The Curial Effect of Vinegar in Reducing the Serious Damages of Lead on the Histological Structure of Some Organs of Embryos and Mature Female Albino Mice

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Abstract: This research aims to study the effectiveness of apple cider vinegar to reduce the harmful impact of lead achieve this female adult mice were divided into three groups and given the first group lead acetate, while the second group was given lead and vineger, the third control group was also treated in the same way. Examined infants of (7-14-21 days). And demonstrated by histological examination over the harmful effects of lead on spleentissue and thymus in embryos. Sharp in all components of the tissue with low density of lymphocytes. The appearance of hemorrhage tissue. Proliferation in epithelial vertical glands of the uterus was observed. Also an imbalance in the number of uteringlands, lead has a devastating impact on the fabric of the ovary. This led to the lack of mature vesicles, with the appearance of hemorrhage and fibrosis in the tissue. The absence of corpus luteum while the addition of vinegar to lead led to improved tissue. In neonatal or maternal tissues and the return to almost normal structure.

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1. Introduction

Roiha., (1974) mentioned that an addition of 50 g of vinegar mixed with drinking water of pregnant cow twice daily led to delivering of normal calf with normal weight, heavy hair and strong legs enable them to stand just after their delivery by five minutes. Vinegar was also used to elevate their sexual ability. It is well known that toxic effects of a xenobiotic can be modified by other substances (Skoczyńska and Smolik, 1994; Brus *et al*., 1999; Institoris *et al*., 1999; Gupta and Gill, 2000). As simultaneous exposure to two or more xenobiotics can take place in the environment and/or under occupational conditions, the investigation of interactions between toxic substances is an important problem in modern toxicology. The interaction between lead can be a good example. Exposure of certain human populations to lead is often rather high (World Health Organization, 1992; Schrey*et al*., 2000) consumption continues to rise worldwide (Samson and Harris, 1992; Meyer *et al*., 2000); Some publications provide data on lead -vinger interactions (Sharma *et al*., 1991, 1992; Brus *et al*., 1995) but many aspects are still not fully recognized. According to our earlier results short- and long-term vinger administration affects lead turnover in rats, and also modifies changes in the metabolism of some essential elements by this heavy metal, (Moniuszko-Jakoniuk *et al*., 1999, 2001; Brzóska *et al*., 2000, 2002). As the uterus is an important target organ of viger (Bunout, 1999; Thurman *et al*., 1999), and the ovary of lead toxicity (Kjellström, 1986; World Health Organization, 1992; Nordberg *et al*., 1994) we have also assessed spleen, ovary and uterus histology.

Honsho *et al*., (2005) suggest that previously described hypotensive action of the beverage may be induced by the inhibition of angiotensin – converting enzyme, Fushimi and Sato (2005) conclude that a diet containing acetic acid may enhance glycogen repletion but not induce super compensation, a large increase in the glycogen level that is beneficial in improving performance ,in liver and skeletal muscle by transitory inhibition of glycolysis. Further, they indicate the possibility of transient enhancement of fatty acid oxidation in liver by acetic acid, Wang *et al*., (2006) conclude that ethyl acetate can decrease the level of serum markers of hepatic fibrosis and the expression of TGF-beta 1, Fushimi *et al*., (2006)examined the effect of dietary acetic acid the main component of vinegar for prevent hyperlipidaemia in rats and they found that dietary acetic acid reduced serum total cholesterol and triacylglycerol: first due to the inhibition of lipogenesis in liver; second due to the increment in faecal bile acid excretion in rats fed a diet containing cholesterol, Zardi et al., (2007) result show that mortality in the acetic acid -treated group was greater than in ethanol- treated group presumably due to greater acetic acid systemic diffusion and its metabolic side effect and this could be the reason why some human studies have concluded similar or even better safety and efficacy with PAI compared to PEI, Panovska et al., (2007) histomorphological. So this study substantiates the potential activity of the acetate extract lead induced spleen damage. Moon and Cha, (2008) suggest that supplementation of persimmon-

vinegar prevents metabolic disorders induced by chronic administration of alcohol. Luster et al., (1978) suggest that the T-lymphocyte rather than the B-lymphocyte is affected by lead exposure, Klein & Koch (1981) found that lead accumulated in the hepatic tissue of infants after 11-20 days of delivery. Overmann *et al* .,(1981)found that wet weight of spleen and thymus were not altered at any post natal lead treatment, Regarding lead, researches indicated that the embryo exposed to significant level of heavy metals via the blood of mother and through placenta. The lactating embryo was also affected when mother exposed to these metals during lactation. Corpas *et al.,* (2002) added that exposed mothers during gestation and lactation to the lead toxicity led to changes in the hepatic architecture in the newly born and lactating infants .Hsu and Guo (2002) suggest that lead exposure causes generation of reactive oxygen species and alteration of antioxidant defense ,the mechanisms for lead include the effect of lead on membrane, DNA, and antioxidant defense system of cells, while Death et al., (2002) suggest that the action of lead in decreasing circulating growth factor-1 contributes to the delayed puberty, the detrimental effect occurred regardless of the developmental time of exposure, although gestational exposure appeared more sensitive to the effect of lead ,the study of Gorbel et al., (2002) shows that chronic exposure to lead causes a double sexual disorder in rats: first , disorder deals with the hormonal function ,which is affected at the early stages of poisoning ,but is rapidly corrected ;second, disorder deals with the genital tract ,affecting the testis and ovary, resulting in a reduced fertility in females, in spite of presence of a normal oestrus. **Peixoto *et al* (2004)** also mentioned that exposing to heavy metals as lead caused toxicity and the level of toxicity depended on the stage of formation and the treated tissue, where the younger rats were more sensitive to the heavy metals exposure than mature ones. **ZhuZw *et al* (2005)** found the lead level of blood of infants of 14 days age was lower than that of infants of 7 days age and declared that this change depended on both the concentration and duration of exposure**. Pillet et al., (2005)** conclude that neonatal exposures to cadmium through maternal milk lead to both transitory and persistent immunotoxic effect, Nampoothiri and Gupta (2006) demonstrated that lead and cadmium are known reproductive toxicants,which accumulate in granulose cells of the ovary**, Karaca and Simsek (2007) Jihen et. al., (2011),** results indicate that lead induced increase mast cells in the ovary during the oestrous cycle of rats .

2. Materials and Methods:

Mature female mice were divided into three groups: the first group is the control group, the second group was provided with a daily dose of 0.5 ml/kg of lead acetate for a month and the third group was provided with a daily dose of lead with equivalent dose of apple vinegar **(Roiha, 1974**). Female mice, during lactation were divided into three groups from the first day of delivery to the 21st day. The first group was provided with distilled water and this is the control group. the second group was provided with a daily dose of 0.5 ml/kg of lead acetate for a month. The third group was provided with equivalent dose of apple vinegar. Female mice were dissected and specimens of the uterus and ovary were taken. Specimens of spleen and lymphatic gland were taken from dissected embryos. All organ specimens were fixed in neutral formalin 10% and the standard procedure of dehydration and clearing in xylol was followed. Specimens were sectioned and stained by eosin and heamtoxyline.

3. Results:

Lymphatic gland

At newly born age, the gland composed of the cortex only without the formation of the lobe or the lobules. It surrounded by a capsule of fiberous tissue with small lymphatic cells spreaded throughout the cortex. It was also observed that the lymphocytes number was low and presence of decaying in the lymphatic tissue (fig 1).

At two weeks after delivery, It was observed the beginning of the lobules formation but they were not complete. Despite the increasing size of the gland, the lymphocytes number was reduced. Odeama and decaying in the lymphatic tissue were also observed and the lobe did not obviously formed at this age.While,

the complete structure of the gland could be nearly recognized at this age with lobulation and differentiation of the gland to the cortex containing the lymphocytes and lobe containing lymphocytes, reticularocytes and Hasal bodies, these bodies were aggregation of flattened cells. Hasal bodies and lymphocytes were less in number especially in the cortex with decaying regions in the tissue.

2-The histological investigation of the reproductive system of treated females

A -Uterus:

Secretory columnar epithelium were proliferated that caused structural disturbance in the uterine gland. This proliferation also led to a disorder in the nuclei position shifting them away from the basement membrane and pressing of cells due to the increasing in their number. There were not disordering in the number of the uterine gland despite presence of loosen lining cells and some of these cells were observed with decayed nuclei. It was also observed that arteries were convoluted in the deep layers of the uterus lining,

while the uterus stroma was composed of fiberous connective tissues. The reticular connective tissues was less dense than that of the control group. The basal layer of the uterus was represented by muscular layer; circular and longitudinal smooth muscles separated by fine barriers of connective tissue. It could be recognized that the size of the muscular layer was reduced with expanded blood vessels and filled with blood corpuscles(fig2).

Ovary:

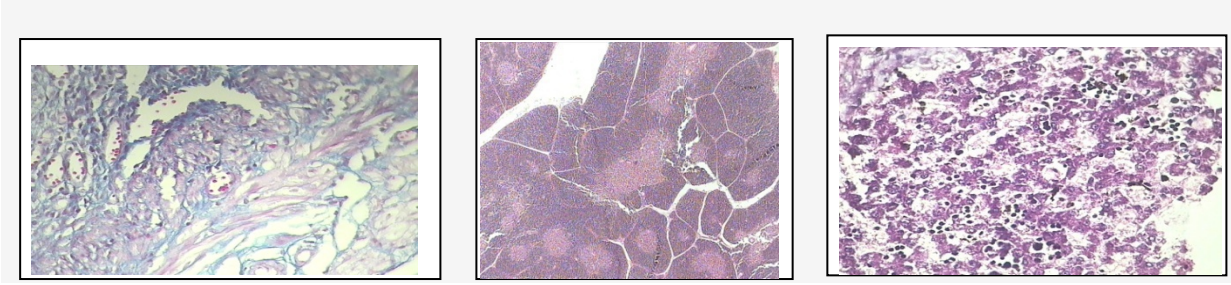
Number, decayed ova in the follicles, smaller outer wall of the follicles due to reduction in the follicular cells and presence of spaces between them with appearing some of them as compact cellular masses. A limited occurrence of primary and secondary follicles was recognized. Also spaces between follicular cells were observed indicating their decaying with decayed ovum in some due to disappearing of the radiating regions that formed by cells and supplied ovum with nutrients. Therefore, there was not any nutrient supply to the ova causing ova decaying, odeama and fibrosis of the tissue. Also the corpus luteum did not appear indicating absence of ovulation. The drug also caused a severe decrease in the ovary stroma and obvious fibrosis in all regions of the tissue.

It was observed that the ovarian columnar secretory cells and the uterine glands resumed their normal structure in the treated group. The muscular layer separated by fine barriers of reticular connective tissue. The rate of blood corpuscles filtration decreased in the blood vessels. For ovary, where all follicles stages, primary, secondary and mature were observed with ova surrounded by discus proligerus and the corpus luteum was appeared in different stages. The ovary stroma resumed its normal size and structure (fig3).

Spleen

In newly born the histological investigation showed a severe decaying in all components of the tissue including veins and arteries with their lining cells. A serious decaying in the strands of the spleen, sinusoids and nodules was also observed with little presence of lymphatic cells and disappearing of the main barriers of the connective tissue. This led to a decreasing in the number of the veins and arteries and undifferentiation of white and red lobes due to the spreeding of the lymphatic cells in the whole tissue despite of their reducing number.

In one week born infant it was observed that the spleen strands decayed seriously in some regions and disarranged in others with reducing number of lymphatic cells . The white lobe was obvious while the red one was pale stained indicating less spreading of lymphatic cells and accumulation of fats between cells with more density in the white lobe. It was also observed that arteries and veins were enlarged and expanded with blood stasis in some regions and their rupture and decaying in others. Phagocytotic, mononucleated and polynucleated cells were obviously observed while the germinal center was not clear in the splenic nodules while it would be recognized clearly in the control group. In two week individuals, section lost its ability for staining with the continuity of the disassociation and decaying of the spleenic strands. This changes led to widening of the spleenic sinusoids with rupture of the rectangular lining cells and less number of lymphatic cells especially the darker ones and absence of the lymphatic nodules. Spleen was obviously composed of the red lobe indicating the increase in the number of the lymphatic cells B and decrease in the number of T-cells. It was also observed that there was an odeama in the tissue, enlarged arteries and veins, proliferation of phagocytic cells and polymorphic nuclear cells. These histological changes were continued till the weaning age, three weeks (fig4).



A **B** **C**

Fig. (1): Optical micrograph of the sector in the rat lymphatic gland at the age of three weeks after birth to mothers in the group shot and the vinegar treatment for the duration of breastfeeding (0-21) describes the approach to the installation of natural fabric ((40 ×-H α E E), A-normal B- lead+ vinegar C- lead.

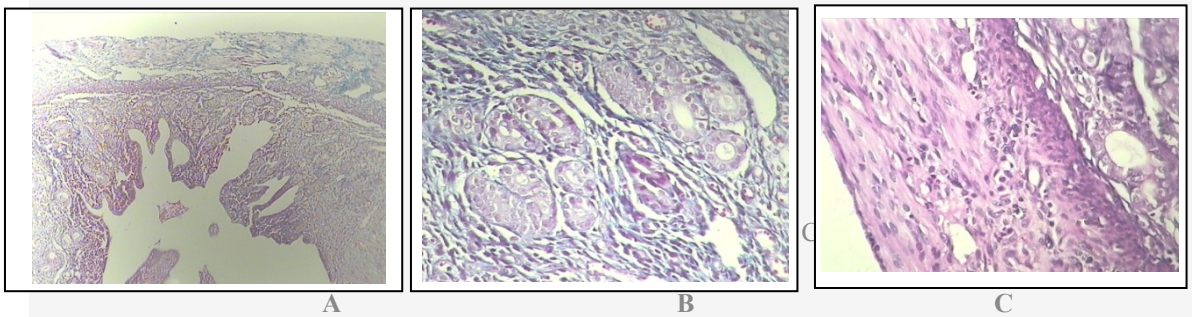


Fig. (2): Optical micrograph of the sector in the uterus of female mouse in the group shot and the vinegar treatment describes the regularity of epithelial secretory glands and increase the thickness of the uterine muscle layer (10 ×-H α E) A-normal B- lead+ vinegar C- lead. A-normal B- lead+ vinegar C- lead.

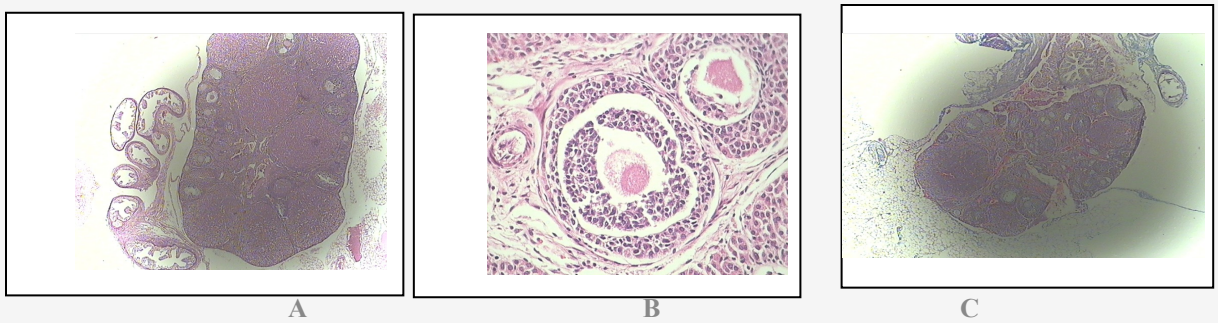


Fig. (3): Optical micrograph of the sector in the female mouse ovary in the treatment group shot shows disruption of installation are: mature follicles (A) and developing B)) and the corpus luteum ((C(10×-H α) A-normal B- lead+ vinegar C- lead.

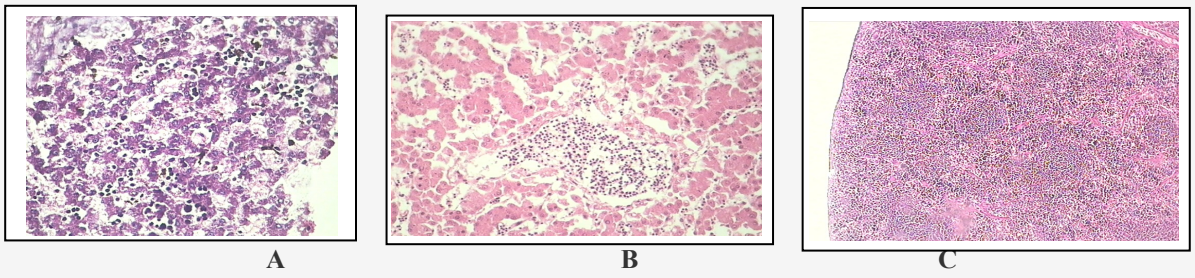


Fig. (4) : Optical micrograph of the sector in the rat spleen at the age of three weeks after birth to mothers in the group shot and the vinegar treatment for the duration of breastfeeding (0-21) describes the approach to the installation of natural fabric ((40 ×-H α E E). A-normal B- lead+ vinegar C- lead.

4. Discussion:

The present study showed a sever decaying in all components of the spleen tissue of the newly born infants after exposure and provided daily with doses of lead acetate. the decaying represents by disappearing of the main barriers of the connective tissue and decreasing in number of veins and arteries and spreading of the lymphatic cells. These histopathological alterations extends to three weeks age after delivery and till the weaning age in which the number of the lymphatic cells B increase and decrease in the number of T cells and an odeama was also observed in the tissue.

The histological investigation of the thymus gland of newly born infants till three weeks age after delivery from females exposed to lead toxicity during gestation and lactation showed that the lobules formation were not complete after two weeks and the lymphocytes number was reduced with decaying regions in the tissue of three weeks age after delivery, these finding agree with studies of **Hsu and Guo., (2002**) who suggest that exposure causes generation of reactive oxygen species and alteration of antioxidant

defense and illustrated that the mechanisms for lead include membranes ,DNA and antioxidant defense system of cells that is the reason for decaying tissue.

The spleen and thymus gland appeared structurally normal in the rope which treated with Lead and vinegar**, Wang et al,(2007)** conclude that a cupuncture of 'Zusanli'(ST 36) can suppress alcohol and vinegar induced decrease of serum gastrin and cortisol ,which may contribute to its effect in the treatment of spleen deficiency syndrome in the rats**, Teriele and Bodensteiner (2006)** investigate the mechanism of dibromo-acetic acid during pregnant and lactating female ,reproductive parameters of female neonatal rats exposed to DBA were examined maternal weight ,size and major organs weights (spleen, liver, kidneys ,uterus and ovary) and there was no different from control, and thus exposed to DBA during the period of follicular formation did not affect follicular populations in neonatal rats.

As concerning the effect of lead on the reproductive system of the treated females ,The examination of uterus showed disturbance in the uterine gland and the uterus stroma was composed of fibrous connective tissue and The reticular connective tissue was less dense than that of the control group and the lead toxicity led to reduced the size of the muscular layer, while the observation of ovaries shows a serious damage of the ovarian tissues odeama and fibrosis of the ovarian tissues which led to absence of ovulation , these finding agree with studies of **Death et al.,(2002) and Gorbel et al.,(2002)**who suggest the action of lead in decreasing circulating growth factor which led to delayed puberty and causes aduble sexual disorder deals with the hormonal function resulting in a reduced fertility.

The present study was undertaken to evaluate the function of admenstrating vinger,to protect organs against lead they affect these organs in different ways **(Kjellström, 1986; World Health Organization, 1992; Nordberg *et al*., 1994; Epstein, 1997; Sakurama, 1998; Bunout, 1999; Thurman *et al*., 1999).** Long-term EtOH consumption damages mainly the liver **(Bunout, 1999; Thurman *et al*., 1999)**, whereas chronic exposure to Cd results, first of all, in tubular dysfunction **(Kjellström, 1986; World Health Organization, 1992; Nordberg *et al*., 1994)**. Unfortunately, no data are available on the function and structure of both organs in conditions of co-exposure to Cd and EtOH.

The level of lead treatment used in this study corresponds to rats occupational exposure to this heavy metal, or environmental exposure in heavily contaminated areas **(World Health Organization, 1992**). The level of intoxication with EtOH may be tantamount to its misuse in man (**Wis′niewska-Knypl and Wrońska-Nofer, 1994).**

Since the relative weights did not change in the co-exposed rats, the decrease in their weights reflects a retardation in body weight gain, which is a consequence of reduced food **(Brzóska *et al*., 2002**) and water intake, and of Cd–EtOH interaction. Other authors also reported the unfavourable effect of co-exposure to Cd and EtOH on body weight gain **(Tandon and Tewari, 1987;Gupta and Gill, 2000**).

Lead accumulation in the thymus gland of rats exposed to this metal alone as well as in combination with vinger resulted in serious changes in the histology and function of this organs. Similar or more advanced changes in spleen and ovary histology and function under lead influence, have been reported by others **(Aughey *et al*., 1984; Kjellström, 1986; Mitsumori *et al*., 1998). Aughey *et al.* (1984)** noted early pathological changes in rat kidney already after 6 weeks of administration of 50 mg Cd/l in drinking water. After 12 weeks, they revealed signs of tubular necrosis, interstitial fibrosis and glomerular epithelial cell hypertrophy in small areas of the kidney cortex. Pathological changes in kidney ultrastructure (were observed when leadconcentration in this organ exceeded 10 μg/g and they became more pronounced as concentration increased. At a Cd level of about 30 μg/g, necrotic changes were observed **(Aughey *et al*., 1984).**

The results of this study and of other investigations **(Aughey *et al*., 1984**) show that the critical Cd concentration in the kidney cortex is lower than 200 μg/g (the kidney cortex/whole kidney ratio of Cd concentration is about 1.25). Such high Cd concentrations in the kidney cortex were measured in rats fed with diet containing 200 mg Cd/kg for 2–4 months **(Mitsumori *et al*., 1998).**

Morphological observations, together with functional tests, show that lead and vingar, administered separately and especially in combination, lead to spleen and uterus injury, thus posing a serious risk for health. The changes observed in these organs of co-exposed rats can be a result of an independent effect of lead and vingar and also of their interaction. Since vingar alone also had affected the spleen and uterus, on the basis of this study it is difficult to make any definite assessment as to whether vingar influenced lead toxicity, and if so, to what extent. However, such an effect of vingar is very likely, and can be linked to changes in lead body burden. In this work, we measured the We have noted that in the vinger group the whole lead pool in the internal organs was at the same level as in those receiving lead alone, in spite of its lower intake. In the absence of the modifying effect of viger, the concentrations and content of lead in the co-exposed animals should be lower, compared to the lead-only exposed ones.

Due to the different intakes of lead and vigar during their co-administration, than after their separate

dosages, we cannot correctly interpret the interactive effects of the two substances on the liver and kidney. Nevertheless, our findings allow us to conclude that viger increases lead nephrotoxicity, although the present results give no clear evidence of enhanced lead toxicity. However, it seems likely that, if the consumption of lead and vinger were the same in co-exposed and separately exposed animals, the disturbances in liver and kidney function as well as histology, would be more serious in the co-exposed ones. On the basis of the present and previous studies **(Brzóska *et al*., 2000, 2002),** we hypothesize that subjects exposed simultaneously to lead andvinger are more vulnerable to lead accumulation and thus its deleterious health effects, including kidney damage. Further studies are needed to explain lead- vinger interactions in conditions of long-term co-exposure and their consequences for health.However, the activity of of heavy metals is related to their physiological interaction with biological receptors depending on their concentrations. **Jang et al., (2011)** concluded that low level of lead inducephosphatidylserine exposure and erythrophagocytosis associated with anemia. Also **Jihen et. al., (2011**), explain the interrelationship between cadmium, zinc and antioxidants inliver of the rat exposed orally to relativily high doses of cadmium and zinc. Heavy metals affected polycystic ovary syndromewhile garlic treatment reduce some heavy metal accumulation in liver of wistar rats.

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