Histological Study for the Effect of Tribulus terrestris Extract Against Hepatotoxicity After Cytarabine (Ara C) Chemotherapy in Male Rats

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***Abstract*— Hepatotoxicity is a common clinical manifestation associated with a wide range of anticancer therapies. Because of the inherent toxicity of anticancer therapies, oncologists must maintain a broad understanding of their effects on the body, including the liver. Therefore, the study was conducted to examine the effects T. terrestris extract on damaged liver as a result of giving cytarabine. In the experiment, twenty-four male rats were employed. The rats divided to four group each group with six rats, lasted about during 28 days the rats were administration as the following groups, which include: group (G1) control negative: control negative: six rats were administered with normal saline, and were euthanized after four weeks, group (G2) of cytarabine (Ara-C 25): in this group six rats will be administrating by cytarabine (Ara-C 25 mg/kg bw) intraperitoneally every day for four weeks is the control positive: in this group six rats will be administered by T. terrestris extract (250 mg/kg body weight) orally for four weeks, group (G3) experimental group: in this group six rats will be administrating by cytarabine (Ara-C 25 mg/kg bw) intraperitoneally + T. terrestris extract (250 mg/kg bw) orally for four weeks, group (G4) is the control positive: in this group six rats will be administered by T. terrestris extract (250 mg/kg body weight) orally for four weeks. The purpose of this study was to evaluate the protective role T. terrestris extract on cytarabine induced hepatotoxicity on liver tissue in male rats.**

***Keywords* — T. terrestris extract, Cytarabine (Ara-C), T. terrestris, histopathological studies, liver.**

I. INTRODUCTION

THE liver performs various metabolic tasks and is a critical organ in the food and drugs biotransformation. Hepatic disorders are a primary global health concern. Because of its remarkable potential for regeneration, toxic substances are the primary cause of hepatic diseases. Drug toxicity, xenobiotic toxicity, and oxidative stress all have a significant impact on the liver. The liver is a primary carcinogen target due to its active proliferative response. Since it is crucial for metabolizing many medications and poisons, including cytotoxic chemotherapy regimens, it is particularly vulnerable to harm [1].

The liver is known only in vertebrates. It is a critical organ due to its numerous essential biological activities, such as removing toxins, producing important and necessary compounds for food digestion, and growing the organism [2].

Xenobiotic compounds can cause severe damage to the body. The liver can protect against damage, so it is considered an essential organ in metabolizing substances. Bio activation of some compounds in the liver can be associated with liver damage of course, the features of restoration and regeneration power have made it considered a powerful organ. In case of lack of regeneration or high severity of liver damage, the person will suffer liver failure or death. An increase in the arbitrary use of some drugs, either orally or by prescription, or more interest in the excessive use of dietary supplements or dietary drugs, or the use of xenobiotic chemical compounds can provide the basis for further damage to the liver [3].

II. MATERIALS AND METHODS

A. Experimental Animals

Twenty-four albino rats with Wight ranging 280-300 g were prepared from the College of Veterinary Medicine University of Kerbala laboratory, kept in plastic cages with diameters of 50×35×15 cm and under appropriate laboratory conditions (25-28 C°, 40٪ - 60٪humidity, and ventilation and the light system was 12 hours per day. Each cage consists of not more than four rats. Male rats were fed on the standard chow and drinking water ad libitum throughout the experiment. To acclimatize, they were kept fifteen days before the experimental assay.

B. Experiment Design

A total of 24 male rats were classified into 4 groups (6 rats in each group):

1- Group (G1) control negative: control negative: Six rats were administered with normal saline, and were euthanized after four weeks.

2- Group (G2) of Cytarabine (Ara-C 25): in this group six rats will be administrating by Cytarabine (Ara-C 25 mg/kg bw) intraperitoneally every day for four weeks [4].

3-Group (G3) experimental group: in this group six rats will

be administrating by Cytarabine (Ara-C 25 mg/kg bw) intraperitoneally + T. terrestris extract (250 mg/kg bw) orally for four weeks [5].

4- Group (G4) is the control positive: in this group six rats will be administered by T. terrestris extract (250 mg/kg body weight) orally for four weeks [5].

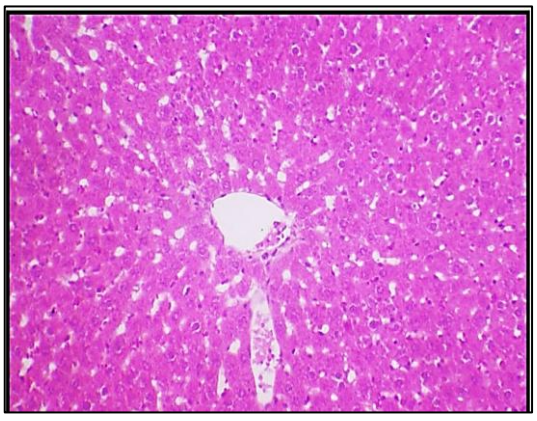
Sample collection and tissue preparation:

After the end of the experiment period testes and epididymis samples have been taken after sacrifice the animal and they were immediately put into a 10% fixative formalin solution and left there for 24 hours before being processed. The samples were first dehydrated in graded alcohol at room temperature for 2 hours each at 70%, 80%, 90%, and 100% concentration before being submerged in xylene for 2 hours and then melted paraffin wax for 3 hours. The samples were then positioned and implanted in brand-new paraffin (paraffin blocks). To examine the sections under a microscope, the blocks were sectioned with a microtome at a thickness of 5 m. The sections were subjected to standard hematoxylin and eosin (H&E) staining procedures. Photomicrographs of each section were taken using a digital camera (canon, japan) using a light microscope to analyze the sections under examination [6].

III. Results and Discussion

A. Histological Study of liver in control group

The histopathological examination to the third group of the liver tissue treated with cytarabine and T. terrestris (H and E,10X). Showing reversible histological changes manifested by mild congestion in central vein and sinusoides, mild hepatocytes degeneration and presence of hepatocytes vacuolation and mild inflammation as shown in figure (1.A). Examination under (H&E,40X) showing slight reversible histological changes characterized by mild congestion inflammatory cells infiltration in portal area, mild hepatocytes degeneration with proliferation of newly formed bile ductules. As shown in figure (1.B).



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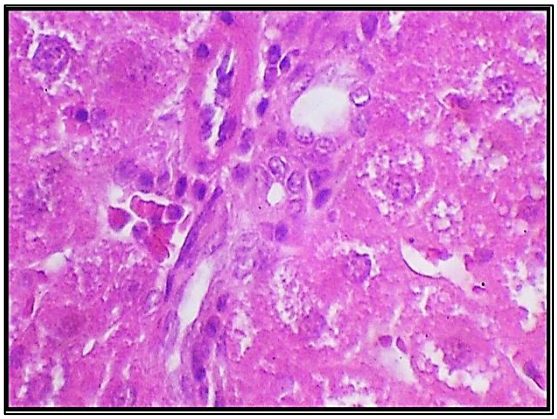
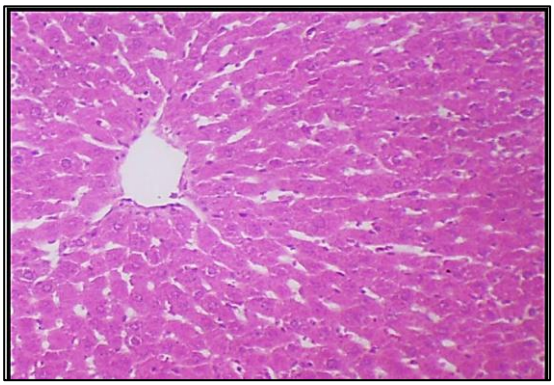


B

(Figure 1): Photomicrograph of hepatic section for a cytarabine and T. terrestris treated rat A: showing reversible histological changes manifested by mild congestion in central vein and sinusoids (black arrow), mild hepatocytes degeneration and presence of hepatocytes vacuolation (white arrow) and mild inflammation (red arrow), (H & E, 10X) B: showing slight reversible histological changes characterized by mild congestion inflammatory cells infiltration in portal area (black arrow), mild hepatocytes degeneration (white arrow) with proliferation of newly formed bile ductules (red arrow), (H & E,40X).

B. Histological Study of liver in T. terrestris group

The histopathological examination to the fourth group of the liver tissue treated with T. terrestris showed no histological change and it was closed to normal liver histology but mild hepatocytes degeneration was found as shown in figure (2.A) Examination also showing normal histological section and mild hepatocytes degeneration as shown in figure (2.B).



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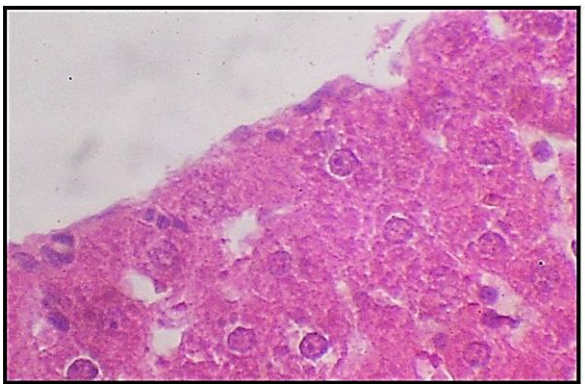

B

(Figure 2): Photomicrograph of hepatic section for a T. terrestris treated rat A: showing closed to normal histological changes manifested by slight congestion in central vein (black arrow), mild hepatocytes degeneration (white arrow), (H & E, 10X). B: showing closed to normal histological changes, mild hepatocytes degeneration (white arrow), (H & E, 40X).

IV. Discussion

Effect of cytarabine and in combination with T. terrestris extract on liver histology

This research shows severe congestion in the central vein in the hepatic histology of the cytarabine group. This result could occur due to the toxic side effect of cytarabine, which can lead to congestion of the hepatic vein due to the destruction of the hepatic cells. Also, cytarabine can increase ROS production, which leads to hepatic destruction. This finding is in consensus with [7] [8].

Cytarabine is a chemotherapy drug that treats various cancers, including leukemia and lymphoma. While it primarily affects the rapidly dividing cancer cells, it can also have some side effects on healthy cells, including those in the liver [9]. Cytarabine can cause liver toxicity, which may result in liver histological alterations such as steatosis, necrosis, and fibrosis. Steatosis refers to fat buildup in liver cells, while necrosis is the death of liver cells. Fibrosis is the buildup of scars in the liver tissue [10].

On the other hand, the combination group shows a significant difference when cumbered to the cytarabine group. This result may occur due to T.terrestris containing a beneficial chemical to the liver. One of the main active components of T.terrestris is saponins, a plant compound shown to have anti-inflammatory and antioxidant properties. These properties may help to protect the liver from injury caused by oxidative stress and inflammation. This finding is in consensus with [11] [12].

T.terrestris may help reduce the production of reactive oxygen species (ROS) in the liver tissue, which could benefit liver health. Some animal studies have suggested that T.terrestris may have hepatoprotective effects, meaning that it could help to protect the liver from damage caused by toxins or other harmful substances, saponins found in T.terrestris may have antioxidant properties that can help to neutralize ROS in the liver [13] [14].

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