.5±2.81	42.25±1.03	46.25±0.30
R5	170±2.04 *	259.5±2.63	64.85±1.80	53.25±2.69*	51.9±0.53 *
R10	155.25±1.7 *	236±2.94	61.8±2.93	46.25±1.75	47.2±0.59 *
LSD	15.42	14.68	15.37	12.1	2.93

Values are mean ±SE. *significantly different at p<0.05 between control group and study groups.

C: control, AD: atherogenic diet, S5: 5 mg/kg silver nanoparticles, S10:10 mg/kg silver nanoparticles, R5:5mg/kg rosuvastatin drug, R10:10mg/kg rosuvastatin drug

Table 2: The difference in mean of the serum lipid profile among study groups

Parameters / Groups	Mean ± SE				
	Cholesterol mg/dl	TG mg/dl	LDL mg/dl	HDL mg/dl	VLDL mg/dl
C	138.75±1.49	217.50±1.04	55.75±1.96	39.50±2.10	43.50±0.21
AD2	182.75±1.11	275.00±1.22	76.25±0.75	51.50±0.96	55.00±0.24
AD3	191.75±1.18	286.00±1.68	70.05±1.96	64.50±1.66	57.20±0.34
S2	168.00±2.48	245.75±1.44	67.10±1.80	51.75±1.18	49.15±0.29
S3	148.50±3.01	232.50±2.78	57.00±3.93	45.00±1.22	46.50±0.56
R2	170.00±4.56	250.75±2.29	65.60±5.33	54.25±1.44	50.15±0.46
R3	155.25±1.70	236.75±2.14	63.65±1.86	44.25±1.44	47.35±0.43
LSD	14.71	11.12	17.04	8.64	2.22

Values are mean ±SE. *significantly different at p<0.05 between control group and study groups.

C: control, AD: atherogenic diet, S5: 5 mg/kg silver nanoparticles, S10:10 mg/kg silver nanoparticles, R5:5mg/kg rosuvastatin drug, R10:10mg/kg rosuvastatin drug

DISCUSSION

The current study revealed a significant elevation (P<0.05) in serum cholesterol, Triglyceride, LDL, HDL, VLDL in male rats fed on atherogenic diet when compared groups of atherogenic with a control group as presented in table (1).

These findings are in agreement with that stated by [18, 19, 20]. Some studies confirmed that a rise in fat diet consumption in animals led to hypercholesterolemia [21, 22]. Previous study suggested that for active distribution and metabolism of the lipids, the lipoprotein was most necessary [23]. Study of Mustad *et al.,* (1997) showed that the high cholesterol in the diet causes down regulation in LDL receptors. So that, this study was descripted that the plasma LDL concentration elevated in hypercholesterolemic rats [24]. Therefore, the rises in LDL-C indicate more cholesterol in the blood that represents the risk of heart disease. [25, 26].

Some recent studies explained the rise of HDL level after consumption of high cholesterol diet. This study confirmed that the HLD elevation due to the boost of HDL production mainly in the liver and partially in the small intestine. HDL particle is consisted mostly from ApoAI and apoAII Apo lipoproteins, which was influenced by nutritional interference, like a change from high-carbohydrate to a high-fat diet to lipid rich diet that was stated to elevate the formational ratio of apoA-I. In addition, HDL is commonly named as “good cholesterol” because high levels of (HDL) represent a rise in the transport of cholesterol from adipose tissue to the liver, where it is modified [27, 28]. So that, this increase in HDL decreases the risk of cardiovascular diseases and hypertension [28, 29, 30]. The current study showed a significant decline in lipid profile in male rats fed on atherogenic diet after administration of rosuvastatin drug in comparision with atherogenic groups. These findings were in agreement with the previous studies [31, 32, 33, 34, 35]. Previous study suggested that because the ability of statin to decrease of LDL, it was used as the main pharmacological treatment of dyslipidemia [36, 37, 38].

The statin drug is occupying the position of HMG-CoA in the enzyme because it is identical to HMG-CoA on a molecular level and decreases the ratio of mevalonate production, which is finally lead to cholesterol production [38]. Therefore, the statin stops the synthesis of cholesterol in the liver. It reduces the LDL, the "bad" cholesterol, and triglycerides and has a minor influence in increasing of HDL [40].

Study of Istvan and Deisenhofer (2001) show that rosuvastatin has the most binding interactions with HMG-CoA reductase of all the statins [41]. This is important because most circulating cholesterol arrives from the inner production rather than the diet. When the liver cannot synthesis cholesterol, the plasma cholesterol will decline in the body [39]. So that, rosuvastatin is more effective than other statins in decreasing lipids profile [42, 43].

The results obtain from this study show, there was a significant decline ($P<0.05$) in serum lipid profile in male rats fed on atherogenic diet after administration of silver nanoparticle. Previous studies suggested that when the NP enters the blood stream, it is cleared by macrophage which is the first cell that interacts with NP and cholesterol via scavenger receptor [44, 45].Therefore, this interaction between AgNP and receptor on the surface of macrophage facilities the uptake and apoptosis [46].The scavenger receptor is contributing in the progression of atherosclerosis through interfile with metabolic rate of the lipids [47].

Some study found that the administration of WSC-NP had an advance result in the decreasing of lipids in rats that intake of atherogenic diet [48, 49]. Previous study suggested that chitosan effect the emulsification of lipids by binding them with hydrophobic bonds [50]. Zhang et al., (2012) confirmed that WSC-NP was acting agonist of glycerol-3-phosphate, therefore, consumption of it increase triglycerides in experimental animal [51].

Recent study indicated that the silver nanoparticle was improved lipid profile, energy compensation, oxidative stress and the glycemic in diabetes [52]. Also, previous study revealed that the treatment with gold nanoparticles [53] and nano ammonium vanadate [54] had an advantageous effect in lowering of TC, LDL, VLDL and TG levels in diabetic mice near to normal.

Umrani & Paknikar (2013) reported that intake of zinc oxide nanoparticles caused in important effects antidiabetic – which is, reduced non-esterified fatty acids, reduced triglycerides, increase insulin in the blood and decrease glucose in serum [55].

Study of Hosseini (2013) indicated that administration of silver nano-particle was effective in decreasing triglyceride amount of blood in mice [56]. Adversely Ahmadi (2012) reported that silver nano-particle was induced a statistically elevation in chicken serum Triglyceride. These influences may be associated

with oxidative stress that caused peroxidation of lipid and liberation of free radical in the body [15]. Also, Yildirimer *et al*. (2011) demonstrated that nano-silver affects the lipid peroxidation and structure of cell membranes, so that, the structural fat of membrane break and this lead to changes in the concentration of plasma lipids [57].

REFRENCES

[1] Pešek K, Pešek T, Roginić S (2011). Book edited by Dr. Ksenija Pesek (Ed.). ISBN: 978-953-307-695-9.
[2] Harikumar K, Abdul Althaf S, Kishore kumar B, Ramunaik M, Suvarna CH. International Journal of Novel Trends in Pharmaceutical Sciences 2013; 3 (4): 95-71.
[3] Montori VM, Brito JP, Ting HH. JAMA 2014; 311:465–466.
[4] Perk J, De Backer G, Gohlke H, Graham I, Reiner Z, Verschuren M, Albus C, Benlian P, Boysen G, Cifkova R, Deaton C, Ebrahim S, Fisher M, Germano G, Hobbs R, Hoes A, Karadeniz S, Mezzani A, Prescott E, Ryden L, Scherer M, Syvanne M, Reimer WJ S, Vrints C, Wood D, Zamorano JL and Zannad F . Eur Heart J 2012; 33:1635–1701.
[5] Olsson AG, McTaggart F, Raza A. Cardiovascular Drug Reviews 2002; 20 (4): 303–328.
[6] Rabbani SA, Ali SM. Br j med health res 2014; 2(4):2394-2967.
[7] Jones SP, Gibson MF, Rimmer DM, Gibson TM, Sharp BR, Lefer DJ. J Am Coll Cardiol 2002; 40: 1172–1178.
[8] Soumya RS, Hela PG. Scholars Research Library 2013; 5 (4):189-197.
[9] Martınez-Gutierrez F, Guajardo-Pacheco JM, Noriega- Trevino ME. Future Microbiology 2013; 8(3):403–411.
[10] Ahamed M, AlSalhi MS, Siddiqui, MKJ. Clinica Chimica Acta 2010; 411: 1841–1848.
[11] Shrivastava S, Bera T, Roy A. Nanotechnology 2007; 18:225103–12.
[12] Martinez-Gutierrez F, Olive PL, Banuelos A. Nanomed- Nanotechnol 2010; 6:681–8.
[13] Xing ZC, Chae WP, Huh MW. J Nanosci Nanotechnol 2011; 11:61–5.
[14] Huang Z, Jiang X, Guo D, Gu N. J Nanosci Nanotechnol 2011;11:9395–408.
[15] Ahmadi F. Pak Vet J 2012; 32(3): 325-328.
[16] Hosseini E. BEPLS 2013; 2 (4): 21-26.
[17] Hansen SF, Michelson ES, Kamper A, Borling P, Stuer-Lauridsen F, Baun A. Ecotoxicology, 2008; 17: 438-47.
[18] Jenner A. Free Rad Biol Med 2007; 42: 559-566.
[19] Prasad K. Journal of Cardiovascular Pharmacology and Therapeutics 2007; 12 (4).
[20] Nigris F, Paolo F. Nitric Oxide 2008; 19:57-63**.**
[21] Kishida T, Nogami H, Ogawa H, Ebihara K. J. Nutr 2002; 132: 2519-2524.
[22] Asashina M, Sato M, Imaizumi K. J. Lipid. Res 2005; 46: 2289-2294.
[23] Adekunle AS, Adedeji AL, Oyewo EO, Adedosu OT, Omotoso AT. Asian Journal of Natural & Applied Sciences, 2013; 2 (1).
[24] Mustad VA, Etherton T, DCooper A, DMastro A, MPearson T, AJonnalagadda SS, Kris-Etherton PM. J. Lipid Res 1997; 38: 459-468.
[25] Ahmed S. MClasen MD, Donnelly MD. Amer, Family Physician, 1998; 57: 1-16.
[26] Costet, P. Pharmacol Ther 2010;126: 263-78. Ahmadi F. Pak Vet J 2012; 32(3): 325-328.
[27] Lewis, G. F. Rader, D. J. C*irc Res,* 2005*96*(12), 1221-1232.
[28] Jiang J, Nilsson-Ehle P, Xu N. Lipids in Health and Disease 2006; 5(4), 186.
[29] Ginsberg HN, Goldberg IJ. In: Principles of Internal Medicine 15th edition. New York: McGraw-Hill; 2001; pp. 2245–2257.
[30] Onyeike EN, Monanu MO, Okoye CN. Annals of Biological Research 2012; 3 (11):5186-5191.
[31] Cheng JW. Clin. Ther 2004*;* 26:1368–1387.
[32] Anitha N, Rao JV, Kavimani S, Himabindu V, Begam A, Kumar R. Pharmacologyonline 2008; 3: 65-72.
[33] Wani TA, Samad A, Tandon M, Saini GS, Sharma PL, Pillai, KK. AAPS Pharm Sci. Tech 2010; 11: 425–432
[34] Fraulob JC. Souza-Mello V, Aguila MB, Mandarim-de-Lacerda CA. Clin Sci (Lond) 2012; 123(4):259–270.
[35] Ansari AJ, Bhandari U, Pillai KK, Haque ES. Indian Journal of Experimental Biology 2012; 50:216-222.
[36] Shepherd J, Cobbe SM, Ford I. N Engl J Med 1995; 333:1301–1307.
[37] Sacks FM, Pfeffer MA, Moye LA. N Engl J Med 1996; 335:1001–1009.
[38] Downs JR, Clearfield M, Weis S. JAMA 1998; 279:1616–1622.

[39] Black DM. Curr Atheroscler Rep 2002; 4:34-41.
[40] Ma H. Nature and Science 20042(4).
[41] Istvan ES, Deisenhofer J. Science 2001; 292: 1160-1164.
[42] Blasetto JW, Stein EA, Brown WV. Am. J. Cardiol 2003; 91 (5):3-10
[43] Vijan S, Hayward RA. Ann Intern Med 2004; 140(8):650–658.
[44] Shannahan JH, Sowrirajan H, Persaud I, Podila R, Brown JM. Journal of Nanomaterials 2015; pp:12.
[45] Rigotti A, Miettinen HE, Krieger M. Endocrine Reviews 2003; 24 (3): 357–387.
[46] Singh RP, Ramarao P. Toxicology Letters 2012; 213 (2): 249–259.
[47] Rigotti A, Trigatti BL, Penman M, Rayburn H, Herz J, Krieger M. Proceedings of the National Academy of Sciences of the United States of America 1997; 94 (23): 12610–12615.
[48] Tao Y, Zhang, HL, Gao B, Guo J, Hu YM, Su ZQ. J Nanomater 2011; pp: 5.
[49] Zhang HL, Tao Y, Guo J, Hu YM, Su ZQ. Int Immunopharmacol. 2011;11(4):457–461
[50] Park GY, Mun S, Park Y, Rhee S, Decker EA, Weiss J, McClements DJ, Park Y. Food Chem 2007; 104: 761–767.
[51] Zhang HL, Zhong XB, Tao Y, Wu SH, Su ZQ. Int. J. Nanomed 2012; 7, 4069–4076.
[52] Pourkhalili N, Hosseini A, Nili-Ahmadabadi A, Hassani S, Pakzad M, Baeeri M, Mohammadirad A, Abdollahi M. World J. Diabetes, 2011; 2: 204–210.
[53] BarathManiKanth S, Kalishwaralal K, Sriram M, Pandian SRK, Youn H, Eom S, Gurunathan S. Journal of Nanobiotechnology 2010; 8:16.
[54] Keyshams N, Fatemi SR, Najafzadehvarzi H, Ashrafi A. Zahedan J Res Med Sci 2013; 15(10): 59-64.
[55] Umrani ID, Paknikar KM. Nanomedicine 2013; 9 (1): 89-104.
[56] Yildirimer L, Thanh NTK, Loizidou M, Seifalian AM. Nanotechnology Today 2011; 6: 585-607
[57] Hosseini E. Bull. Env. Pharmacol. Life Sci 2013; 2 (4).