

Cancer protective Effects of L. Serriole Extract against Carcinogen Benzo (A) Pyrene in White Mice Liver: Histological Study

Roaa Waleed Dawood¹, Shaimaa Hijlan Sayer², Ashwaq Talib Hameed³

^{1, 2, 3}College of Education for women, University of Anbar, Iraq

Email: rou20w4016@Uoanbar.edu.

Abstract

This study was conducted to investigate the possibility of using the alcoholic extract of *Lactuca serriola* as a protective agent against the cancer-causing chemical benzopyrene, study included dividing male white mice into five groups 7 mice per group. The results showed a Significant changes were found in the normal liver structure in the group of animals that had been treated with the carcinogenic substance benzopyrene, including liver damage, which is represented by the infiltration of inflammatory cells in various places, especially around the central and inflammation cellular veins, and clear fibrosis around the portal and central veins. The research showed when mice were dosed with alcoholic extract of the wild lettuce plant *L. serriola* at a concentration of 0.006mg/kg ((0.003mg/kg)) 0.0015 mg/kg for 30 days and in conjunction with dosing it with the carcinogenic substance Benzo(a)pyrene at a concentration of 0.001mml, it was found that there was no pathological change in the normal structure of the liver tissue, that is, without damage to the hepatocytes and sinusoids in addition to the blood vessels compared to the control group for the first concentration 0.006mg/kg, as it was found that the histological shape was close to normal with the expansion and congestion of the hepatic portal vein in addition to the presence of vinegar Hepatocytes binucleated and the sinusoids expanded in comparison with the control group for the second concentration 0.003mg/kg and it was found from the histological shape of the liver that there were histological changes represented by the infiltration of inflammatory mononuclear cells with the dilatation of the hepatic veins and hematopoietic congestion, as well as the multinucleated cells of the focus.

Keywords: histological study; carcinogen Benz (a) pyrene; *L. serriola*

1. Introduction

Cancer is one of the dangerous and widespread diseases worldwide, and it occurs as a result of defects in some cells due to their deviation from the normal course of division and growth, and the reason for this is due to the effects of carcinogens, such as chemical, radiological, bacterial and viral causes (Cooper, 2004), currently Cancer has become the second leading cause of death in the world after cardiovascular disease, where global statistics indicate that cancer will become the number one cause of death worldwide by the twenty-first century, as the World Health Organization -WHO issued a statement in which it stated that The number of deaths reached 5.6 million deaths worldwide in 2018, the highest recorded in East Asian countries (Ferly et al., 2019).

Iraq witnessed an increase in the number of cancer patients, according to what was indicated by the official Iraqi Cancer Registry, the ninth edition of which was issued at the end of 2015, in which it was found that there were 10,278 cancer-related deaths. The higher percentage was in males compared to females, as lung cancer was It occupies the first place in males, while breast cancer ranked first in females, and in children, blood and brain cancers came in the first place, and thus Iraq has the highest percentage among the countries of the Middle East, and the reasons are due to the wars that Iraq was subjected to. In recent decades (Mula-Hussain,

2019 ; Alwan, 2016 ; Salih et al., 2015) .At the present time, there are many types of treatments for cancer, including chemotherapy, surgery, and radiation, but these treatment methods have great collateral damage to human health, as their effect on cancer cells affects at the same time on the natural body cell, and for this The reason is that recent research has aimed to find new ways to treat cancer, including the use of natural sources as sources of treatment, by heading towards nature, because it contains natural plants and herbs characterized by the possession of many chemically active substances (Balunas & Kinghorn, 2005; Pandey, 2019).

Due to the fact that the plant genera belonging to the compound family Asteraceae, including the wild *L. serriola*, is characterized by being rich in active compounds (Koc et al., 2015), as most of the active substances present in it are phenols and flavonoids that are highly effective against cancer (Muniyandi et al. ., 2019), in addition to its antioxidant activity (Ahmed et al., 2016), as wild lettuce contains the milk of latex plants (Sessa et al., 2000), which is called *Lactucarium*, which is used medically because of its many medicinal properties. Such as its effectiveness as Anticancer, Diuretic, Emollient, Fever reliever, Hypnotic, Narcotic, Tonic, Galactagogue, Sedative, It is also used to treat Anxiety, Neuroses (Mifsud, 2006), the study aimed the effect of alcoholic extract of wild lettuce on some histological aspects in mice.

2. Materials and Methods

Collect plant sample

Wild lettuce plant *L. serriola* was collected from separate areas in Fallujah district and clean, free from bush, insects and undamaged parts were obtained. Taking into account its constant stirring, and after making sure that the plant was completely dry, it was ground using the electric grinder, then the plant powder was placed inside filter papers to prevent exposure to the effects of moisture, and then they were kept inside glass containers (Al-Hashimi, 2005). Soak 4g of plant powder in 100ml of methyl alcohol 99% for 24 hours in a tabletop shaking incubator. Then, the alcohol was evaporated at 37°C by leaving the extract in the incubator for 48 hours, then the extract was suspended with 10ml of distilled water, sterilized and kept at 20°C.

Histological study

35 adult white male mice were used in this study, which were brought from the National Center for Drug Control in Baghdad, and were placed in plastic cages for animal husbandry, which were sprinkled with sawdust, taking care to clean the cages and change the sawdust. An average of three times a week. Mice in cages with 7 mice in one cage, while the number of cages was 5 cages. Mice were subjected to appropriate laboratory conditions in terms of ventilation, appropriate temperature and lighting, while they were continuously given water and fed the standard diet. The negative control group, which was given water only, the positive control group, which was given orally benzopyrene, purchased from Guokang (China) in the development of cancer in experimental animals, which is a water-insoluble solid. Dissolve it in vegetable corn oil at a concentration of 0.001 mm and one dose per week according to (Wattenberg, 1993 & Richard). As for the groups of wild lettuce extract *L. serriola*, they were distributed according to the concentration of the extract into three groups, the group that was dosed with the extract at a concentration of 0.006 mm and the group that took doses. With 0.003 mM extract and the group dosed with 0.0015 mM extract on a daily basis for 30 days. The livers of each animal were excised and placed in plastic containers of formalin at a concentration of 10% for the purpose of histological study.

3. Results and Discussion

The histological changes of the liver were studied and diagnosed in male white mice using a light microscope. The results of the histological examinations of the animal groups treated with the carcinogen benzopyrene showed clear histological changes in the liver tissue when compared with the control group, when the mice were dosed with benzopyrene at a concentration of 0.001mg/kg. With one dose per week for 30 days, the histological profile showed significant changes in the structure of the liver tissue, including liver damage resulting from treatment with benzopyrene, which is

represented by the infiltration of inflammatory cells in multiple places, especially around the central veins and cellular inflammation, and clear fibrosis around the vein. Pyloric and central, as it shows multi-nucleated cells with different sizes in addition to the widening of the sinusoids of the liver and the presence of interstitial hemorrhage [picture 2](#). When mice were dosed with alcoholic extract of *L. serriola* at a concentration of 0.006 mg/kg for 30 days, in conjunction with the carcinogenic substance benzo (a) pyrene at a concentration of 0.001mg/kg at a concentration of one dose per week for 30 days, it was found that there was no change Patient with the normal structure of the liver tissue, that is, without damage to the hepatocytes and sinusoids, in addition to the blood vessels compared to the control group. [Fig.1 C](#).

And when mice were dosed with alcoholic extract of wild *L. serriola* at a concentration of 0.003ml for 30 days, which was administered concomitantly with the carcinogenic substance Benzopyrene at a concentration of 0.001ml at a single dose weekly for 30 days, it was found that the histological shape was close to normal with the expansion of the portal vein. Hepatitis and congestion in addition to the presence of binucleated hepatocytes and enlargement of the sinusoids compared to the control group [fig. 1.D](#). And when mice were dosed with alcoholic extract of *L. serriola* at a concentration of 0.0015ml for 30 days in conjunction with the carcinogenic substance Benzopyrene at a concentration of 0.001 ml at a single dose weekly for 30 days, it was found from the histological profile of the liver that there were histological changes represented by the infiltration of inflammatory mononuclear cells. With the expansion of the hepatic veins and blood congestion, as it shows multinucleated cells.

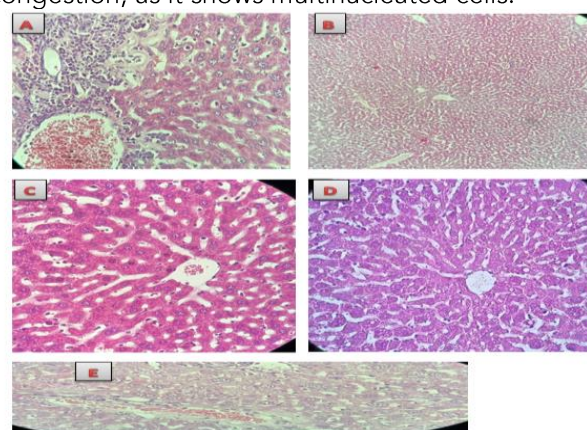


Figure 1 : section Of Liver , (A) control showing normal histology, (B) Liver treated with benzo(a)pyrene showing abnormal histology when compare with control group (A), where they appear hepatic veins expansion and blood congestion and hepatic sinusoidal expansion and inflammatory cell infiltration, (C) Liver treated with alcoholic extract showing (0.006mg/kg) normal histology homologous when compare with control group (A), (D) Liver treated with alcoholic extract (0.003mg/kg) showing histological form close to normal with hepatic sinusoidal expansion and presence binuclear cells when compare with control group (A), (E) Liver treated with alcoholic extract (0.0015mg/kg) showing inflammatory cell infiltration and hepatic sinusoidal expansion and blood congestion .

Through the histological study of the liver in the group of animals that were dosed only with the carcinogenic substance benzopyrene, it was found that there were significant histological changes in the structure of the liver tissue. And fibrosis around the central and portal veins, in addition to the expansion of the hepatic sinusoids, and this is consistent with (Uba et al., 2020), which proved that benzopyrene causes hepatotoxicity, as it showed similar changes in animals, as it caused the infiltration of inflammatory cells around the portal area in addition to widening Liver sinusoids.

Also, Wang (2015)) confirmed that benzopyrene causes cancer and cancerous lesions in the liver, stomach, and kidneys after 90 days of exposure. Liver cells of animals treated with B (a) p benzopyrene, in addition to the enlargement of the hepatic sinusoids when compared with control animals, as this expansion increases with the increase in the density of metabolites of benzopyrene during its conversion to other forms in animals that have been dosed with it.

The protective or mitigating effect of the leaves and stems of *L. serriola* against the hepatotoxicity caused by chemical compounds was also observed. The alcoholic extract of the leaves and stems of *L. serriola* showed less toxic effects on the liver tissue in white mice, and this confirms the protective role of the alcoholic extract. Plant in stabilizing the cell membrane the phenol present in it may be responsible for the protective effect of the liver accompanied by the antioxidant mechanisms. In the group of animals that were dosed with alcoholic extract of wild lettuce with a concentration of 0.006 mml in conjunction with the carcinogenic substance benzopyrene the extract showed Alcohol has a high efficiency in protecting the liver from the toxic effects of benzopyrene, as it helped in an improvement in the hepatic tissue, which was accompanied by the return of hepatocytes and sinusoids to their normal position. The vegetarian is considered the best because of the results it showed in the protection and prevention against the carcinogen benzopyrene, and this agrees with (Bouimeja et al., 2019), which proved that giving the alcoholic extract to the experimental animals had a significant protective effect on the liver tissue, as it restored the liver tissue to its natural structure, as it works to protect the liver against toxicity caused by chemicals through the active substances present in it, which Acting as antioxidants, *L. serriole* has a protective effect against many hepatotoxic drugs, in agreement with (Asif et al., 2020), which proved that the alcoholic extract of wild lettuce leaves and stems had a significant effect in reducing liver toxicity. Caused by paracetamol and this is due to the presence of the polyphenol compound responsible for antioxidants and the ability to remove free radicals. The results are also in agreement with (James et al., 2019) who demonstrated the protective effect of *Launaea taraxacifolia* Willd extract against hepatotoxicity caused by the chemical compound carbon

tetrachloride CCL₄, where the alcoholic extract showed significant protective effects against liver injury caused by it, as the use of the extract Alcohol in advance helped prevent damage to liver cells by helping to maintain the normal structure of liver tissue

Some previous studies on several plant extracts to reduce the toxicity of benzopyrene on tissues of some laboratory animals showed that the ethanolic extract of the leaves of *Combretum Zenkeri* has the ability to reduce liver damage caused by benzopyrene due to free radicals (Okwu et al., 2014), and the results are in agreement with (Kolade & Oladiji, 2019), where the effect of curcumin extract was proven to protect the liver against toxicity caused by benzopyrene in albino laboratory rats, as curcumin did not affect liver tissues, and no expansion of liver sinusoids was observed when compared to the control group. The protective and curative properties of the extract against Benzopyrene is due to its ability to remove free radicals.

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