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Research Article

Histopathological effect of *Conium maculatum* aqueous extract on liver in Rats

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Abstract

Conium maculatum is amongst the most poisonous species throughout higher plants. Humans and livestock are also both poisoned by *Conium maculatum*. Cosequently, *Conium* can be found growing alongside highways, purple-spotted, glabrous, and up to 3-meter-high , and branching. The leaves are decompounding pinnately like several edible and medicinal herbs. *Coniine* and -coniceine, two alkaloids found abundantly, are thought to be responsible for the plant's toxicity and teratogenicity, the relative ratio of distinct *Conium* alkaloids appears to be affected by several conditions such as temperature, hydration, period, and stage of growth. *Conium* includes piperidine alkaloids that are structurally similar to nicotine. They bind to nicotinic-type acetylcholine receptors and behave as agonists. The Rats used in this study were all from the Animal Resource Center at the University of Kerbala's College of Veterinary Medicine. In the current experiment, several doses of aqueous extract of conium were used at concentrations of 2, 5 and 10 mg/kg to get whatever effect these may have on the liver in Rats. 24 mature rats were divided into 4 groups, six rats for each concentration and control as well. The results showed massive changes on the liver tissues for all groups in comparison with control. However, all groups receiving *Conium maculatum* extract infusions at rates of 2 , 5 and 10 mg/kg of drinking aqueous revealed toxic changes in the liver in Rats, according to the findings of the research study.

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1. Introduction: -

Conium maculatum is a poisonous plant[1, 2]. *C. maculatum* poisoning directly impacts the gut, neurological system, neuromuscular paralysis of respiratory, cardiovascular system, and respiratory tract, as well as, causing bronchoconstriction and bronchorrhoea[1, 3].

Human, cattle, sheep, horses, pigs, goats, and poultry have all been harmed by *Conium maculatum* poison. [4, 5]. The harmful plant *C. maculatum*, sometimes known as poison hemlock, appears in a variety of species, each with its own set of alkaloids [6]. Alkaloids are found in every part of the plant, such as the leaves, seeds, and blossoms. *Coniine*, N-methyl-coniine, pseudoconhydrine, gamma-coniceine, and conhydrine are the most prevalent alkaloids identified in *C.maculatum*[7, 8]. *Coniine* is a highly toxic liquid alkaloid that affords the plant its characteristic smell. Mucous membranes and the skin readily absorbs it. It has a stimulating influence in modest dosages, but at higher amounts, it has a destructive and hard effect on the spinal cord's motor centres[9]. However, these alkaloids serve as a selective agonist by binding to nicotinic acetylcholine receptors (nAChRs)[10]. The central and autonomic nervous systems, neuromuscular junctions, and the adrenal medulla generally include nicotinic-type acetylcholine receptors[10, 11].Consequently , the most dangerous side effect of *Coniine* is Rhabdomyolysis with acute renal failure, also known as renal damage, a condition that is typically seen in humans who have been poisoned[12]. *Coniine* -induced respiratory paralysis can result in death if the respiratory center in the medullary nerve is damaged. Conium alkaloids, which act resemble biphasic nicotine, cause tachycardia and bradycardia. However, this plant's teratogenic effect on animals has been observed[13]. In homeopathy, fresh poison hemlock herbs are applied. Pyridine alkaloids are significantly identified in all plant parts, involving coniine, N-methyl-coniine, conhydrine, coniceine and pseudoconhydrine, [2]. A technique for the biosynthesis of pseudoconhydrine has been proposed, in which c-coniceine undergoes a tautomeric double bond shift, resulting in an intermediate that is then oxidized at C5 to generate a second intermediate, which is then whittled down to pseudoconhydrine[14]. However, reducing c-coniceine is stochiometrically desirable. It has been proven that c-coniceine can produce conhydrine and conhydrinone. The allylic oxidation of c-coniceine output 10 -hydroxy-c-coniceine, which is ultimately minimize c-coniceine to conhydrine by a tautomeric shift of the double bond. Similarly, c-coniceine can operate as a precursor to pseudoconhydrine directly[7].

2. Materials and methods

2.1. Plant extraction

2.1.1. Pre-extraction or plant samples preparation

Plant sampling preparation was the first stage in researching therapeutic plants since it preserves the biomolecules in the herbs prior to extraction. To extract pieces such as leaves, you can use fresh or leaf powder *Conium maculatum*. Other pretreatments of bioactive components of herb, such as grinding and drying, affect the retention of phytochemicals in the final extracts[15].

2.1.2. Herbal drying and Grinding

Primary processing refers to the immediate post-harvest treatments given to herbs harvested through cultivation, wildcrafting, or field collecting in order to remove foreign substances, unintended plant parts, and other impurities, and includes, for example, sorting (garbling), washing, and areal drying powdered samples, on the

other hand, have a more homogenized and smaller particle size, resulting in increased surface contact with extractants. Because excellent extraction necessitates the vehicle making contact with the target analytes, particles smaller than 0.5 mm are ideal for solubilization [16].

2.1.3. Aqueous extraction of plant

The maceration extraction process is used to extract bioactive components from plants. Plant materials (coarse or powdered) were soaked in a sterile container with a liquid and left to stand at room temperature for at least three days with constant stirring, followed by compressing or separating and filtration. Heat is transported by convection and conduction in traditional methods, and the extractor is chosen based on the substance to be extracted. Infusion and decoction are similar to maceration in that they are immersed in cold water[17].

2.2. Experimental Design

Determining the right animal models for the planned experiments[18], rats were divided into four groups, six rats for each subgroup which included control and three groups treated with different concentration of extract (2, 5 and 10 mg/kg) . By consequence, after hospitalizing of rats in our animal house for two ten days, the experiment started by treating with oral extract for all groups of animal for two weeks in a daily basis .

2.3. Procedures for histological analysis and cell quantification

Liver of rats subsequently fixed in10% formalin and then dehydrated in a gradient of ethanol (70, 80, 95, and 100%) prior to getting embedded in paraffin, sections were cut at 5 m thicknesses, and soaked with hematoxylin and eosin [19]. Using a light microscope, the slides were examined (Olympus, Tokyo, Japan) ; each sample was randomly examined under the microscope with a 10X and 40X objective lens in total fields.

3. Results:-

Liver tissue section of rats treated with aqueous extraction of Conium maculatum 2 ,5 and 10 mg/kg induced different histopathological changes in the hepatic tissue, significant enlargement and congestion of central vein with degeneration of hepatocytes(fig 3,4),while the livers of control group animal showed normal histological picture represented by the normal arrangements of hepatic tissue(fig 1,2). The groups of animals treated with 5mg/kg and 10mg/kg of the exraction ,respectively revealed sever histopathological alterations on hepatic tissue represented by abundant inflammatory cells infiltration (fig.6); coagulative necrosis of hepatocytes and fibroblasts , inflammatory cells infiltration , (fig.7 & 8) liver tissue fibrosis (fig 7) are the predominant alterations.

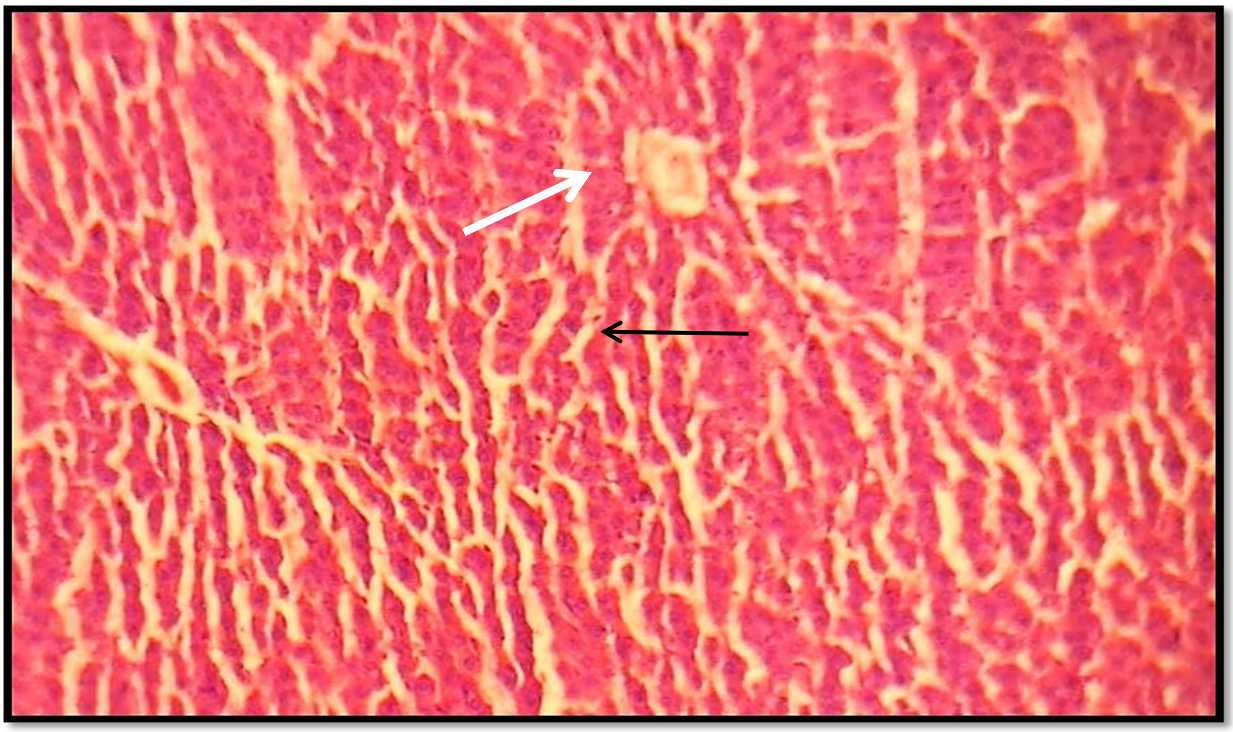

Figure 1 . Histopathological section for liver of control rats group ,showed the normal hepatic architecture, normal hepatocytes cords arranged (black arrow) around hepatic central veins (white arrow) .(10X, Hematoxylin and Eosin Stain).

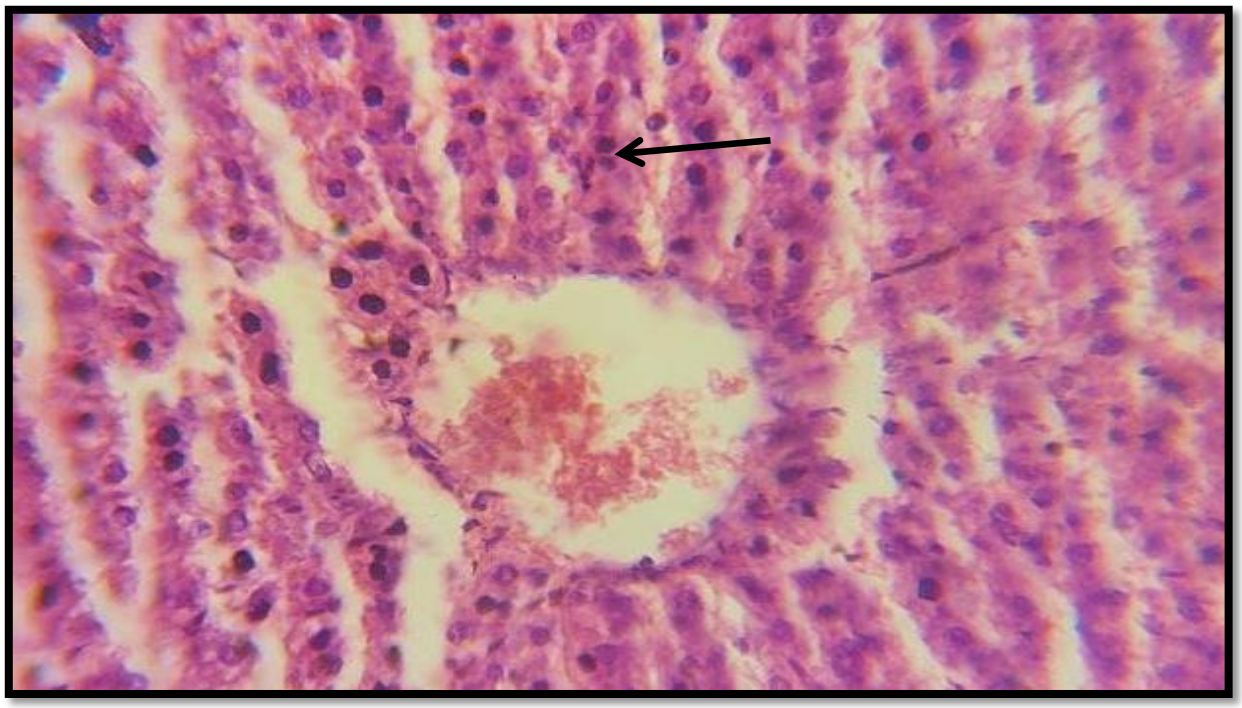

Figure 2. Histopathological section of control group liver with a high magnification revealed the normal histological appearance for the hepatic tissue , normal arrangments of hepatocytes cords (black arrow) around central vein.(40X, Hematoxylin and Eosin Stain).

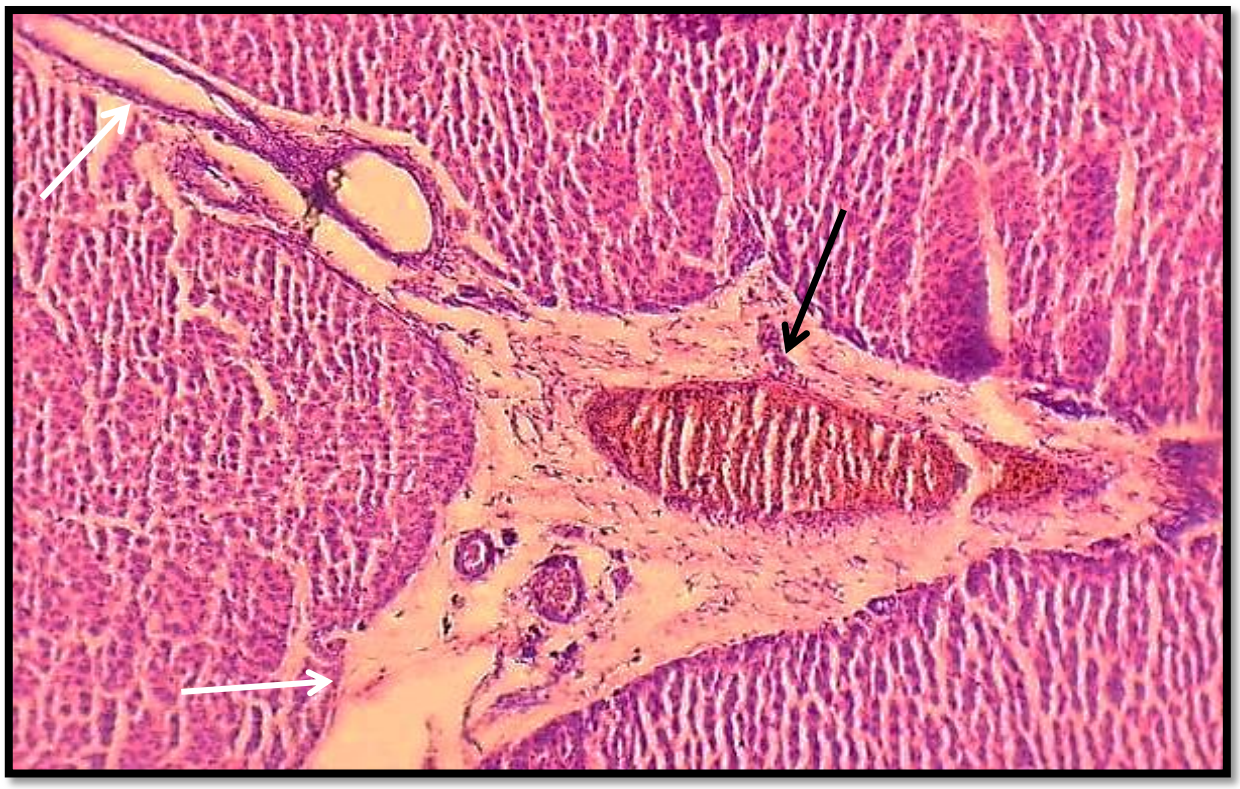

Figure 3. Histopathological section of Rats group treated with 2 mg/kg aqueous extraction of *conium maculatum*, showed sever congestion in hepatic central vein (black arrow) ,hepatic sinusoides and dilation in portal vein(white arrows) and portal artery. (10X, Hematoxylin and Eosin Stain).

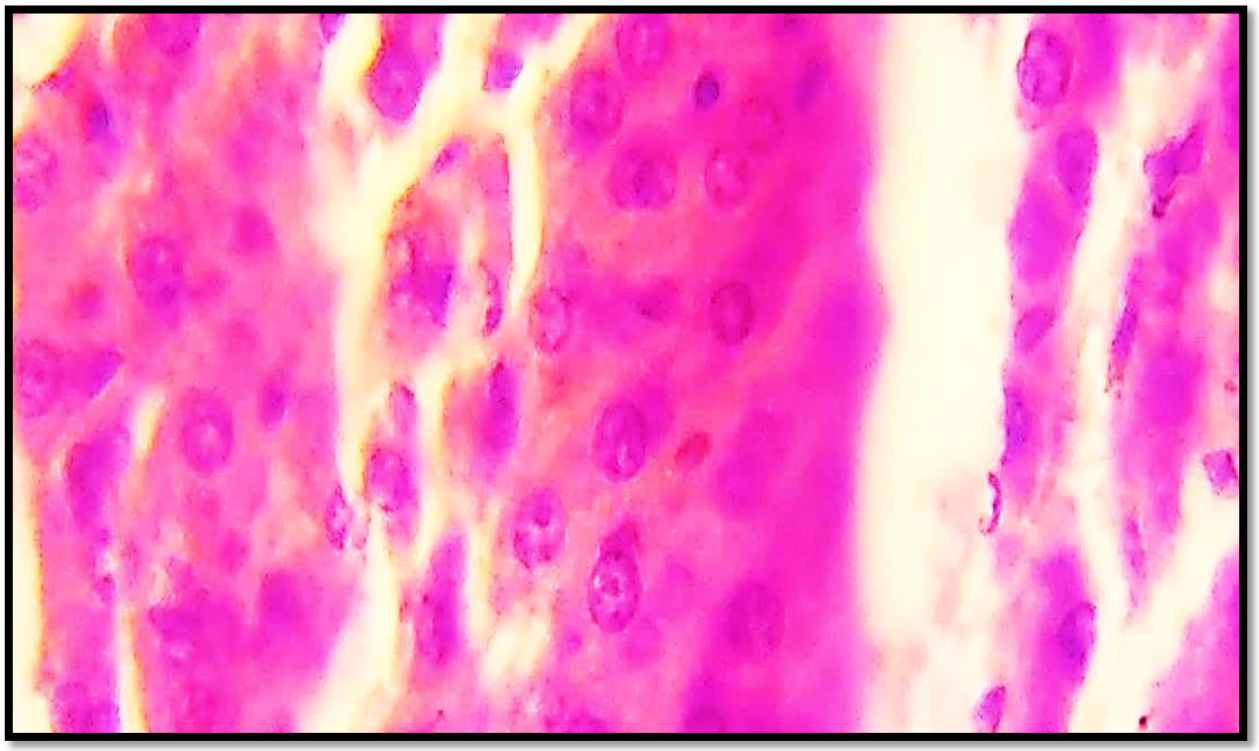

Figure 4. Histopathological section of Rats group treated with 2 mg/kg aqueous extraction of *conium maculatum* ,showed the hepatocytes injury represented by degenerative changes (cloudy swelling) black arrow .(40X, Hematoxylin and Eosin Stain).

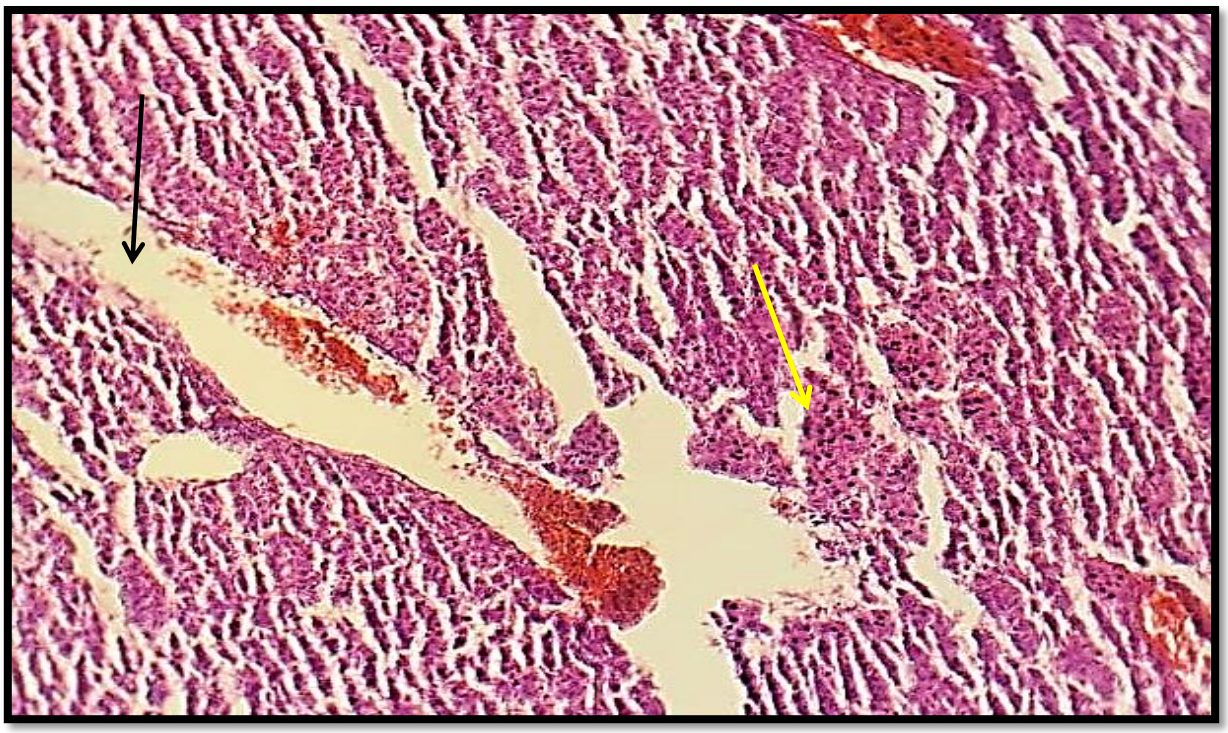

Figure 5. Histopathological section of Rats group treated with 5 mg/kg aqueous extraction of *conium maculatum* , revealed sinusoidal spaces dilation with congestion of hepatic central vein (black arrow) , loss of hepatic architecture and significant hepatocytes necrotic changes (yellow arrow). (10X, Hematoxylin and Eosin Stain).

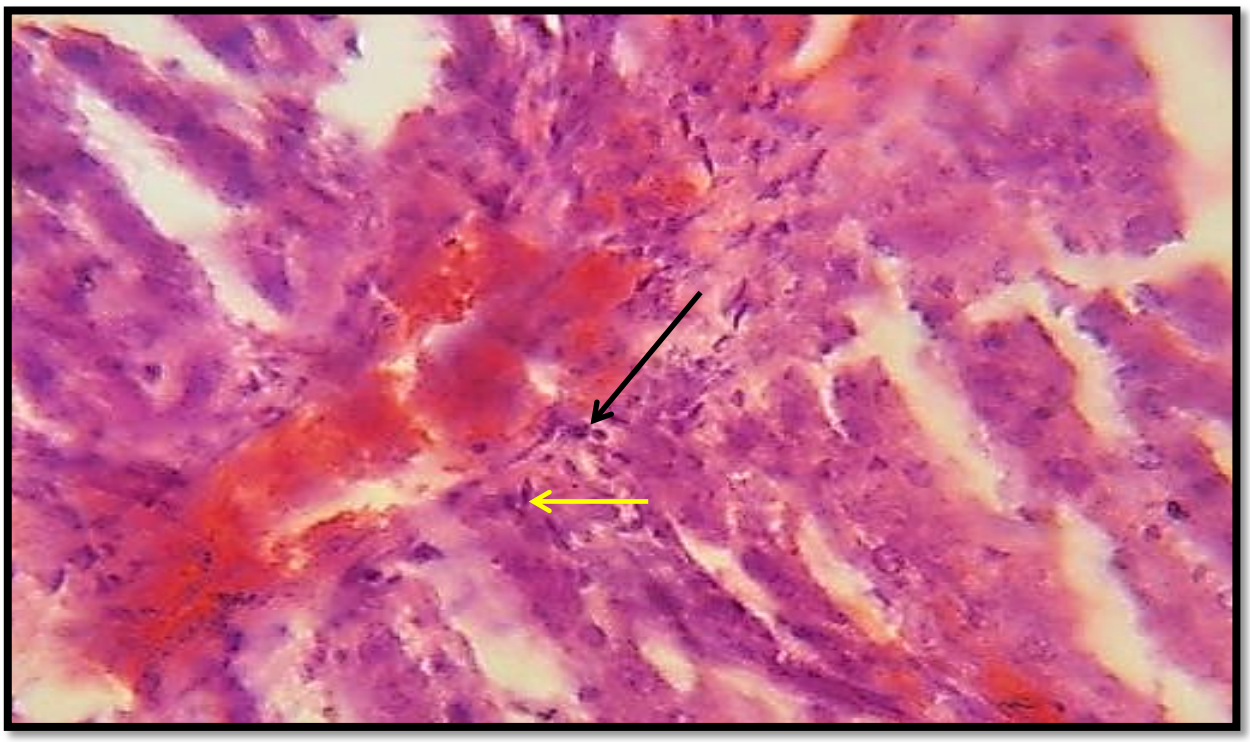

Figure 6 . Histopathological section of Rats group treated with 5 mg/kg aqueous extraction of *conium maculatum* , showed sever congestion of hepatic vein , inflammatory cells infiltration (black arrow) and fibroblasts proliferation around the congested blood vessel (yellow arrow) . (40X, Hematoxylin and Eosin Stain).

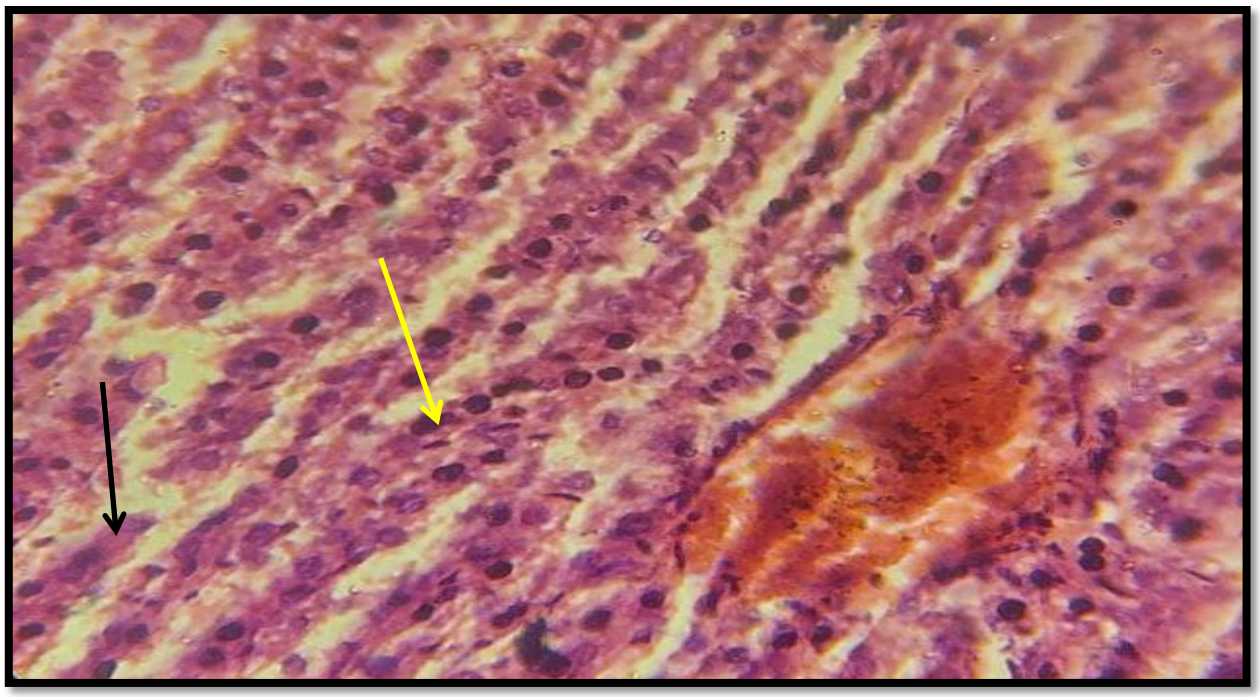

Figure 7 . Histopathological section of Rats group treated with 10 mg/kg aqueous extraction of *conium maculatum*, revealed significant hepatic fibrosis (collagen fibers proliferation) black arrow , with necrosis of hepatocytes manifested by pyknotic nuclei (yellow arrow). (10X, Hematoxylin and Eosin Stain).

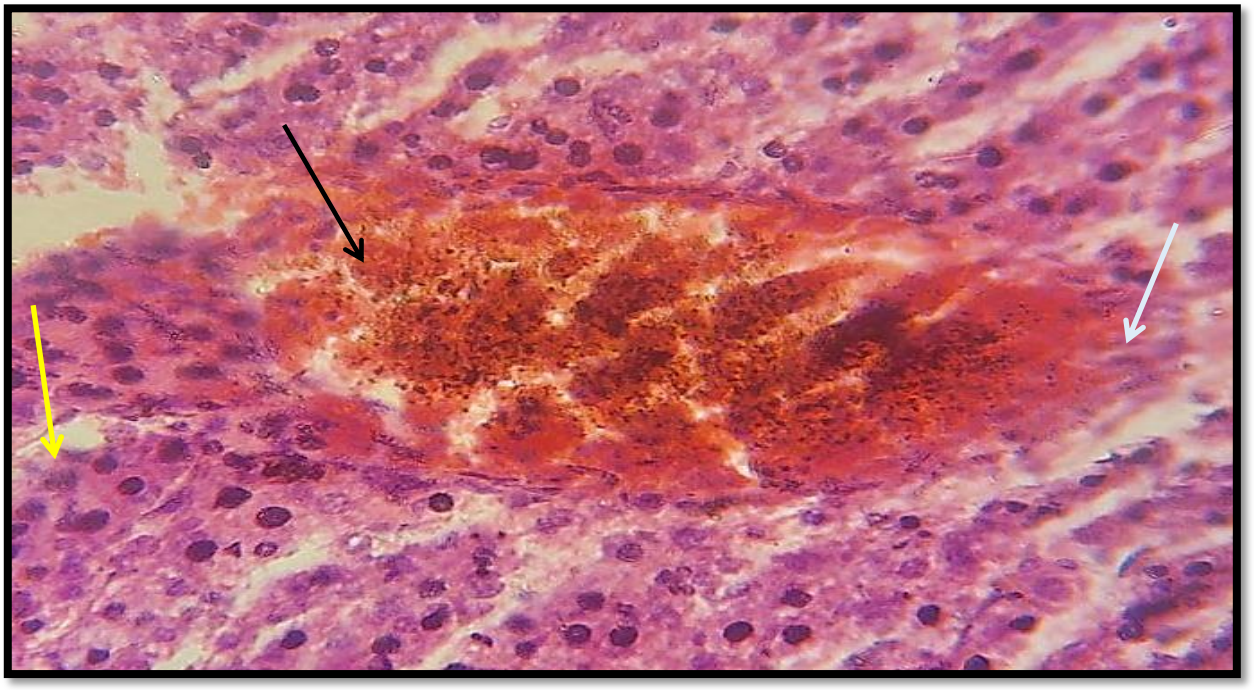

Figure 8 . Histopathological section of Rats group treated with 10 mg/kg mg/kg aqueous extraction of *conium maculatum* , showed the massive congestion of the hepatic central vein with hemosiderin (black arrow) , sever infiltration of mononuclear inflammatory cells , fibroblasts infiltration (blue arrow) and areas coagulative necrosis of hepatocytes (yellow arrow) .
(40X, Hematoxylin and Eosin Stain) .

4. Discussion: -

Conium maculatum included alkaloids, flavonoids, coumarins, polyacetylenes, vitamins, oils, and a variety of other actively metabolites, according to a chemical study. Although some of these were incredibly effective in treatment of illnesses, many of the plant ingredients had adverse side effects and might cause life-threatening conditions[20]. The alkaloidal fraction of Conium maculatum aerial parts exhibited remarkable anti-inflammatory activity in rats and strong peripheral and central antinociceptive properties in mice at a range of doses of 10–20 mg/kg. Doses more than 20 mg/kg were found to be lethal. Hemlock (*Conium maculatum*) was one of the most dangerous plants for animal models, domesticated animals, and people due to the presence of piperidine alkaloids in all sections of the plant, even the leaves [9].

C. maculatum is toxic in general, according to field research, although its limited, and risky effects of death following acute poisoning [21].

The alkaloid residues in avian muscle and liver tissues may support the theory that 'coturnism,' an acute toxicity of humans caused by quail consumption, which induced after feeding on *C. maculatum* seeds by those animals prior or within their migratory flights; Coturnism has been recognized since ancient times, and the cause of the disease is still a topic of contention today. There are a few scientific publications with conclusions that are worth looking at;Coniine, when given to turkeys in single doses, has been observed to remain in muscle and the liver (at concentrations of 80±120 and 100±200 ppm, respectively)[22]. The possibility of *C.maculatum* alkaloids infiltrating the liver tissue and causing damage ,cellular injury and histological changes has been indicated, fibrosis among the most characteristic alterations on liver tissues . In addition to inflammation , necrosis of hepatocytes and sever congestion of hepatic blood vessles and sinusoids[6] are observed.

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