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INVESTIGATING ANTIOXIDANT EFFECT OF CINNAMON EXTRACT ON ELIMINATION OF TOXICITY OF GELOFEN DRUG IN KIDNEY TISSUE OF FEMALE RATS

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ABSTRACT

Gelofen is such as anti-inflammatory drugs that through inhibit prostaglandins and inhibiting cyclooxygenase enzyme, preventing conversion of arachidonic acid to the intermediate Endo peroxides and it has numerous effects on various tissues of the body. Cinnamon bark has many Therapeutic properties, so that its use strengthens the heart, stomach and intestines, and improving kidney activities. So finding a suitable antioxidant in order to reducing side effects of gelofen drug that is as common drug to reduce menstrual cramps is essential. 49 female Wistar rats were randomly divided into 7 groups. The first group (control group) did not receive any medication. The second group (sham group) was injected only normal saline. Experimental group 1 was given only gelofen Drug (400 mg / kg) intraperitoneally. Experimental group 2 received only cinnamon extract (50 mg/kg) and experimental group 3 received cinnamon extract

with dose of (200 mg/kg). Experimental groups 3 and 4, in addition gelofen Drug (400 mg / kg) received cinnamon extract with doses of (50 mg / kg) and (200 mg / kg). At the end of 21 days, rats were anesthetized and kidney tissue were removed and it was sent to laboratory for histopathological studies .Results revealed that in Diameter of Bowman's capsule in G100 group has significant decrease compared to the control group. Cortex diameter in G100 and GCi 50 groups has significant decrease compared to the control group. Medullary diameter in G100 group showed significant decrease compared to control group. Distance curved pipe diameter in G100 and GCi50 groups has significant decrease compared to the control group. Close curved pipe diameter in experimental group GCi200 has significant increase compared to control group ($P<0.05$). In conclusions, Cinnamon extract has antioxidant properties; thereby it reduces nephrotoxicity due to gelofen consumption.

Keywords: Cinnamon, Gelofen, Kidney Tissue, Rat

INTRODUCTION

Since kidney diseases is a major problem in today's society, so pay careful attention to the structure and function of it can play an important role in the health of the individuals **[1]**. Today, because of successful effects of synthetic drugs, these medications have been developed, but Synthesis problems, high cost and side effects has led researchers to study the effects of these drugs on various parts of body **[2]**. Cinnamon has scientific name of Cinnamomum Zeylanicum Nees and common name of Cinnamon that is aromatic and pleasant plant **[3]**; Cinnamon is from laurel family (Lauraceae) that smells fragrant from all parts of plant **[4]**. Cinnamon is the cause of being young and daily use keeps people healthy and young. Cinnamon is also used to increase and retrieve sexual power, keep kidney warm and it eliminate fatigue and waist and leg weak, and it treat and anemia. Cinnamon is the best medicine for muscle pain. Cinnamon has calm and happiness effects, and it is better than many tranquilizers. Another important effect of cinnamon is decreasing fever **[4]**. Cinnamon bark contains more than 50 different compounds that 60-80% of it includes the cinnamaldehyde. Other compounds include: cinnamic acid, phenolic compounds such as eugenol, Flandren and Safrul, terpene compounds such as limonene and linalool, Trans cinnamaldehydes, tannins, coumarin, resins, phenyl propany compounds such as hydroxy cinnamaldehyde, cinnamon sweet flavor is due to the mannitol. One teaspoon of cinnamon contains 28 gr of calcium, one

gram iron and more than one gram fiber and lots of vitamin c, k, and manganese. Also, it contains 1.2 grams of carbohydrates **[5]**. The dried bark of the cinnamon tree is used for therapeutic purposes. Bark of the plant has 0/5 to 2/5 percent of the Essence that the bulk of it contains cinnamaldehyde, Eugenol and Trans cinnamic acid. Also another phenyl propany compounds such as hydroxy cinnamaldehyde, Ortho-methoxy cinnamaldehyde, cinnamyl alcohol and acetate and terpene compounds found in essence. Tannins are another polyphenolic or polymeric compounds similar to Lignin with high molecular weight that plays important protective role against adverse conditions. Cinnamon is a very powerful anti-free radical **[6]**. Research results have shown that the tannins in some herbs have valuable properties that can briefly be mentioned as following; reducing the inflammation and swelling, preventing bleeding in superficial and small wounds, reduction of intrauterine bleeding, wash eyes, dysentery and diarrhea treatment, reducing runny nose and hot flashes **[7]**. Anti-inflammatory activity of NSAID drugs is carried out mainly through the inhibition of prostaglandin biosynthesis. NSAID medicines through inhibition of cyclooxygenase enzymes prevents converting arachidonic acid to Endo peroxide interfaces and consequently do not synthesize prostaglandins. Also different NSAID may also have an additional mechanisms that includes inhibition of chemotaxis, negative regulation of interleukin-1 production, and interfere with intracellular events mediated by calcium . One of the most High consumption NSAID drugs is gelofen (Ibuprofen) that is a simple derivative of phenyl propionic acid with a molecular weight of 206 /28 **[8]**. gelofen generic name is ibuprofen . This medication is part of nonsteroidal anti-inflammatory drugs, non-narcotic analgesic and antipyretic **[9]**. This material is practically insoluble in water **[10]**. The study found that ibuprofen inhibits the formation of prostaglandins and endo-peroxide, and it affects histamine and quinine system **[11]**. Also it is determined that gelofen causes reduction of Glumer filtration and renal plasma compared to acetaminophen **[12]**. So with regard to possible effects of gelofen on various tissues of the body, especially the kidneys, the purpose of this study is to identify the appropriate antioxidants to reduce the effects of gelofen in the kidney tissue changes.

MATERIALS AND METHODS

This research was conducted in a completely randomized experiment. All ethic about working with laboratory animals comply with

ethical principles. 49 adult female Wistar rats weighing 200±5% gr and aged 100-120 days were obtained from research center of Jahrom city. Rats were placed at animals house of Islamic Azad university of Jahrom for 21 days in laboratory conditions including temperature of 21 ± 2 ° C and the cycle of 12 hours light and 12 hours dark. Standard food (pellete) was used for Rats. Also water was given to them by special Glass bottle. Cages were disinfected with 70% alcohol three times a week. Preparation and prescribing method of gelofen is as follow that this medication was purchased from pharmacy of Jahrom and it made by pharmaceutical company of Dana that was in 400 mg capsules, then the material in the capsule emptied and after dilution with distilled water, it was injected daily by insulin syringe and needle with doses of (400 mg/kg) to related rats groups intraperitoneally. To prepare the cinnamon extract 1 kg cinnamon stick were purchased from the market and then fine grinding and were completely powder. Soxhlet method was used for extraction, In this way, for every 10 grams of cinnamon powder, 200 ml of the solvent containing ethanol and water is added to it and then throw in a soxhlet machine, and finally the solvent removed from the extract by Rotavapor apparatus **[13]**. The rats were randomly divided into 7 groups of 7 that includes:

Control: In normal condition without any medication was maintained.

Sham: Daily 0/2 ml of distilled water as a solvent, was injected intraperitoneally.

Experimental 1: Daily 400 mg / kg of gelofen drug were given intraperitoneally.

Experimental 2: Daily 50 mg / kg of cinnamon extract were given intraperitoneally.

Experimental 3: Daily 200 mg / kg of cinnamon extract were given intraperitoneally.

Experimental 4: Daily 400 mg/kg of gelofen drug and 50 mg/kg of cinnamon extract were received intraperitoneally.

Experimental 5: Daily 400 mg/kg of gelofen drug and 200 mg/kg of cinnamon extract were received intraperitoneally.

After 21 days period, all groups of rats after weighing were anesthetized by ether and the kidney tissue was removed and for various tissue stages and preparing slides were sent to the laboratory. One-way ANOVA for comparison between treatments (ANOVA) followed by t-test and Duncan test was used for multiple comparisons between groups. ($P<0.05$) was significant level. Data analysis and statistical testing was performed using SPSS, version 18.

RESULTS

Cortex diameter in G100 and GCi 50 has significant decrease compared to the control group. Cortex diameter in GCi50 had significant reduction compared to the Ci50 and Ci200. Also in GCi 200 group significant increase in Cortex diameter was observed compared to the G100 group ($P<0.05$) **(Figure 1)**.

Medulla diameter in G100 group showed significant decrease compared to control group . Also the medulla diameter in Ci50 and Ci200 and GCI200 groups showed a significant increase compared to the G100 group . Distance curved pipe diameter in G100 and GCi 50 groups has significant decrease compared to the control group **(Figure 2)**.

Bowman's capsule diameter in the G100 group has significant decrease compared to the control group. Also Bowman's capsule diameter in Ci50 and Ci200 showed significant increase compared to experimental group G100 **(Figure 3)**.

Close curved pipe diameter showed significant decrease compared to the G100 group. Also in experimental group Gci200 significant increase was observed compared to control group. In experimental groups Ci50 and Ci200 showed significant increase compared to G100 group **(Figure 4)**. Distance Curved pipe diameter in G100 and Gci50 groups has significant decrease compared to control group. Distance Curved pipe diameter in Ci50 and Ci200 and Gci200 groups has significant increase compared to G100 group. In GCi50 group distance Curved pipe diameter showed significant decrease compared to Ci50 group **(Figure 5)**.

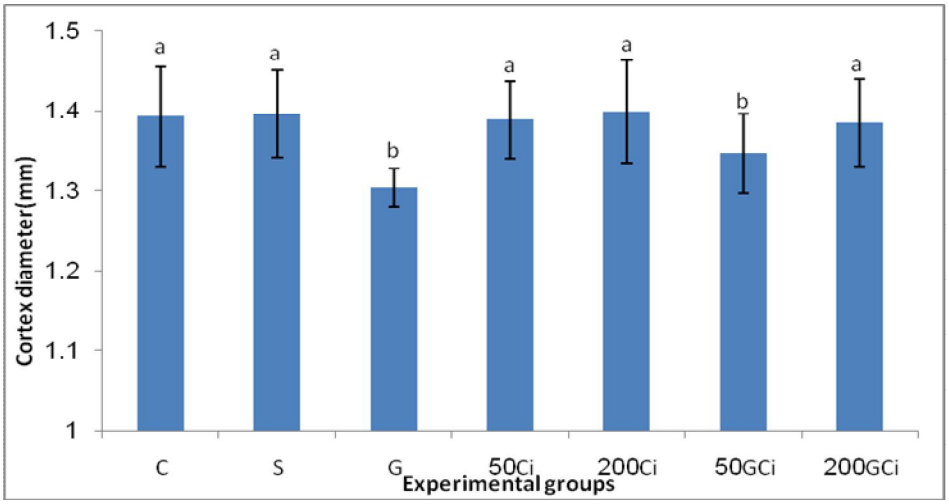

Figure 1: Effect of Cinnamon and Gelophenon cortex diameter. The Columns that Have at Least One Common Letter, Have Not Significant Different From Each Other at the Level of P<0.05

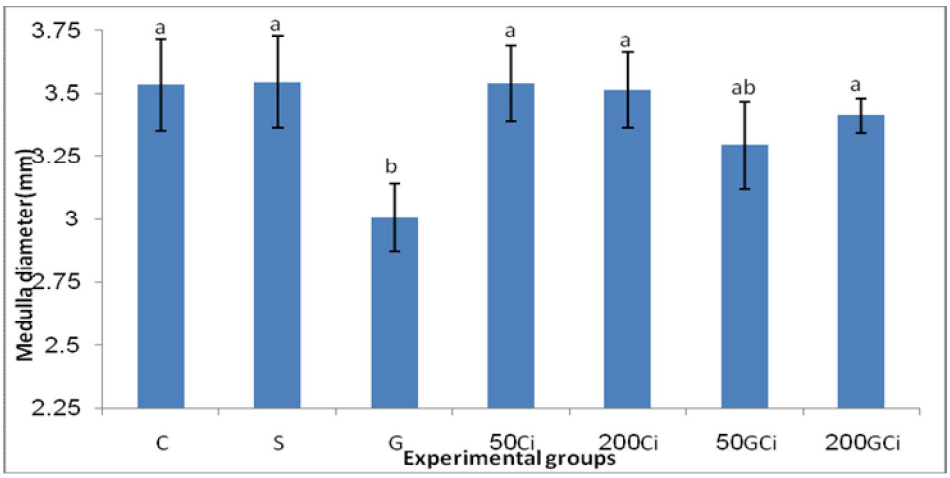

Figure 2: Effect of Cinnamon and Gelophenon Medulla Diameter. The Columns That Have at Least One Common Letter, Have Not Significant Different From Each Other at the Level of P<0.05

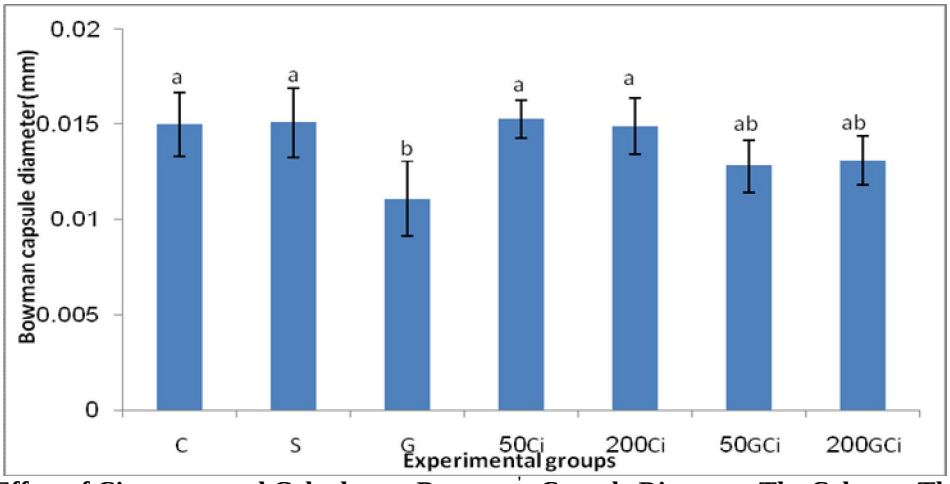

Figure 3: Effect of Cinnamon and Gelophenon Bowman's Capsule Diameter. The Columns That Have at Least One Common Letter, Have Not Significant Different From Each Other at the Level of P <0.05

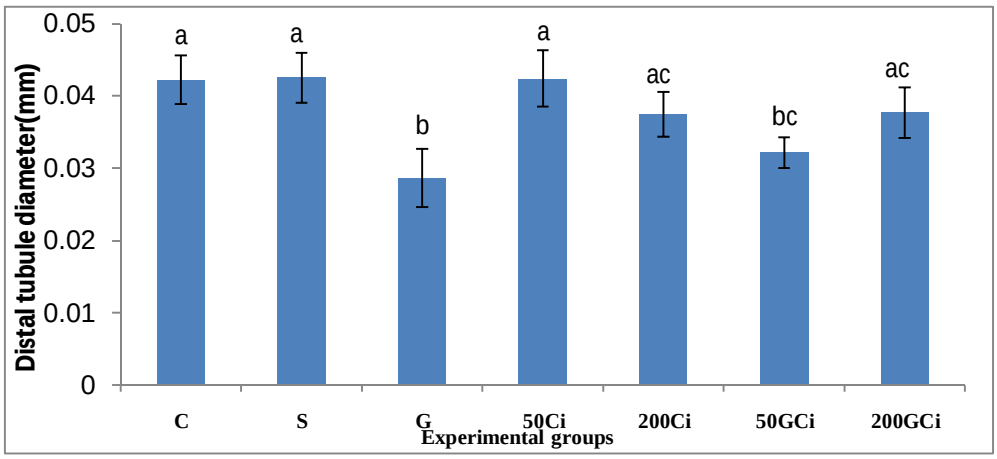

Figure 4: Effect of Cinnamon and Gelophenon Distal Tubule Diameter. The Columns That Have at Least One Common Letter, Have Not Significant Different From Each Other at the Level of P<0.05

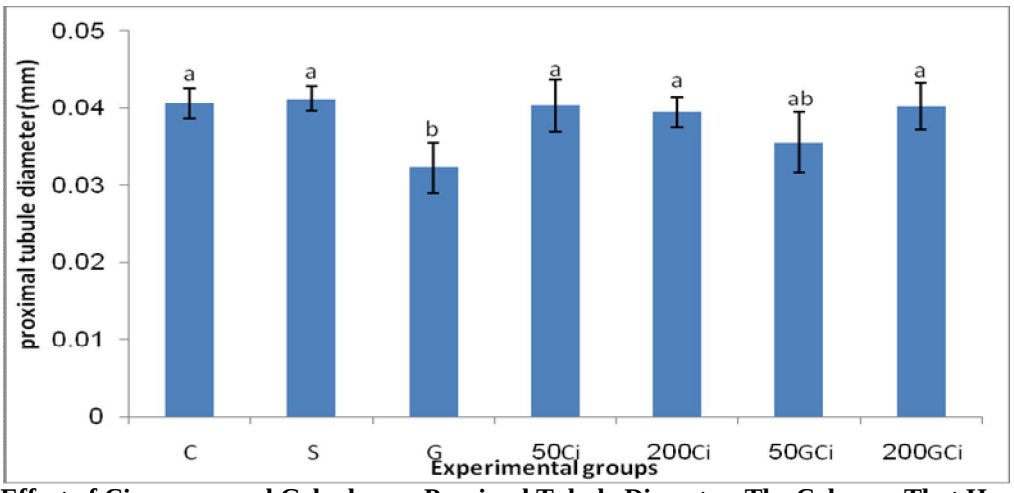

Figure 5: Effect of Cinnamon and Gelophenon Proximal Tubule Diameter. The Columns That Have at Least One Common Letter, Have Not Significant Different From Each Other at the level of P <0.05.

DISCUSSION

According to the above results indicated that gelofen causes abnormal tissue changes in different parts of the kidney. In Medical and veterinary, non-steroidal anti-inflammatory drugs used in many diseases as analgesics, antipyretic and anti-inflammatory **[14]**. Nonsteroidal anti-inflammatory drugs in different animal species have different effects **[16]**. Also the mechanism of action of these drugs is different. It is possible synthesis inhibits special groups of prostaglandins and Endo peroxides or may inhibit certain biochemical reactions. Therefore, before using these drugs in a particular species, it should be reviewed and evaluated **[15, 16]**. The review stated that nonsteroidal drugs can reduce renal collagen composition cells **[17].** It is likely that the collagen is used to reinforce the walls of the pipes and ducts, reducing this material causes tissue clutter. It also stated that nonsteroidal drugs can prevent the proliferation of mesenchymal cells **[19]**. That this function does through inhibition of AP-1 mechanism **[18]**. It also stated that non-steroidal drug with injection to kidney bilaterally causes production of hydroxyl radicals and tubular damage and use of this material can be effective in assessing and measuring impairment **[20]**. Another study stated that nonsteroidal drugs such as raloxifene act as modulators of estrogen receptor,for preventing Histological and functional changes in kidney of type 2 diabetes of rats has been investigated . The result suggests that raloxifene significantly reduces proliferation of Mzanzhyal cells and fibronectin accumulation in kidneys of diabetic rats **[6, 19]**. Thus it can be stated that the production of free radicals may also be

involved in causing the damage. As it is expressed use of medicinal plants has developed today. The study found that cinnamon contains amydon, mucilage, tannin, dye, calcium oxalate, glucose, Sinamumin, essence and resins . The physiological effect is due to essence and tannins **[21]**. It also stated that the main component of the cinnamon essence is cinnamaldehyde and essence of bark contains 55-57% dialdehydes and 5-18% eugenol , and reported that cinnamaldehyde is the cause of anti-spasmodic effects of cinnamon . Pharmacology and toxicology studies show that there is not a risk for cinnamon consumption in humans **[22]**. The investigation determined that the antioxidant property of cinnamon is due to eugenol, acetyl eugenol, Karunil, cineol and cinnamaldehyde. Many studies have shown the antioxidant effect of eugenol. Eugenol has non-toxic and protective properties and it facilitate exiting toxic materials from the intestines, and food consumption of eugenol causing lipid peroxidation and normal glutathione peroxidase activity , superoxide dismutase and catalase in rat intestine **[12]**. In another study stated that high levels of phenolic compounds and the potential inhibitory effect of free radicals in extract, leaves, fruit and cinnamon oils have been reported and this inhibitory activity of free radicals has been attributed to phenolic rings in the eugenol of cinnamon **[23]**. Thus, positive changes in renal tissue in this study in groups that consumed cinnamon have also confirmed this subject. In Ci50 and Ci200 groups that have received only cinnamon extract showed a significant increase in the diameter of Bowman's capsule, close curved pipe, distance curved pipe and medulla compared to the G100 has been observed. Also in GCi200 group, distance curved pipe diameter, close curved, cortex and medulla that have received the maximum dose of extract, significant increase have been showed compared to G100 group that received only gelofen.

CONCLUSION

According to the studies and the results of this study could be stated that gelofen by effecting on the diameter of Bowman's capsule, distance curved pipe and close curved pipe, cortex and medulla, as well as changes in sodium pump and changes in antioxidant systems, all cause harmful changes of renal tissue . Using antioxidant of Cinnamon improve status of renal tissue. Therefore cinnamon extract can be used to reduce the side effects of gelofen.

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