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The Effect of Depakin Physiologically and Histology on the Kidney of Pregnant Female White Rats and the Investigation of the Protective Role of the Portulacea Oleracea Plant

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ABSTRACT

Aim: Knowledge of histological and physiological changes of the kidneys in female rats treated with lepipakine, and the possible protective role of the use of Portulacea Oleracea plant extract.

Materials and Methods: Female rats were divided into six groups (1) control group (2) treatment group with therapeutic dose (0.5mg/kg), depakine (3) double dose treatment group (1mg/kg) of depakine.(4) Portulacea Oleracea -aqueous extract group at 2mg/kg, (5) therapeutic dose of depakine (0.5mg/kg) with Portulacea Oleracea -aqueous extract (2mg/kg), (6) double dose of depakine (1mg/kg) with Portulacea Oleracea -aqueous extract (2mg/kg) Any day for 18 days, and the female rats were dissected on the 19th day of pregnancy, and the kidneys were taken for histological examination and blood was drawn from the heart for urea and creatinine tests.

Results: Laboratory examination of kidney function showed a significant difference P001, where high urea and creatine were observed in the two groups treated with depakine with different dose concentrations, and the aqueous extract of the Portulacea Oleracea plant showed its protective role in reducing creatine and urea levels as shown in the table(1-1). The histological examination showed that Depakin led to histological changes in the kidneys of the therapeutic and double dose group of the drug, which was represented by atrophy in the glomerulus, hemorrhage within the tissue area and the appearance of a plug in the tubules in addition to thickening in the vessel as shown in the picture (A, B, C). Compared to the control group . As for the plant extract, the Portulacea Oleracea contributed to reducing the negative effects of the drug as shown in the pictures (E, F, G).

Conclusion: The drug led to many histological and physiological changes in the kidneys, and the aqueous extract of the Portulacea Oleracea plant also contributed to improving the kidney injury caused by the drug by reducing urea and creatinine levels, and reducing renal histological damage.

Introduction

Anomalies is the science that studies the abnormal growth of the fetus inside the mother's womb, which causes an impediment in the growth of the fetus, and phenotypic abnormalities can be observed on the body of the newborn Where the percentage of malformations is about 3% of live births, due to many factors, including primary genetic factors or environmental factors that include chemicals, drugs and overlapping environmental genetic factors [1]

Depakine is one of the anti-epileptic drugs and its chemical formula C8H15NaO2 is used for many cases of epileptic seizures, migraines and depression for all genders and ages because of its positive role in the treatment of epileptic seizures, But it may cause many negative effects, including it may affect the process of embryogenesis when used during the first trimester of

pregnancy as a result of which results in many phenotypic abnormalities, including cleft palate, shortening the limbs of the fetus, small head size and delay in the fetal growth process.

Medicinal plants have recently aroused great interest and have been used as a treatment for many diseases, and have become one of the health and preventive means in many countries, Including the plant Portulacea Oleracea, one of the medicinal plants that belongs to the manly family Portulacaceae, spread globally in multiple countries[2], including Iraq, a wild herbaceous plant that grows naturally and has medical importance, Previous studies have shown that the ethanolic extract of the flowers and leaves of the Portulacea Oleracea plant is used to treat renal and liver disorders, atherosclerosis, diabetes, colitis, muscle spasms and bloody vomiting[3], The plant improves lipid metabolism and lowers blood sugar, and plant seeds are used to lower triglyceride and cholesterol levels in the blood[4], He also showed that the methanolic extract of the perbens plant has shown antioxidant, anti-inflammatory, bacteriological and antimicrobial activities.[5]

Materials and Methods: The drug Depakin used 500 mg/kg was determined by the effective dose method (to calculate the oral dose on the basis of the equivalent human dose, and the dose used (0.5-1 mg / kg) of the body weight of the drug Depakine was determined[6], as for the Portulacea Oleracea was collected from different areas of Salah al-Din Governorate, where it was extracted by warm water according to [7]

Animals used in this Study: 18 animals of white rats were used, with weights ranging from 200-180 g, and these animals were subjected to appropriate laboratory conditions in terms of temperature taking into account the ventilation factor, they were fed with diet freely throughout the experiment duration of 19 days. It was placed with males of the same breed inside a plastic cage during the night and then the next morning the females were examined, as the vaginal plugs or the appearance of sperm in the vaginal fluid were formed as evidence of the occurrence of the insemination process, and the females are considered on the zero day of pregnancy [8]

Experimental Design: The study was designed on the basis of the use of 18 female white rats randomly distributed into six groups for each group according to the following treatments: the first group was dosed with distilled water only, the second group (therapeutic) was dosed with 0.5 mg/kg of depakine and the third group (doubled) was dosed by 1 mg / kg of depakine. While the fourth group treated with aqueous extract of the perpen plant at a rate of 2 mg / kg, the fifth group treated with the therapeutic dose of depakin with the aqueous extract of the perpene plant and the sixth group treated with the drug depakin double dose with the aqueous extract of the perpen plant The groups were dosed once a day throughout the pregnancy period

Prepare histological sections: Isolation of the kidneys after dissection, rinsing with ordinary saline, fixing it in 10% formalin / 24 hours, drying it with ascending concentrations of ethanol, disinfecting it in xylene, immersing it in paraffin at 56 ° C / 24 hours, dividing it with a thickness of 4 microns, fixing it on a glass slide, smeared with hematoxylin and osin and examining it under a light microscope[9]

Results of kidney function levels (urea and creatinine)

Table (1-1) shows a significant increase $P \leq 0.01$ in urea and creatinine levels in groups dosed with depakine at therapeutic doses of 0.5 mg/kg and doubling 1 mg/kg and a significant decrease $P \leq 0.01$ in the concentration of urea and creatinine levels in the groups dosed with paraben extract 2 mg/kg

Table (1-1)

Group Name	creatinin	Uerea
Control Group	0.400±0.100 d	36.0±1.00 C
Therapeutic dose	0.667±0.115 b	39.0±1.00 B
Double dose	0.866±0.057 a	41.00±1.00 A
Extract Dosage	0.333±0.115 d	33.33±1.528 D
Therapeutic dose with extract	0.566±0.115 c	38.0±1.00 B
Double dose with extract	0.700±1.00 b	0. 0.38±1.67 C

Kidney tissue:

The results of the kidney tissue of pregnant female rats through microscopic examination showed that the group dosed with the drug depakine therapeutic dose with a concentration of 0.5 mg / kg, which included renal glomerular atrophy and degeneration of the endothelium cells of the tubules in addition to hemorrhage within the kidney tissue as shown in the image (B) compared to control.

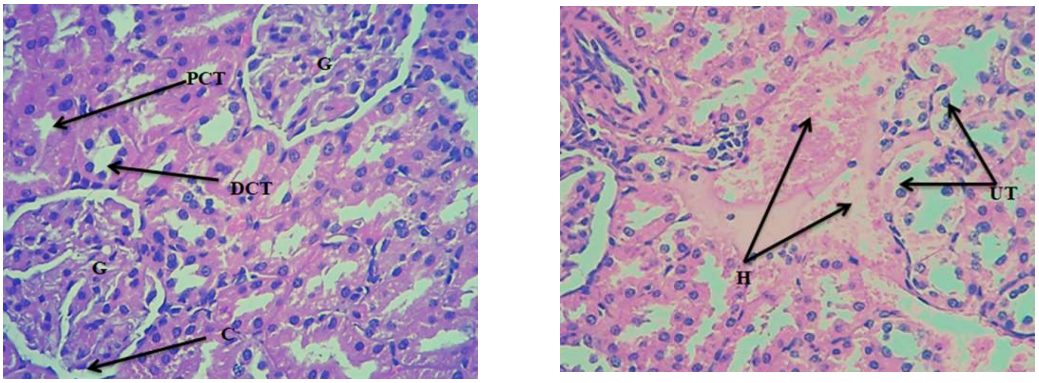
Kidney histology of pregnant rats dosed with depakine at a concentration of 1 mg/kg showed double dose of histological changes, including the appearance of a plug in the tubules and thickening of the blood vessel wall, in addition to atrophy of some glomeruli and degeneration of tube lining cells as shown in the image (C).

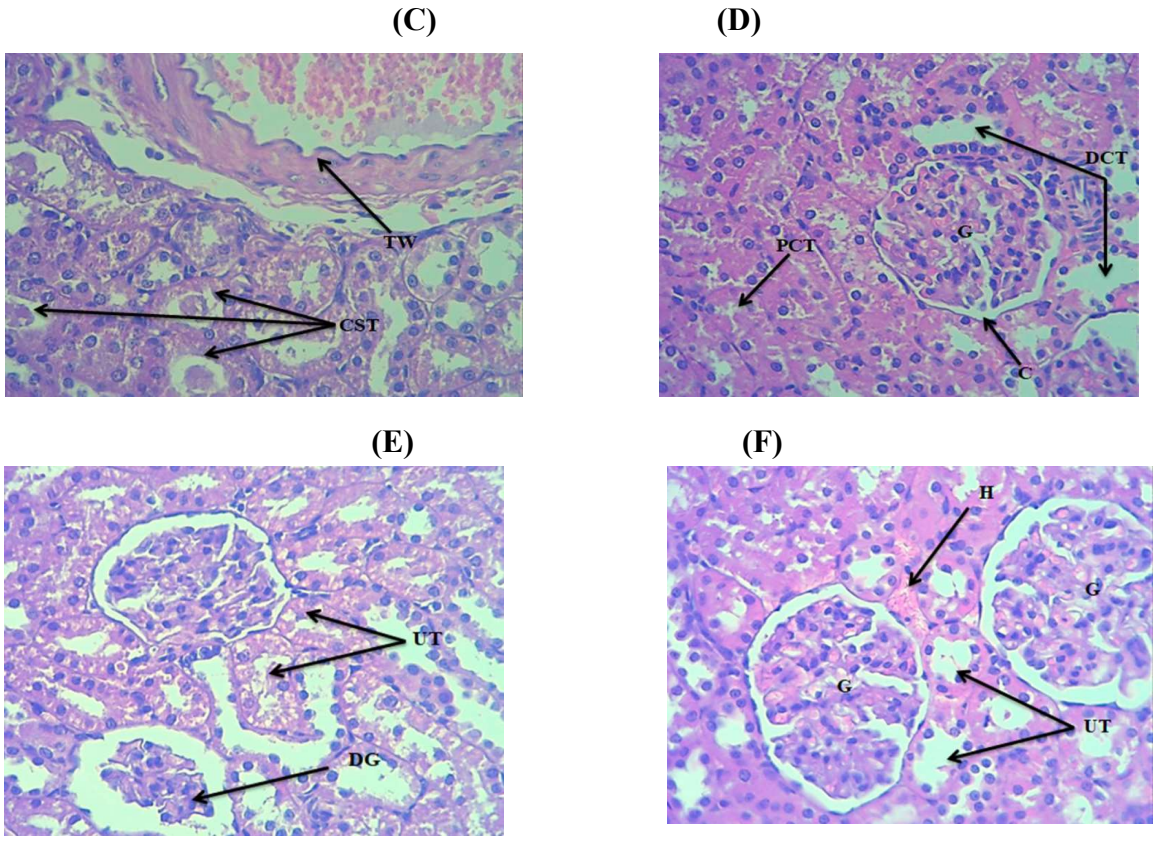
Kidney histological sections in the group treated with aqueous extract of the perpen plant No changes were observed in the kidney tissue compared to the control group, they appeared in their normal form as shown in the image(D)

Histological changes of the kidneys in the group treated with depakine Therapeutic dose with aqueous extract of the perpen plant The histological sections of the kidneys showed some changes, including the occurrence of bleeding within the tissue area, while the renal glomeruli and urinary tubules as shown in the image(E)

Histological changes of the kidneys in the group treated with depakine Double dose with aqueous extract of the perpen plant showed the presence of degeneration in the endothelial cells of some tubules, but for the renal glomeruli, they were normal as shown in the picture were normal as shown in the image(F)

(A) **(B)**





Discussion:

The results of the current study showed a significant increase in the levels of urea and creatinine in blood serum in the group treated with the therapeutic dose of Depakene and doubling respectively in pregnant white rats mainly due to their elevation due to tissue damage and nephronal dysfunction as shown in the kidney histology study in the above images(B,C). Creatinine and urea are forms of metabolic waste filtered by glomeruli in the kidneys [10], serum concentrations of urea and creatinine are elevated as a result of functional disorder of kidney cells or reduced glomerular filtration rate of the kidneys (Mouton and [11] Creatinine is produced through the demolition of phosphoratinine (creatinine phosphate) in the muscles and to be filtered and excreted by the kidneys to prevent its reabsorption, as for urea is formed as a result of the metabolism of protein substances through a series of chemical reactions and the removal of an amine group of amino acids in the liver and excreted into the bloodstream to be eliminated by the kidneys, The results of the current study agreed with [12], that raising the levels of urea and creatinine in serum very high as a result of reducing antioxidants in tissues, in return for increasing lipid peroxide and ROS in the kidneys and renal glutathione permeability, in addition to the contribution of oxidative stress to the occurrence of renal mitochondrial dysfunction and thus resulting in injury to the kidney tissue[13] reported that damage to the renal brush boundaries as a result of breakdown of the cellular structure that responds to actin polymerase sensitivity at cellular ATP levels, the decrease in which leads to F-actin loss of apical microvilli and stress fibers, while the results of the current study did not agree with [14]. Depakine was found to have mitigated kidney injury caused by diabetes by inhibiting endoplasmic reticulocular stress. The results of the current study showed that there is damage in the kidney or that it has been affected by different doses of depakine through the size of the damage to its tissues, atrophy of the renal glomeruli, degeneration of the lining cells of the tubules with thickening in the vessel wall to varying degrees. In addition to the occurrence of bleeding within the tissue and the appearance of a plug in the tubules, the reason for this may be due to its action related to the mineral balance and the harmful effects of the drug as well, if

many research and reports indicate that between 20-5% of cases of acute renal failure are mainly due to chemicals and drugs[15],Inflammation is defined as the primary response to the process of entering the pathogen and is achieved by increasing the movement of plasma and white blood cells WBC from the blood to the affected tissues, which results in congestion of blood vessels due to increased blood flow and varicose veins, and as a result of these changes, the tissue sections reveal them form congestion or bleeding [16], as Kumar et al. [17] showed the main cause of erythrocyte lysis It is carried out by phagocytes due to local hemorrhage. The current results of the histological study of the kidneys showed the presence of histological changes as a result of the effect of the drug according to the doses given, including renal glomerular atrophy, bleeding of vessels within the renal tissue, cellular degeneration of the lining of the tubules, in addition to thickening of the vessel wall and the appearance of stamens in the tubules. Our results coincided with the results of [18] where the increase in the size of the tubes results in the process of reabsorption , Which causes hyperfiltration of the glomerulus, and the greater the hyperfiltration, the greater the absorption in return as a result of the glomerular capillary pressure, which may lead to infection of the Padocyte, Mesangial endothelial with the increase in the quantities of proteins filtered into the tubular cavity, which works on the occurrence of intensive tubulitis. , as found by[19][18] lymphatic infiltration into the renal tissue of depakin-treated mice. The effectiveness of the aqueous extract of the perpen plant, which in turn contributed to reducing the side effects of the drug within the renal tissue of pregnant female rats, it was noted that the renal glomeruli and urinary tubules appeared in their normal form, in addition to the presence of bleeding and degeneration of the endothelial cells of some tubules. The antioxidant effect of the extract used is due to the antioxidant effect of the extract used. to its high phenolic compounds, which are an added value and a source of use in biomedicine due to their superior ability to produce various antioxidants that can be based on their chemical structures by membrane stabilization activity through the generation of ROS [20]

Conclusions

High indicators of urea and creatine in the therapeutic groups 0.5mg/kg and double 1mg/kg treatment with depakine and the occurrence of tissue damage in the kidneys, which were represented by renal glomerular atrophy DG, hemorrhage H with endothelial cell degeneration of the renal tubules UT, in addition to thickening of the vessel wall TW and the appearance of a plug also in the tubules The aqueous extract of the perpen plant showed a protective role in reducing the levels of urea and cretianine, as for the histological section, it improved and showed it within the normal form with the presence of hemorrhage and degeneration of some cells.

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