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The Effect of Hydro Alcoholic Cinnamon Extract on Changes of Gonadotropins (LH and FSH) in Mice Treated with Co-codamol

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ABSTRACT

Cinnamon with scientific name of Cinnamomum Zeylanicum Nees and common name of Cinnamon is aromatic and pleasant plant. The treatment plant has anti spasmodic, carminative, anti-diarrhea, anti-bacterial, anti-parasitic, and cooling effects. Due to the possible side effects of Co-codamol on the body and cinnamon benefits, the current study seeks to investigate the possible effects of cinnamon on Co-codamol complications. 42 female Wistar rats were randomly divided into 7 groups. The first group (control group) did not receive any medication. Experimental group 1 received a dose of 50 mg / kg cinnamon, experimental group 2 received, 200 mg / kg cinnamon, experimental group 3 received, 400 mg / kg Co-codamol alone, experimental groups 4 and 5; in addition Co-codamol medicine received 50 mg / kg and 400 mg / kg cinnamon intraperitoneally. At the end of 21 days, blood samples were prepared from the rats and the LH and FSH serum concentrations were measured by ELISA. The data is then tested by ANOVA (One-way analysis of variance) at a significance level ($P<0.05$) using SPSS software version 18. Experimental results show that the concentrations of LH in the experimental group received 50 mg/kg cinnamon has a significant increase compared to controls. Concentrations of FSH in the experimental group who received a dose of 50 mg/kg cinnamon have a significant increase compared to the control group ($P< 0.05$). : The results suggest that cinnamon extract in a dose-dependent manner with its antioxidant properties reduces the side effects of Co-codamol medicine on Gonadotropins hormones.

Key words: Cinnamon, Co-codamol, LH, FSH, rat.

INTRODUCTION

Chemicals are extensively updated; however, complications such as autoimmune phenomena and drug resistance caused by constant and indiscriminate self-medication as well as long-term use of drugs and in some cases, stopping use of drugs cause other side effects that can be more dangerous than the disease itself. Although today synthetic drugs have been developed due to the successful effects, synthesis problems, high cost and side effects has led researchers to study the side effects of these drugs on different parts of the body[1].

Co-codamol generic name is ibuprofen and is a nonsteroidal anti-inflammatory drug (NSAID) derivative of propionic acid used for relieving pain,

helping with fever and reducing inflammation[2] that is used in the treatment of the following: In the treatment of inflammatory diseases (such as rheumatoid arthritis and osteoarthritis), relief of mild to moderate pain, inflammation and pain control in dental surgery, bone surgery and obstetrics, as adjunctive therapy in the treatment of painful menstruation to reduce pain (2). Among the possible side effects of this drug can be dizziness, mild nausea, heartburn and headache. The red spots on skin, hives, itchy skin, black tarry stools, bloody urine, vomit, blood streaked, gums abnormal bleeding, unusual bruising, wheezing, shortness of breath, swelling of the legs or ankles, a rapid increase in body weight, confusion, seizures and coma are also dangerous side effects of this drug[3].

Previous studies indicate that flavonoids play an important role in the regulation of the hypothalamus - pituitary axis and gonad. The function of the ovaries and uterus is controlled by the hypothalamus - pituitary axis and gonad and their hormones[4,5]. Cinnamon with scientific name of Cinnamomum Zeylanicum Nees and common name of Cinnamon is aromatic and pleasant plant. The treatment plant has anti spasmodic, carminative, anti-diarrhea, anti-bacterial, anti-parasitic, and cooling effects. Also cinnamon is used for the treatment of anorexia, intestinal colic, diarrhea in children, colds, flu and especially for colic associated with bloating and digestive disorders with nausea[6].

Cinnamon bark contains more than 50 different compounds, with 80-60-80 % Cinnamaldehyde. Other ingredients include: Cinnamic acid, and phenolic compounds, such as Eugenol, Phellandrene and Safrole, Terpene compounds such as Limonene and Linalool, Trans Cinnamaldehyde, Tanin, Coumarin, Resins, and phenylpropan compounds such as hydroxy Cinnamaldehyde. Cinnamon sweet flavor is due to the Mannitol content[7,8]

In our country, there is a general trend towards the use of herbs to treat disease. This is of crucial importance regarding the sexual diseases due to the chronic nature of disease in which the long-term use of medications; adverse drug effects are more frequent. This study aimed to evaluate the antioxidant effect of cinnamon extract on the levels of LH and FSH under treatment by Co-codamol.

METHODS

This study is experimental and is completely random. All ethical principles in animals study are adhered to. 49 adult female Wistar rats weighing 200 ± 5% g aged 100-120 days were obtained from Jahrom Islamic Azad University, Center. Animals were kept in animal laboratory for 21 days in conditions include a temperature of 21°± 2 C and 12 hours light and 12 hours dark cycle. Rats fed with standard pellet and special glass water bottles. The cage is disinfected with 70% alcohol three times a week. The Co-codamol drug was prepared and administrated after being purchased from Jahrom pharmacy hostel produced by Dana pharmaceutical company in the 400 mg capsules, then capsules was evacuated and after dilution with distilled water, daily dose of (400 mg/ kg) was injected intraperitoneally using insulin syringe and needle to the rats. To prepare the cinnamon extract, 1 kg cinnamon stick was purchased from the market, then fine grinding and was completely powdered. Soxlet method of extraction was used, in this method, for every 10 grams of cinnamon powder, 200 cc solvent which includes water and ethanol is added, and then poured in soxhlet mixture, and in the end the solvent is separated from the extract using Rotavapor device[8]. The rats were randomly divided into 7 groups of 7, including:

Control	Was maintained at normal without any medication.
Experimental 1	Received daily dose of 50 mg / kg cinnamon extract intraperitoneally.
Experimental 2	Received daily dose of 200 mg / kg cinnamon extract intraperitoneally.
Experimental 3	Received daily dose of 400 mg / kg Co-codamol intraperitoneally.
Experimental 4	Received daily dose of 400 mg / kg Co-codamol and 50 mg / kg cinnamon hydro alcohol extract intraperitoneally.
Experimental 5	Received daily dose of 400 mg / kg Co-codamol and 200 mg / kg cinnamon hydro alcohol extract intraperitoneally.

After the 21 day period, all groups' rates were weighted and then anesthetized and the heart blood sample was collected by 5 ml syringe after separation of serum, FSH and LH concentrations were measured in the laboratory of Jahrom Medical Sciences University. ANOVA test was used for comparison between treatments and then followed by t-test and Duncan test for multiple comparisons between different groups. (P>0.05) was considered the significant level. Data analysis and statistical testing was performed using SPSS, version 18.

RESULTS

Results show that the concentrations of LH in the experimental group received daily dose of 50 mg / kg cinnamon extract has a significant increase compared to controls. Moreover, the experimental group received Co-codamol alone has a significant decrease compared to the experimental group received daily dose of 50 mg / kg cinnamon extract (P <0.05) (Figure 1). There are no significant differences regarding other experimental groups.

Results show that the concentrations of FSH in the experimental group received daily dose of 50 mg / kg cinnamon extract has a significant increase compared to controls. Moreover, the experimental group received daily dose of 200 mg / kg cinnamon extract has a significant increase compared to the experimental group received daily dose of 50 mg / kg cinnamon extract. The experimental group received Co-codamol alone has a significant decrease compared to the experimental group received daily dose of 50 mg / kg cinnamon extract (P <0.05) (Figure 2).

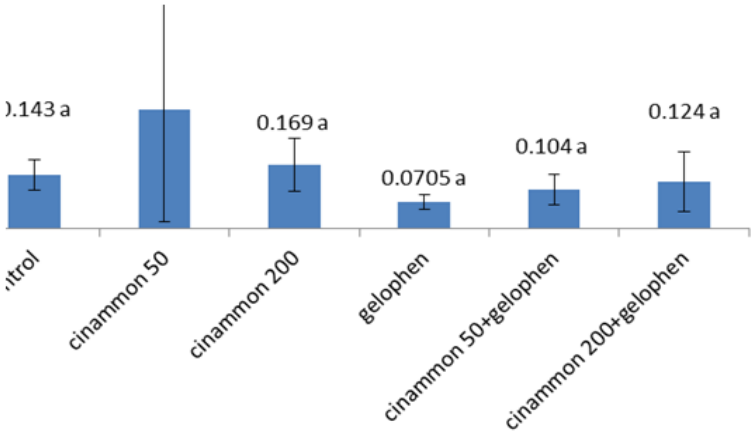

Fig. 1: Changes on LH hormone

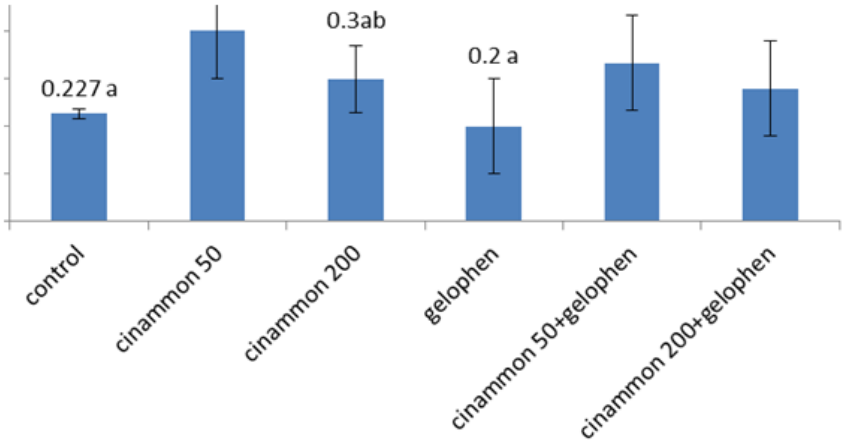

Fig. 2:

DISCUSSION

The results in the current study show that the experimental group received Co-codamol alone has a significant decrease in serum LH and FSH were compared to extract received groups. The investigation determined that the anti-inflammatory activity of this class of drugs takes place mainly through inhibition of prostaglandin biosynthesis. NSAID medicines through inhibition of cyclooxygenase enzymes prevent arachidonic acid conversion to intermediate prostaglandins and as a result prostaglandins cannot be synthesized. Mechanisms of NSAID may also have other effects, including inhibition of chemotaxis, negative regulation of interleukin-1 production and interfere with intracellular events mediated by calcium. Co-codamol (Ibuprofen) is one of the most frequent NSAID drug that is a simple derivative of phenyl propionic acid with a molecular weight of 28.206 [9].

we know that NSAIDs can prevent the proliferation of mesenchymal cells[10], that they act through inhibition of AP-1 mechanisms[11]. Also the drug injected bilaterally into the various tissues of the body stimulates the production of hydroxyl radicals and tissue damage, and use of this substance can be effective in measuring damage[12]. So it can be stated that production of free radicals may also be involved in causing damage to the pituitary-gonad and is possibly the cause of reduced gonadotropin hormones in the two groups received Co-codamol alone than the experimental group received a minimal dose of cinnamon.

On the other hand, in the current study cinnamon recipient groups showed a significant increase in serum gonadotropin hormone (LH, FSH), which indicates a positive effect compared to the group receiving Co-codamol.

Nitric Oxide is a free radical gas with a short-term effect occurred from L - arginine and it is considered the main mediator in many cardiovascular, reproductive, digestive and immune system functions[13]. According to various studies, the ovaries are able to synthesize nitric oxide[14]. Probably this matter involves in ovarian steroidogenesis, ovulation and corpus luteum loss[15, 14]. Nitric oxide ISO maker enzymes are active in different parts of the ovary in which the activity is controlled by gonadotropins[16]. Nitric oxide in the ovaries takes effect of gonadotropin, but it affects them in hypothalamus[17]. Place of nitric oxide-producing neurons is in close proximity to GnRH neurons in the hypothalamus[16]. Nitric oxide also appears to affect ovarian artery[18] with this interpretation, the increased nitric oxide, increases the LH secretion rate and nitric oxide effect of on pituitary causes the release of LH, which is consistent with the present study. So cinnamon increases levels of LH and FSH. However, in the present study using Co-codamol reduces hormones and the concurrent use of extract and drug improves the effectiveness indicative of the positive effects of the extract.

Another study stated that the use cinnamon increases levels of LH and FSH due the active ingredients in cinnamon, it also stimulates the pituitary, resulting in increased secretion of follicle stimulating hormone and luteinizing stimulus[19, 20]. Mehrani et al also stated that the Deltacadin in cinnamon leads to increased LH secretion[21] which is consistent with the present study.

CONCLUSIONS

According to the above it can be stated that the cinnamon extract with antioxidant properties and is especially effective material such as Cinnamaldehyde, Tanin and etc. and effect on nitric oxide release and changes in the pituitary-gonadal axis prevented Co-codamol side effects that may produce harmful reactive oxygen species and inhibition of cyclooxygenase enzyme in rat. Therefore, cinnamon extract is recommended to reduce the effects of Co-codamol intake on gonadotropines.

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