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Amelioration of Gentamicin Induced Dyslipidemia in Guinea Pigs by Curcumin and Rosemary

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Abstract: The present study aimed to evaluate the effectiveness of curcumin, and Rosemary as a natural source of antioxidants to minimize the harmful effects of gentamicin induced dyslipidemia in Guinea pigs. Guinea pigs were divided into five groups. The first group (control) was injected intraperitoneal with saline. The 2nd group was injected intraperitoneal with gentamicin at a dose of 100 mg/kg body weight /day. The 3th , 4th , and 5th groups were injected intraperitoneal with gentamicin (100 mg/kg b. wt /day) concurrently with curcumin, rosemary, and curcumin with rosemary at the doses of 200 mg, 220 mg, and 200 mg with 220 mg /kg body weight /day respectively orally by gavage for 10 days. Blood samples were obtained for assessment of serum cholesterol, triglycerides, high density lipids, low density lipids, and very low density lipids concentrations. Gentamicin treatment induced dyslipidemia. Guinea pigs that injected intraperitonally with gentamicin at a dose of 100 mg/kg body weight daily for 10 days had significantly ($p<0.05$) increase the concentrations of serum cholesterol, triglycerides, low density lipids cholesterol, very low density lipids cholesterol concentrations, and the atherogenic ratios based on lipid profile parameters (Castelli's Risk Index I, Castelli's Risk Index II, Atherogenic Coefficient and Atherogenic Index of Plasma) and decreased the serum high density lipids cholesterol concentration. Co-administration of rosemary and/or curcumin with gentamicin significantly improved of all lipid profile parameters and atherogenic ratios parameters. It can be concluded that, gentamicin had adverse effects on lipid profile parameters, and the atherogenic ratios parameters. Rosemary and/or curcumin supplementation showed a remarkable amelioration of these abnormalities in gentamicin treated male Guinea pigs. It is recommended that the use of gentamicin must be limited and use of rosemary and curcumin as antioxidants to prevent the dyslipidemia. Further studies are necessary to elucidate exact mechanism of protection of hyperlipidemia, atherogenic and potential usefulness of rosemary and curcumin as a protective agent against gentamicin induced dyslipidemia and atherogenic in clinical trials.

Keywords: Dyslipidemia; Curcumin; Gentamicin; Rosemary; Hypolipidemic effect; Guinea Pigs.

1. Introduction

Gentamicin is an aminoglycoside antibiotic derived from *micomonospora* purpurea. It is effective against most of the life threatening Gram negative bacterial infection [1, 2]. Free radicals and reactive oxygen species are continuously produced in the human body. These oxygen species are the cause of cell damage and the initiation and progression of chronic diseases [3]. Gentamicin induces an increase in the oxidative stress and production of free radicals and suppresses the antioxidant defense system in liver. The suppressive effect of gentamicin on the non enzymatic and enzymatic antioxidants results in an excess production of reactive oxygen species which not only deleteriously affects membrane lipids but also deteriorates proteins and nucleic acids [4]. Many investigators reported that treatment of experimental animals with gentamicin were induced elevation on the levels of total cholesterol, triglycerides and LDL in serum [5-7]. Hypercholesterolemia is one of the most important risk factors for atherosclerosis [8]. So, hypercholesterolemia and hypertriglyceridemia are risk factor for predicting coronary heart disease [5, 9].

There is an epidemiological evidence that showed consumption of various herbs and spices is associated with positive health benefits [3]. Several natural products have been used to protect the toxicities induced by drugs. Herbs are generally considered safe and proved to be effective against various human ailments and their medicinal uses have been gradually increasing in developed countries [10]. Natural antioxidants strengthen the endogenous antioxidants defenses from reactive oxygen species and restore the optimal balance by neutralizing the reactive species [11].

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Curcumin (diferuloylmethane) is a yellow colouring ingredient of the spice turmeric obtained from the rhizome of *Curcuma longa* Linn (Zingiberaceae). It has been used since ancient times for promoting human health. It represents a class of anti-inflammatory and antioxidant reported to be a potent inhibitor of reactive oxygen species (ROS) formation [12]. Antioxidative properties of curcumin are well documented [13-15]. Curcumin could exert antioxidative effects either directly as a chemical antioxidant due to its ability to scavenge reactive oxygen and nitrogen free radicals or by modulating cellular defenses which themselves exert antioxidant effects [13, 14]. It is a potent scavenger of reactive oxygen species including superoxide anion radicals and hydroxyl radicals [16].

Rosemary (*Rosmarinus officinalis* L.) belongs to the family Lamiaceae (Labiatae) is a well-known aromatic plant used as spice, flavoring agent in food processing and in different medicinal purposes [3]. The aqueous extract of rosemary used as a drug with strong antioxidant properties for eliminating the generated free radicals, reinforce the antioxidant system and prevent oxidative stress [17]. It is composed of dried leaves and flowers constitutes a particularly interesting source of biologically active phytochemicals as it contains a variety of phenolic compounds including carnosol, carnosic acid, rosmanol, 7-methyl-epirosemanol, isorosmanol, rosmadial and caffeic acid [11]. Rosemary and its constituents especially caffeic acid derivatives such as rosmarinic acid have a therapeutic potential in prevention of bronchial asthma, spasmogenic disorders, peptic ulcer, inflammatory diseases, hepatotoxicity, atherosclerosis, ischemic heart disease, cataract, cancer [18]. Rosemary extracts have a high scavenging capacity of different types of reactive oxygen and nitrogen species, mostly free radicals[15, 19].

Most of the previous literatures studied the protective effects of one antioxidant substance on alteration in lipids profiles induced by gentamicin. Also, to our knowledge, the evidence reporting the hypolipidemic effect of curcumin and rosemary against gentamicin induced hyperlipidemia are very few. So, the present work aimed to evaluate effectiveness of curcumin, and rosemary against gentamicin induced dyslipidemia in male guinea pigs.

2. Materials and Methods

2.1. Chemicals

The gentamicin and curcumin were purchased from Sigma Chemical Co. (St. Louis, Mo, USA). Rosemary was purchased as dried rosemary leaves from a herbal store in Sabratha city, Libya. Aqueous rosemary extract was prepared according to the method of Amin and Hamza [20]. Briefly, ten gm of dried plants was slowly boiled in 100 ml of distilled water and heated for 30 minutes. The extracts were then filtered and directly administered orally by gavage to the animals. The given dose was 220 mg/kg b.wt. Gentamicin was intreperitoneally administered at dose of 100 mg/kg body weight/day [4, 21, 22], for ten successive days.

The choice of the doses of curcumin and rosemary were based on the results of the previous studies, where the antioxidant effects of these agents were confirmed. Curcumin was given orally at a dose of 200 mg/kg b. wt by gavage [23, 24]. Rosemary was given at a dose of 220 mg/kg b. wt orally by gavage [25, 26].

2.2. Animals

30 adult male guinea pigs (*Cavia porcellus*) weighting 490-530 gm were used for this study. The animals were obtained from animal house unit in the Faculty of Veterinary Medicine, Ttipoli University, Libya. The animals were housed in a room under standard conditions of ventilation, temperature (25 ± 2°C), humidity (60-70%) and light/dark condition (12/12). The animals were provided with tape water *ad libitum* and fed with the standard commercial chow. The animal procedures were performed in accordance with Guide Lines for Ethical Conduct in the Care and Use of Animals.

2.3. Experimental Design

After one week of acclimation, the animals were randomized and divided into 5 groups (6 guinea pigs for each) as follow:

Group 1 (control group): The animals received intraperitoneal injection of saline (0.5 ml/day for 10 days).

Group 2 (gentamicin treated group): The animals received intraperitoneal injection of gentamicin only (100 mg/kg b.wt/day) for 10 days.

Group 3 (gentamicin /curcumin co-administered): The animals received intraperitoneal injection of gentamicin (100 mg/kg b.wt /day) concurrently with curcumin (200 mg/kg b.wt /day) orally for 10 days.

Group 4 (gentamicin/rosemary co-administered): The animals received intraperitoneal injection of gentamicin (100 mg/kg b. wt/day) concurrently with rosemary (220 mg/kg b.wt /day) orally for 10 days.

Group 5 (gentamicin/ curcumin and rosemary co-administered): The animals received intraperitoneal injection of gentamicin (100 mg/kg b. wt /day) concurrently with curcumin (200 mg/kg b. wt /day), and rosemary (220 mg/kg b. wt /day) orally for 10 days.

At the end of the experimentation and 24 hours after the last dose, all animals were sacrificed under light ether anesthesia, then rapidly dissected and subjected to the following examinations:

2.4. Biochemical Analysis

Blood samples were drown by cardiac puncture. The samples were collected in clean dry tubes and centrifuged at 3000 rpm for 15 minutes then serum was separated and kept in a deep freezer at -20ºC until biochemical measurements were carried out. Total cholesterol concentration was estimated according to Allain, *et al.* [27],

triglycerides concentration also by the method of Fossoti and Prencipe [28] and HDLcholesterol by Burstein, *et al.* [29]. VLDL-cholesterol and LDL-cholesterol concentrations were estimated by using the Friedwald, *et al.* [30]. The atherogenic ratios were calculated as follows: Castelli's Risk Index (CRI-I) = TC/HDLc, Castelli's Risk Index (CRI-II) = LDLc/HDLc, Atherogenic Coefficient (AC)=(TC– HDLc) /HDLc and Atherogenic Index of Plasma (AIP)= log TG/HDLc.

2.5. Statistical Analysis

The values were presented as means ± SD of different groups. Differences between the mean values were estimated using one way ANOVA. The results were considered statistically significant when $p < 0.05$.

3. Results

Lipid profile parameters in serum of the different groups are shown in Table 1. Guinea pigs that received intraperitoneal injection of gentamicin only (100 mg/kg body weight /day) for 10 days had significantly ($p<0.05$), increased the serum cholesterol, triglycerides, non HDLc, LDLc and VLDL concentrations. Co-administration of gentamicin with rosemary and/or curcumin were significantly ($p<0.05$) prevented the changes recorded in serum cholesterol, triglycerides, non HDLc, LDLc and VLDL concentrations as compared with gentamicin group (Fig. 1, 2, 4 & 5). On the other hand, serum HDL cholesterol concentration of gentamicin treated animals was significantly ($p<0.05$) decreased as compared to the control group (Fig. 3). Co-administration of gentamicin with rosemary and/or curcumin were significantly ($p<0.05$) prevented the changes recorded in serum HDLc concentration as compared with gentamicin group.

Table 2 showed the means and standard deviations for Castelli's Risk Index I, Castelli's Risk Index II, Atherogenic Coefficient and Atherogenic Index of Plasma in control group, gentamicin group, co-administrated of gentamicin with rosemary and/or curcumin groups. These ratios were elevated in gentamicin treated male Guinea pigs group compared with the control group with statistically significant differences ($p<0.05$). Co-administration of gentamicin with rosemary and/or curcumin were declined these ratios with statistically significant differences ($p<0.05$), when compared with gentamicin group (Figs. 6, 7, 8, 9 & 10).

Table-1. Effect of rosemary and /or curcumin on lipid profile parameters in gentamicin treated Guinea pigs

Parameters	**Experimental groups**				
	Control	**Gentamicin**	**Gentamicin + Rosemary**	**Gentamicin + Curcumin**	**Gentamicin + Rosemary + Curcumin**
	Mean ± SD	**Mean ± SD**	**Mean ± SD**	**Mean ± SD**	**Mean ± SD**
Serum cholesterol (mg/dl)	45.17±1.17	75.33±2.16*	49.35±2.15**	52.17±1.33**	42.17±1.72**
Serum triglycerides (mg/dl)	43.33±1.37	63.00±1.41*	44.00±0.89**	41.33±1.03**	40.67±1.75**
Serum HDL- cholesterol (mg/dl)	5.05±0.19	4.30±0.09*	5.30±0.09**	5.20±0.14**	5.47±0.12**
Serum LDL- cholesterol (mg/dl)	31.45±1.13	58.43±1.98*	35.25±1.99**	38.70±1.17**	28.57±1.69**
Serum VLDL- cholesterol (mg/dl)	8.67±0.27	12.60±0.28*	8.80±0.18**	8.27±0.21**	8.13±0.35**
Non HDLc (TC-HDLc) (mg/dl	40.12±1.27	71.03±2.18*	44.05±2.09**	46.97±1.28**	36.70±1.72**

*: Significant differences as compared with control group ($P < 0.05$). **: Significant differences as compared with gentamicin treated group ($P < 0.05$). All data are mean of 6 individuals.

Table-2. Effect of rosemary and /or curcumin on the ratios based on lipid profile parameters in gentamicin treated Guinea pigs

Parameters	**Experimental groups**				
	Control	**Gentamicin**	**Gentamicin + Rosemary**	**Gentamicin + Curcumin**	**Gentamicin + Rosemary + Curcumin**
	Mean ± SD	**Mean ± SD**	**Mean ± SD**	**Mean ± SD**	**Mean ± SD**
CRR-I (TC/HDLC)	8.96±0.49	17.53±0.69*	9.31±0.33**	10.04±0.28**	7.72±0.35**
CRR-II (LDLc/HDLc)	6.24±0.41	13.60±0.60*	6.65±0.32**	7.45±0.24**	5.23±0.32**
AC [(TC- HDLc)/HDLc]	7.96±0.49	16.53±0.69*	8.31±0.33**	9.04±0.28**	6.72±0.35**
AIP [log(TG/HDLC)]	0.93±0.02	1.17±0.02*	0.92±0.01**	0.90±0.02**	0.87±0.03**

CRR-I: Castelli's Risk Index I, CRR-II: Castelli's Risk Index II, AIP: Atherogenic Index of Plasma, AC: Atherogenic Coefficient.
*: Significant differences as compared with control group ($P < 0.05$).
**: Significant differences as compared with gentamicin treated group ($P < 0.05$). All data are mean of 6 individuals

Figure-1. Serum cholesterol concentration in different animals groups.

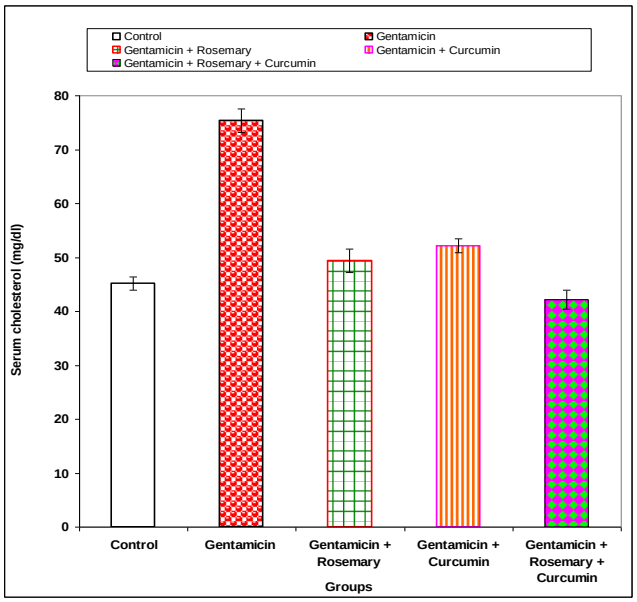


Figure-2. Serum triglycerides concentration in different animals groups.

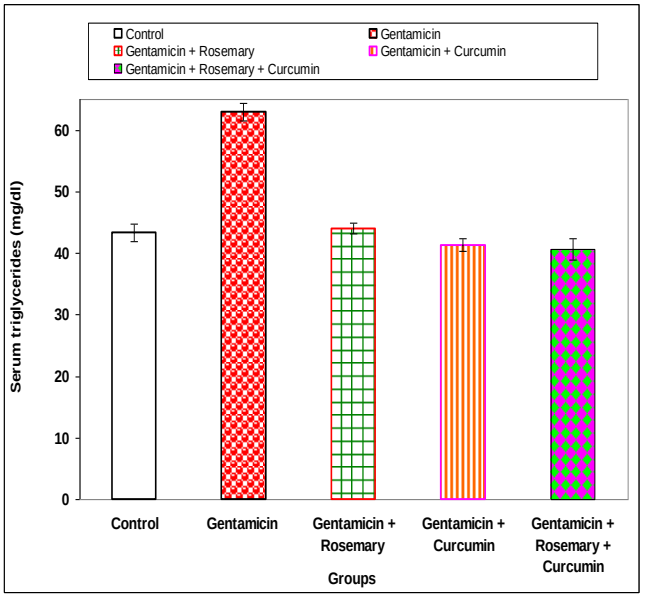


Figure-3. Serum HDL-cholesterol concentration in different animals groups.

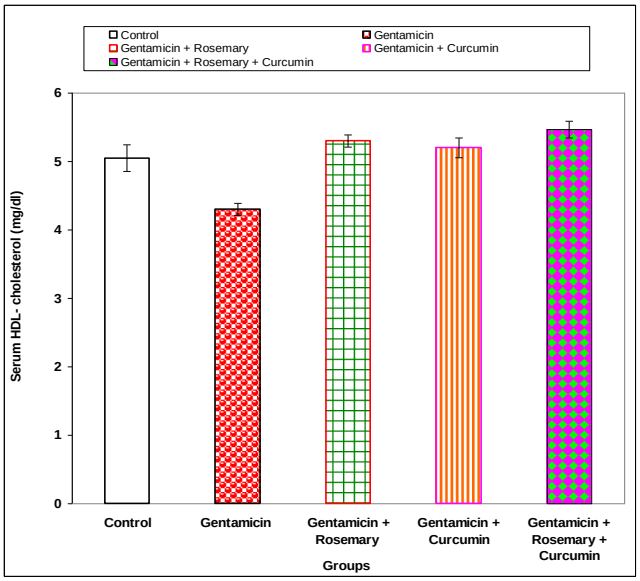


Figure-4. Serum LDL-cholesterol concentration in different animals groups.

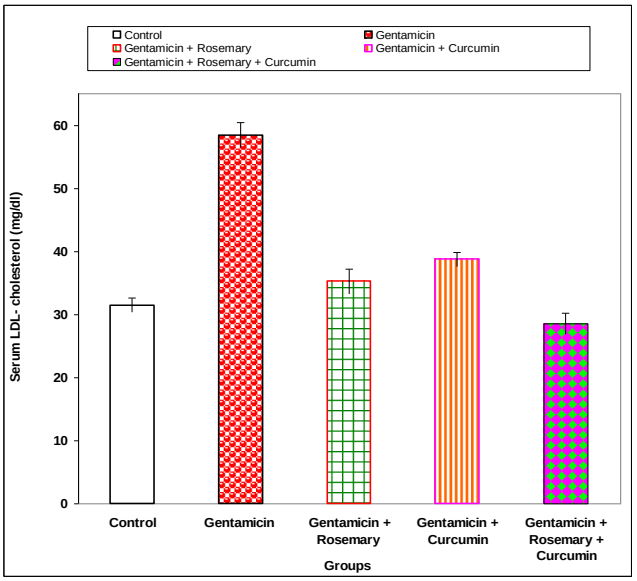


Figure-5. Serum VLDL-cholesterol concentration in different animals groups.

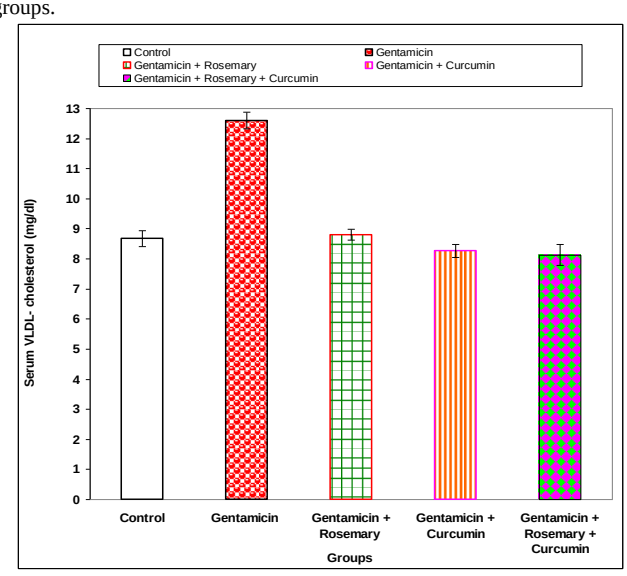


Figure-6. Serum Non HDLc concentration in different animals groups.

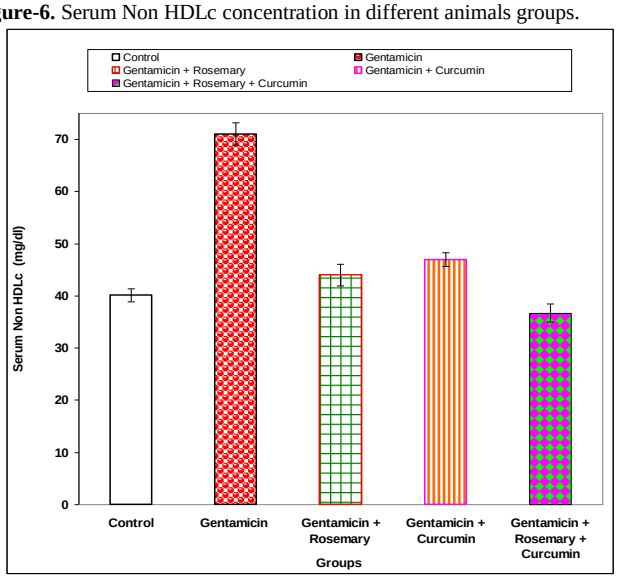


Figure-7. Castelli's Risk Index I in different animals groups.

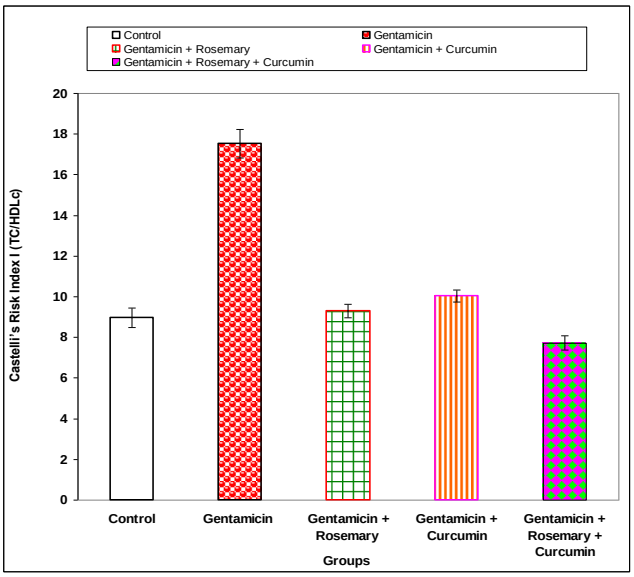


Figure-8. Castelli's Risk Index II in different animals groups.

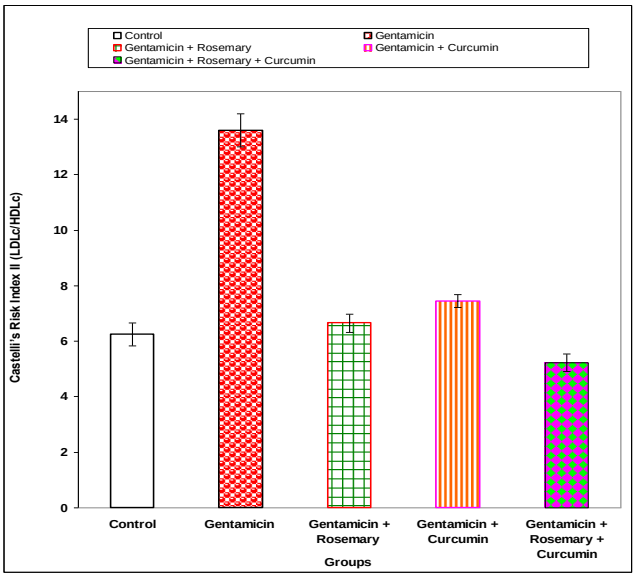


Figure-9. Atherogenic Coefficient in different animals groups.

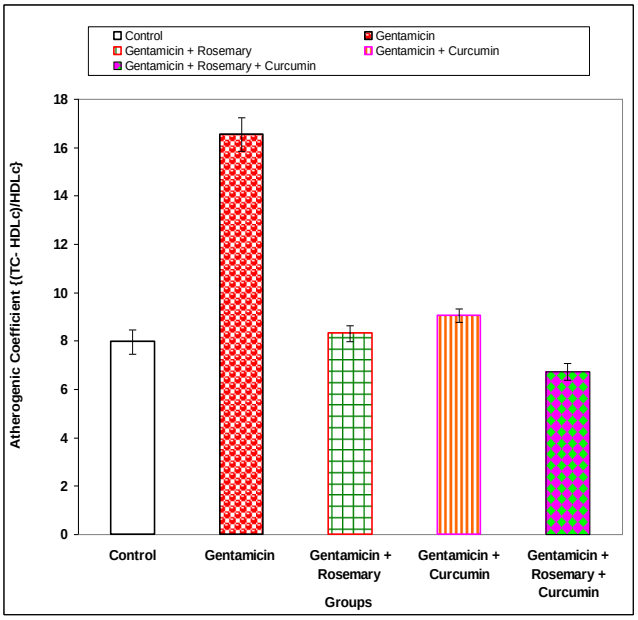
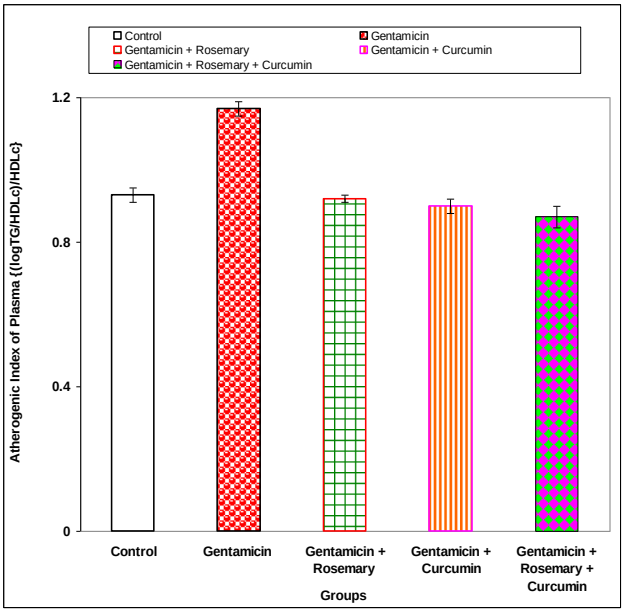


Figure-10. Atherogenic Index of Plasma in different animals groups.



4. Discussion

Oxidative stress, resulting from an imbalance in the generation of free radicals and antioxidant defense molecules, affects biological macromolecules causing their structural alterations that lead to cell damage and its death, [31, 32]. Certain drugs may induce oxidative stress by forming drug-derived radicals that can not only deplete the antioxidant defenses but can also react directly with biomolecules [33]. Gentamicin induces an increase in the oxidative stress and production of free radicals and suppresses the antioxidant defense system in liver [34]. The exacerbated increase of lipid peroxidation by gentamicin impairs membrane lipids. The suppressive effect of gentamicin on the nonenzymatic and enzymatic antioxidants results in an excess production of reactive oxygen species which not only deleteriously affects membrane lipids but also deteriorates proteins and nucleic acids [34]. Antioxidants, on the other hand, try to combat the oxidative stress and minimize its deteriorated effects [4, 35].

The present study demonstrated that gentamicin treatment caused significant increases in the serum cholesterol, triglycerides, non HDLc, LDLc and VLDL concentrations. This is in agreement with Rashid and Khan [7] who reported that treatment of rats with gentamicin (80 mg/kg) increased the levels of total cholesterol, triglycerides and LDL in serum as compared with control animals. Ahmadvand, *et al.* [6] reported that gentamicin significantly increased TG, TC, LDL, VLDL in rats treated with 100 mg/kg/day for 12 days as compared with control group. Also, Ademiluyi, *et al.* [5] reported that the plasma atherogenic lipids (triglycerides and total cholesterol) were increased in gentamicin treated rats. The high levels of triglycerides may be due to inhibition of 7a-hydroxylase activity [8, 36]. Also, the high levels of LDL-C may be attributed to a down regulation in LDL receptors [8, 37], moreover, this increase in LDL-c level might be explained via involvement of two enzymes namely cholesterol ester hydrolase and cholesterol ester synthetase. These enzymes balance the cholesterol levels in the

blood. Hence, it is logical to assume that the elevation in plasma cholesterol is mediated through increased cholesterol turnover and influenced by the relative balance between cholesterol ester hydrolase and cholesterol ester synthetase activity. With increased esterifying activity (when cholesterol ester hydrolase: cholesterol ester synthetase is lowered) cholesterol will be predominantly in its ester form (as in LDLc) and can lead to the development and progression of atherosclerosis [8, 38]. HDL plays an essential role in the transport of cholesterol to the liver for excretion into bile [5]. Azab, *et al.* [15] reported that treatment of guinea pigs with 100mg/kg body weight/ day gentamicin for 10 days induced hepatotoxicity. Furthermore, impaired hepatic function may also have affected cholesterol metabolism leading to hypercholesterolemia and hypertriglyceridemia [5].

The present results showed that injection of guinea pigs with 100 mg/kg/day gentamicin for 10 days significantly induced decrease in serum HDL-C level compared with control animals. This results is run in accordance with the results of Ahmadvand, *et al.* [6] who found that gentamicin significantly decreased HDL-C level in rats treated with 100 mg/kg/day for 12 days as compared with control group. Also, Ademiluyi, *et al.* [5] reported that the plasma HDLcholesterol was decrease in gentamicin treated rats .

The present data showed that the serum Castelli's Risk Index I, Castelli's Risk Index II, Atherogenic Coefficient and Atherogenic Index of Plasma were significantly increased in gentamicin treated guinea pigs compared with control animals. These results run parallel with the results of Ahmadvand, *et al.* [6] who reported that gentamicin significantly increased atherogenic index, atherogenic coefficient (AC), and cardiac risk ratio (CRR) in rats treated with 100 mg/kg/day for 12 days as compared with control group. Azab, *et al.* [39] recorded that elevations in Castelli's Risk Index I, Castelli's Risk Index II, Atherogenic Coefficient and Atherogenic Index of Plasma in mice treated with lead acetate. Also, Azab, *et al.* [40] found that Castelli's Risk Index I, Castelli's Risk Index II, Atherogenic Coefficient in serum and Atherogenic Index of Plasma were significantly increased in sodium nitrite treated guinea pigs when campared with control animals. In addition, Bhardwaj, *et al.* [41] reported that lipid ratios like Atherogenic Index of Plasma, Castelli risk index and Atherogenic coefficient could be used for identifying individuals at higher risk of cardiovascular disease in Indian population in the clinical setting especially when the absolute values of individual lipoproteins seem normal and in individuals with elevated triglycerides concentrations. Thus, the use of these indexes should be encouraged to complement the existing profile of tests for identifying high risk individuals for Coronary Artery Disease and effective drug management.

The present study showed that co-administration of gentamicin and curcumin significantly decreased the elevations in the serum cholesterol, triglycerides, non HDLc, LDLc and VLDL concentrations, and significantly increased decline in serum HDL-cholesterol. These findings are similar to Hussein, *et al.* [8] who found that treatment with curcumin to high cholesterol diet-induced hypercholesterolemia rats lowered serum total cholesterol, triacylglycerols, LDL-C, and VLDL-C concentration, in addition to, increasing HDL-C. Chowdhury, *et al.* [42] found that oral administration of turmeric to guinea pigs reduced cholesterol level significantly. Kempaiah and Srinivasan [43] recorded that female rats treated with 0.2% curcumin and fed a high fat diet showed decreases in the elevated plasma triglycerides, LDL, VLDL, and hepatic triglycerides which was decreased near to normal range. Also, Manjunatha and Srinivasan [44] reported that the beneficial hypolipidemic effect of the dietary curcumin in rats fed a high fat diet for 8 weeks. In addition, Ramirez-Tortosa, *et al.* [34] found hypo-cholesterolemic effect in rabbits fed by a high-cholesterol diet. Anticholesterol action turmeric, as well as curcumin, is reported to reduce the uptake of cholesterol from the gut and increase the high-density lipids cholesterol and decrease low-density lipids type. It can also inhibit the peroxidation of serum LDL, which can lead to atherosclerotic lesions. Thus, turmeric can prevent coronary problems and heart diseases [45, 46]. Turmeric and its active principle-curcumin were found to be effective as hypocholesterolemic agent under various conditions of experimentally induced hypercholesterolemia/ hyperlipidemia in rats [47-49]. Curcumin may be effective in controlling cholesterolemic status and improving dyslipidemia and has the potential in reducing cardiovascular complications due to hypercholesterolemia [8].

The ingestion of curcumin-containing spices in diet, especially rich in fat, could have a lipid-lowering effect. Hypocholesterolemic effect of curcumin my be due to an effect on cholesterol absorption, degradation, or elimination, but not due to an antioxidant mechanism [46, 50]. The mechanism is assumed through increased cholesterol excretion in the gall bladder together with decreased saturation of biliary cholesterol and increased fat excretion in the feces [8, 42, 51]. The reduced cholesterol levels in turmeric-treated animals is a clear indication of stimulated bile fluid secretion as well as biliary cholesterol secretion and enhanced excretion of bile acids and cholesterol in feces which is almost similar to the report published by many authors [42, 51-53]. Curcumin might decrease absorption of cholesterol and increase the activity of cholesterol-7α-hydroxylase [54]. This hypocholesterolemic effect of curcumin may be attributed to its stimulatory effect on hepatic cholesterol-7α-hydroxylase enzyme, an enzyme that regulates cholesterol catabolism [8, 55]. Curcumin also reported to modulate (decrease) 3-hydroxy-3-methylglutarylcoenzyme A (HMG-CoA) reductase enzyme activity to decrease serum and liver cholesterol, triglycerides and free fatty acid levels [8, 56].

Hussein, *et al.* [8] reported that HDL-C levels were significantly increased in curcumin treated group this proves that curcumin not only regulate hyperlipidemia through decreased blood cholesterol and triglyceride levels but it also enhance the levels of lipid removing cholesterol i.e. HDL-C in blood with increased Apo A I and paraoxonase enzyme activity [8, 57].

The present study reveled that co-administration of gentamicin and aqueous extract of rosemary significantly decreased the elevations in the serum cholesterol, triglycerides, non HDLc, LDLc and VLDL concentrations, and significantly increased decline in serum HDL-cholesterol. These similar to the results of Al-Jamal and Alqadi [58]

who reported that oral administration of rosemary leaf extract to diabetic rats shows a decrease in the blood levels of triglycerides, total cholesterol, LDL-cholesterol, by 24%, 22%, and by 27%, respectively, and an increase by 18% in HDL-cholesterol. The findings of this study indicate that the administration of rosemary resulted in a better lipid profile in both normal and diabetic rats. Also, Olmedilla, *et al.* [59] reported that basal diets containing goadaid reduced the levels of LDL-cholesterol, TC and TG. On the other hand, HDL-cholesterol level was raised in diet with goadaid. Exposure to high fruit and vegetable content in diet increases antioxidant concentrations in blood and tissues and potentially protects against oxidative damage of cells and tissues.

Phytochemical studies have shown that rosemary contains essential oils, terpenoids, flavonoids and alkaloids. Some of its constituents such as rosmarinic acid have been reported as powerful antioxidant protecting against free radicals damage [60]. The active constituents of rosemary like carnosol, carnosic acid, caffeic acid, rosmarinic acid, ursolic acid, different diterpenes, phenols and flavonoids are reported to have antioxidant, antimutagenic, radioprotective properties [61]. It has been shown that rosemary extract and its antioxidant compounds inhibit free radicals generations in vivo [62]. Rosmarinic acid [63], diterpenoids such as carnosic acid, carnosol, rosmanol, epirosmanol [64], carotenoid, and alpha-tocopherol [65] have been documented as the principal antioxidant constituents of rosemary extracts. The chemopreventive action of rosemary can alternatively be mediated through the induction of detoxification enzymes [66, 67]. These protective effects of rosemary may be attributed to its antioxidant and free radical scavenging activities due to its higher contents of polyphenolic compounds [67, 68]. Metabolic control of rosemary leaf extract on mechanisms involved in elimination of the lipids from the body, this hypolipidemic properties have been confirmed in many plant species and plant products in medicinal use [58, 69-71]. The most important constituents of rosemary are caffeic acid and its derivatives such as rosmarinic acid. These compounds have antioxidant effect [18]. A variety of phenolic compounds, in addition to flavonoids, are found in fruit, vegetables and many herbs. The phenolic compounds (such as caffeic, ellagic, and ferulic acids, sesamol, and vanillin) inhibit atherosclerosis [72]. In addition to a well documented role in reverse cholesterol transport, HDL-cholesterol has recently been recognized to have several other important cardio protective properties including the ability to protect LDL from oxidative modification [73]. Fuhrman, *et al.* [74] reported that polyphenols glabridin (derived from licorice), rosmarinic acid or carnosic acid (derived from rosemary) inhibited LDL oxidation in a dose-dependent manner. Moreover, several studies showed that plant extracts lowered LDL oxidation [34, 58, 70, 75]. In this respect, Tapsell, *et al.* [76] reported that the antioxidant properties of rosemary are of particular interest in view of the impact of oxidative modification of low-density lipoprotein cholesterol in the development of atherosclerosis. Herbs and spices have an important role in dietary flavonoids intake. Chamomile, onions, rosemary, sage and thyme have high flavonoids contents, but there is little evidence apart from epidemiological studies to support a direct cardiovascular health benefit from these herbs and spices.

In the current work the serum Castelli's Risk Index I, Castelli's Risk Index II, Atherogenic Coefficient and Atherogenic Index of Plasma in guinea pigs co-administrated of gentamicin with rosemary and/or curcumin groups were significantly decreased when compared with gentamicin group. This is in agreement with Azab, *et al.* [15] who found that co-administration of sodium nitrite with propolis were reduced Castelli's risk index I, Castelli's risk index II, atherogenic coefficient and atherogenic index of plasma with statistically significant differences ($p<0.05$), when compared with sodium nitrite treated group. Also, Azab, *et al.* [39] recorded that a decreases in Castelli's risk index I, Castelli's risk index II, atherogenic coefficient and atherogenic index of plasma with statistically significant differences ($p<0.05$) in mice co-administrated of lead acetate with propolis , when compared with lead acetate treated group.

The mechanism of hypolipidemic and antiatherogenic action of natural antioxidant may be due to the inhibition of dietary lipid digestion and absorption and lipid and lipoprotein metabolism pathways [6, 77-79]. Also, antioxidants prevent glycation lipoproteins, enzymes, and proteins that involve lipid and lipoprotein metabolism pathways [6, 77, 79-81].

5. Conclusions

Based on the previous findings, it can be concluded that, gentamicin had adverse effects on lipids profile, and atherogenic ratios in the blood serum. Curcumin and/or rosemary administration showed a remarkable amelioration of these abnormalities in gentamicin treated male Guinea pigs, which may be due to its antioxidant property. However, the present data demonstrated that consumption of rosemary and/or curcumin can lead to reduction in the risk of hyperlipidemic symptoms and heart diseases. So, the patients should be advised to take curcumin and rosemary in combination while they are treated by gentamicin. Further studies are necessary to elucidate exact mechanism of control of dyslipidemia and potential usefulness of curcumin and rosemary as a protective agent against gentamicin induced dyslipidemia in clinical trials.

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