

Full length Research Paper

Evaluation of the ability of ginger to treat the adverse effects of tetracycline drug in the liver of albino rats' embryos in the second trimester of pregnancy

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Abstract

This research aims to study the effect of drug tetracycline and ginger as well as study the ability of ginger to treat the adverse effects of drug tetracycline on liver embryos during the second period of pregnancy. Therefore, pregnant female rats were divide into four groups, (G1): control group, (G2) was treated with a drug tetracycline during the second week of pregnancy with a dose of 0.7mg \ kg, (G3) was treated with a dose similar to ginger syrup during the second week of pregnancy, and (G4) was treated with tetracycline drug and ginger syrup together in the same period. The results revealed that, a severe shortage and significant loss in liver weight and total weight of the embryos' body in all treatment groups with lesser decrease in (G3), in addition, vascular disorders with acute inflammation and large number of Kupffer's cells were observed in histological examination of liver embryos at the age of 20 days in the group (G2). In ultra structure examination of the liver, degradation in the cytoplasm of hepatocytes was observed. Group (G3), however, was much better and Moreover, the ultra structure examining of the liver showed that most of the cellular organelles are in good positions. In Group (G4) a decline in the severity of vascular disorders and limited number of Kupffer's cells were noticed. The ultra structure of the liver, clarified cytoplasmic degradation in cells and acute changes in hepatic fats. We conclude that ginger is safe to embryo liver and has a limited capacity in the treatment of the effects of tetracycline drug. Therefore, we recommend pregnant women keep away from antibiotics during the period of organization so as not to cause delay or disrupt embryo growth. Ginger is to be used with the antibiotic and not alone during pregnancy.

Keywords: Tetracycline, ginger, embryo and rat.

INTRODUCTION

• Tetracycline drug

Tetracycline is an antibiotic drug. (Bokor and Brkanić 2000) reported different forms of tetracycline. Older group of tetracycline has appeared in the fifties and sixties and include tetracycline and Oxtetracycline and chlortetracycline and Demecloxytetracycline while the latest group of tetracyclines include doxycycline, minocycline and methatetracycline. Tetracycline was recommended

by Centers for Disease Control and Prevention (2001) as a good option for children and pregnant women and as a preventative treatment against microbes and treatment of skin diseases. Because many of pregnant women are susceptible to microbe's infection, that is difficult to treat, such as Chlamydia, which need tetracycline to eliminate it. Ferjani *et al.*, (2006) recorded that group B of Streptococcal Bacteria is one of the most common types of bacteria that cause various infections in newborns. To investigate this, the researcher infected 300 pregnant women with a group B of vaginal and anal Streptococcal Bacteria, 10% of them in the second trimester and 17% in the third trimester, tetracycline, erythromycin and lincomycin were used for healing. Rise in the rate of

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resistance by 97.4% was found when using tetracycline, while that percentage is different when using other antibiotics (51.3%: erythromycin; 46.3%: lincomycin) with no transmission of infection to newborns.

• Ginger

Fresh and dry ginger are widely used in the medical field under several names and is used to treat vomiting, inflammation, fever, stomach ulcers, an antioxidant and lowers cholesterol, blood pressure (Sanjay *et al.* 2004). Moreover, Nordeng and Havnen (2004) reported that, 36% of pregnant women resort to the use of herbal extracts such as extract of ginger during pregnancy and lactation without medical advice and without prior knowledge of side effects. Nausea is one of the painful symptoms associated with pregnancy in more than 85% of women during early pregnancy, and since the anti-vomiting traditional exposed fetuses to the risk of deformation potential during the critical stage of early pregnancy, the women prefer to take a natural substance or herbal antidote for nausea and vomiting (Woolhouse 2006). (Forster *et al.* 2006) stressed that the data on the extent of use by women of herbs during pregnancy is still limited despite the fact that knowledge of the benefit or harm many of these products is limited, especially in pregnancy, and the objective of the study to know the extent of use of Herbal Medicine in pregnant women and find out why eating these herbs. In his study were given herbal supplements for pregnant women in the 36-38 week of pregnancy, where that 36% of women took at least one herbal supplement during pregnancy. Concluded that the use of herbal supplements in pregnancy is relatively high, so it is important to verify whether the supplements taken by pregnant women safe and has no damage. In the study conducted by (Khalifa 2006) using urine and milk of camel, ginger and mix of honey with black bean to stop the toxic of anti-depressants (haloperidol drug) on the histology of the testes of male rats, the results showed a significant improvement in pathological changes to the tissue of the testis caused by the toxicity of the drug, confirming the possibility of using urine and milk mixture, ginger, honey and black seed in alleviating the side effects resulting from the toxicity of the drug. (Suekawa *et al.* 1984) said that the components of ginger that are likely to be responsible for its activities are Gingerols and Shogaols. These compounds work to lower blood sugar, stimulate the vagus nerve, reduce the rate of cholesterol, inhibition of synthesis prostaglandin and platelet aggregation. And causing the anti-nausea properties of ginger by their ability to stop the contraction of the stomach and increase the natural movement of the intestines. Ginger root also contains 50% of the carbohydrate, 9% proteins and 6-8% amino acids and triglycerides (Leung 1984).

MATERIALS AND METHODS

In this study, 80 pregnant rats weighing between 180-200 g are taken at the beginning of pregnancy and then divided into four groups, G1: a control group which does not treated with any kind of drugs, G2: this group was treated with tetracycline drug during the second week of pregnancy (from day 7 - day to 14) (Slonitkaia and Mikhailets 1975) and using the amount of therapeutic dose 0.7mg \ kg, which is equal to the therapeutic dose in humans (Goodman and Gilman 2001), G3: this group was treated with ginger syrup during the second week of pregnancy at a dose equal to the therapeutic dose of the tetracycline drug, G4: this group was treated with both of tetracycline drug and ginger syrup at the same period. After the end of treatment pregnant females were left until the end of pregnancy period and autopsy at day 20 of pregnancy and extraction of embryos and determine the body and liver weight of embryos Results were then statistically analyzed by One Way ANOVA method in SPSS program version 11. Liver tissue was examined by the light and electronic microscope.

RESULTS AND DISCUSSION

Statistical results

Body weight

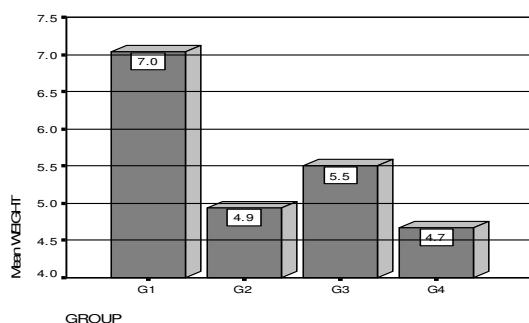
The result of body weight was shown in Table (1) and Histogram (1). A significant decrease in the average body weight of fetuses in each treatment groups (G2, G3, G4) compared with the control group (G1), but the average weight in the group treated with ginger syrup (G3) is higher than the two other groups. Weight loss may be due to the period of treatment which represents phase of organization in the embryo, This is in agreement with (Cohlan *et al.* 1963), indicating that tetracycline affects the weight of embryos and explained the effect of tetracycline drug on the bones, where they noted that the deposition of tetracycline hydrochloride in the bones of rat fetuses cause weight loss. And also agrees with us (Goyal and Kadnur 2006) in that the treatment with ginger lead to a decrease in body weight, high glucose, insulin and fat level.

Liver weight

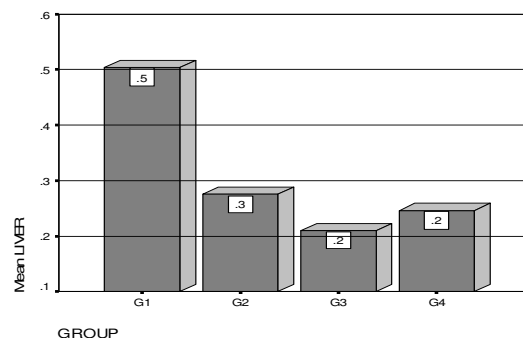
Results in Table (a) and Histogram (2), convergence of data in the average liver weight of embryos in each treatment groups and the results showed a significant decrease in the average liver weight in the treatment groups (G2, G3, G4) compared with the control group (G1). (Olin *et al.*, 1995) Have been interpreted effect of

Table 1. shows weight of body and liver in the embryo at the age of 20 days of pregnancy in the treatment and control groups

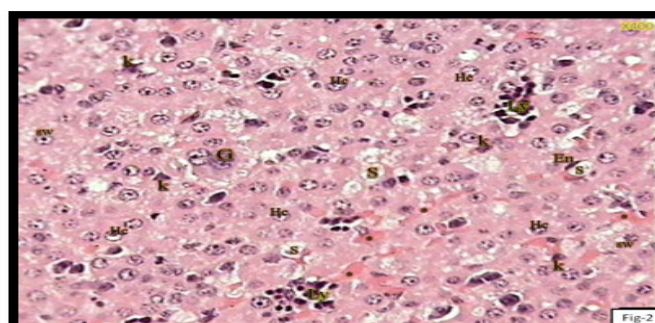
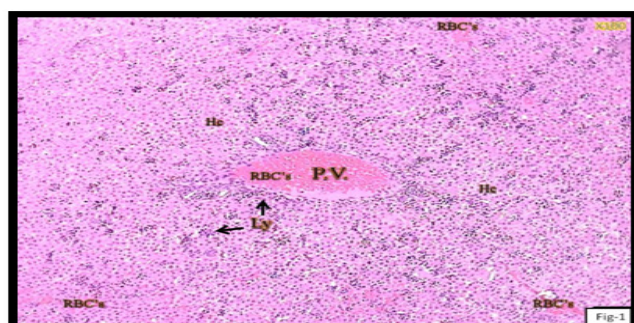
Groups	body weights	liver weights
G1	7.03±0.13	0.504±0.00
G2	4.93±0.23*	0.275±0.00*
G3	5.50 ±0.06*	0.210±0.00*
G4	4.67 ±0.12*	0.246±0.01*



Histogram 1



Histogram 2



antibiotics occur as malfunctioning in the cells because they play a role in stopping the synthesis of DNA and RNA, leading to delay or stop the process of cell division, that leads to the loss of organs weight such as liver.

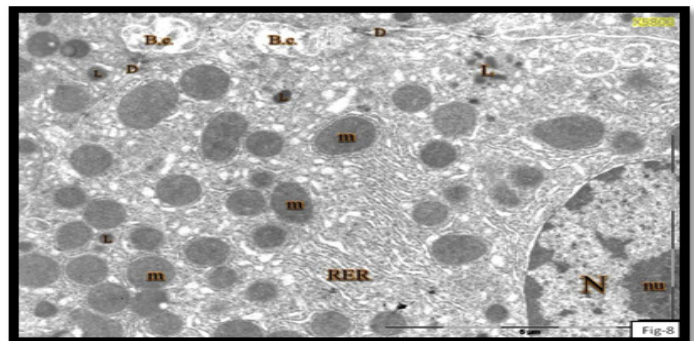
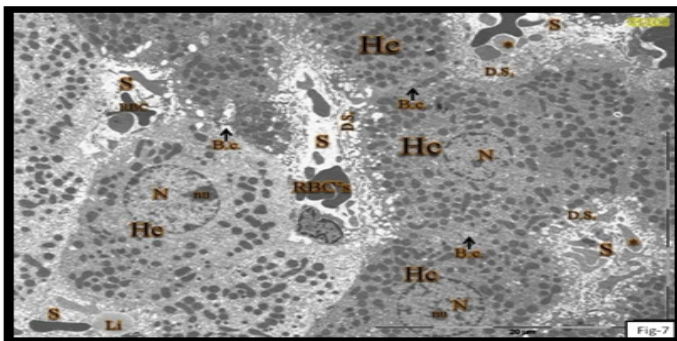
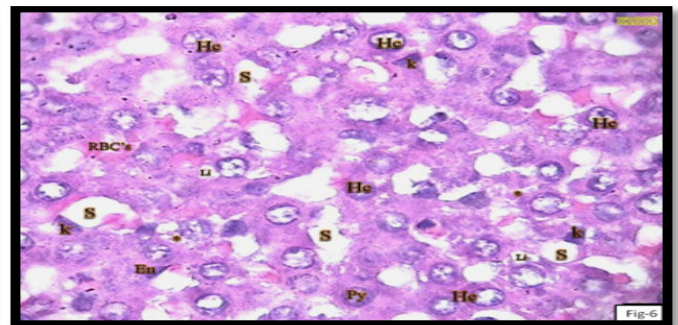
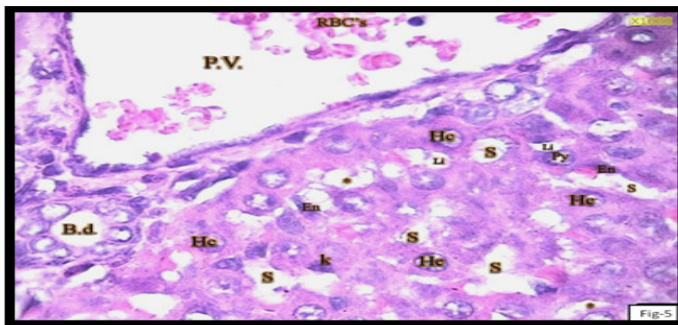
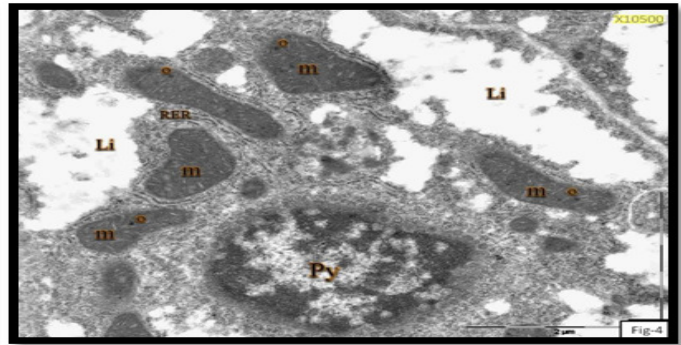
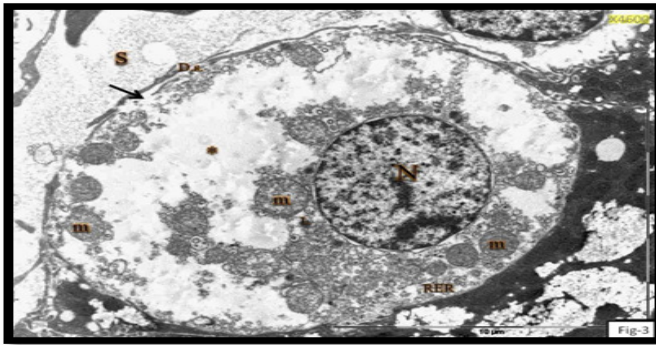
Histological and Ultra structural Results of the liver

Histological examination of the fetal liver at the age of 20 days of gestation in the group G2, showed circulatory disturbance in the form of expansion and blood congestion in the portal vein (P.V.) as well as congestion of blood in the sinusoids (S) with an acute inflammation around the portal vein and focal inflammation in the sinusoids (S) (figure 1). In addition to the appearance of giant cells and Ito cells (I). Expansion of some sinusoids as a result of fatty infiltration (Li) was observed together with a swelling in some hepatocytes, there were drops of

varying sizes of the fat in the cytoplasm of other hepatocytes with the occurrence of pyknotic (Py) in some of them. The large number of Kupfer's cells (k) was also observed (Figure 2).

The ultra structure of the liver of embryos in group G2, revealed some of swollen hepatocytes, lack of numbers of cellular organelles, mitochondrial swelling and fragmentation of rough endoplasmic reticulum. Concerning the results of nuclei, there is different kinds of damages; some of them appeared pyknotic or karyolysis in some hepatocytes and irregular nuclear membrane. A large fat drops with high electronic density was recorded (Figure 3 and Figure 4).

So, tetracycline drug caused a variety of histopathological changes in the liver of embryos in the two groups G2 and G4. These results have coincided with (Machado et al. 2003) study, in the presence of liver damage in modern newborns in the groups treated with tetracycline on the

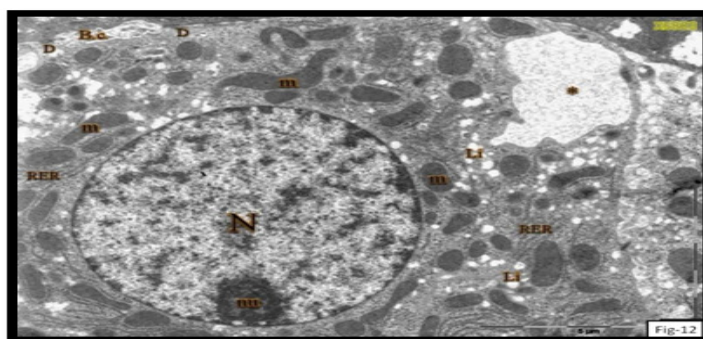
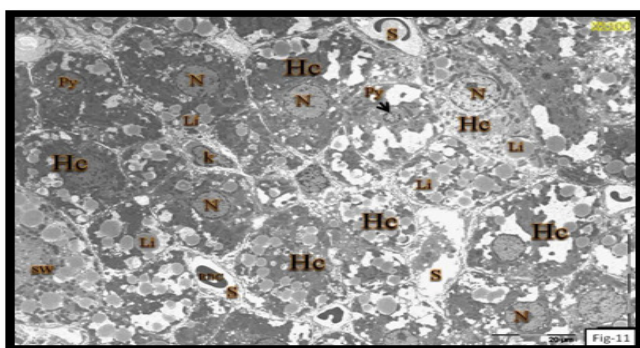
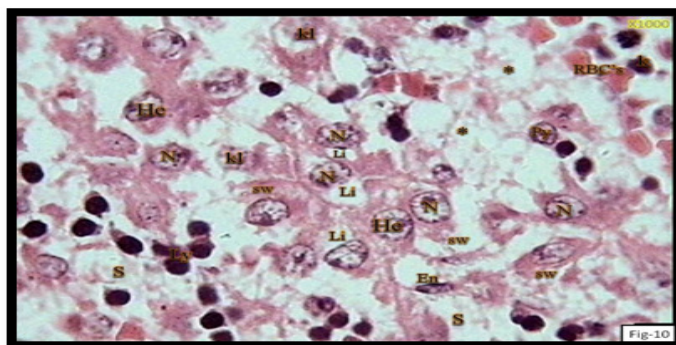
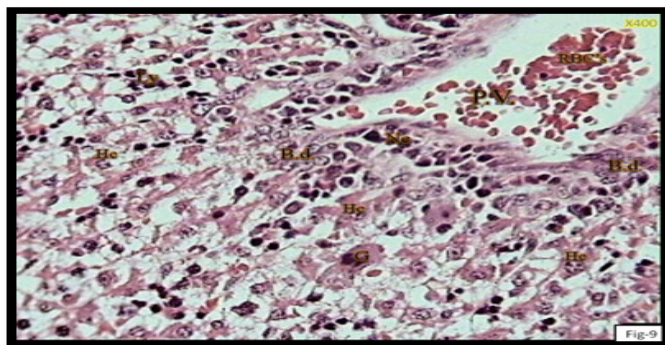


tenth day of pregnancy such as vesicles in the hepatocytes, expansion of the sinuses, focal necrosis and inflammation. (Silva and Rocha 1995) agree with them, where vesicles appeared small, medium and large-sized in hepatocytes of embryos treated with small doses of tetracycline during mid-pregnancy. (Curran. 1996) said that the cellular infiltration of lymphocytes and macrophages is one of the signs of chronic inflammation, where macrophages taking up pathogens and damaged tissues while lymphocytes produce anti-toxins and speed up repairs of the cell. The results of (Awodele *et al.* 2010) search showed that Rifampicin antibiotic cause tissue damage in the liver.

Results of the histological examination of liver fetuses at the age of 20 days of gestation in the group G3, indicated that, the portal vein (P.V) has well structure and

most of the hepatocytes seem in good structure (Figure 5) with fatty changes (Li) in some hepatocytes (Hc) and pyknosis (Py) and there are cytoplasmic hydrolysis in hepatocytes in limited areas, and large numbers of Kupffer's cells (k) was noticed (Figure 6).

On the other hand ultra structural examination of hepatocyte showed that most of them have circular nuclei (N), and a regular envelope nuclear while there were some nuclei with irregular nuclear envelope. Rough endoplasmic reticulum (RER) is spread in the cytoplasm and smooth endoplasmic reticulum (SER) appear in the form of membrane-free ribosome. The occurrence of the mitochondria (m) is moderately to appear as circular and oval shape. In some hepatocytes a large number of lysosomes (L) spread in the cytoplasm was recorded (Figure 7 and Figure 8).



In the group G4, we found that tissue susceptibility to pigmentation and indicate a decline in the severity of circulatory disturbance with infiltration of neutrophil (Ne) and lymphocytes (Ly) around the portal vein (PV) (Figure 9). And the emergence of acute fatty changes, pyknosis (Py) or karyolysis (kl) in some hepatocytes (Hc) and appearance of giant cells (G) in a limited way. There was also a swelling (sw) in some hepatocytes. Appeared severe focal analyze in hepatic tissue led to expansion of sinuses (S) and the lack of presence Kupffer's cells (k) (figure10).

When examining the ultra structure of hepatocytes in this group we have seen appearance most of the hepatocytes (Hc) in different forms and have circular nuclei (N) lost the central situation in most cells. The nucleons (nu) appear either central or non-central position. It is noted the cytoplasmic hydrolysis in hepatocytes (Hc) and acute fatty changes and the presence of rough endoplasmic reticulum (RER) with appropriate content of ribosome and surrounding mitochondria (m) (figure 11 and figure 12).

The effect of ginger on the liver of embryos is well in the group G3, and had a protective effect on harmful effect of tetracycline drug on the liver in the group G4. We have supported by (Al-Zubairi et al., 2010) who reported that ginger has shown anti-cancer and anti-apoptosis properties. (McMahon and Pergament 2001) said they did not notice any side effects to the mother and fetus when using ginger during pregnancy. And

(Nammi et al., 2010) said that the ginger plant leads to lower levels of triglycerides and cholesterol in the liver of rats fed fat-rich meal. This is due to the contents of ginger anti-inflammatory and anti-oxidant.

CONCLUSION

From the present study, we can conclude that tetracycline drug and ginger are capable of penetrating the placental barrier and that tetracycline drug has adverse effects on the liver tissue and body weight in fetuses in the second period of pregnancy. Ginger has some capacity to treat these effects, so we recommend that pregnant women do not use antibiotics, especially tetracycline, except in when strictly necessary and with an option the use of ginger as a treatment companion to the antibiotic to reduce its effects.

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