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Protective Effects of Cinnamon Bark Hydroalcoholic Extract on Gentamicin-induced Nephrotoxicity in Mature Rats

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Abstract

Background and Methodology: Gentamicin is a broad-spectrum antibiotic with restricted application in man and stock due to its side effects such as Nephrotoxicity and autotoxicity. Cinnamon bark has antioxidant properties. This is the first study on the protective effects of the hydroalcoholic extract of cinnamon on gentamicin-induced nephrotoxicity.**Methods and Materials:** Thirty-six mature female Wistar rats were divided into six equal groups. The control group did not receive any solvents or medicines. The experimental group I received Gentamicin with the daily dose of 80 mg/kg through intraperitoneal injection, and the experimental group II the daily 200 mg/kg gavage dose of hydroalcoholic extract of cinnamon. The experimental groups III, IV, and V were given the daily dose of 80 mg/kg of Gentamicin through intraperitoneal injection together with 50, 100, and 200 milligrams of cinnamon extract, respectively, by gavage for 21 days. **Results:** Serum uric acid concentration in the experimental group I increased significantly compared to the control group at the 5% probability level, and urea and creatinine concentrations in the experimental groups I and III showed a significant increase compared to the control group at the 1% probability level. **Conclusions:** Cinnamon extract was able to protect rats against Gentamicin-induced nephrotoxicity due to its contents of phenolic compounds and of other antioxidant substances.

Keywords: Cinnamon, Antioxidant, Gentamicin, Nephrotoxicity

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Introduction

Gentamicin is an antibiotic with known side effects, and 10 to 20 percent of patients receiving it develop nephrotoxicity (1). Some studies have reported that oxidative stress is involved in Gentamicin-induced toxicity (2). Gentamicin increases superoxide anion, hydrogen peroxide, and hydroxyl radical production by renal mitochondria (3). Free radicals cause peroxidation of membrane phospholipids, break DNA strands, and denature proteins (4). The most conspicuous biological damage inflicted by active oxygen metabolites is their reaction with unsaturated lipids, which leads to the oxidation of these lipids. This will cause changes in membrane fluidity and, hence, membranes become permeable to molecules as large as enzymes (5). Hydroalcoholic extracts of cinnamon are used to prevent damages caused by oxygen free radicals and, hence, to reduce Gentamicin-induced renal toxicity. Cinnamon, with the scientific name of Cinnamomum zeylanicum, is an evergreen tree of the Lauraceae family and a native of Sri Lanka and Southeastern India (6). Although cinnamon with its pungent flavor is mostly used in kitchens, its medicinal applications should not be ignored. Cinnamon is one of the oldest medicinal plants and had important medical applications in ancient medicine. Different parts of this plant, including its bark, have therapeutic properties and function as a tonic for the heart, the stomach, and the intestines, improve kidney function, and act as a libido enhancer (7). The medicinal value of this plan is mostly due to its volatile essential oils, the main constituents of which include cinnamaldehyde, eugenol, and safrole (that has activities similar to insulin and can be useful for diabetics) (8). These compounds also have positive effects in reducing blood triglyceride, cholesterol, and LDL (9). Cinnamon has many applications because of its antifungal and antibacterial properties against various important pathogens of the human body including Escherichia coli, Heliobacter pylori, and Candida albicans (10). In this research, the possible effects of Gentamicin and various concentrations of hydroalcoholic extracts of cinnamon on kidney structure were studied.

Materials and methodology

In this research the big laboratory Wistar rats (170±20 grams) of Islamic Azad University of Jahrom were used. The samples were randomly divided into 6 groups of six (total number 36) including: control group, experimental 1, experimental 2, experimental 3, experimental 4 and experimental 5. Each of these groups was placed in a different cage. During the two weeks of samples compatibility with experimental environment and during injection period, all rats used available water and food, constant temperature of 28-32 C and natural light.

Extraction method

First of all cinnamon bark was powdered using the mill and 24 grams of the powder was dissolved in 20 CC medical ethyl alcohol 96%. The resulting mixture was maintained for 24 hours at room temperature (25 C). Then it was completely mixed for 4 minutes using magnetic stirring device (shaker) and filtrated using a Whatman paper whose initial weight was written down. The paper and the remaining powder were dried in 50 C for 1/5 hours using Avon devise. The amount of the dissolved powder was determined comparing the eight difference of the remaining dried powder on the filter paper and the initial amount of the cinnamon. The extraction achieved using this method (Forman) contains a large amount of alcohol (about 20 ml). In order to eliminate the alcohol, the extraction was placed in a pollution-free environment for 48 hours so that the additional alcohol is evaporated and reduced to the least possible amount (about 5 ml). Then the extract volume is increased to 150 ml using 9% saline (normal saline injection).

After the 21 days period, the 36 rats were anesthetized with ether and five milliliters of blood were drawn from the heart of each one with a 5 cc syringe. After blood serum was separated, the serum levels of

creatinine, urea and uric acid levels were measured.ANOVA was used to compare the treatments and Duncan's new multiple range test was employed for the comparison of the various groups. SPSS (version 18) was used for data analysis and for performing statistical tests.

Results and Discussion

Gentamicin is an aminoglycoside derived from Micromonospora purpurea and is used to treat Gram-negative bacterial infections in man and animals. One of the important side effects of Gentamicin administration is renal toxicity. Results of this research suggest that Gentamicin significantly affects serum uric acid, urea, and creatinine. Serum uric acid concentration in the experimental group I significantly increased compared to the control group at $p< 0.05$, and serum urea and creatinine concentrations in the experimental groups I and III were significantly higher compared to the control group at $p< 0.05$. These results are similar to those found by Goodman Gilman et al. (1991) and Wedeen et al. (1983) (11-12).

Comparison of various groups with respect to the studied parameters

Parameter / Group	urea (mg/dl)	creatinine(mg/dl)	uric acid(mg/dl)
Control	24/440a	0/757a	5/927a
Experimental group I	28/933b	0/743b	6/227b
Experimental group II	32/353a	0/8018a	7/164a
Experimental group III	28/555a	0/7583b	6/594b
Experimental group IV	30/443ab	0/6094ab	7/977ab
Experimental group V	32/500ab	0/7278ab	6/227ab

*Columns that have at least one letter in common are not significantly different

In this research, serum creatinine, urea, and uric acid increased with the administration of Gentamicin. This increase probably results from damage in the glomeruli caused by Gentamicin. These results conform to those found by Derakhshanfar et al. (2009) (13-14). Moreover, Zareifard et al. (2001) reported that injection of Gentamicin in sheep for 63 days(once every 12 hours) increased serum urea nitrogen and creatinine (and these results agree with those found in this research) (15). The glomerular filtration rate of creatinine and urea nitrogen can be considered as a direct index measuring glomerular filtration rate, although their changes in weeks following Gentamicin administration are substantial. It seems that Gentamicin manifests its effects mostly in the form of pathological failures, and that these effects can be observed even at low doses of this medicine. The simultaneous application of antioxidants and Gentamicin was able to somewhat reduce kidney tissue damages resulting from Gentamicin administration (16-18). Research has indicated there are antioxidant compounds in cinnamon (19). Given the adverse effects of free radicals, and of oxidative stress reactions, it seems necessary to have

antioxidant compounds capable of protecting the body against oxidative stress damages. Antioxidants play a special role in preventing, and in curing, diseases (20-21).

Conclusions

In this research, the protective effects of cinnamon against Gentamicin-induced nephrotoxicity were proved for the first time. Considering the antioxidant properties of cinnamon, it seems this plant can be used, when Gentamicin is administered, to minimize damage inflicted on the kidneys.

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