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STUDY THE EFFECT OF *URTICA PULLIFERIA* LEAVES ON IBUPROFEN INDUCED HEPATIC RENAL DAMAGE IN ALBINO RATS

Dina Saadoon Dheyab & Sawsan Kadhim Mashi
Physiology, Pharmacology and Biochemistry Department, College of Veterinary Medicine, University of Baghdad, Iraq

ABSTRACT
This study designed to prepare the effect of *Urtica pilluferia* on liver, kidney and some blood parameters that's damage by ibuprofen 200mg/kg/b.w. 40 adults male albino rats (1000-2000g), which divided into equal 4 groups: first control group (no treatment only food and water) second group :which was given ibuprofen 200mg/kg/ b.w. to induce damage, third group was treated by ibuprofen 200mg/kg/b.w. with *Urtica pilliferia* 1-2g/kg/ b.w. (ethanolic extract orally), fourth group:1-2g/kg/ b.w. orally. The results of this of this experiments showed no change in Hb, PCV with increase in AST, ALT urea and creatine after treating by ibuprofin200mg/kg/b.w. while seen increase in Hb, PCV with decrease in AST, ALT urea, creatinine after treating plant in 3rd,4th groups. The histological changes seen in compared with control, the NSAIDS cause serious damage to liver, kidney sections such as congestion necrosis hemorrhages and swelling to tissues organ .The most characteristics changes of hepatic renal tissues were removed after treating by extract *Urtica pulliferia*. Liver section showed moderated central venous congestion only with appears a few of mild hemorrhagic foci in kidneys after giving ibuprofen, *Urtica pulliferia*. Present study proved that the UP has antioxidants hepato renal protective against non steroid anti inflammatory drugs in rat used as a model.

KEYWORDS: PCV (packed cell volume), Hb hemoglobin, ALT (Alanine aminotransferase, AST (asparate aminotransferase), urea.

INTRODUCTION

Ibuprofen apropoinic acid derivative is an example of the non steroidal anti-inflammatory drugs (NSAIDS)[1,2]. Its used for relief pains and anti-inflammatory conditions from the joints, muscle pain than most other analgesics[3]. Ibuprofen can increase danger of fatal heart attack or stroke, especially if you use in long term and take high doses, or if you have heart disease. Ibuprofen may also cause gastro intestinal bleeding, which can be fatal. These conditions can occur without warning while you are using NSAIDs, especially in older adults. An ibuprofen overdose can damage your stomach or intestines. Use only the smallest amount of medication needed to get relief from your pain, swelling, or fever, Its is commonly associated with gastrointestinal toxicity and alter liver and PGE1, PGE2 improve hepatic blood flow, renal function that's largest internal organ in the body[4,5]. The risk of gastrointestinal bleeding from this drug is compound by adverse effects an systemic clotting resulting in abnormality thrombocyte[5,6]. NSDAIDs are frequently used agent for post operative pain in combination with other analgesic, its inhibition cyclooxygenase (COX) prostaglandins synthase G2/H2 enzymes, which produce important PG2 and PG1 especially in kidney PG2regulating important processes related with blood pressure such as salt,water tone following inhibition of PG synthesis by NSDAIDs salt retention increased vascular tone in glomerular vascular bed, filteration rate . *Urtica pilulifera* L. is a member of family Urticaceae. Urt plant extract there increasing toward medical plants and their active ingredients since 1980 *Urtica pulliferia* (up) is a good plant found in Palestine area, the antioxidants supplements and active compounds such as caffeoyl, malic acid, caffeoyl quinic acid, essential oil, formic and acetic acid histamine tannins mucilage, vitamins (A, B1, B2, CK1 folic and panatothesic acids) may be contributing to help the body in reducing oxidative damage by free radicals and active oxygen. *Urtica pilulifera* used in ointment as agent for skin regeneration. *Urtica pilulifera* was reported as one of the most effective medicinal plant to treat benign prostate. The *Urtica pilulifera* is widely used in folk remedy to treat hyperglycemia, hypertension and inflammation of some organs such as uvula and uterus, uterus bleeding, anemia, wound healing. *Urtica pilulifera* is used for various immune disorder and applied either topically or taken orally. Extract of *Urtica* plant is useful for bladder disorder, it reduced postoperative blood loss, bacteriuria, and prevented hemorrhagic and purulent inflammation following adenomectomy. Amino acids as organic nitrogenous compounds are the building blocks in the process of protein biosynthesis Amino acids are particularly important for cell growth stimulation. Many world traditional medicine it has been used this plant for many diseases include bleeding ,anemia excessive menstruation ,hemorrhage arthritis, hay fever, kidney and skin pain, eczema[7,8] and acts as asource of biological activity such as antihistamine, antitumor, stringent, diuretic, antidandruff, galctogogue, deputative and anti-hyperglycemia.

MATERIALS & METHODS

40adults male albino rats (1000-2000)g put in Animal houses stabling under normal condition air and heat for 30 days ,which divided into 4equall groups: first group known control group (give only food and water) second

group :which was given ibuprofen 200mg/kg/bw to induce damage ,third group :was treated by ibuprofen 200mg/kg/bw with *Urtica pilliferia* 1-2g/kg/bw (ethanolic extract orally), fourth group:1-2g/kg/b.w. orally. Iboprofen 200mg/kg/bw[9] was brought from the pharmacy produce sigma company, dissolve in distlled water before administration orally using stomach tube for 30 days leaves of *Urtica pilluferia* collect from super market and crushed to give powder 500mg/kg [10] was put on soxlett cold extractor with absolute methanol solvent and remained for 3days ,the extract concentrated to dryness in rotary evaporator under 45°C to yield a viscous greenish color extract and stored in freeze in 4cin glass container until use. Sample collection blood sample collected from cardiac of animals after anathezied and put in EDTA tube to determine some hematological testes Hb, PCV with centrifuge another blood to measure biochemical liver, kidney parameters and remains the plasma under -20cuntil the day to measurement s.

Statistical analysis: The result of this experiment as mean+_SD were analyzed by one way Anova test and propably level 0.05(11).

Hematological parameters: Hb g/dl measure by cyanomethhemoglobin method [12].

Pcv %: use the method of microhematocrite[13].

ALT: use kit of linear company.

AST: use kit linear company.

Urea and cratinine: according to methods of lineart kit.

Histological tissue: after did the animals take the tissue organs and put in 10%formaldehyde bloked of liver, kidney were then sectioned 4-5m in thickness with hematoxylin and eosin pigment take the slides and examine under microscope to note the changes in this organs.

RESULTS

Table-1 shows the effect of Ibuprofen 200mg/kg/bw and *Urtica pilluferia* 50mg/kg on some blood and biochemical tests in rats

TABLE 1: effect of Ibuprofen 200mg/kg/bw and *Urtica pilluferia* 50mg/kg on blood

Group / tests	Control group	T1	T2	T3
pcv	2.9a± 36.6	2.5a±35.6	2.1bc±40.4	1.06de±44.2
Hb	0.33a±10.5	0.38a±10.9	0.95c±15.7	1.7cd±21.0
ALT	1.8a±4.0	2.3cd±5.3	1.9bc±4.9	1.9a±4.4
AST	2.7a±10.1	3.0d±22.1	2.8cd±14.8	2.7b±12.1
urea	3.6a±37.1	4.0c±48.3	3.8cd±41.1	3.7c±38.6
creatinine	0.19a±0.83	0.24de±1.8	0.20c±1.2	0.1b±0.93

Means with different letters in the column differ significantly (P< 0.05)((

C=control group

T1=group which treatment by ibuprofen 200mg/kg/BW

T2=group which give ibuprofen 200mg/kg/bw +*Urtica pilluferia* 50 mg/kg

T3= group give *Urtica pilluferia* 50 mg/kg /BW

Observe from this table the effect of ibuprofen 200mg/kg/BW and *Urtica pulliferia* on hematological, biochemical parameters, T1(Hbg/dl, PCV%), it was no significant differences (p>0.05)(2.5a ±35.6)(0.38a ±10.9a) compared with control, T3 groups, while after treating by ibuprofen and *Urtica pilluferia* (T2)(2.1bc ±40.4)(0.95c ±15.7) show increase slightly value and recoded significant differences (p<0.05) also increase the value result in T3 group (1.06de ±44.2) (1.7cd ±21.0).

Effect of drugs on biochemical tests in this study also indicate ALT, AST increased significantly p<0.05 in ibuprofen group (2.3cd ±5.3)(3.0d ±22.1) as compared to control group (1.8a ±4.0)(2.7a ±10.1), column 3seen (T2) that's treatment with ibuprofen, *Urtica pilluferia* (1.9bc ±4.9) (2.8cd ±14.8) slightly reduce but significantly differences p<0.05along another line that's treats by *Urtica pilluferia* (1.9a ±4.4) (2.7b ±12.1) record decreased significantly p<0.05 also seen increased value significantly p<0.05in biochemical test of kidney (urea, creatinine) in T1(4.0c ±48.3) 0.24de ±1.8) copmared with control group (3.6a ±37.1)(0.19a ±0.83). By contrast, after treatment by *Urtica pilluferia* (3.7c±38.6) (0.1b±0.93) show lower in urea and creatinine level p<0.05compared with control (3.6a±37.1) (0.19a ±0.83) and T1 group(4.0c ±48.3)(0.24de ±1.8).

Histological changes: in liver

In compared with control (fig.1) the sections showed multiple portal amyloidosis and congestion (fig. 2). Other sections showed moderate central venous congestion with disappearance of lobular sinusoid, the liver parenchyma showed acute degenerative changes that characterized by cellular swelling and necrosis of hepatocytes that lead to compress the sinusoids (fig. 3). In compared with control (fig.4), the most characteristics changes of kidney section were multiple focal hemorrhages (fig. 5). Most of glomeruli showed distended in the lumen of Bowman's capsules. The changes within the renal tubule showed degeneration of epithelial cells of renal tubules which showed massive nuclear pyknosis, karyorrhexis and necrosis (fig. 6).

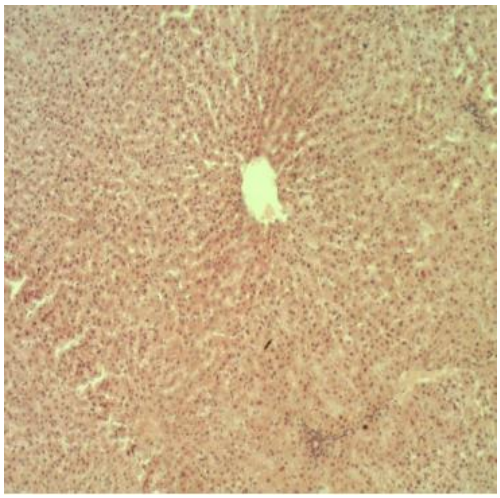

FIGURE 1: Section of liver (control). H&E 100X

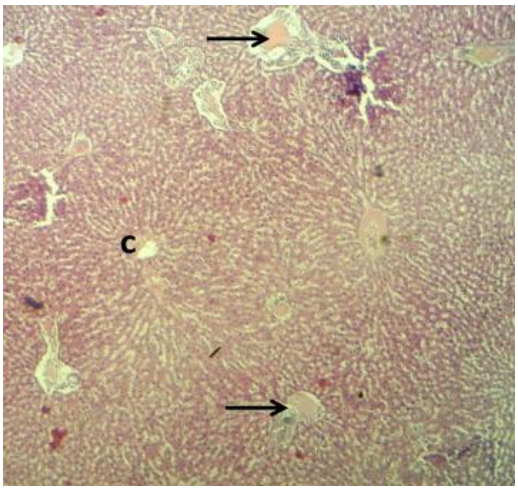

FIGURE 2: section of liver (P) shows: central venous congestion (c) & multiple focal

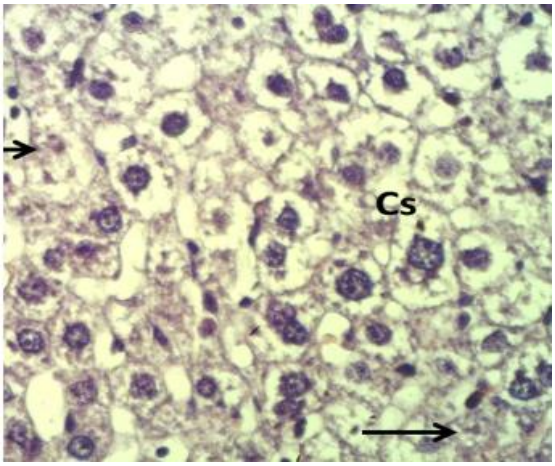

FIGURE 3: : Shows: acute cellular swelling (Cs), necrosis of hepatocytes (black arrows) H&E 400X

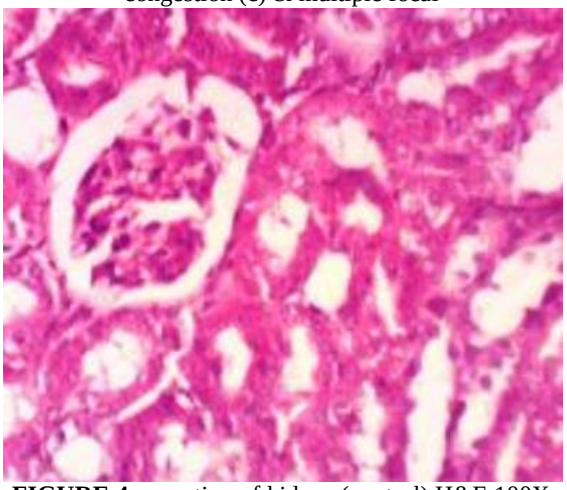

FIGURE 4: : section of kidney (control) H&E 100X

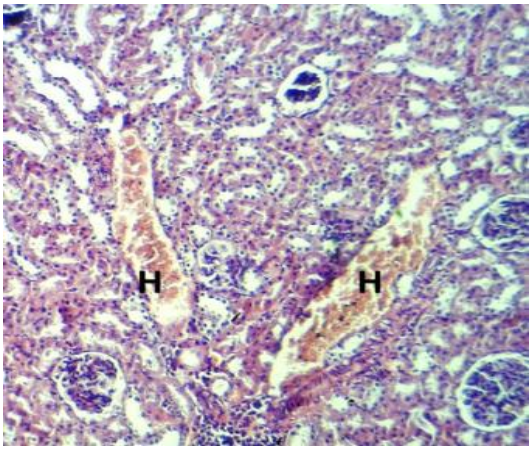

FIGURE 5: renal cortex shows: multiple hemorrhages (H). H&E 100X

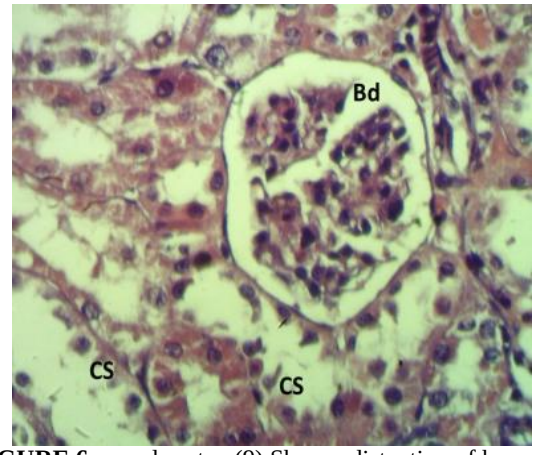

FIGURE 6: renal cortex (9) Shows: distention of bowman space (Bd) and cellular swelling of cells of renal tubules (CS) H&E 400X

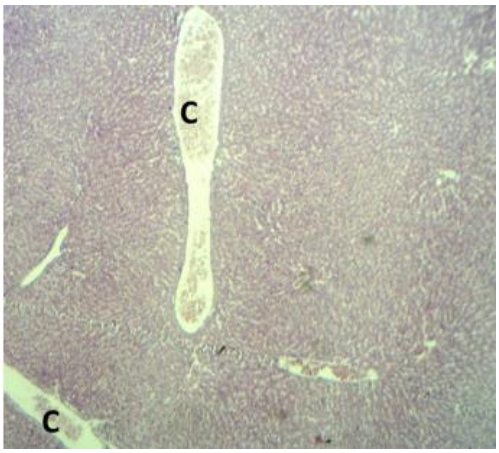

FIGURE 7: Section of liver (PE) shows: marked venous congestion (C). H&E 40X

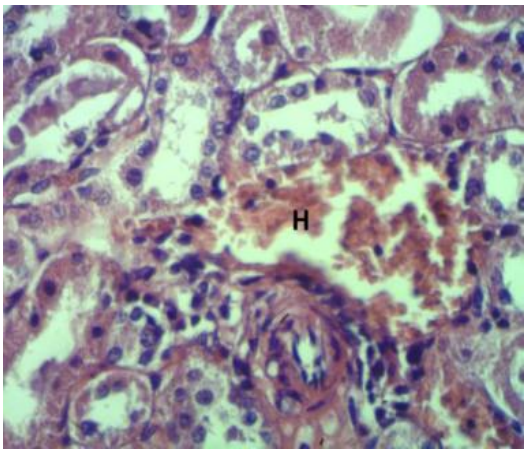

FIGURE 8: renal cortex (PE) shows: marked little focal hemorrhage (H). H&E 400X

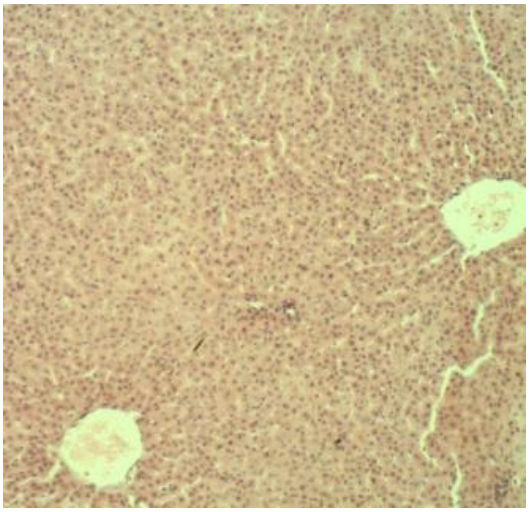

FIGURE 9: section of liver show near to control group H&E400 x

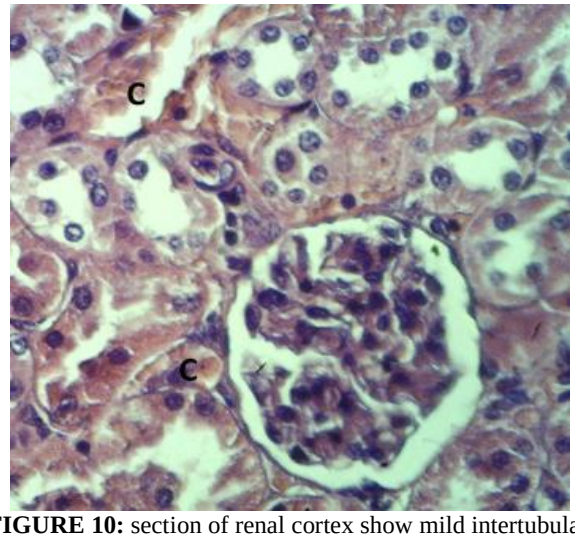

FIGURE 10: section of renal cortex show mild intertubular congestion (C) H&E 400X

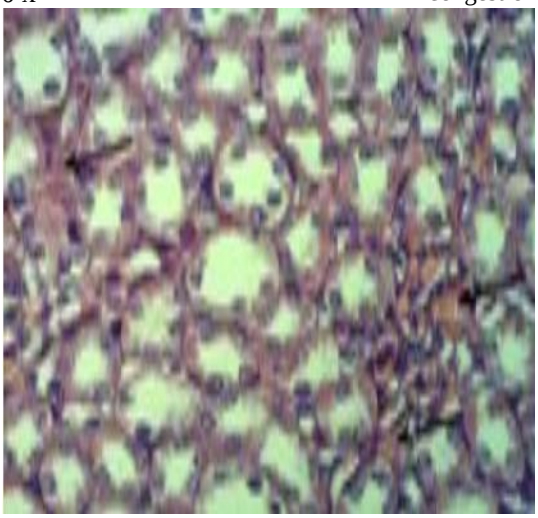

FIGURE 11: magnified section of renal medulla shows mild intertubular congestion (arrows). H&E 400X

In group ibuprofen with *Urtica pulliferia* the sections of liver showed moderated central venous congestion only (fig.7) and those of the kidneys appear few of mild hemorrhagic foci (fig.8).

While in group of *Urtica pulliferia* seen, the section of liver were similar those of control (fig. 9) while those of kidney showed mild congestion in inter tubular arterioles in renal cortex and medulla (fig.10 &11).

DISCUSSION

Ibuprofen is used routines in animals and human for relief of mild painful condition such as arthritis, muscle pain, abdomen pain, skin lesion, fight wound and skin abscess [14]. The study show non-significant differences in value of Hb and PCV after administration ibuprofen 200mg/kg /b.w. this agreement with[15] compared with control and *Urtica pilluferia* 50mg/kg this lead to the plant have antioxidants vitamins and minerals necessary for RBC build and increase the hemoglobin such as iron, magnesium, when improperly used NSAID could serve as source of harm animals and increase in ALT, AST level (lead to liver damage) this associated with bile duct damage [16] and cause increase in TSB which also secrete in bile indication liver damage[17], while seen decrease in level of this biochemical tests in T2, T3 because antioxidants activity of this plants, poly phenols specially inhibits the cytochrome p450 enzyme [18] minerals Zn, Se, mg, copper also hepatoprotective to xenobiotics[19] extensively protein bound with drug and metabolism occur mainly by oxidation and conjugation in the liver and renal elimination[20] causes increase in urea severe adverse and prolong use NSAIDS due to vasoconstriction and inhibition of renal prostaglandin mediated vasodilatation with decreasing renal blood flow and resulting in reduction in glomerular filtration rate[21]. PG play role in GIT mucosal and thrombocyte accumulation[22] this lead to renal failure, hypertensive disease and organ damage because increase in salt retention and vascular tone in glomerular vascular bed but decrease in value in T2, T3 creatinine show increase significantly in T1 may be the ibuprofen effect on renal and glomerular and cause retention in salts with freely both filtered by the glomerulus and creatine reabsorption remain the same mineral reabsorption if urea reabsorbed by the tubules, while a decrease in value of groups treatment with *Urtica pilluferia*_lead to a plant have contributed to various mechanisms, which prevention of chain initiation binding of transition metal ion catalysts, decomposion of peroxides prevention of contributed hydrogen ,obstruction reductive capacity and radicals scavenging [23] and phytochemical have been flavonoids, coumarius, some sterols, alkaloids and hydrocarbons. In histology the effect size of ibuprofen drug cause liver and gastrointestinal injury [24] appear as multiple portal amyloidosis and congestion, with dysfunction in renal multiple focal hemorrhages, glomeruli showed distended in the lumen of Bowman's capsules may be this drug induced renal damage to this organs[25]. While a powerful of antioxidants activity to *Urtica pilluferia* such as flavonoids (phenolic acids) coumarines, alkaloids, B-carotene[26,27] have a good effect with a decrease in the size of injury to the liver and kidney of T2,T3.

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