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Original Article

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The Cytotoxic Effects of *Datura Stramonium* Plant on Liver in Laboratory Rats

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Abstract

The goal of this study is to demonstrate the pathological effects of Datura extract on liver tissue as well as some physiological, biochemical, and haematological indicators in laboratory rats. When the animals were given the Datura plant filtrate, which contains many special and effective compounds, it caused histopathological changes in the liver tissue, such as dilatation and congestion in the central vein, expansion and congestion in the sinusoids, severe fatty infiltration in the liver cells, necrosis of the hepatocytes, endothelial cell necrosis, and vacuolar degeneration in large areas of the liver compared to the control. The current study found a significant reduction in blood and biochemical parameters when compared to the control group.

Key word: Datura, Liver, plant extract

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Introduction

Datura stramonium, also known as "Jimson weed," is a flowering plant that belongs to the Solanaceae family and can be found throughout tropical and warm temperate regions of the world (Chinedu et al., 2019). It has been identified as an annual herb that grows in gardens, roadsides, and other waste or cultivated land (Jonson and Afshari, 2016). Datura is an important source for many medical drugs. Datura can be poisonous if used incorrectly (Kayode et al., 2016).

Traditionally, Datura was used to treat asthma, abscesses, arthritis, gastrointestinal problems,

headaches, aches, sprains, haemorrhoids, snake bites, swellings, and tumours; it was also used as an ointment to relieve the pains of rheumatism and sciatica, and to ease Parkinson's disease spasms (Williams, 2013).

Hyoscyamine, atropine, and scopolamine were the most significant alkaloids that have been discovered in the Datura plant, and they are typically found in seeds with high numbers and in leaves (Kayode et al., 2016; Fernández et al., 2021). Toxicity may result from the presence of "toxic tropane alkaloids" with methylated nitrogen atoms (N-CH3), such as the anticholinergic medications atropine and scopolamine (Henry et al., 1974).

Atropine scopolamine, and competitive antagonists of muscarinic cholinergic receptors, are employed as inhibitors of the central nervous system (Halpern, 2004). The minor alkaloids in Datura stramonium, according to Das et al. (2012), include scopolamine N-oxide, apoatropin hyoscyamine Ν oxide, tigloidin, 7hydroxyhyoscyamine, and Apo scopolamine. Datura stramonium has been used in fatal poisonings due to its capacity to alter consciousness, as well as eating and chewing Datura during suicide attempts (Uddin et al. 2017). The total alkaloids content in the leaves is 0.25-0.45%, and the content in the seeds is 0.47-0.65%. Hyoscine content in leaves is 0.1%, stems are 0.05%, and roots are 0.1%; and hyoscyamine content in leaves is 0.4%, stems are 0.2%, and roots are 0.1% (Kaur et al., 2020). For adults, the lethal dose is 15-100 g of leaf or 15-25 g of seeds (Nayyar et al., 2020). The HTIS annual reports from 2005 to 2017 were examined to identify plant-related poisoning cases (Kerchner & Farkas, 2020).

Anticholinergic toxicity symptoms included: acute confusion, impaired short-term memory, tachycardia, delirium, hot flushed dry skin, convulsions, seizures. hallucinations, fever. urinary retention, dilated pupils, psychosis, headache, agitated delirium, dry mouth, rapid and weak pulse, coma, and death (Adekomi et al.,2011, Amini et al.,2012; Babiker et al.,2017;Ogunmoyole et al.,2019).

Datura toxicity made it a good tool as insecticidal against "Spodoptera litura Fabricius (Lepidoptera:Noctuidae), Dysdercus cingulatus Fabricius (Hemiptera:Pyrrhocoridae) ,and Pericallia ricini Fabricius(Lepidoptera:Noctuidae) (Priyanka et al.,2012) , used as antimicrobial against clinical bacteria such as: Bacillus subtilis, Escherichia coli and Staphylococcus aureus and two strains of fungi of clinical use (Candida allbicans and Aspergillus niger) (Al-Snafi ,2017).

Uddin et al., (2017) reported several cases of Datura stramonium poisoning caused by accidental consumption of this plant when mothers prepared it for fetus by decoction in cold and asthma situations, resulting in permanent damage to the fetus. Materials and Methods Collection of plant and preparation of plant extracts

The Datura leafs have been collected, identified by a specialist, washed, sun-dried, and finally crushed to powder. 250 g of powder was extracted with 70% ethanol via cold maceration for 48 hours and filtered before being evaporated to dryness. The concentrations of the extracts were made in normal saline for the experiment.

Experimental Design

The experiments involved a total of 20 rats. These animals weighed between (25-32) gm on average. The animals were housed in cages under standard environmental conditions, with free access to food and water. These animals were divided into four groups of five mice each; ten mice were given 0.5mg/kg/ml for seven weeks, while the remaining ten rats served as controls. The extract was given to the rats intragastrically through a BMI feeding tube.

Histological Parameters

Histological studies were done on the liver according to Drury and Wellington (1967).

Haematological Parameter measurements

The rats were sacrificed 24 hours after the last treatment, and blood was collected in clean and dry centrifuge tubes. After allowing the blood to clot, the serum was extracted. The calculation of Haemoglobin Concentration (g/100 ml) was done 24 h before the last treatment according to Sahli method (Coles, 1980).

Packed Cell Volume(PCV) (%) was calculated using microhematocrit (Sood, 1987). Coles, 1980) was used to calculate the total number of white blood cells (WBCs) and red blood cells (WBCs). Mean corpuscular volume (MCV) and mean corpuscular haemoglobin (MCH) are blood indicators (Coles, 1980).

Biochemical Testes

IRON-TPTZm Test (Itano, 1978) was used to determine the iron concentration in serum. Alanine Aminotransferase Activity in Blood Serum (ALT) was determined using a chemical kit (Young, 1990). Young (1990) used a chemical kit to determine Aspartate Aminotransferase (AST) in blood serum.

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Statistical Analysis

The experiment results were statistically analysed using the Statistical Package for the Social Sciences, Version 20 (SPSS) (2008), with the averages calculated at the probability level (P0.05) according to the Dunkin test (Duncan, 1955).

Results and Discussion

Datura stramonium is a pharmaceutical plant, it is a local source for tropane alkaloids Which is the important anticholinergic alkaloids which has a methylated nitrogen atom (N-CH3), also Datura stramonium contain the anti-cholinergic drugs scopolamine (Uddin et al. 2017).

The current study has been indicated a significant decrease in body weight, haematological and biochemical parameters in the Datura stramonium extract group compared to the control group (Table 1) (Fig 1,2), as well as a significant increase in WBCs in the treated group (Table 1) (Fig 3).

These results agree with the results of Ali A. Eltayeib and Siddige (2021), in Histological and body weight effects of Datura innoxia seeds and leaves extracts in rats and the results of KaliliNajabadim and Atabis(2004), in evaluation of analgesic effect of Datura stramonium leaves in hot plate and formalin test on male rats.

All These variations are due to the extract effect on the liver and kidney tissues, which resulted in lack of erythropoietin, that is necessary for the production of blood cells in the bone marrow. Our study has been also suggested that active substances which is found in the plant, such as atropine and scopolamine may be the cause of these histological changes.

Furthermore, the histopathological changes in rat due to Datura plant has also revealed in the liver (picture 2,3,4) compared to control group (picture 1) including sinusoid extension, hepatocyte necrosis, haemorrhage, vacuoles in the cells, rupture of the inner lining of the liver vein, apoptosis, nucleus matter lysis, hepatocyte necrosis and finally nucleus hyperplasia.

We suggest that Datura stramonium has a toxic effect on this organ due to the presence of biologically active substance "Atropine and scopolamine" and this is consistent with the results of (Alwirfli et al.,2021) when he experimented the effect of Datura stramonium plant extract on the liver of rat.

Table (1): Shows Weight of rats (gm), Hemoglobin concentration(Hb) (g/100ml), Packed cell volume (PCV)(%), Red blood cells count (RBCs) (cell/mm3), White blood cells count (WBCs) (cell / mm 3), Mean cell volume (MCV), Mean cell hemoglobin (MCH), Alanine aminotransferase (ALT) and Aspartate.

Biomarkers	Control group Mean+SD	<i>Datura</i> extract group Mean+SD
Body weight (gm)	233.76±0.95 (a)	193.7±1.5 (b)
(Hb) (g/100ml)	13.95+0.39 (a)	9.95±0.38 (b)
(PCV)(%)	45.5+1.29 (a)	34.8±1.72 (b)
(RBCs) (cell/mm3)	8.240000+0.138 (a)	6.220000±0.18 (b)
(MCV)	48 (a)	38.9 (b)
(MCH)	15.8(a)	12.7(b)
(WBCs) (cell / mm 3)	8757+84.988 (a)	9450±129.09 (b)
Iron concentration (mg/dl)	105.0±2.160(a)	55.25±1.707(b)
(ALT)	13.5425±0.5525(a)	8.50±0.3522(b)
(AST) (IU/L)	42.99±4.70(a)	27.615±0.083(b)

The current study, result of all of the parameters that have been done, revealed a significance difference between the control group of rat and the infected group of rat. For example, for the WBC test it was (8757+84.988) for control group and (9450 ± 129.09) for infected mice group, for the Hb test the control was(13.95+0.39) and (9.95 ± 0.38) for the infected mice group.



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The (PCV)(%) test it was (45.5+1.29) and (34.8 ± 1.72) for the infected mice group, also RBCs test it was (8.240000+0.138) for control group and (6.220000 ± 0.18) for the infected mice group, MCV test it was (48) for control group and (38.9) for the infected mice group.

Also MCH test was(15,8) for the control group and (12,7) for the infected mice group, for Iron concentration test was (105.0 ± 2.160) for control group and(55.25 \pm 1.707) was for the infected mice group, ALT test was (13.5425 \pm 0.5525) for control group and(8.50 \pm 0.3522) for the infected mice group, (AST) (IU/L) test was (42.99 \pm 4.70) for control group and(27.615 \pm 0.083) for the infected mice group, and finally Body weight decreases from (233.76 \pm 0.95) for control group to(193.7 \pm 1.5) for the infected mice group.

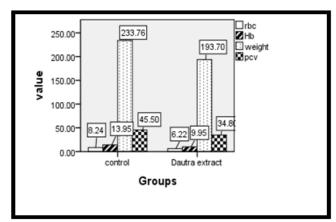


Figure (1): Show Weight of rats (gm (Hb) (g/100ml), (PCV)(%), and (RBCs) (cell/mm3 in all groups)

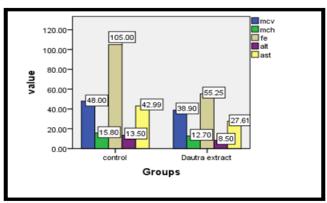


Figure (2) : Show (WBCs) (cell / mm 3), (MCV), (MCH), (ALT) and (AST) (IU/L), iron concentration (mg/dl)in all groups .

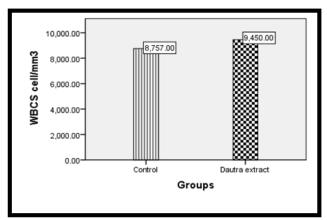
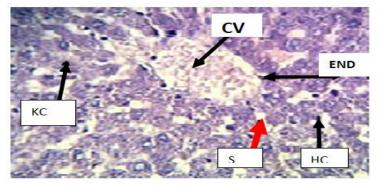
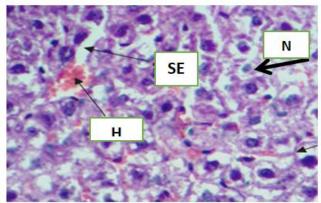


Figure (3): Show (WBCs) (cell / mm 3in all groups .

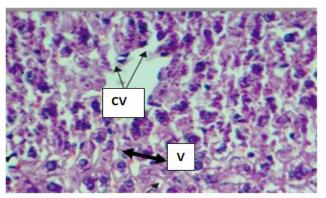
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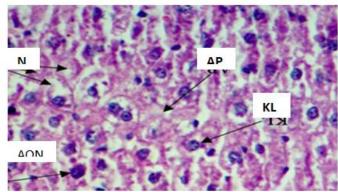
Picture(1): Rat liver control group showing epithelial cells (EP), hepatocyte (HC), sinusoids (S), central vein (CV), kupffur cell(KC) endothelial cell (END), E&H dyes(400x).



Picture(2):Rat liver *Datura* Extract showing sinusoid extansion (SE), hepatocyte necrosis (N). hemorrhage (H), E&H dyes(400x).



Picture(3):Rat liver *Datura* Extract showing pigment (V), vacuoles in the cells (CV), Rupture of the inner lining of the vein, E&H dyes(400x).



Picture(4):Rat liver *Datura* Extract showing apoptosis (kl), nucleus matter lysis (N),hepatocyte necrosis(AP), Nucleus hyperplasia(AON), E&H dyes(400x).

Conclusion :

Datura stramonium is an important medicinal plant but, Researches studies about its effect on the rat liver is very minimum, and this study is the first.We recommend that further studies about this medicinal plant should be done because of its medicinal Importance.

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