The Role of Silver Nanoparticles Against Amoxicillin/ Clavulanate-Induced Liver Damage in the Female Rats

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Abstract

The current study was designed to evaluate the protective effect of silver nanoparticles against toxicity induced by amoxicillin/clavulanate acid. Number of rats in the experiment are nine divided into three groups each group has three rats. The first group is kept as control group and administrated normal saline, the second is administered amoxicillin/clavulanate acid at dose 80 mg/kg and third group is administered amoxicillin/ clavulanate acid at dose 80 mg/kg and silver nanoparticles at dose 50 mg/kg for 30 days. The results show significant increase ($p<0.05$) in the liver aminotransferase levels (AST, ALT and ALP), total protein and albumin in addition significant increase ($p<0.05$) in the lipid profile total cholesterol TC, triglyceride TG, low density lipoprotein LDL, very low density lipoprotein VLDL and significant decrease ($p<0.05$) in the high density lipoprotein HDL incompare with control group. In conclusion: silver nanoparticles has beneficial effectagainst side effects induced by amoxicillin/clavulanate acid in rats.

Keywords: *Amoxicillin/Clavulanate acid, Silver Nanoparticles, Liver Damage*

Introduction

Medication prompted liver injury is getting mainstream around the globe. Anti-microbials are known as one of the reasons for liver injury, because of its high openness rate [1, 2].

Amoxicillin/clavulanic corrosive (AC) is an oral Broad-range antibacterial compound composite of an anti-infection semi-manufactured penicillin (amoxicillin) and an inhibitor of β-lactamase (potassium clavulanate). It has been viably utilized for more than 20 years in the treatment of different bacterial contaminations [3].

Despite the fact that AC has gotten one of the anti-microbials most regularly recommended, the organization of the medication may be corresponded with cholestatic and hepatocellular liver injury, which seemed, by all accounts, to be essentially due to the clavulanate part (4). demonstrated to have amazing cell reinforcement properties of the decrease responsive oxygen species (ROS, for example, superoxide anions, hydrogen peroxide, hydroxyl revolutionaries and hypochlorous corrosive [5].

Nanomaterials (1–100 nm materials) have been drawing in much consideration in the previous few decades in numerous fields, for example, biomedicine, catalysis, energy stockpiling, and sensors, because of their special physicochemical properties when contrasted with their mass structures. Silver nanoparticles (AgNPs) have gotten extraordinary interest, particularly in biomedicine. AgNPs are popular for their wide range and exceptionally productive antimicrobial and anticancer exercises[6]. Other natural exercises of AgNPs have been likewise investigated, including advancing bone recuperating and wound fix, improving the immunogenicity of immunizations, and hostile to diabetic impacts. Unraveling the organic components

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and possible cytotoxicity of AgNPs will encourage their better clinical applications[7].

The current work was planned to assessthe scavenging antioxidative bioactivities ofsilver nanoparticles on oxidative stress relatedinjury of liver in experimental ratspoisoned with amoxicillin/clavulanic acid.

Materials & Methods

Using nine female rats (Rattusnorvegicus) weighting 200-250 gm were obtained from the animals house in the faculty of science/university of kufa. the animals were kept under standard environment condition for one week (temperature 25-28 C° and 12 hr light-dark cycle) and allowed access to standard laboratory diet and water for acclimation after the animals were divided into three groups each group contain three animals : group one received orally amoxicillin/clavulinac acid at dose 80 mg/kg , group two received orally amoxicillin/clavulinac acid at dose 80 mg/kg with silver nanoparticles at dose 50 mg/kg and the last group as control group received distal water and standard diet for one month. At the end of experiment. Each animal was anaesthetized by the mixture of xylazine 0.1 ml and ketamine 0.5 ml and they were scarified [8].

Determination of lipid profile activity

Total cholesterol kit for quantitative determination of total cholesterol in serum was supplied by Biolabo SA, France, Serum HDL(High Density Lipoproteins), Cholesterol level and Triglycerides Kit was supplied by Biolabo, France,Very low density lipoprotein (VLDL) were measured by using the following formula: VLDL = TG (mg/dl) / 5 ,Low density lipoprotein (LDL) were measured by using the next formula: LDL=TC(mmol/l)-VLDL(mmol/l)-HDL(mmol/l).

Determination of Serum Transaminase Activity Transaminases – Kits

Alanine Transaminase (ALT)& Aspartate Transaminase (AST) activity were determine by colorimetric method according to the biolabo kit,france and ALP according to biomerieux kit

Statistical Analysis

Data were presented as means ± S.E. and statistically analyzed using (ANOVA) test followed by least significant difference (L.S.D.) analyses at 0.05% probability of levels. Using computerized SPSS program.

The Results

According to table (1), the current study showed a high significant decrease in the levels of liver enzymes (AST, ALT, ALP) in the group treated withamoxicillin 80 mg/kg + silver nano. 50 mg/kg. The present study also revealed that there was a significant decrease in serum albumin (g/dl) total protein (g/dl) bilirubin (g/dl) in the group treated withamoxicillin 80 mg/kg + silver nano. 50 mg/kgas shown in table (2) . Regarding table (3), the current study showed a high significant decrease in the levels of lipid profile (TC , TG; HDL, LDL ,VLDL) in the group treated withamoxicillin 80 mg/kg + silver nano. 50 mg/kg .

Table (1) : Effect of amoxicillin and silver nanoparticles in the levels of liver enzymes in the female rats for 30 days

Groups	AST(U/L)	ALT(U/L)	ALP(U/L)
amoxicillin 80 mg/kg	165.61	94.03	223.61
amoxicillin 80 mg/kg + silver nano. 50 mg/kg	148.58	59.86	196.6
control	130.56	31.35	179.82
F-test : 24.67 ; P value : 0.000			

Table (2) : Effect of amoxicillin and silver nanoparticles in the levels of serum albumin, total protein and bilirubin in the female rats for 30 days.

Groups	Serum albumin (g/dl)	Total protein (g/dl)	Bilirubin (g/dl)
Amoxicillin 80 mg/kg	4.3	2.4	1.56
Amoxicillin 80 mg/kg + silver-nano. 50 mg/kg	2.5	4.4	0.9
control	3.5	1.8	0.68
F-test : 4.9 ; P value : 0.05			

Table (3) : Effect of amoxicillin and silver nanoparticles in the levels of lipid profile in the female rats for 30 days.

	TC (mg/dl)	TG (mg/dl)	HDL (mg/dl)	LDL (mg/dl)	VLDL (mg/dl)
amoxicillin 80 mg/kg	180.27	268.48	28.21	85.23	72.86
amoxicillin 80 mg/kg + silver nano. 50mg/kg	151.9	240.14	32.5	65.2	60.26
control	136.38	218.51	39.28	52.68	42.16
F-test : 67.61 ; P value : 0.000					

TC : Total Cholesterol ; TG : Triglycerides ; HDL : High Density Lipoproteins ; LDL : Low Density Lipoproteins ; VLDL : Very Low Density Lipoproteins

Discussion

Our information uncovered a critical upregulation in the degree of complete cholesterol also, fatty oils in amoxicillin/clavulanate corrosive gathering which are steady with the investigation [9]. The raised levels may demonstrate an unsettling influence in fat digestion because of the peroxidation of films and adjustment of the cell structure because of harmfulness portion of amoxicillin/clavulanate corrosive just as overproduction of free revolutionaries [10]. The aftereffects of our investigation are in amicability with the past reports that indicated an elevated level of absolute cholesterol, fatty substances, low thickness lipoprotein and low thickness lipoprotein after amoxicillin clavulanate treatment. Such change in the degrees of absolute cholesterol, fatty oils, low thickness lipoprotein and low thickness lipoprotein prompted shift in the film porousness [11].

The degrees of lipids profiles, that is, plasma all out cholesterol, HDLcholesterol, LDL-cholesterol and fatty substances were high in the treated gathering. Examinations on layer lipids demonstrated that cholesterol/phospholipids molar proportion combined with different boundaries are the main determinants of film ease. The outcome may recommend a reduction in film ease and could bring about adjusted layer work [12].

The current examination uncovered a huge rise (P<0.05) in serum cholesterol, Triglyceride, LDL, VLDL and critical lessening (p<0.05) in HDL level in female rodents controlled amoxicillin at portion 80 mg/kg when thought about a benchmark group.

These discoveries are in concurrence with that expressed by [13]. A few investigations affirmed that an ascent in fat eating regimen utilization in creatures prompted hypercholesterolemia. Past investigation proposed that for dynamic appropriation and digestion of the lipids, the lipoprotein was most essential. the elevated cholesterol in the eating routine causes down guideline in LDL receptors. So that, this examination was descripted that the plasma LDL fixation raised in rodents. Accordingly, the ascents in LDL-C show more cholesterol in the blood that speaks to the danger of coronary illness[14].

Some new investigations clarified the reduction of HDL level after admission amoxicillin . This investigation affirmed that the HDL decreased because of the increase in HDL creation chiefly in the liver and halfway in the small digestive tract. HDL molecule is comprised generally from ApoAI and apoAII Apo lipoproteins, which was impacted by nourishing impedance, What's more, HDL is normally named as "great cholesterol" since significant levels of (HDL) speak to an ascent in the vehicle of cholesterol from fat tissue to the liver, where it is adjusted [15]. So that, this expansion in HDL diminishes the danger of cardiovascular sicknesses and hypertension [16].

These discoveries were in concurrence with the past investigations. Past examination recommended that in light of the fact that the capacity of amoxicillin to diminish of LDL, it was utilized as the primary pharmacological treatment of dyslipidemia [17].

The evaluation of liver harm by xenobiotics and drugs, which are passing and processed into poisonous intermediates in hepatic cells. The serum boundariesidentified with liver capacities which have been concentrated in the current work uncovered that intense dosages of amoxicillin-clavulanate actuated critical expansion in the degree of AST, ALT, ALP, egg whites and absolute protein. Comparative discoveries were seen that amoxicillin-clavulanate corrosive organization prompted liver injury [18]. AST, ALT and ALP are ordinarily situated in mitochondria, cytoplasm or microsomes of hepatic cells; their expanded serum levels may show a harm in the hepatic cells and thusly liver harm [19]. The expanded serum level of such proteins may likewise be ascribed to changes in the cell layer penetrability and expanded/diminished catabolism of aminotransferases and it was accounted for in conditions including rot of hepatocytes [20]. Also, the expansion in egg whites and all out protein saw in the current examination are not in assent with different discoveries that demonstrated decreased degrees of egg whites and aggregate protein instigated by amoxicillin-clavulanate harming [21].

Then again, our information concurred with those acquired by Agbaforand his team[22] when their trial creatures were given anti-microbials, for example, ofloxacin and ciprofloxacin. They ascribed the unaltered or raised egg whites and complete protein level to the liver which keeps its typical capacities inside the given portions of the anti-toxins. We concur with the previously mentioned creators that the exploratory portions of anti-toxin utilized were not sufficiently able to cause broad hepatocytes harm to down control the blend of proteins, along these lines keeping the protein levels as high as would be expected in solid liver.

Liver is a primary site of collection of AgNPs along with spleen [23]. Park and his co-workers found that oral organization of 1mg/kg of AgNPs in mice prompted diminished degrees of AST and ALT in both male and female mice with increment of ALT in female mice just and didn′t show histopathological changes in the liver [24] . El Mahdy et al. exhibited histopathological changes in the liver after intraperitoneal organization of various portions of AgNPs (1000 and 4000 mg/kg) in pale skinned person rodents every day for 28 days[25]. Then again Cho and his co-workersindicated that the intraperitoneal organization of little estimated AgNPs (10 nm) in mice prompted huge lessening in AST

with a diminishing inclination in ALT. While Qin and his co-workersdetailed that lone AST was essentially diminished in rodents after oral organization of a 0.5 and 1 mg/kg AgNPs every day for 28 days notwithstanding minor histological changes in the liver and kidneys. As opposed to our outcomes, Pourhamzehand his co-workers, found that oral organization of AgNPs orally to test rodents for 28 days didn't show impressive changes in the serum level of AST and ALT when given in various portions[26]. These outcomes might be because of the utilization of huge estimated nanoparticles (78.59 nm) than that utilized in our test study.

Conclusion

In conclusion, our results suggest that silver nanoparticles have a hepatoprotective effect on liver dysfunction caused by amoxicillin-clavulanate acid and this effect is attributed to its antioxidant properties and this could be clinically beneficial to reduce the hepatotoxic adverse effect of amoxicillin-clavulanate acid.It was found that silver nanoparticles has beneficial effect against side effects induced by amoxicillin/ clavulanate acid in rats regarding liver enzymes , proteins , bilirubin , and lipid profile .

Ethical Clearance : Taken from University of Kufa ethical committee

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Conflict of Interest : Nil

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