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Physiological and histological effect of Captopril on kidney and the protective role of Brassica nigra seed extract in male rats

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ABSTRACT

The experiment was designed to determine the protective role of Brassica nigra seed extract on Kidney function and tissue against the negative effects induced by the drug Captopril (CPT25 and CPT50).

In this experiment, 30 animals (Rats male) were used. Kidney efficiency was measured by measuring The level of urea and creatinine and level of Glutathion (GSH), Malondialdehyde (MDA) and Superoxide dismutase (SOD) in kidney tissue, as well as studying the histological effects of the drug Captopril (CPT25 and CPT50). against ،Kidney tissue and the protective role of Brassica nigra seed extract . The results showed that the treatment of animals with drug Captopril (CPT25 and CPT50) at a dose of 1.9 and 3.8 mg / kg bw for 30 days led to a significant increase in The level of urea, creatinine, (MDA), (SOD) and decrease in The level of (GSH).

The treatment of animals with drug Captopril (CPT25 and CPT50) has shown Effected on kidney tissues cases the infiltration and inflammatory of inflammatory cells between the urinary tubules, the presence of hemorrhage within the kidney tissue and the renal glomeruli, and cellular degeneration of some cells of the urinary tubules. Brassica nigra seed extract improves most of the negative effects caused by drug Captopril (CPT25 and CPT50).

The aim of this study is to investigate the negative effects of captopril on kidney tissues, and to identify the protective role of Brassica nigra seed extract against the negative effected of captopril on some biochemical and histological parameters.

The conclusion from this study is that the drug Captopril showed an effected on the kidneys of the experimental animals, represented by the emergence of tissue lesions in the organ tissues, and through the results of the results, the protective effected of Brassica nigra seed extract against the effects of captopril was identified.

1- Introduction

High blood pressure is a common disease that afflicts millions of people in different parts of the world, and it is called the (silent killer), because most of them sufferers do not complain of any symptoms. The severity of the disease comes from the complications it causes, such as atherosclerosis, poor performance of the heart and its enlargement, heart and brain clots, kidney failure, and the effect on the retina[1].

The blood pressure is the force that pushes blood through the blood vessels to provide oxygen and nutrients to the various organs and tissues of the body, while at the same time carrying waste and food products. High blood pressure is higher than 90/140 mm Hg, and it is a common health problem all over the world with the ongoing global increase in high blood pressure. Approximately 25% of the adult population was affected from high blood pressure[2].

There are currently three main commonly used classes of antihypertensive drugs:[3]

1- Angiotensin blocking drugs.

2- Calcium channel blockers (CCB).

3- Diuretic drugs.

Captopril is an angiotensin converting enzyme that contains a sulfhydryl (SH) group manufactured in

1976 by Ondetti and colleagues at ER Squibb and Sons. It was known under the generic name SQ14,255 and then the name was changed to Captopril. Captopril is a new drug, specifically designed to compete for the active binding site (ACE)[4].

Captopril is used to treat mild to moderate high blood pressure, and in hypertensive crisis. It is the only one Angiotensin converting enzyme inhibitor (ACEI) that can be used for high blood pressure in newborns and infants. The drug is used within the category of drugs used in the treatment of heart diseases and has been used in the treatment of primary hypertension[5]. It is also given to patients suffering from cases of myocardial infraction or congestive heart failure and nephrotoxicity, as well as used in the protection of renal function in nephropathy of the injured Diabetes and in cancer treatment[6].

Brassica nigra It is an annual herbaceous plant that belongs to the family Brassicaceae, which is one of the large and widespread families where there are more than 500 genera and more than 2000 species in the world. Its effectiveness lies in its seeds containing oily compounds (30.35%) as well as glycosides, phenolic compounds, enzymes and others. It is a bioactive compound[7].

Brassica nigra seed contain glycosides, alkaloids, resins, flavones, phenols, and saponins. They are devoid of tannins, and they also contain proteins 23.30% and 28.30% carbohydrates, as well as contain minerals, beneficial antioxidants, nutritional fibers and oils and Vitamin A, Vitamin C, Vitamin D, and Vitamin B compounds such as Niacin B3, Thiamine B1, Riboflavin B2 and Pyridoxine B6, also contain large amounts of minerals such as - Calcium - Iron - Zinc - Copper - Manganese – Selenium[8]. The aim of this study is to investigate the negative effects of captopril on kidney tissues, and to identify the protective role of Brassica nigra seed extract against the negative effected of captopril on some biochemical and histological parameters.

2- Material and Methods

2-1 Experimental Design: The Experimental was designed on the basis of the use of 30 male white rats, It weighs 180-200 kg and age 4 months, divided into 6 groups each group continent 5 animals according to the material treated with them as follows:

1. The Control group.
2. The treatment group with captopril 25 mg at a dose of (1.9 ml/kg orally) of body weight, in addition to the standard diet with drinking water throughout the trial period[9].
3. The treatment group with captopril 50 mg and a dose of (3.8 ml/kg orally) of body weight, in addition to the standard diet with drinking water throughout the trial period[9].
4. The group treated with aqueous Brassica nigra seed extract at a dose of (100 ml/kg) of body weight.
5. The group treated with captopril 25 mg (1.9 mg/kg) + Brassica nigra seed extract (100 mg/kg).
6. The group treated with captopril 50 mg (3.8 mg/kg) + Brassica nigra seed extract (100 mg/kg).

2-2 Seeds collection and extraction Experimental: The Brassica nigra plant was collected from several areas of Salah al-Din Governorate during the period of May to the end of June of the year 2019 and the plant was taken and the seeds were extracted from it, then the seeds were brushed to obtain a sample free of impurities, then the seeds were left to dry in the shade, then the seeds were crushed With an electric grinder, the mixture was placed in airtight and opaque cans and kept at room temperature, until the extraction process took place. The seeds of the Brassica nigra plant were extracted by the warm water method [10], where 50 grams of crushed seeds were taken and placed in a beaker containing 500 milliliters of warm water and stirred by hand to mix the mixture and then the beaker was placed in the Shaker vibrator for 24 hours. Then the mixture was filtered by several layers of medical gauze in order to ensure that the parts not well crushed, then the mixture was put after filtering in several glass dishes that were transferred to the electric oven so that the mixture was completely dried at a temperature of 40°C, and after that it was stored in packages An opaque sealed glass bottle was placed in the refrigerator until it was used and its information was written down.

2-3 Hematological Examination: After the end of the 30-day experiment, the animals were starved for 24 hours after which blood samples were drawn through a jugular vein cut. The blood was placed in test tubes and placed in the incubator at a temperature of 37º for 30 minutes, after which a 3000 rpm centrifuge was used for 15 minutes, in order for the serum to be separated from the other ingredients using a micropipette and placed in deep freeze at a temperature of 82- A degree until the biochemical tests are performed. They estimate the concentrations of urea, creatinine, glutathione, SOD, MDA. Measurements includes (Physiological parameters and Oxidative stress factors: MDA (malonedialdehyied), by thiobarbituric acid (TBA) according to method [11], and Glutathione (GSH) by using DTNB according to method[12] ,and SOD by using MPNT according to method[13]

2-4 The histological study: kidney tissue samples were fixed in 10% formalin since 24 hours, dehydration by ethyl alcohol in increasing concentrations (70%, 80%, 95%, 100% and100%), clearing with xylene and then embedded with paraffin. When analyzed, all paraffin embedded tissue was sectioned at 5 µm ,and stained with Hematoxylin and eosin stain. These specimens were examined under a light microscope at 40X magnification power. Corresponding digital images were captured for later analysis[14].

3- Statistical Analysis

The results of this study were statistically analyzed by using variance analysis software (IBM SPSS

Statistics for Windows, Version 23.0., NY: IBM Corp.), and ANOVA test was used to analyze the variance between six groups at the probability level ($P \leq 0.05$).

4- Results

The results of the current study showed a significant increase in the level of urea and creatinine in the group treated with captopril (CPT25 -50) compared with the control group. The results also showed a decrease in the levels of urea and creatinine in the group treated with captopril (CPT25 -50) and Brassica nigra seed extract.

The results of the current study showed a decrease in the level of (GSH) and (SOD) and increase level of (MDA) in kidney tissue in the group treated with captopril (CPT25 -50) compared with the control group. The results also showed a significant increase in the level of (GSH) and (SOD) and a decrease in the level of (MDA) in the group treated with captopril (CPT25 -50) and Brassica nigra seed extract.

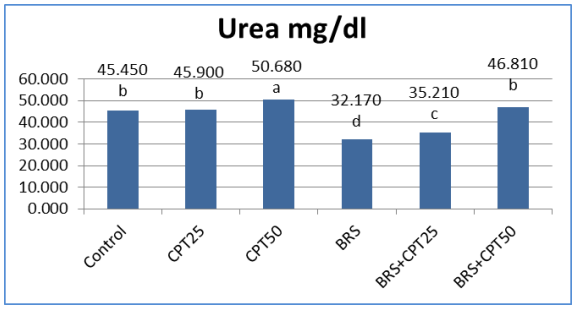

Fig. 1: shows the effect of treatment with captopril (CPT25) (at a dose of 1.9 mg / kg) and the effect of treatment with captopril (CPT50) (at a dose of 3.8 mg / kg) and the Brassica nigra seed extract (at a dose of 100 mg / kg) on the concentration of Urea in serum Blood of male white rats.

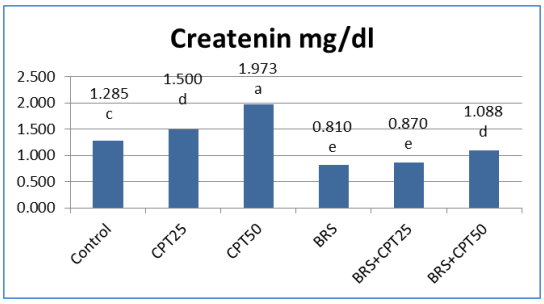

Fig. 2: shows the effect of treatment with captopril (CPT25) (at a dose of 1.9 mg / kg) and the effect of treatment with captopril (CPT50) (at a dose of 3.8 mg / kg) and the Brassica nigra seed extract (at a dose of 100 mg / kg) on the serum creatinine concentration of male white rats.

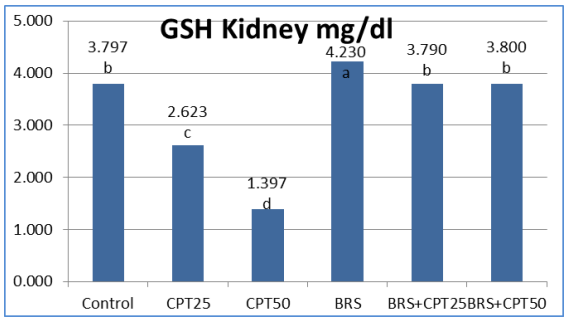

Fig. 3: shows the effect of treatment with captopril (CPT25) (at a dose of 1.9 mg / kg) and the effect of treatment with captopril (CPT50) (at a dose of 3.8 mg / kg) and the Brassica nigra seed extract (at a dose of 100 mg / kg) on the activity of GSH on kidney tissue of male white rats.

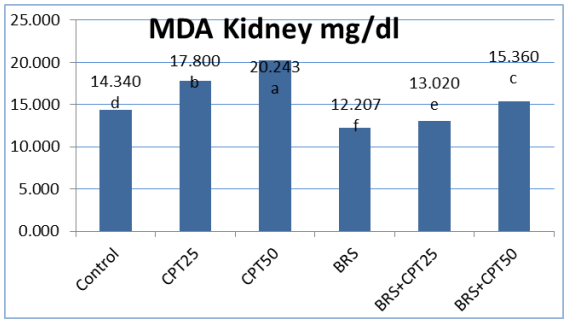

Fig. 4: shows the effect of treatment with captopril (CPT25) (at a dose of 1.9 mg / kg) and the effect of treatment with captopril (CPT50) (at a dose of 3.8 mg / kg) and the Brassica nigra seed extract (at a dose of 100 mg / kg) on the effectiveness of MDA on the kidney tissue of male white rats.

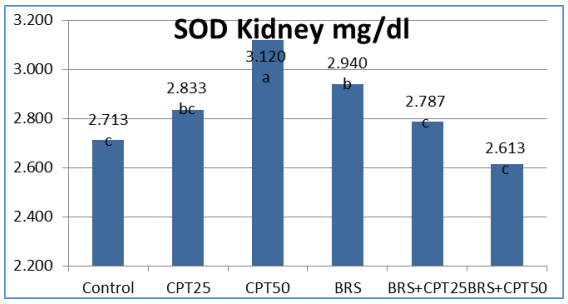

Fig. 5: shows the effect of treatment with captopril (CPT25) (at a dose of 1.9 mg / kg) and the effect of treatment with captopril (CPT50) (at a dose of 3.8 mg / kg) and the Brassica nigra seed extract (at a dose of 100 mg / kg) the effect of SOD on the kidney tissue of white male rats.

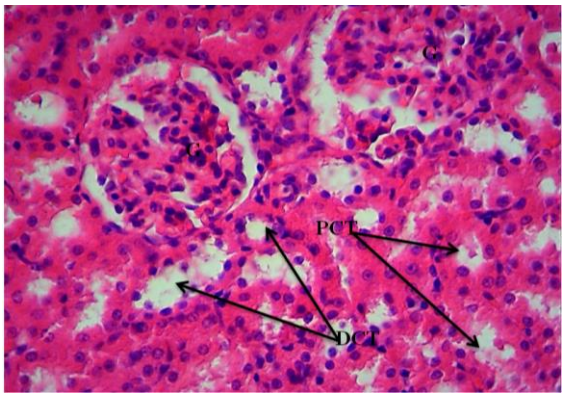

Image 1: a control group rat kidney section showing the proximal convoluted tubule (PCT) and distal tubule (DCT) as well as the renal glomeruli (G) in a clear and normal way, H&E 400X.

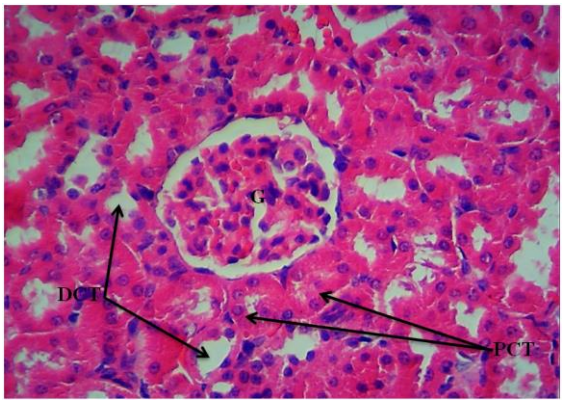

Image 2: a group rat kidney section treated with mustard seed extract illustrates proximal convoluted tubule (PCT) and distal tubule (DCT) as well as normal (G) renal glomeruli, H&E 400X.

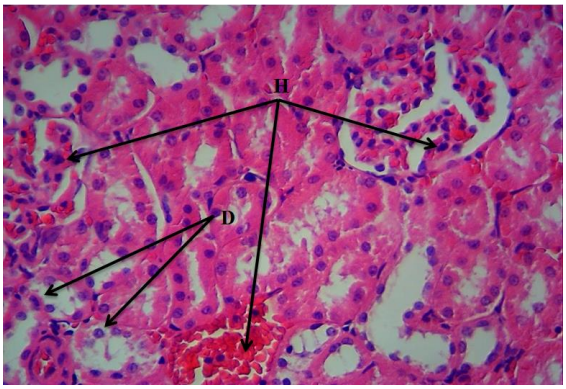

Image 3: section of a rat kidney of the group treated with the drug Captopril at a dose of 1.9 mg / kg shows the presence of hemorrhage (H) within the kidney tissue and the renal glomeruli, and (D) cellular degeneration of some cells of the urinary tubules, H & E 400X.

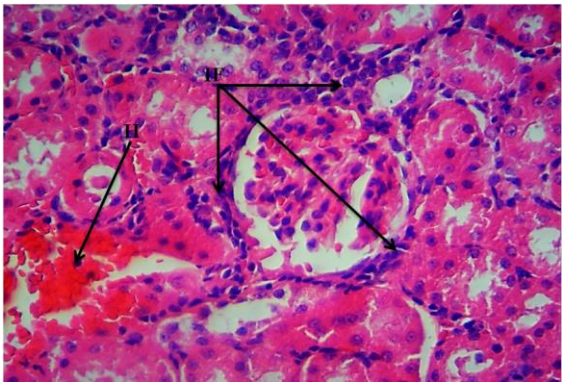

Image 4: section of a rat kidney of the group treated with the drug Captopril at a dose of 3.8 mg / kg shows the presence of hemorrhage (H) within the kidney tissue and clear infiltration of inflammatory cells (IF), H & E 400X.

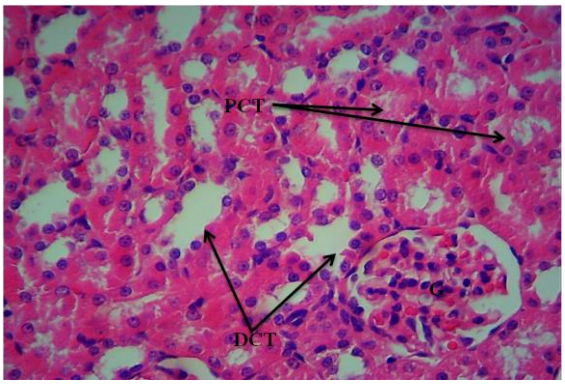

Image 5: section of a group of rat kidneys treated with Captopril at a dose of 1.9 mg / kg and mustard seed extract showing proximal convoluted tubules (PCT) and distal (DCT) as well as normal renal glomeruli (G), H&E 400X.

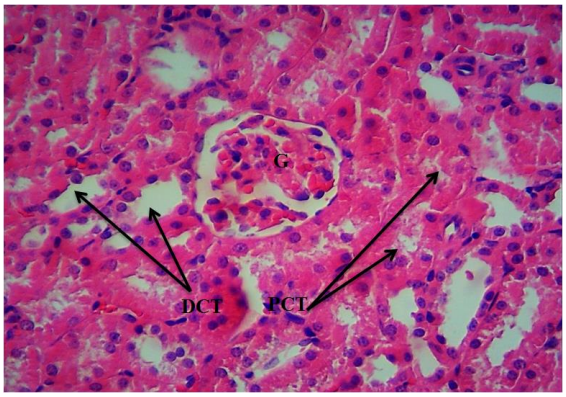

Image 6: section of the rat kidney of the group treated with the drug Captopril at a dose of 3.8 mg / kg and mustard seed extract showing the proximal convoluted tubules (PCT) and distal (DCT) as well as the normal renal glomeruli (G),H&E 400X.

5- Discussion

The results of the current study showed a significant increase in the concentration of urea and creatinine in the captopril drug-treated group compared to the control group. Several studies have indicated that widespread use of captopril for several days and months may lead to harmful side effects and a decrease in kidney function due to decreased renal perfusion[15]. And that the increased levels of urea and creatinine in the blood serum due to the inability of the nephrons to be excreted in the urine due to the damage that occurred in the convoluted tubules, which caused an imbalance in the efficiency of the nephron in ridding the body of the waste of cellular metabolism as the ability of the kidneys to excrete urea and creatinine is one of the important vital indicators in the evaluation of Kidney performance[16].

The increase in urea in the group treated with the drug captopril with a dose of (3.8 mg/kg ,1.9 mg/kg) was consistent with [17]. The same study indicates that the use of angiotcinin inhibitors (Captopril) may be associated with functional renal syndrome, a form of acute renal failure.

The results of the current study also showed a decrease in the level of urea and creatinine in the group treated with the drug captopril with the aqueous extract of mustard seeds due to the effective compounds that the plant contains that have the ability to suppress free radicals and preserve the nephron tissue. It turns out that the most important compounds are phenols, flavonoids, glycosides, alkalis and tannins.

The results of the current study also showed a significant decrease in the group treated with captopril drug glutathione and SOD in kidney tissue and raised levels of MDA.

Also, the current study was in agreement with a previous study [18], where it was found that captopril accumulates in the kidneys after glomerular filtration. To other parts of the kidneys, it works to reduce levels of Glutathione and SOD.

The current study showed a higher level of GSH and SOD in kidney tissue in the group treated with the Brassica nigra seed extract with captopril drug compared with the infected control group.

Microscopic examination of kidney tissue in animals of the group treated with captopril drug at a dose of (3.8) mg / kg showed the presence of hemorrhage within the kidney tissue and clear infiltration of inflammatory cells with severe congestion. As for the group treated with the drug Captopril (1.9) mg / kg, it was found that there is infiltration of inflammatory cells between the urinary tubules, as revealed in the microscopic examination of the kidney tissue in this group, the presence of hemorrhage within the kidney tissue and the renal glomeruli, and cellular degeneration of some cells of the urinary tubules, as the results of the current study were in agreement. With [19] it was shown that captopil has significant negative effects on kidney tissues and thus causes kidney failure due to the low average glomerular filtration rate (GFR).

The results of the histological sections of the kidneys of the animals of the group treated with captopril at a dose of (3.8) mg / kg with the Brassica nigra seed extract showed that there was a return between the normal proximal and distal tubules, as well as the normal renal glomeruli. Also, the group treated with captopril drug at a dose of (1.9) mg / kg with the Brassica nigra seed extract clearly shows the proximal and distal convoluted tubules, as well as the renal glomeruli, clearly and naturally.

6- Conclusion

The results of the research showed clear negative effects of captopril on the functions and tissues of the kidneys, as it led to an increase in the level of urea and creatinine, severe bleeding and infiltration of inflammatory cells with severe congestion. The results also showed the protective role of the Brassica nigra seed extract in reducing the negative effects.

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التأثير النسيجي والفسيولوجي لعقار الكابتوبريل على الكلى والدور الوقائي لمستخلص بذور الخردل الأسود في ذكور الجرذان

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الملخص

صممت هذه الدراسة لتحديد الدور الوقائي لمستخلص بذور الخردل الأسود في وظائف الكلى والأنسجة ضد الآثار السلبية التي يسببها عقار كابتوبريل (CPT25 و CPT50).

في هذه الدراسة تم استخدام 30 حيوان (ذكور جرذان). تم قياس كفاءة الكلى عن طريق قياس مستوى اليوريا والكرياتينين ومستوى الجلوتاثيون (GSH) والمالون الدهايد (MDA) وسوبراوكسيد ديسموتاز (SOD) في أنسجة الكلى، وكذلك دراسة التأثيرات النسيجية لعقار كابتوبريل ضد أنسجة الكلى والدور الوقائي لمستخلص بذور الخردل الأسود. أظهرت النتائج أن معاملة الحيوانات بعقار كابتوبريل (CPT25 و CPT50) بجرعة 1.9 و 3.8 ملغم / كغم من وزن الجسم لمدة 30 يومًا أدى إلى زيادة معنوية في مستوى اليوريا والكرياتينين (MDA) و (SOD) وانخفاض مستوى (GSH).

أظهر علاج الحيوانات بعقار كابتوبريل (CPT25 و CPT50) تأثيرًا على أنسجة الكلى من حيث تسلل الخلايا الالتهابية بين الأنابيب البولية، ووجود نزيف داخل أنسجة الكلى والكبيبات الكلوية، والتنكس الخلوي لبعض خلايا المسالك النبيبات البولية. يحسن مستخلص بذور الخردل الاسود معظم التأثيرات السلبية التي يسببها عقار كابتوبريل (CPT25 و CPT50).

نستنتج من هذه الدراسة بأن عقار الكابتوبريل أظهر تأثيراً على كلى حيوانات التجربة تمثلت بظهور آفات نسجية في أنسجة الأعضاء. ومن خلال النتائج المتوصلة تم التعرف على الدور الوقائي لمستخلص بذور نبات الخردل ضد تأثيرات عقار الكابتوبريل .