

## Nephrotoxicity effect of *Cannabis sativa* (Marijuana) plant on the male albino rats.

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(Received: 15 / 8 / 2012 ---- Accepted: 31 / 10 / 2012)

### Abstract:

The objective of this study was to investigate the effects of cannabis (marijuana) induced toxicity in kidney tissue. Thirty mature male rats of six to 8-week-old male rats were divided into three groups, ten animals in each group. Group 1, served as control and received standard diet and tap water (*ad libitum*), while animals of second group injected intrapretoneously with 1ml of the solution (5mg/1kg) body weight, while the animals of third group injected intrapretoneously with 1ml of the solution (10mg/1kg) body weight. Histological examination of rats kidney treated, with cannabis showed many lesions characterized by coagulative necrosis in epithelium lining proximal convoluted tubules some of glommeruli revealed bowman's capsules dilatation and other showed a trophy or loss of glommeruli.

**Key words:** Cannabis, cannabinoids, marijuana, histopathology, kidney

### Introduction:

Cannabis refers to the dried flower tops of the female plant of Cannabis (*Cannabis sativa*). This herbal product is also commonly known as marijuana or marihuana. The main way to administer cannabis is by smoking, which is also the way most medicinal users consume it. Cannabis or single cannabinoids may have medicinal value for certain diseases and under certain conditions [1, 2].

Marijuana is the most widely used a illegal l drug in the world. The United Nations Office of Drugs and Crime (UNODC) estimates that, across all nations, 160 million people used cannabis in the course of 2005, 4% of the global adult populations - far more than the number that used any other illicit drug, though far less than the number that consumed alcohol or tobacco [3, 4].

Delta-9-tetrahydrocannabinol (THC), is the pharmacologically and toxicologically most relevant constituent found in the Cannabis plant, producing a myriad of effects in animals and humans. The most well-established palliative effect of THC is the inhibition of chemotherapy- induced nausea and vomiting, mainly in cancer patients. Pure THC can be derived from natural sources (extraction from cannabis plants) or produced synthetically [5, 6].

Up to date, more than 100 different cannabinoids have been described, but only a few of the major ones have been characterized for biological activities, including cannabidiol and cannabinal [5].

The cannabis use among adolescents and young adults led to a strong reaction in much of the developed world, which still results in large rates per capita of arrests for cannabis possession and use in nations such as Switzerland, Australia and the United States. The emergence of a new stream of research findings documenting that cannabis can trigger adverse mental health consequences for some users has recently increased popular concern [7].

The aim of this study was to determined the histological changes caused by cannabis on kidney tissue in expermental albino rats.

### Materials and Methods: (Cannabis)

Six to 8-week-old male rats (*Rattus norvigicus*) were obtained from the animal house of Science College. The animals were housed in plastic cages bedded with wooden chips. All animals were kept in a temperature-controlled environment with a 12-h light/dark cycle and were allowed free access to food and water *ad libitum*.

In this experiment the animals were randomly allocated to three experimental groups of 10 rats each: (1) the rats of this group were received tap water and regarded as control group. The rats of the second group daily injected with (5mg/1kg) body weight and the rats of third group were injected daily with (10mg /1kg) body weight.

### Drug Preparation:

Cannabis extract used in the present study was provided by the directorate of narcotics control in Erbil province-Iraq. Stock solution of the extract was prepared by suspending 500mg of cannabis extract in 1ml Tween 80 and diluted to 50ml with (20%) diluted ethanol, giving a final concentration of 10mg/ml. Each 1kg of rat body weight was injected intrapretoneously with 1ml of the solution (10mg/1kg) body weight. Further dilution was prepared for the other dose by resuspending the stock solution in 20% ethanol solution.

### Results and discussions:

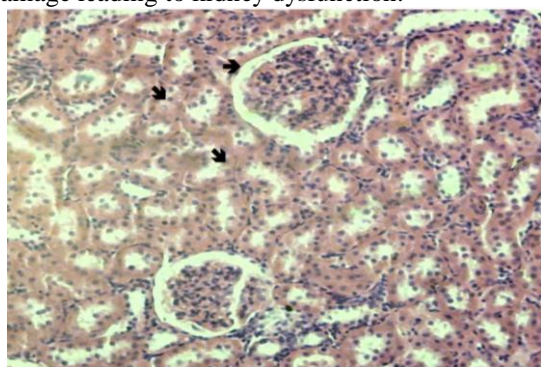
Marijuana is a crude drug derived from the plant Cannabis sativa. It contains more than 400 compounds [8], many of them distributed widely in the brain and spinal cord [9], and in the enteric nervous system, where it regulates gastrointestinal motility. It is also found in several other organs, such as the uterus, prostate, adrenals, urinary bladder, liver, heart, and blood vessels. and they closely associated with the immune system, being prevalent in peripheral immune cells, such as white blood cells [10].

In the present study, the effects of marijuana, on rat kidneys section was studies. And according to [11] the effects of cannabis depend on the dose received, and the mode of administration.

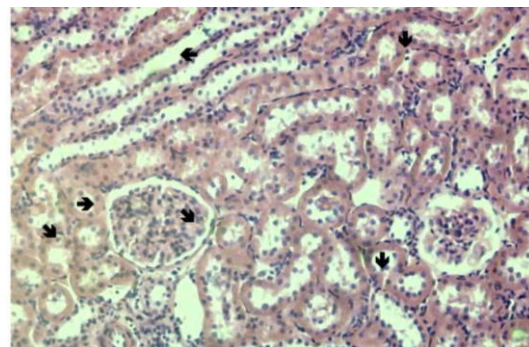
Histological examination of kidney treated with 5 mg cannabis showed many lesions represented by atrophy of proximal convoluted tubules, some of these suffered from coagulative necrosis in addition to dilation of bowman's capsules associated with expansion of glomerular tuft (hyper trophy). Also mild infiltration of mononuclear inflammatory cells has been seen also (figure 3 and 4). In contrast, kidneys sections of control group showed unremarkable changes (figure 1 and 2).

Kidney and liver are important organs of metabolism, detoxification, storage and excretion of xenobiotics and their metabolites, and are especially vulnerable to damage [12, 13]. The cannabis considers as toxic material with lethal dose about 50% [14]. In addition to it is a histopathological effect, cannabis affected markedly on the brain in the form of shrunken cells. The liver cells were affected in the form of refraction of the cytoplasm, while it led to severe congestion in the kidneys [12].

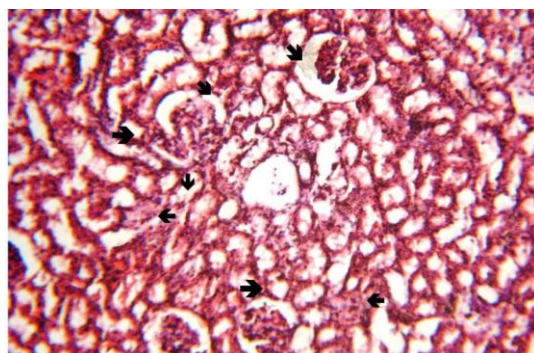
Histopathological section of kidney treated with 10 mg cannabis showed many lesions characterized by coagulative necrosis in epithelium lining proximal convoluted tubules some of glomeruli revealed dilatation in bowmans capsules and other showed a trophy or loss of glomeruli, in addition of congestion of blood vessels and infiltration of mononuclear inflammatory cells have been seen (Figure 5 and 6). According to [15] the cannabis abuse rarely led to renal complications, but [16] reported that heavy cannabis smoking cause renal infarction. While [17, 18, 19] represented that since the central role of liver and kidney is drug metabolism that predisposes them to toxic injury. Metabolites may have higher activity and/or greater toxicity than the original drug. Metabolites of the drugs that are excreted from kidneys cause cellular damage leading to kidney dysfunction.



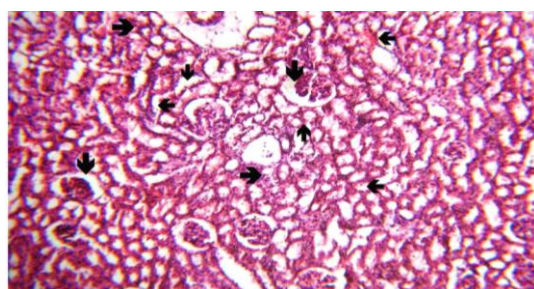
**Figure (1):** histological section of normal kidney, revealed glomerular tuft (➔) and proximal convoluted tubule which lined by simple cuboidal epithelial cells with present of brush border in the lumen (➔) (H&E 20X).



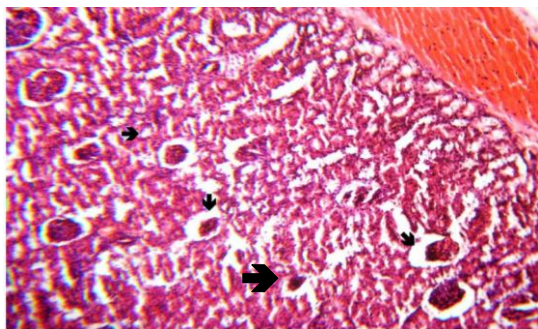
**Figure (2):** histological section of normal kidney, revealed glomerular tuft (➔) proximal convoluted tubule (➔), collecting tubules (➔) and distal convoluted tubule (➔) (H&E 30X).



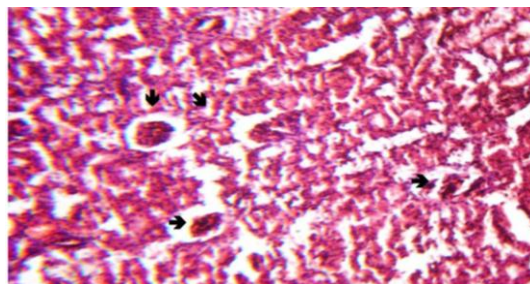
**Figure (3):** Histopathological section of kidney treated with 5 mg cannabis showed many lesions represented by atrophy of proximal convoluted tubules (➔), some of these suffer from coagulative necrosis (➔) in addition to dilation of bowman space associated with expansion of glomerular tuft (➔). Also mild infiltration of mononuclear inflammatory cells has been seen (➔) (H&E 30X).



**Figure (4):** Histopathological section of kidney treated with 5 mg cannabis showed many lesions represented by congested blood vessels (➔) some of the proximal convoluted tubules suffer from coagulative necrosis (➔) in addition to dilation of bowman capsules associated with expansion of glomerular tuft (➔) (H&E 20X)..



**Figure (5):** Histopathological section of kidney treated with 10 mg cannabis showed many lesions characterized by coagulative necrosis in epithelium lining proximal convoluted tubules (➔) some of glomeruli revealed dilatation in bowmans space (⬇) and other showed a trophy or lost of glomeruli (⬇). (H& E 20X)



**Figure (6):** Histopathological section of kidney treated with cannabis 10 mg showed highly lesions characterized by coagulative necrosis in epithelium lining proximal convoluted tubules (⬇) some of glomeruli revealed dilatation in bowmans capsules (⬇) and other showed atrophy of glomeruli tuft (➔) (H& E 20X)..

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## التأثير السمي لنبات الماريجونا *Cannabis sativa* على خلايا الكلوية في ذكور الجرذان البيض

لأنه سردار صالح العالم

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( تاريخ الاستلام: 18 / 8 / 2012 ---- تاريخ القبول: 31 / 10 / 2012 )

### الملخص:

الغرض من الدراسة هو معرفة مدى التغير النسيجي في كلية الجرذان البيض مع معاملتها مع مستخلص نبات الماريجونا. أشتملت الدراسة على 30 جرذا والتي تروحت أعمارهم بين ستة الى ثمانية أسابيع. قسمت الجرذان الى ثلاثة مجاميع، المجموعة الاولى تمثل السيطرة، بينما حقنت المجموعة الثانية (داخل الغشاء البريتوني) ب(5ملغم/1كلغم) من الماريجونا اما المجموعة الثالثة حقنت (داخل الغشاء البريتوني) ب(10ملغم/1كلغم) من الماريجونا.

سبب الماريجونا تغيرات نسيجية في الكلية بصورة عامة متمثلة بظهور ضمير في الخلايا الطلائية المبطنة للنبيبات الكلوية و ظهور تمدات في محفظة بومان بالاضافة الى تنخر الخلايا الطلائية المبطنة للنبيبات الكلوية عند استعمال كلا جرعتين 10ملغم من مستخلص نبات الماريجونا.