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INHIBITORY EFFECTS OF DIANTHUS CARYOPHYLLUS EXTRACT ON GENTAMICIN-INDUCED NEPHROTOXICITY IN ADULT RAT

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ABSTRACT

One of the causes of acute renal failure and toxicity of these drugs is of great importance, especially with the aminoglycoside gentamicin. The prevalence of gentamicin nephrotoxicity by 7-36% (average 14%) and in critically ill patients is two-fold. Dianthus caryophyllus has a variety of antioxidant agents. In this study the inhibitory effect of dianthus caryophyllus extract on renal failure induced by gentamicin is investigated. 49 Wistar rats were randomly divided into 7 groups. Group C was given no medication. S group, the saline solution was injected intraperitoneally. Group D100 extract of dianthus caryophyllus (100mg/kg B.W), Group G100 gentamicin (100mg/kg B.W), Groups GD25, GD50 and GD100 order gentamicin with the dosages of 25, 50 and 100 mg per kg body weight of ethanol extracts of dianthus caryophyllus in the injections. During the experimental period was 28 days. Later samples were taken at the end of day 28, rats were killed and serum urea nitrogen, uric acid and creatinine levels were measured. The concentration of blood urea nitrogen G100, GD25 and GD50, a significant increase compared to group C is shown ($P<0.05$). Creatinine concentrations in G100 and GD25 group showed a significant increase compared to the C group ($P<0.05$) and GD100 is a significant reduction compared to G100 ($P<0.05$). Uric acid concentrations in G100 showed a significant increase compared to C group and GD100 showed a significant decrease compared to G100. The concentration of uric acid in the G100 group also showed a significant increase compared to the D100 ($P<0.05$). Dianthus caryophyllus extract was able to protect the enzyme

changes and nephrotoxicity induced by gentamicin. This protective effect may be related to the antioxidant properties of these extracts.

Keywords: Dianthus Caryophyllus, Gentamicin, Nephrotoxicity, Rat

INTRODUCTION

Antibiotics are among the most common drugs that are prescribed by doctors and used by the patients themselves **[1]**. They had saved millions of lives and prevent many problems are caused by infections. If these drugs were not found in many were cases of infectious complications like Kerry, Murray, paralysis, organ failure, and heart valves, etc. **[2-4]**. However, antibiotics can have side effects and can affect various organs of the body such as blood, skin, eyes, mouth, etc. **[5-9]**. Aminoglycoside antibiotics, especially gentamicin are widely used to treat severe infections Gram-negative bacteria **[10]**. Nephrotoxicity is important side effects of drugs that are responsible for acute renal failure in a significant number of people are taking this medication. According to one of the major side effects of gentamicin nephrotoxicity in a significant percentage of people taking this medication may face limitations **[10-12]**. The actual mechanism of gentamicin-induced nephrotoxicity is not yet fully identified **[10-13]**. Some researchers believe that the increased production of Reactive Oxygen Species ROS in cells following gentamicin seen in drug-induced toxic effects on structure and function of the kidneys is effective **[11-15]**. ROS have also been expressed as cell death in various other pathological conditions has been proposed **[13]**. Studies have shown that gentamicin also crosses the placenta **[16-18]**. Auditory toxicity of gentamicin nephrotoxicity in two separate studies on embryos studied, and although this effect was not proven to be excluded, but nephrotoxicity **[19-20]**. Studies show that consumption of compounds with antioxidant activity are reduced gentamicin-induced nephrotoxicity **[13, 15, 21]**. Carnation plant family Myrtaceae and its scientific name is Dianthus caryophyllus **[22]**. The whole world has more than 300 species of Dianthus **[23, 24]** that 30 species are in Iran. Dianthus caryophyllus is a tonic for strengthening the stomach, nausea, fever, worms' cache binding rule. Dianthus caryophyllus are prescribed as an adjunct for the treatment of arterial disease. This medicine is also appetizing. Dianthus caryophyllus essential oil is used for local anesthesia. Dianthus caryophyllus oil is also irritating to the skin **[26-32]**. Dianthus caryophyllus contain a significant amount of

oil is volatile. The essential oil is obtained by distillation from the buds of dianthus caryophyllus, dianthus caryophyllus tree is about 16% and 4.6% of the stems and leaves of the clove tree are about 2%. Dianthus caryophyllus oil contains Eugenol material is 80-90%. Eugenol is non-toxic disinfectant. Moreover Sesquiterpenoids, Caryophyllin, Eugenin, vanillin, glutamic acid and calcium oxalate are also other substances in dianthus caryophyllus. The chemical structure of these plant compounds such as B-caryophyllene, acetyleugenol, methylsalicylate, alpha-humulene, carvacrol, thymol, and there is cinnamaldehyde **[31, 33]**.

METHODOLOGY

This study experimentally and is completely random. All animal experiments in this study comply with the code of conduct has been developed. 49 adult Wistar rats weighing 200±10 g and 75 days of age, was produced from Shiraz Razi Vaccine & Serum Research Center. The rats were housed in Islamic Azad University Jahrom Branch Animal House for 28 days under laboratory conditions include a temperature of 21±2° C and 12 h light and 12 h dark cycle was used. The mice were kept in cages; metal mesh doors and a standard rodent diet (pellete) were used. Glass bottles of water were also provided. Their food and water were free. Cage 3 times a week it was disinfected with 70% alcohol. Gentamicin Caspian Pharmaceutical Company as 80 mg in 2 mL ampoules was bought. Gentamicin dose of 100 mg per kg body weight in rats (100mg/kg Bw) was performed. The dianthus caryophyllus extract was prepared that preparing the plant and verified by expert scientific botanical, extract the Soxhlet method using 50 g of plant powder and 400 ml of alcohol (ethanol 96%) was obtained as a solvent. Then the rotary evaporator apparatus, the extract obtained was concentrated. After extraction, the alcohol was removed by distillation apparatus then it is possible to extract dissolved in saline solution at doses of 25, 50 and 100 mg per kg of body weight in rats (25,50 and 100mg/kg B.W) were prepared **[34]**.

Samples (extract, gentamicin and saline solution) with 0.2ml insulin syringe volume were injected intraperitoneally at 9 am each day.

49 rats were divided randomly into 7 groups as follows:

Group C: were maintained on normal without any medication.

Group S: Rats in this group recevied saline solution as solvent of dianthus caryophyllus extract and gentamicin.

Group D100: Rats in this group recevied dianthus caryophyllus extract 100mg/kg B.W.

Group G100: Rats in this group recevied gentamicin 100mg/kg B.W.

Group GD25: Rats in this group recevied Gentamicin 100mg/kg B.W with dianthus caryophyllus extract 25mg/kg B.W.

Group GD50: Rats in this group recevied gentamicin 100mg/kg B.W with dianthus caryophyllus extract 50mg/kg B.W.

Group GD100: Rats in this group recevied gentamicin 100mg/kg B.W with dianthus caryophyllus extract 100mg/kg B.W.

After 28 days, rats of all groups were comatose after weighing by Ether and the heart by syringe, 5 ml blood was measured after separating the serum concentration of urea nitrogen, uric acid and creatinine were measured in serum. To express the results, compare the amount and distribution of column charts are used to express the values are given as Mean ± SD. One way analysis of variance (ANOVA) followed by Tukey's post hoc test for multiple comparisons were used to compare difference between experimental groups. The criterion for statistical significant was $P<0.05$. For all data analysis software SPSS version 18.0 statistical doing tests were used.

RESULTS

The results showed that the concentration of blood urea nitrogen (BUN) in groups G100, GD25 and GD50 is a significant increase compared to the C group. BUN concentration in groups GD25 and G100 were significantly higher than D100 group, which has received only dianthus caryophyllus extract. GD100 in BUN concentration is significantly reduced compared to GD25 ($P<0.05$).

Serum creatinine concentration were significantly increased in G100 and GD25 groups compared to C group. G100 and GD25 groups showed a significant increase compared to the D100. The GD100 group was significantly decreased compared to G100 and GD25 ($P<0.05$).

The results show that the serum uric acid concentration was significantly increased in G100 group compared to the C and D100 groups. The group G100 is a significant increase compared to the D100 and GD100. In GD25, GD50 and GD100 Groups is a significant reduction compared to G100 ($P<0.05$).

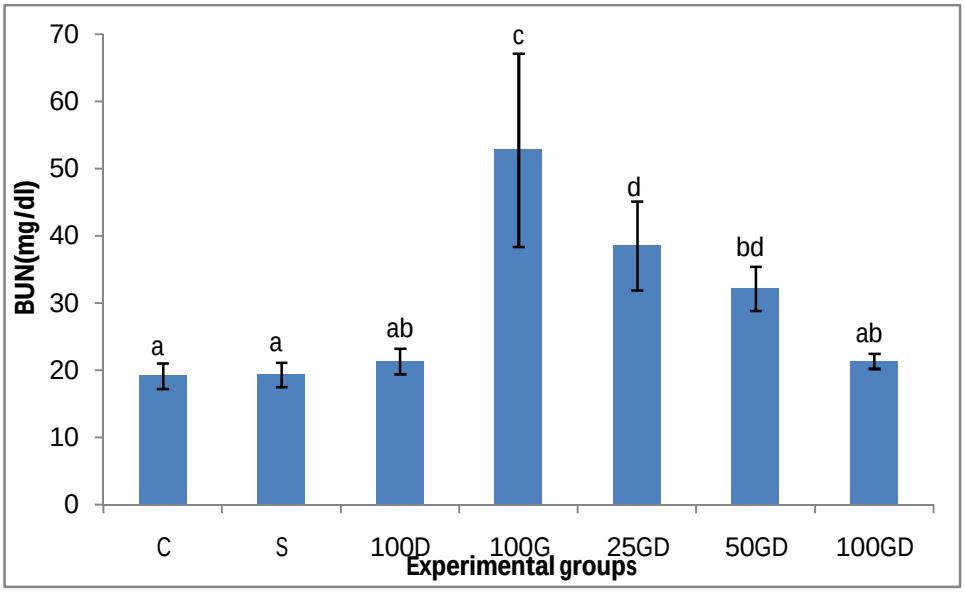

Figure 1: Effect of Gentamicin and Dianthus Caryophyllus on BUN. The Culmnes That Have at Least One Common Letter, Have Not Significant Different From Each Other at the Level of P<0.05

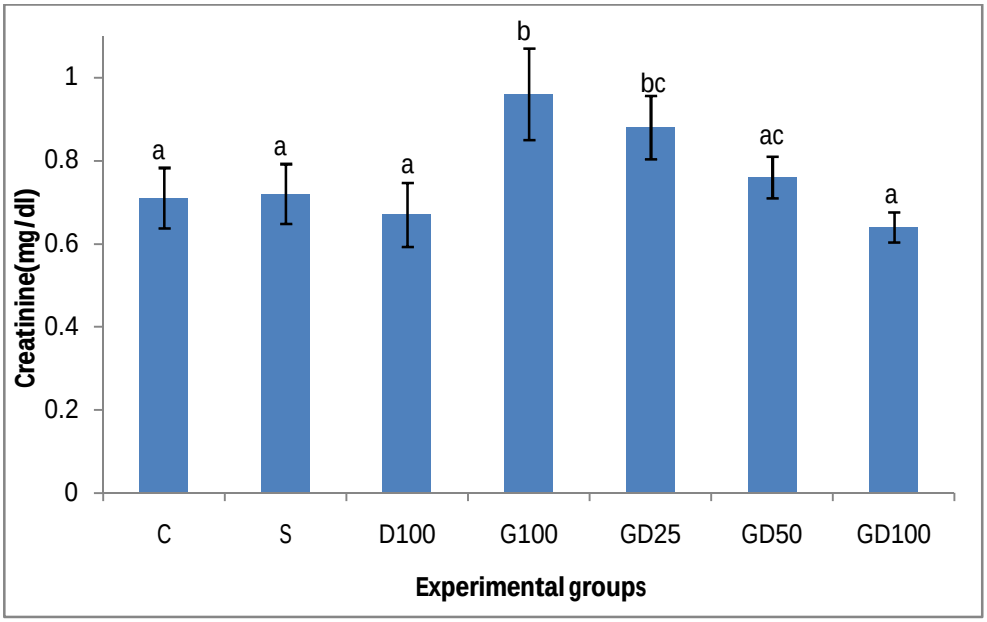

Figure 2: Effect of Gentamycine and Dianthus Caryophyllus on Creatinine. The Culmnes that Have at Least One Common Letter, Have Not Significant Different from Each Other at the Level of P <0.05

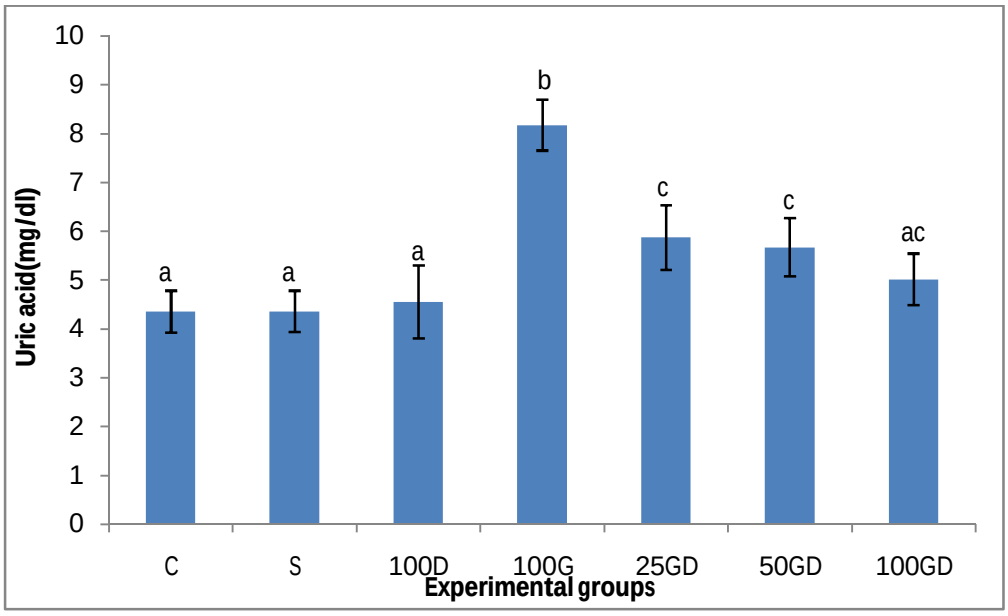

Figure 3: Effect of Gentamycine and Dianthus Caryophyllus on Uric acid. The Culmnes that Have at Least One Common Letter, Have Not Significant Different From Each Other at the Level of P <0.05

DISCUSSION

The body of toxins such as urea, uric acid, creatinine and bilirubin metabolites are excreted via the kidneys **[35]**. Since the kidney is a major problem in today's society, so pay careful attention to the structure and function, it can be important for the health of the individual **[36]**. In research conducted in the past stated that the signs of acute renal failure and renal tubular damage can include: Decreased creatinine clearance, increased BUN and uric acid in serum and increased degree of pathology and tissue damage in other cases **[37]**.

In this study BUN concentration were significantly increased in G100, GD25 and GD50 groups compared to the C group. Gentamicin is probably due to tissue damage in groups. Studies have shown that the major side effects of gentamicin, renal toxicity (nephrotoxicity). Clinical protests aminoglycoside nephrotoxicity glomerular or tubular dysfunction is the first and sometimes the Oliguria and renal failure progresses **[38, 39]**. What is certain is showing the negative effects of increased BUN and gentamicin-induced nephrotoxicity that according to research done that may have caused the production of reactive oxygen species **[11-15]**. This study showed that dianthus caryophyllus extract csuse decrease level of BUN in rats. Serum BUN concentration was significantly decreased in GD100 compared to G100. Some studies have shown that the use of antioxidants is reduced gentamicin-induced nephrotoxicity **[11-13, 15, 21, 40]**,

which is consistent with current research. Also, by increasing the dose of dianthus caryophyllus extract, inhibited the increase in BUN was observed. The results indicate that uric acid in GD50 and G100 were significantly increased compared to in the C group. GD100 significant decrease was observed compared to in the G100 group. Also in the group receiving gentamicin compared to dianthus caryophyllus extract significant increase in serum uric acid was observed. Some researchers increased production of ROS such as superoxide anions, hydrogen peroxide and lipid peroxidation in gentamicin-induced side effects as effective **[41]**. Gentamicin has been reported to cause changes in the lipid composition of cell membranes in the kidney **[42-47]**. These changes are likely to be mediated by the activity of free radicals and lipid peroxidation **[47]**. So it is also possible that changes in the groups receiving gentamicin is due to the same issue. Other causes of increased uric acid in the groups receiving gentamicin It also can be easily filtered by the kidneys and gentamicin uptake in the tube is bent. That's why cell necrosis induced by gentamicin is mainly a curved tube **[46, 48]**. The increased plasma urea occurs due to damage to the pipes and ducts obstruction **[46]**. As explained dianthus caryophyllus extract, probably due to its antioxidant properties are due to the elimination of free radicals in the experimental group received gentamicin GD100 extract the antioxidant effect is seen. The investigation stated that the use of gentamicin in children with urinary tract infections, serum creatinine levels decreased in all patients **[49]**. Greece in serum creatinine during the study drug administration compared with before injection showed a reduction in both term and preterm **[50]**. In two studies on full-term and premature loss of serum creatinine was observed during treatment **[51, 52]**. The concentration of creatinine in groups G100 and GD25 showed a significant increase. With different concentrations of creatinine present study, it is likely that the serum creatinine concentration gradually increases with age. Sex and the subjects could also be involved in this dispute. In another study stated that gentamicin can increase plasma concentrations of biochemical indices of renal function, including creatinine is **[42, 43]**, which is consistent with current research. Likely due to the increase in serum creatinine, glomerular injury is caused by gentamicin **[42-44]**. It also stated that another reason for the increase in creatinine could damage the pipes and necrotic cells was reduced glomerular filtration occurs due to obstruction

of the ducts by **[46]**. However, given the amount of creatinine is dependent on the weight and volume of muscle mass **[53]** is the result of research work. The investigations of the eugenol in dianthus caryophyllus extract at concentrations as low as anti-oxidation, anti-inflammation and act contrary to the high concentration **[54-55]**. Can also cause an increase in serum creatinine GD25 attributed to the antioxidant properties of dianthus caryophyllus extract. What is certain is that the groups received gentamicin and simultaneously extracts the group receiving gentamicin alone will reduce the view that shows the positive effects of extracts of dianthus caryophyllus.

CONCLUSIONS

According to the above consume dianthus caryophyllus extract to reduce the amount of urea nitrogen, uric acid and creatinine levels is effective so that more improvement is seen at higher doses. So it seems dianthus caryophyllus extract can as adjuvant treatment in order to minimize damage of gentamicin to the kidney.

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