



## Studying Protective Role of Nano-Extract of Fruits of Cardi Myxa Plant Against Effects of Indomethacin Drug on Kidneys of Male White Rats.

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### ABSTRACT:

The current study was conducted in the animal house/college of science/University of Kufa, This study aimed to reveal the protective role of the nano-extract of the fruits of the Cardi myxa plant in the histological structure of the kidneys of male albino rats treated with indomethacin, (40) male rats were used , and the ages of the male rats ranged between (8-10) weeks and their weights ranged between (200-250) g, the animals were divided into (8) groups, each group included (5) male rats, the first group represented the control group and the second group was treated with indomethacin drug with a concentration of (0.143) mg/kg, the third group is the ZnO group with a concentration of (1) mg/kg, and the fourth and fifth groups that are treated with the nano-extract group with two concentrations of (20 and 30 mg/kg) respectively, while the sixth and seventh groups are treated with the nano-extract with two concentrations of (20 and 30 mg/kg) + indomethacin drug respectively which was treated with the drug half an hour after dosing with the nano-extract, and the eighth group was dosed with the aqueous extract of Cardi myxa plant with a concentration of (500) mg/kg + indomethacin drug with a concentration of (0.143) mg/kg for the period (40) days, after that the animals were sacrificed and the histological sections of the kidney tissue were made. The results of the histological sections of the kidney of white rats showed that the control group had normal tissue for the kidney, as for the indomethacin drug group, the results showed that shrinkage of the glomerulus, widening of the Bowman's space and necrosis in the renal tubules, also the results of the ZnO group revealed the effect of ZnO on the kidney tissue such as complete renal glomeruli retraction, necrosis of the urenal tubules with infiltration of inflammatory cells, as for the results of the fourth and fifth groups which were treated with the nano-extract groups with two concentrations (20 and 30) mg / kg, the results showed that the histological structure of the kidney was close to normal and the appearance of the epithelial cells of the renal tubules with the normal shape compared to a control group, As for the results of the sixth and seventh groups, the two groups of nano-extract (20 and 30 mg / kg) + indomethacin drug, their results showed a slight effect on the cells lining the renal tubules and the appearance of the normal histological structure of the kidney, and the results of the eighth group which was treated with the plant aqueous extract group with concentration (500 mg / kg) + indomethacin drug at a concentration of (0.143 mg / kg ), as the results showed little necrosis in the lining cells of renal tubules with moderate effects of renal glomeruli.



## Introduction

The *Cardi myxa* plant is locally called (Bumber), it is one of the largest species belonging to the borage family *Boraginaceae*. It is a flowering plant with a length of 12 m and its fruits are spherical or oval, this plant contains chemical compounds in its fruits, seeds and all parts of the plant (Abdel – El Ameen et al., 2017). *Cardi myxa* plant has been known since ancient times for its high medical benefits and its use in medicine in all its parts, bark, leaves, fruits, seeds and it contains inhibitory compounds and secondary receptors such as alkaloids, phenols, sterols, saponins, coumarins, phenolic acids, and others (Musa et al., 2020). Zinc oxide (ZnO) is an insoluble, white powder with a high surface area, these properties make it an important agent for many applications and applications, ZnO is used in cosmetics, biosensing, electronics, and its high absorption of ultraviolet radiation. (Diez-pascual and Diez-vicenle, 2014).

Indomethacin drug is one of the drugs that belong to the nonsteroidal drugs and is anti-inflammatory and one of the most used drugs in all parts of the world (Botlonni et al., 2009), indomethacin drug has been used since its discovery in 1963 to treat several diseases, including gout, arthritis, myopathy, rheumatoid arthritis (Matsui et al., 2011), indomethacin drug is called by many commercial names such as Indocin, Indomin, Indocint, and Indocid (Botting, 2006), this drug is used as an analgesic for pain, antipyretic, arthritis, gout, osteoarthritis and rheumatoid spondylitis (Matsui et al., 2011), the mechanism of action of this drug is similar to that of other nonsteroidal anti-inflammatory drugs that inhibit the biosynthesis of prostoglandins (PGS) by inhibiting the activity of enzymes known as cyclooxygenase (Cox) which exists mainly in two forms Cyclooxygenase-1 (Cox1), and Cyclooxygenase-2 (Cox-2) (Smith et al., 2012), the use of this drug is accompanied by many side effects including the gastrointestinal effect which is considered one of the most harmful aspects and the gastro-intestinal tract is the main target of these drugs (NASIDs), especially indomethacin because it rapidly absorbs substances through the gastrointestinal tract when it is taken orally (Mayo et al., 2016).

Nanotechnology is the manipulation of matter at molecular or atomic scales to build structures or systems. The term nanotechnology consists of two parts

(nano) and technology. (Nano) is derived from the Greek scientist (nanos) means dwarf, either technology is a term that refers to the use or creation of modern technical means that have specific names such as billion (10<sup>9</sup>) (Regers et al., 2014), that nanoscience is the science of the art and processing of matter on the nano level, the value of nano (Nano technology) deals with materials with very small nano sizes and will be called nano particles, One in the range (1-100) nanometers (Tjong and Chan, 2004), the nanoparticles are manufactured in different ways and have professional characteristics. The nanoparticles are left in the way they are prepared, either a method from the smallest to the largest, and it is called the TDA Top-down approach. Top-down approach or bottom-up-approach (BuA) (Wang and Xia., 2004).

## Materials and Methods

### Animals

(40) white rats of the type (*Rattus rattus*) were used, the weights animals ranged between (200-250 gm) and their ages ranged between (8-9) weeks, the experiment was conducted from (3/2022 to 10/2022), the animals were placed in cages made of plastic covered with iron clips, The cages were spread sawdust and changed constantly and the animals were fed according to a natural diet suitable for them with the creation of shameful conditions and lighting and under a temperature of 25 C, the total rats divided into 8 groups, (5) animals for each group and distributed as follows: 1-group :the control group was given a physiological solution of 0.9% only, 2- group was dosed with zinc oxide (ZnO) at a concentration of (1 mg / kg), 3- group was dosed with indomethacin at a concentration of 0.143 mg / kg, 3 and 4 groups were dosed with the nano-extract of *Cardi myxa* plant with a concentration of (20 and 30) mg / kg respectively, and 6-7 groups these two groups were treated with nano-extract *Cardi myxa* plant at concentrations of (20 and 30) mg / kg + indomethacin drug with a concentration of 0.143 mg/kg and 8- group was treated with the plant extract of *Cardi myxa* plant with a concentration of 500 mg/kg+ indomethacin drug with a concentration of 0.143 mg/kg.



## Preparation of aqueous extract from the fruits of *Cardi myxa* plant.

The aqueous extract of *Cardi myxa* plant was prepared by adding 109% of *Cardi myxa* plant fruits powder to (100ml) of distilled water in a glass beaker and placed in a water bath at room temperature for two hours, the solution was left to cool, then filtered with filter paper, then by the central reaction device at 4500 cycles for 15 minutes. Minutes after that, the extract is collected in a clean container and pressed in the refrigerator until use (Cnpta et al., 2017; Inshad et al., 2020).

## Preparation of the nano-extract of *Cardi myxa* plant fruits

This nano-extract was prepared according to the method of (Inshad et al., 2020), Zinc acetate ( $(CH_3COO)_2 Zn \cdot 2H_2O$ ) was added at a concentration of (0.2L/Mol) to (100MI) of plant extract at room temperature, and (NaOH) was added for hot plate acidity equation for (3) hours at 60 m until the color change of the solution is evidence of the formation of zinc oxide nanoparticles, then it is filtered by a centrifuge at 4500 cycles for 15 minutes, the precipitate was taken, then washed (3) times and dried in the electric oven at (40-45) C, then ground with an electric hand mill and kept in a clean box until use.

## Preparation of drug

The indomethacin drug was obtained in the form of pills or tablets at a dose of 50 mg, and then the concentration required in the study was prepared in accordance with the weights of the animals which was estimated at 0.143 mg/kg of body weight (Demosceno et al., 2008).

## Dosage of animals

All rats in the study groups were dosed for a period (40 days) by means of an oral dosing tube, at the rate of one dose per day.

## Anatomy of male rats

After the end of the experiment, the animals were sacrificed and anesthetized with chloroform, Male rats were placed on a dissection dish and fixed with staples and then the abdominal cavity was opened, the kidneys were extracted from the male rats and the surrounding fatty connective tissues were removed and they were placed in a formalin solution with a concentration of

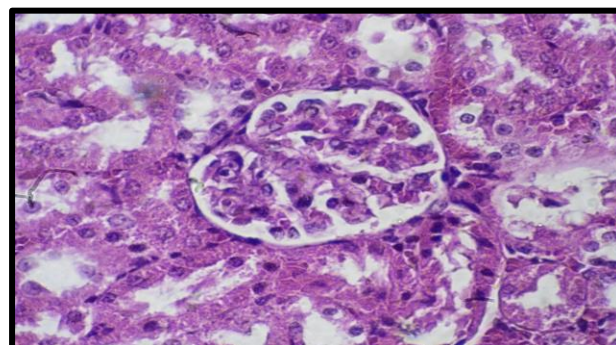
10% for 48 hours for the purpose of preparation for the histological study.

## Results and Discussion

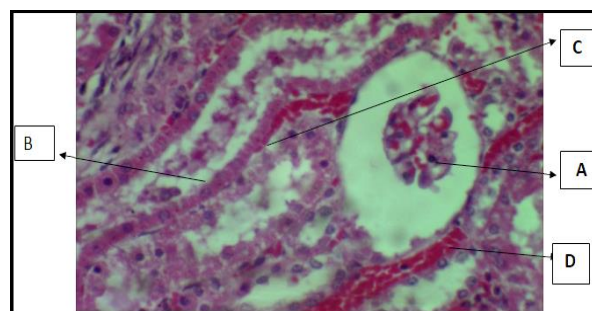
The results of this study indicated that the microscopic examination showed anormal structure of male rat kidneys in the control group as in the figure (1), the kidneys of the animals dosed with the drug Indomethacin at a concentration of (0.143) mg / kg showed a severe effect on the kidney tissue of the rats after administering it for a long-term period of (40) days as in the figure ( 2), and the drug causes a toxic effect on the animal and the appearance of Shrinkage of the renal glomerulus, widening of Bowman's capsule, necrosis and destruction of the cells lining the urinary tubules, necrosis and hemorrhage of the urinary tissue, and infiltration of inflammatory cells as in figure (2), A study (which recorded that this drug caused( Sebeeh and Al -Naimi et la., 2014), histopathological effects in the histological structure varied similar to what was shown in the current study leading to toxic pathological effects ,another studies showed (Mojtaba et al., 2019 and Han et al., 2016), where it was observed that when using this drug which led to atrophy, destruction, and a decrease in the weight of animals, especially when indomethacin was used for a long time, and this was shown by some studies in the liver and kidney (Abdulah et al., 2016; AL-Essawi ,2020) as well as in the gastrointestinal membrane (Han et al., 2016) in the liver( AL- Essawi et al.,2020) and in reproductive organs in male rat treated with indomethacin (Sabeeh et al., 2014), as for the results of the 3-group which treated with zinc oxide (ZnO) with a concentration of (1 mg / kg), the results showed an effect on the kidney tissue and clear histological changes in the The renal glomeruli, in addition to pathological changes in the renal tubules as in figure (3), where severe shrinkage of the renal glomeruli, widening of Bowman's space, and hemorrhage in the cells and their destruction in renal tissue and inflammatory cell infiltration (Alsewi & Alradhi, 2022) and the study of (Surekhe et al., 2012) where the use of different and long-term low doses (5, 10 mg) revealed the cause of toxicity more than the different high doses before (100 mg, 250 mg/), this result can be attributed to the selective hydration union, while the results of 4-5 groups that treated with the nano- extract with concentrations 20 and 30 mg / kg



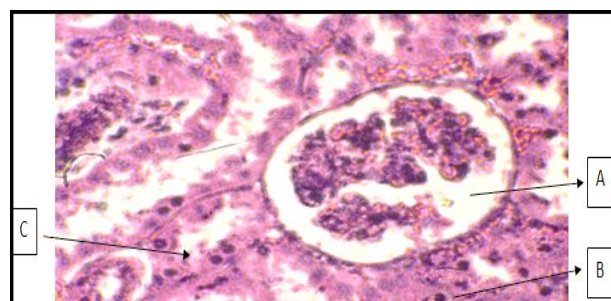
of body weight respectively showed that the histological structure was close to normal and its effects were few as shown in the figures(4, 5) respectively, some studies showed that the nano-extracts of different plants are useful in controlling kidney injury in the case of drug-induced nephrotoxicity and this is due to the therapeutic properties to the presence of complex bound chemicals with a variety of composition in one or more parts of these plants (Alsewi & Alradhi, 2022), as for plant compounds are classified according to their composition in the form of alkaloids, helicosides, corticosteroids, essential oils, flavonoids (Farrell et al., 1975) as the study (Ranjbar et al., 2013) which showed the protective role of *Cardia myxa* plant extracts can be attributed to the antioxidant effect of the flavonoids contained in it, the groups 6-7 that treated with nano-extract with two concentrations of (20 and 30 mg/kg) respectively + indomethacin drug with a concentration of (0.143 mg/kg), Its results showed little effect from the effect of the nano-extract only, these treatments reduced the effect of the drug on the kidney tissue as in figures (6,7) respectively which they showed slight bleeding and a slight breakdown of the cells lining the urinary tubule of the kidney caused by the drug because it inhibited the synthesis of prostaglandin by inhibiting the right oxidative enzymes, in turn depriving the body of self-protection (Albu et al., 1998; - Mohammed and Jabbar 2022), the result of 8-group which treated with aqueous extract of *Cardia myxa* plant with a concentration of (500 mg/kg) + indomethacin drug at a concentration of (0.143 mg/kg) showed a slight damage and occurrence of simple necrosis in the renal cells when compared to the control group and when compared to a group of plant nano-extracts as in the figure (8), the reason for this result may be due to these plant nano-extracts gave a protective role against the drug, the studies of (Mojtaba et al 2019) and (Pan et al., 2014) showed the protective effect of plant extract of *Cardia myxa* and its components (rutin, phytosterol, caffeic acid) on kidney or liver tissue, that the antioxidant and anti-inflammatory effects have a role in maintaining CdCl<sub>2</sub>-treated kidney and liver tissue.



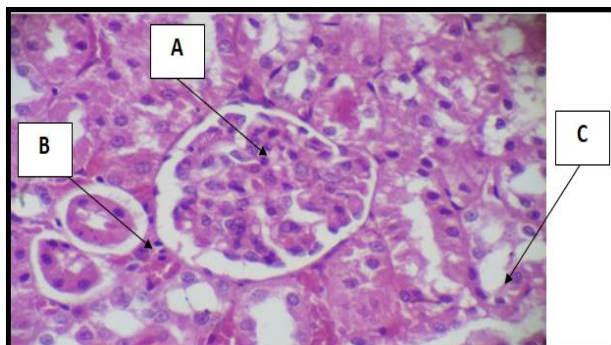
**Figure(1):-**A section of a male rat kidney from negative control group that treated with Physiological solution, in which it is noted: Normal renal glomerulus; Normal renal tubules.(H&E 400X) .



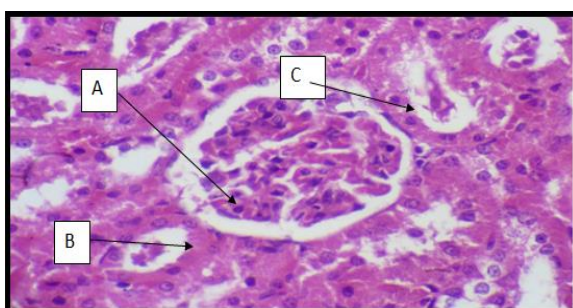
**Figure(2) :-**A section of a male rat kidney from the positive control group that treated with indomethacin drug with concentration of (0.143 mg/kg) , in which it is noted: (A) Shrinkage of renal glomerulus;(B) Expansion of renal tubules;(C) Breakdown of the cells of the inner lining of the renal tubule (D)Hemorrhage into renal tubules. H&E-400X).



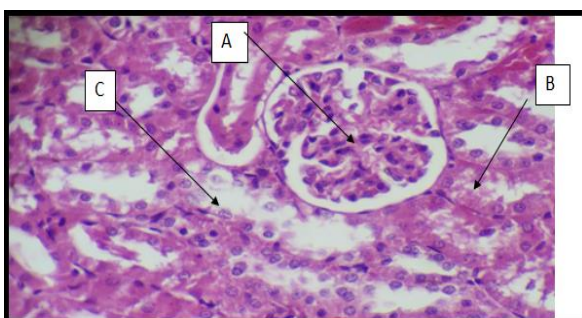
**Figure(3) :-**A section of a male rat kidney from the group that treated with zinc oxide with concentration of (1 mg) , in which it is noted: (A) Shrinkage and degeneration of renal glomerulus;(B) Expansion of Bowman space ;(C) Necrosis into the cells of the inner lining of the renal tubules (H&E-400X).



**Figure(4 ):-**A section of a male rat kidney from the group that treated with nano-extract of *Cardi myxa* plant with concentration of (20 mg /kg) , in which it is noted: (A) Little Shrinkage and degeneration of renal glomerulus;(B) Little Expansion of Bowman space ;(C) Necrosis some the cells of the inner lining of the renal tubules ( H&E-400X).

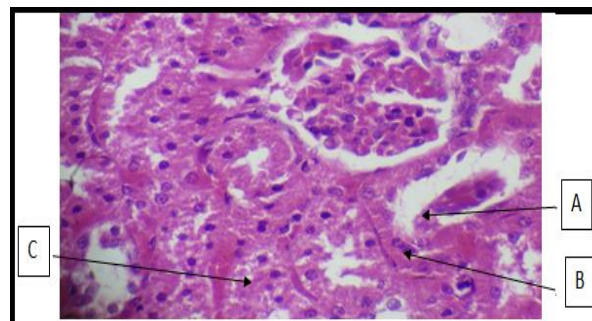


**Figure(5 ):-**A section of a male rat kidney from the group that treated with nano-extract of *Cardi myxa* plant with concentration of (30 mg /kg) , in which it is noted: (A) Little Shrinkage and degeneration of renal glomerulus;(B) Little Expansion of Bowman space ;(C) Necrosis some the cells of the inner lining of the renal tubules ( H&E-400X).

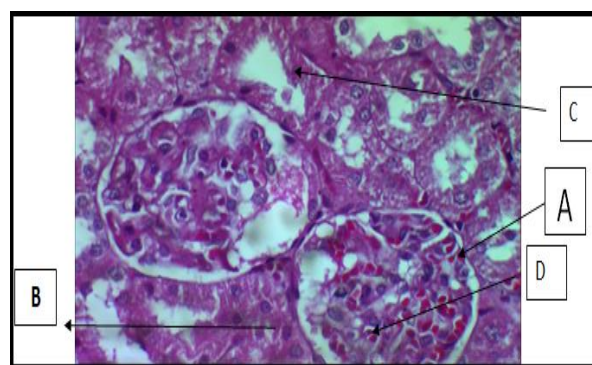


**Figure(6 ):-**A section of a male rat kidney from the group that treated with nano-extract of *Cardi myxa* plant with concentration of (20 mg /kg)+ indomethacin drug with concentration of (0.143 mg/kg) , in which it is

noted: (A) Renal glomerulus closer to normal ;(B) Little Expansion of Bowman space ;(C) Necrosis in some cells of the inner lining of the renal tubules ( H&E-400X).



**Figure(7 ):-**A section of a male rat kidney from the group that treated with nano-extract of *Cardi myxa* plant with concentration of (30 mg /kg)+ indomethacin drug with concentration of (0.143 mg/kg) , in which it is noted: (A) Renal glomerulus closer to normal ;(B) Very little Expansion of Bowman space ;(C) Necrosis in some cells of the inner lining of the renal tubules ( H&E-400X).



**Figure(8 ):-**A section of a male rat kidney from the group that treated with extract of *Cardi myxa* plant with concentration of (500 mg /kg)+ indomethacin drug with concentration of (0.143 mg/kg) , in which it is noted: (A)Mlid shrinkage of renal glomerulus;(B) Necrosis of renal glomerulus;(C) Breakdown of the cells of the inner lining of the renal tubule (D)Mild Hemorrhage into renal glomerulus.( H&E-400X).

### Conclusion

The conclusion of current study that the nano- extract of *Cardi myxa* plant fruits with different concentrations has a protective role against the stimulating negative



effects in the histological structure of the kidney of white male rats when treated with indomethacin drug.

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