The Toxic Effects of Datura stramonium Leaf Extract to liver and kidney Swiss Albino Mice Mus muscullu

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ABSTRACT.

Datura is a genus of plants belonging to the Solanaceae family which possess potent, toxic, anticholinergic properties. One member of this genus is the *Datura stramonium* species, a ubiquitously-growing hallucinogenic plant that has been known by different names - Jimson's weed, Green Dragon, Angel's Tear. In different parts of the world. Though rare, cases of acute intoxication by *D. stramonium* consumption have been reported, with victims often presenting with fulminant anticholinergic symptoms such as dry skin, mydriasis, and tachycardia, often with fatal consequences. The objective of this experiment is to evaluate the toxicity of *Datura stramonium* to male Swiss albino mice and this has been achieved by conventional LD50 biochemical function tests in addition to the histo-physiology approach. Changes in behavior, physical activity, and body weight during the period of study have also been observed, Furthermore, the relative weight of liver and kidney, as well as the blood chemistry and parameters, were studied. This investigation has been designed to examine the toxicity and describe the possible changes in the structural-function of vital organs, following the oral intubation of non-lethal doses of Datura stramonium leaves crude aqueous extract. Through preliminary trials, crude aqueous extract. Of 200mg leaves per kilogram body weight was established as a tolerable non-lethal dose. Three doses 0.36, 0.7, and 4 mg/kg, were orally weekly, administered to the male mice in a 0.1 ml volume. Acute toxicity studies were accomplished through oral intubation of three dosage in each case. Observation and mortality reported for 24 .48, 72 hours. Prolonged toxicity was performed through the administration of weekly, single doses oral for 40 days. Observation were made on the mice body weight, blood parameters (RBC, WBC, HB, HCT, MCT and PLT) and histological abnormality of vital organs.

Key words Datura stramonium Male Mice body weigh Physiology; Histopathology.

التأثيرات السامة لمستخلص أوراق الداتوره سترومنيوم على كبد وكلية ذكور الفأر الأبيض السويسري

الملخص:

جميع أجزاء نبات الداتورة سترامونيوم تعد سامه للإنسان والحيوان، إلا ان هناك تقارير تفيد بأن البذور تبدو الأكثر سميه مقارنه مع الأجزاء الأخرى وتعد المستحضرات التي تدخل في تركيبها مختلف أجزاء الأعشاب والأشجار التي يطلق عليها مصطلح النباتات الطبية في علاج طيف واسع من الأمراض. ان أوراق نبتة الداتوره تستخدم في تحضير مستخلصات مائية ومذيبات عضوية ومراهم وحتى ادخنه للاستنشاق. لقد تجاوزت استخدامات أجزاء هذه النبتة حدود الطب الشعبي لتدخل في مجالات التصنيع الدوائي. استهدفت هذه الدراسة وصف التغيرات المحتمل حصولها في الكيانات التركيبية - الوظيفية للأعضاء الحيوية لذكور الفأر السويسري الأبيض المعرضة لجرعات غير مميتة من الخلاصة المائية لأوراق الداتورا لكيلوغرام من وزن الحيوان اختير الفأر السويسري الأبيض كحيوان لهذا الاختبار، حيث تم إحضار مجموعة من الذكور والإناث من معمل الحيوان التابع لكلية الطب البشري لتشكل النواة التربية للحصول على العدد المطلوب. لقد تم أجراء التجارب السامة الحادة من خلال الفم بواسطة التجريع وقد استخدمت اربع جرعات محسوبة 200,100,50,12.5 مليجرام من المستخلص للكيلوجرام من وزن الفأر. الوفيات واي أعراض أخرى يتم تسجيلها على مدى 24 و 48 و72 ساعة بعد معاملة الفئران. السمية المطولة تم أجراءها من خلال الحقن الأسبوعي بجرعة 0.36 ، 0.7، و 4 مليجرام لكل كيلوجرام من وزن الفأر من المستخلص النباتي ولمدة 40 يوما وقد سجلت الملاحظات ودونت النتائج حول كل من وزن الجسم الأسبوعي، وكيمياء الدم المتمثلة في الكرات الحمراء والكرات البيضاء والهيموجلوبين والهيماتوكريت والصفائح الدموية ووظائف الكبد والكلى .كما تم تشريح الحيوانات وفحص الأعضاء وتحضير القطاعات في كل من الكبد والكلى والقلب والخصي والرئة للحيوانات التي تعرضت للمعاملة. ان نتائج هذه الدراسة تشير إلى مقدرة ذكور الفئران على تحمل الجرعات الأربعة من الخلاصة المائية الخام لأوراق نبتة الداتورا حيث لم يتم تسجيل أي وفيات. كانت الأعراض الوقتية للتسمم العصبي دليلا على فاعلية الجرعات. ان المؤشرات الوظيفية للكبد معززة بالتغيرات التركيبية - الوظيفية التي لوحظت في شرائح الكبد تؤكد حصول تسمم كبدي محدود بالإضافة إلى القلب والرئة وبالمثل يمكن الاستدلال على حصول ضرر محدود في الكليتين من خلال المؤشرات الوظيفية والتغيرات المجهرية - الوظيفية. ان محدودية ووقتية أعراض التسمم العصبي يجب أن يؤخذ بنظر الاعتبار إلى جانب الأضرار المحدودة في الأعضاء الحيوية والتعامل معها على أنها تأثيرات جانبية لهذه الجرعات المتكررة من المستخلص المائي الخام لأوراق الداتورا السترامونيوم. ان من غير المتوقع وصف مركب كيميائي على أنه خال من التأثيرات الجانبية عند تكرار تناوله ولو بجرعات علاجية. فالجرعات العلاجية للعقاقير طبيعية كانت أم مستحضره، لها درجات متفاوتة من الأعراض الجانبية. وفي بعض الأحيان يتم الترحيب بالعقار ولو كان المريض على بينة من مساوئه الجانبية. ان نتائج البحث الحالي قد جلبت الانتباه إلى ضرورة تقصي ابعد لهذه التأثيرات الجانبية غير المرغوب بها ولغاية فترة مناسبة بعد تناول أخر جرعة من المستحضر. ان من الضروري إخضاع مستحضرات نبتة الداتورا والنبات الطبية الأخرى إلى دراسات معمقة مستفيضة لوصف معالم تأثيراتها الجانبية على الوظائف الحيوية المتنوعة وإيجاد الوسائل التي تضمن تقليلها. ومثل هذه الدراسات ستضمن تزويد المرضى بمعلومات وافية عن حدود جرعات المستحضرات النافعة والحالات التي يجب فيها تجنب الاستعمال مع وصف للتأثيرات الجانبية المتوقعة.

Introduction.

Datura is a genus of plants belonging to the Solanaceae family (Angiospermae dicotiledoni). Other plants belonging to this family include: mandrake (Mandrogora officinarum), belladonna (Atropa belladonna), henbane (Hyosyamus niger) and tobacco (Nicotiana tabacum). Some other members of the family are edible fruits such as: tomato (Lycopersicon exculentum), pepper (Capsicum annuum) and potato (Solanum tuberosum). *Adesanya A, et al. (2020).*

Datura genus however is comprised of four species - Datura inoxia, Datura metel, Datura arborea and Datura stramonium - all of which possess potent, toxic, anticholinergic properties The leaves are most commonly used as a narcotic, either smoked or boiled and eaten; seeds are similarly used.

Roots, seeds or leaves are added to alcoholic drinks to increase the intoxicating effect. Side effects include dry mouth and throat, eye pain, blurred vision, restlessness, dizziness, arrythmia, flushing and faintness

Datura species are well known because of their high concentration of tropane alkaloids, which has led to poisoning episodes when Datura is accidentally mixed with edible crops (Fernández et al., 2021)

The toxic anticholinergic effect of this plant is a result of three tropane-alkaloids it contains, including: atropine, hyoscyamine and scopolamine. It is important to note that while all parts of this plant are toxic, the range of toxicity is variable in different parts such as: seeds, roots and leaves.

Atropine and Scopolamine are competitive antagonists of muscarinic cholinergic receptors and are central nervous system depressents (Halpern, 2004). Many cases of accidental poisoning by Datura stramonium species have been reported when these plants were eaten accidentally or decoction prepared from herbal prescription (A-Shaikh and Sablay, 2005; Hirschmann et al., 1990). Fatal poisoning with Datura stramonium for its mind altering properties and eating and chewing of Datura in a suicide attempts (Klein-Schwartz and Odera, 1984; Kurzbaum et al., 2001, SteenKemp et al., 2004; Uddin et al 2017) .

Total alkaloids content in leaves are 0.25–0.45%, and in seeds 0.47–0.65%. Hyoscine content in leaves are 0.1%, in stems 0.05% and in roots 0.1%; and hyoscyamine content are 0.4% in leaves, 0.2% in stems and 0.1% in roots (Boumba et al., 2004; Kaur et al.,2020)

The deadly dose for adults is 15-100 g of leaf or 15-25 g of the seeds (Nayyar et al., 2020). The 2005–2017 annual reports of the HTIS were reviewed to identify plant-related poisoning cases (Kerchner & Farkas, 2020).

MATERIALS AND METHODS.

Test Animals:

A total of 16 adult male and female Swiss albino mice Mus muscullus were brought, from the animal house of the faculty of Medicine, to the Zoology Department, University of Benghazi. The animals were reared in the laboratory,

The chemicals:

Datura stramonium Hematoxylin, eosin and all other chemicals used in this study were of a technical grade with known structures and functions.

The experimentation

LD50 determination (Acute toxicity study):

The acute Toxicity of Datura stramonium was evaluated through using five treatments 200, 100, 50, 25 and 12.5 mg of leaf extract per kg mice body weight. In addition to control treatment receiving only saline water.

Each treatment was replicated two times with four mice per replicate. Mice of 50 to 70 days of age with approximate similar body weight were selected randomly for each treatment. The calculated doses (mg/kg) were orally delivered in a 0.1 ml solution through the mouth intubation. Observation were made on the behavior while other symptoms and mortalities were recorded on 24, 48, 72 and 96 hours post treatment.

Prolonged toxicity study:

A total of 36 male mice were used in this study. The animals were divided into three treatments each treatment contained three replicates and each replicate having three animals. The fourth treatment having 9 mice in three replicates formed the control .Treatment animals were intubated with 0.1 ml solution containing the specified treatment concentration 0.36 , 0.7 and 4 mg/kg leaf extract per kg mice body weight, whereas, control mice were orally intubated with 0.1 ml of saline water .

Blood and Tissue Sample:

The blood was collected for the measures of Erythrocytes RBC, White Blood Cells WBC, Hemoglobin HB, Hematocrit HCT, Mean cell volume MCV, and Platelet Count PLT. Other blood sample was collected without EDTA for blood chemistry mainly for liver and kidney function.

Decapitated animals were then dissected for postmortem observations, including: Liver and kidney and kidney.

All organs of each animal were dissected out and weighted. After washing with normal physiology salin solution, the organs were transferred into glass containers containing formalin –acetic acid-alchol (FAA) fixative solution and kept for weighting and histological studies.

RESULTS

In the acute toxicity symptoms were found to follow dose dependent acute toxicity to male mice receiving an orally single dose of various concentrations.

After 72hr of exposure no mortality was reported for the 200, 100, 50, 25, 12.5 mg/kg body weight.

Body Weight Means:

Body weight mean of the 0.36 mg/kg treatment was o.40± 1.08167g, 0.7mg/kg - 0.6333± 1.87705g and 4 mg/kg 2.0333±0.90738g, whereas, the body weight mean of control was 0.50±0.26458. Increasing body weight mean in the 4mg/kg treatment and decreasing body weight mean in the 0.7 treatment were evident.

The p value of more than 0.05 indicated no significant difference between the compared means of all treatments.

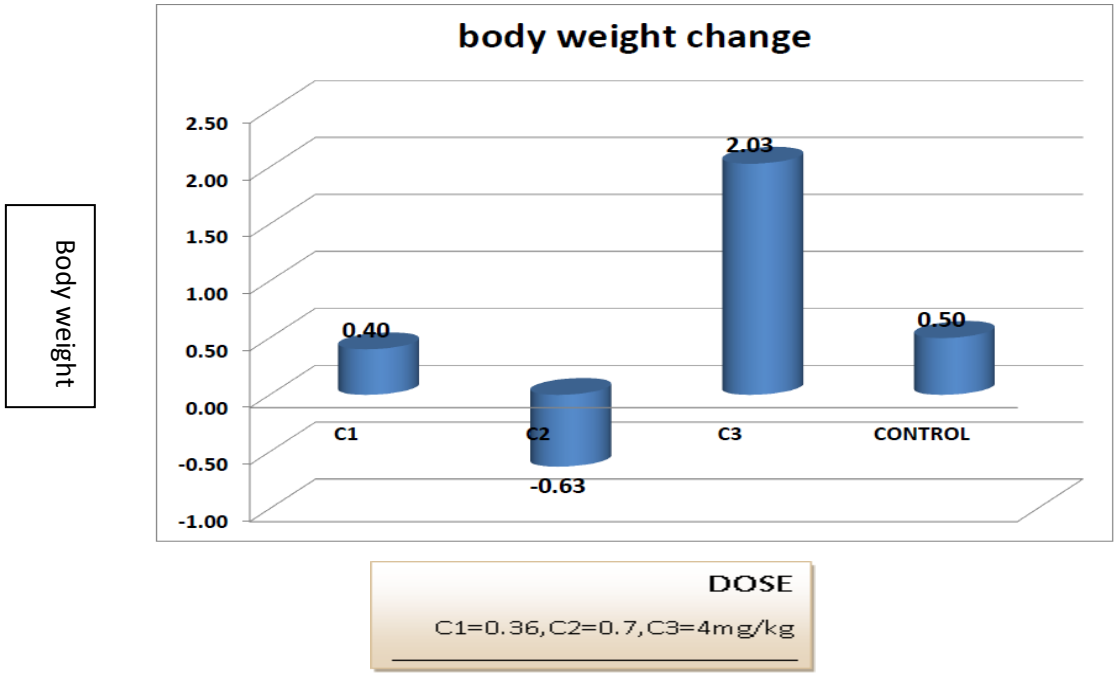


Fig 1 %body weight change of male mice exposed to 0.36, 0.7 and 4mg/kg concentration of *D.sramonium* leaf extract for 40 days.

Percent organ weight / body weight:

The effect of *Datura stramonium* extract on the vital organs including liver and kidney were measured through the relative organ weight per 100g body weight in each treatment and compare that with control treatment after 40 days of exposure.

Liver Weight Mean

The result of liver weight in all three concentrations treated mice revealed insignificant differences as compared to that of control (t-test-p≥0.5). The % means ±SD of all treatments were 4.92±0.47, 4.9±0.74, 5.17±0.43 and 4.9 ±0.31 for C1, C2, C3 and control respectively. (figure .2)

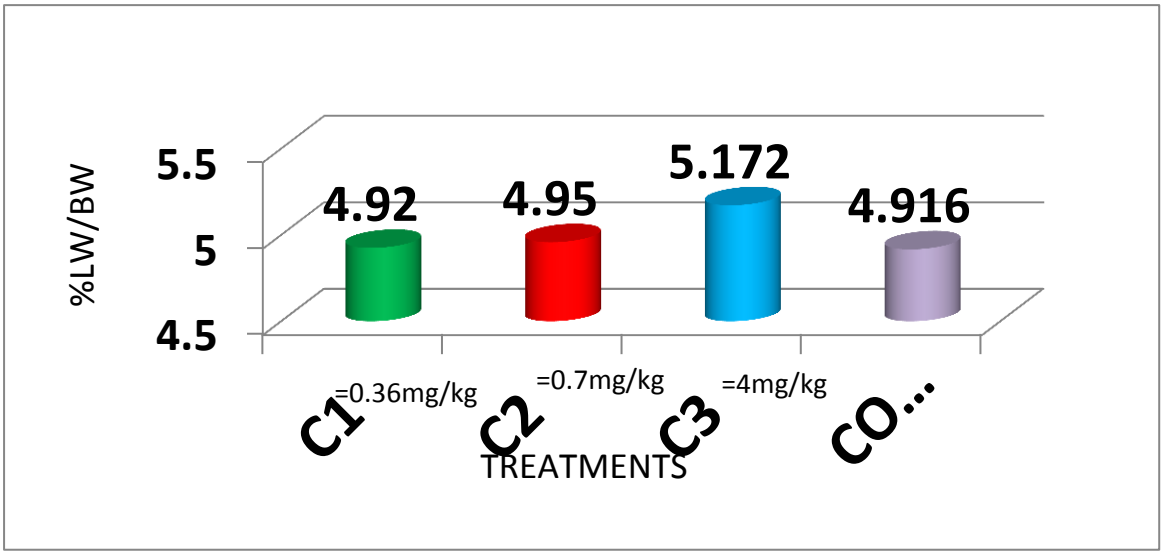


Figure .2 The relative weight mg liver weight /100g body weight of male mice exposed to three dose of *D. stramonium*.

Kidney Weight Mean.

Relative weight mg kidney weight per 100 g body weight revealed a significant differences between treatments (T-test p≤0.5).

The mean±SD of treatment showed that concentration C3 had significantly lower mean than the other two concentrations as well as the control. The mean±SD of all treatments came as 2.12±0.19 for C1, 1.97±0.19 for C2, 1.68±0.35 for C3 compared to 1.95±0.08 for control.

Both C1 and C2 had comparable means to that of control (Fig 3)

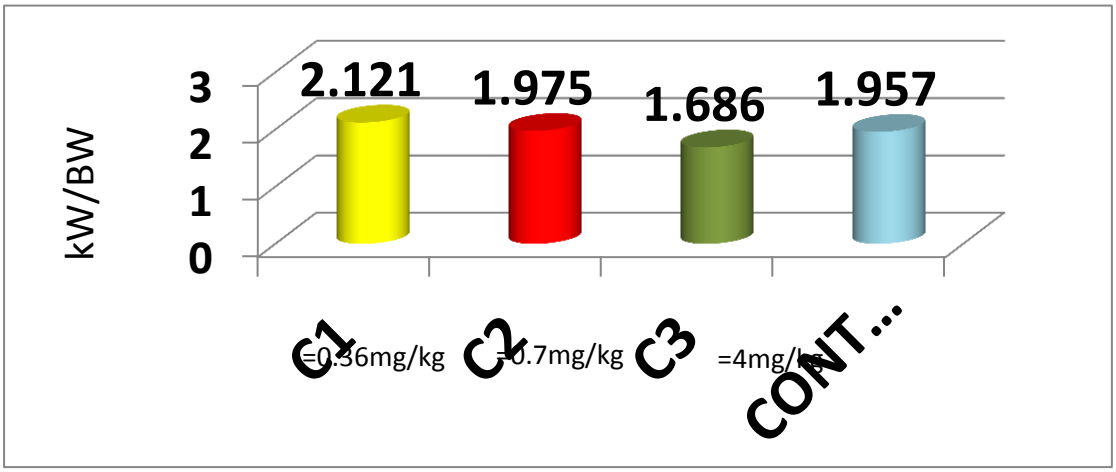


Figure -3 the relative weight mg kidney weight /100 g body weight of control and *D. stramonium* treated male mice for 40 days of exposure.

Blood parameters.

Blood parameters including WBC, RBC, HB, HCT, MCT, and PLT for control and *Datura stramonium* treated male mice are presented in (Fig 4).

The results revealed that HB, MCT were comparable in control and the three concentration treated mice. However, the values of RBC, WBC, HCT and PLT were reduced in C2 compared to control and C1& C3.

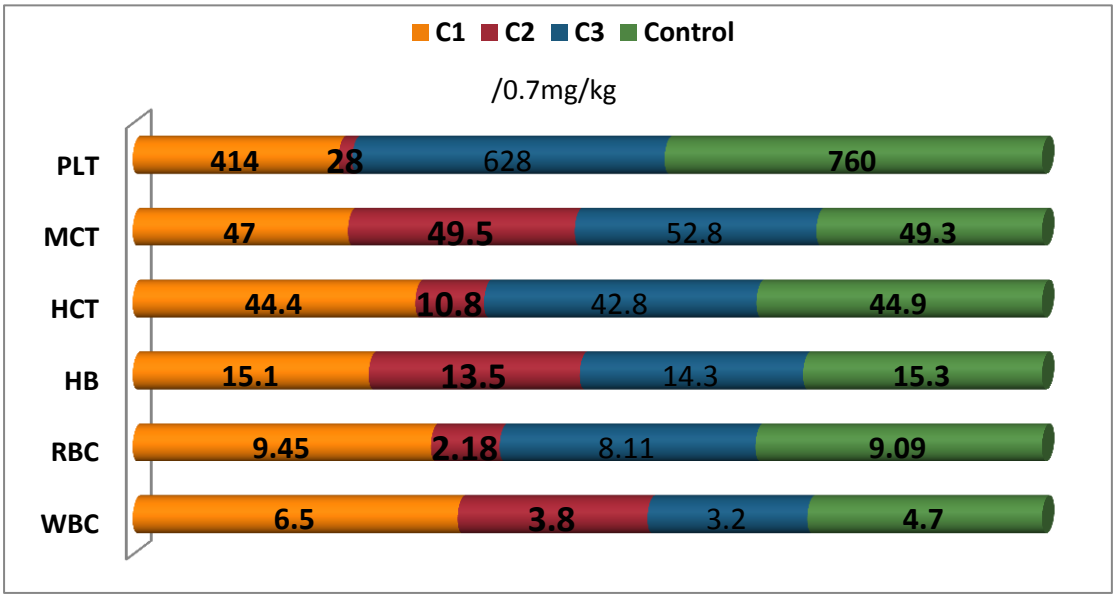


Figure- 4 Blood parameters of control and *D.stramonium* treated male mice

Blood chemistry

The blood chemistry of control and *D.stramonium* treated male mice revealed that control mice had higher values in Urea, createuin, potassium (k+), Total protein and Alanin transferase (ALT) compared to all concentrations treated mice . On the other hand C3 had higher values in Urea , createuin, and Total protein compared to both C1 and C2(Fig 5).

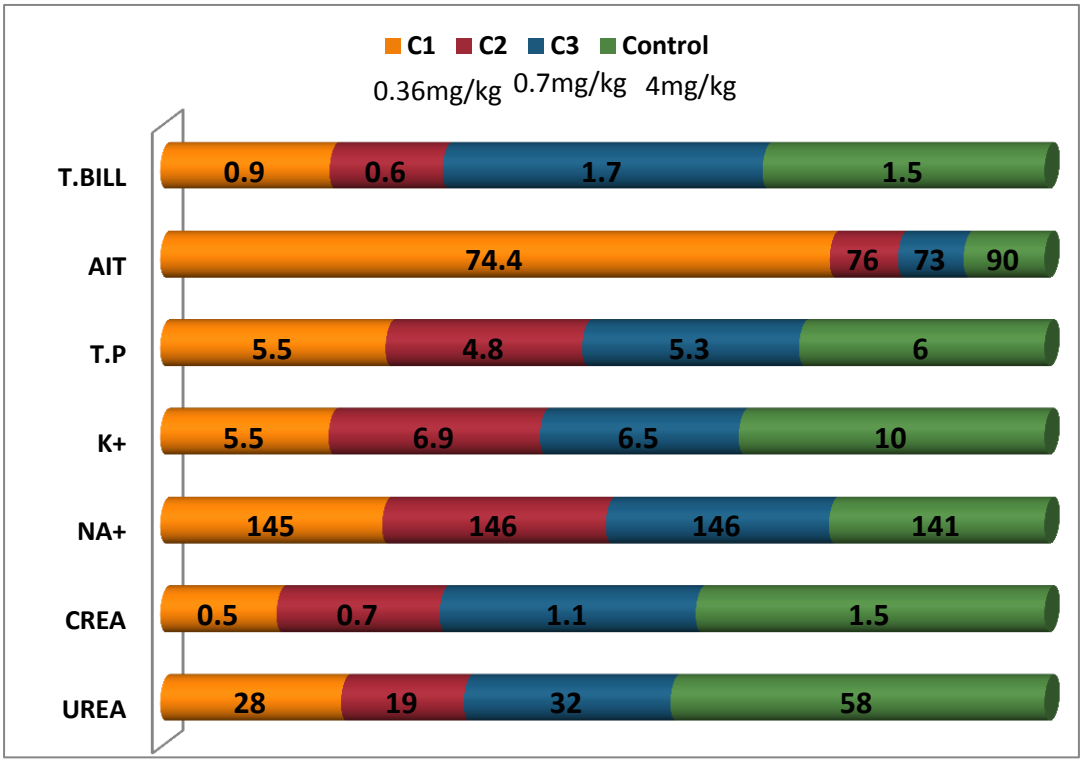


Figure- 5 Blood chemistry of control and *D.stramonium* treated male mice

Organ Histopathology:

Light microscopic examination of the hematoxylin-eosin stained liver and kidney sections pointed out some micro-structural changes due to multi- exposure of the adult male mice to the specified dose of *Datura stramonium* leaves crude aqueous extract. Appearance and organization of the cellular elements of the control liver as well as the characteristic feature of the central vein were within the normal specification (Fig 6.A).

While photograph of liver tissue of showed:

No change between the control and treatment C1 (Fig 6 B).

Higher number of Kupffer cells hepatocytes with microvesicles congested central vein (Fig 6 C, D).

Small focal area of inflammatory cell, nuclear changes (different shapes and sizes), microvesicles, hepatocyte with hydropic degeneration, and high number of kuffer cells (Figs 6 E,F and G).

The renal structure showed:

The control mice had normal microscopic appearance (Fig 7 A).

The extract treated animals contained micromorphologyical changes.

Cellular infiltration between renal tubules (Fig 7 B) whereas kidney cortex showed irregular dilation of tubules.

Heavy cellular infiltrates associated with tubules and glomerular (Fig 7C).

The glomeruli obscured by inflammatory cells diffuse cellular infiltration between renal tubules (Fig 7D).

Two central renal corpuscle in its glomeruli (Fig 7 E).

Obsoured by inflammatory cells forming foreign body- like granuloma (Fig7 F). The renal medulla showed cloudy swelling of large hemorage areas (Fig 7 G).

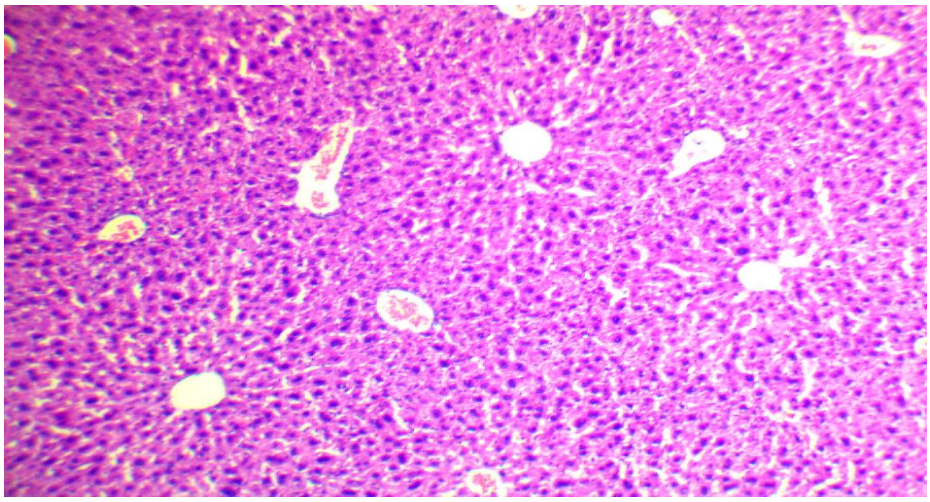


Figure. 6-A. Section in liver of a control mice. Normal appearance of the central vein, bile ducts and hepatocytes (HE., X100)

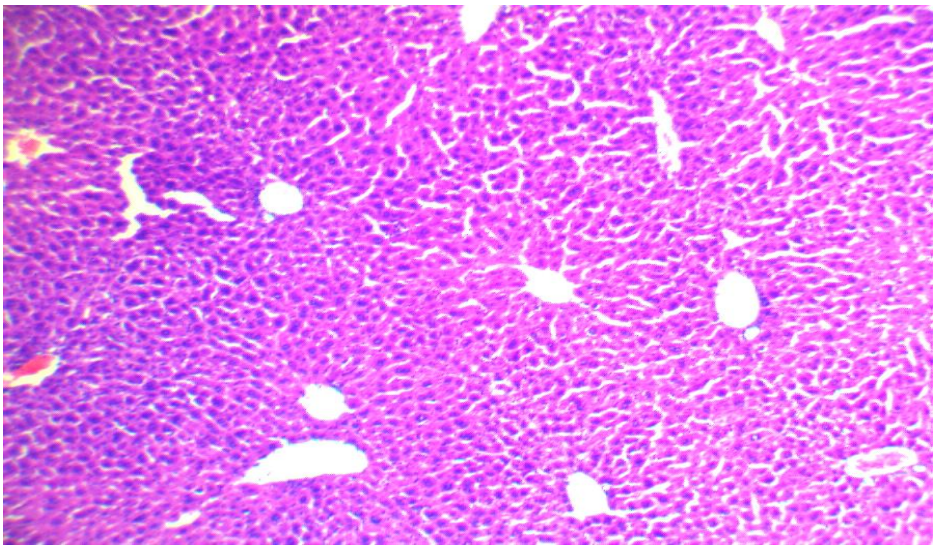
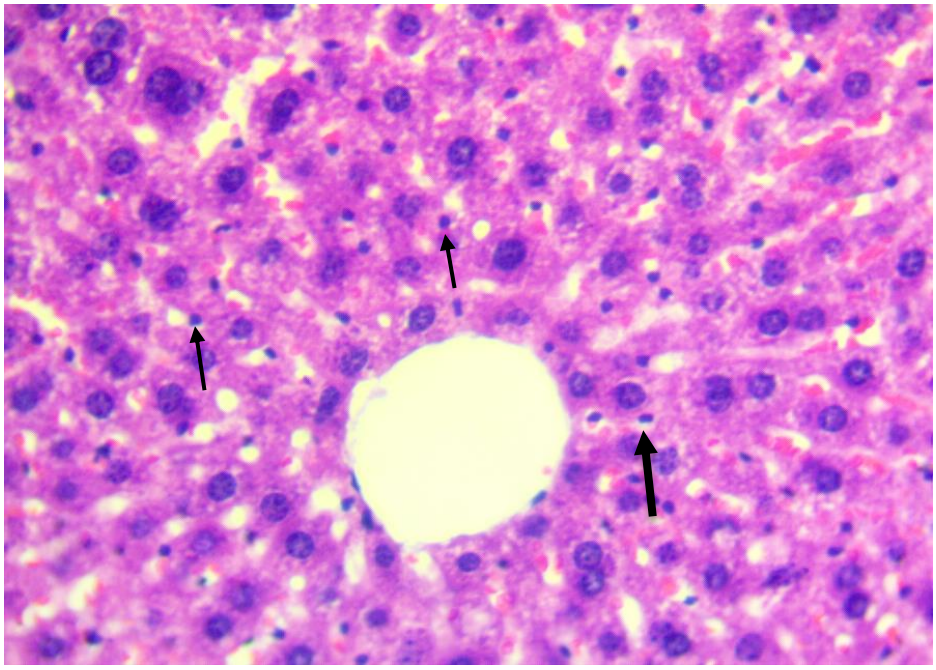


Figure. 6-B. Hematoxylin-eosin stained liver section of a mouse in T1 group. The microscopic appearance was parallel to that in control liver sections (X100)



Figur. 6-C. Photomicrograph of liver tissue of a mice treatment C2 with Datura Stramonium leaves aqueous extract showing high number of Kupffer cells (black Arrow) H&EX400.

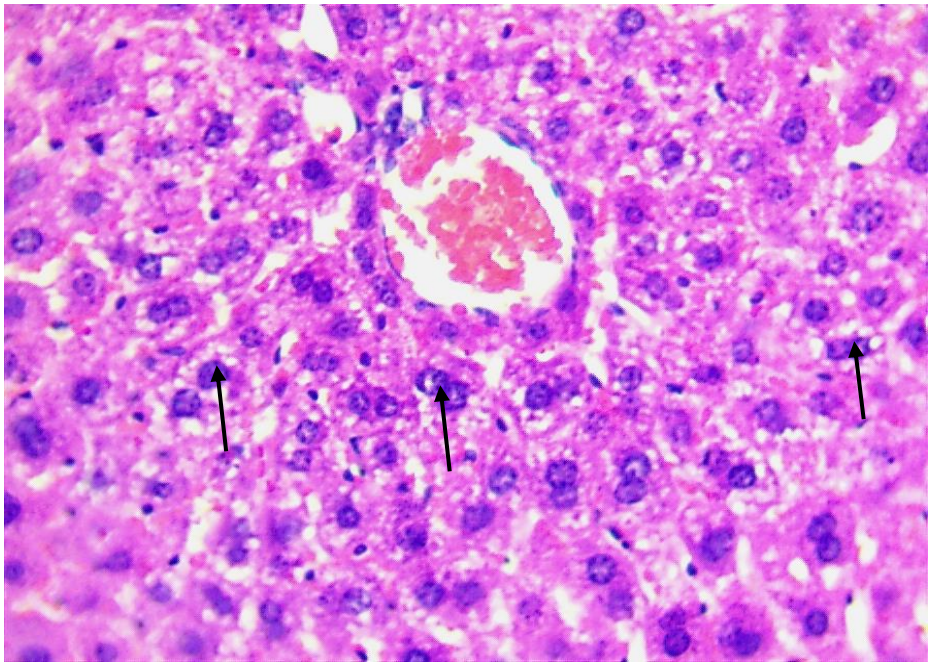


Figure. 6-D. liver section tissue treatment C2, showing hepatocytes with microvesides (black arrows), congested central vein (H&E X 400).

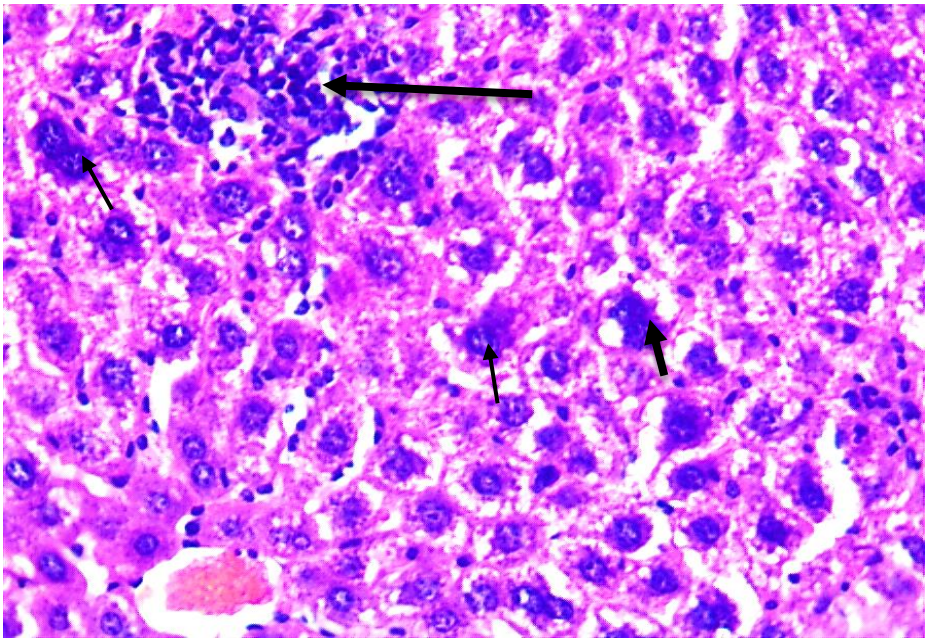


Figure. 6-E. Liver tissue after treatment C3, showing small focal area of inflammatory cells (long arrow), nuclear changes (different shapes and size) short arrows.

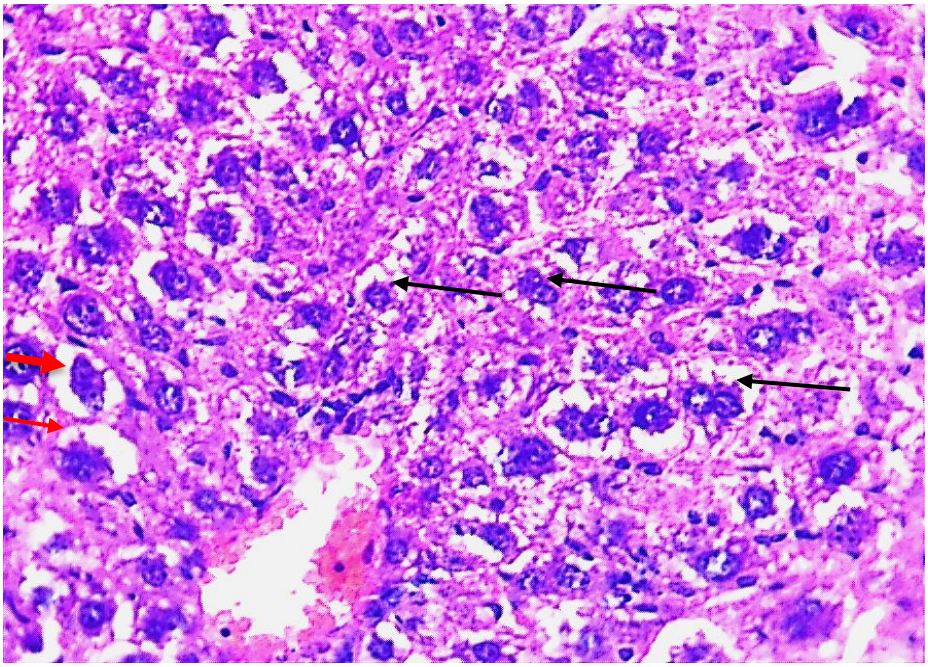


Figure.6-F. liver section T3 showing microvesides (arrows), hepatocytes with hydropic degeneration. (Red arrows), and high number of kupffer cells (small arrows)(H&E X400)

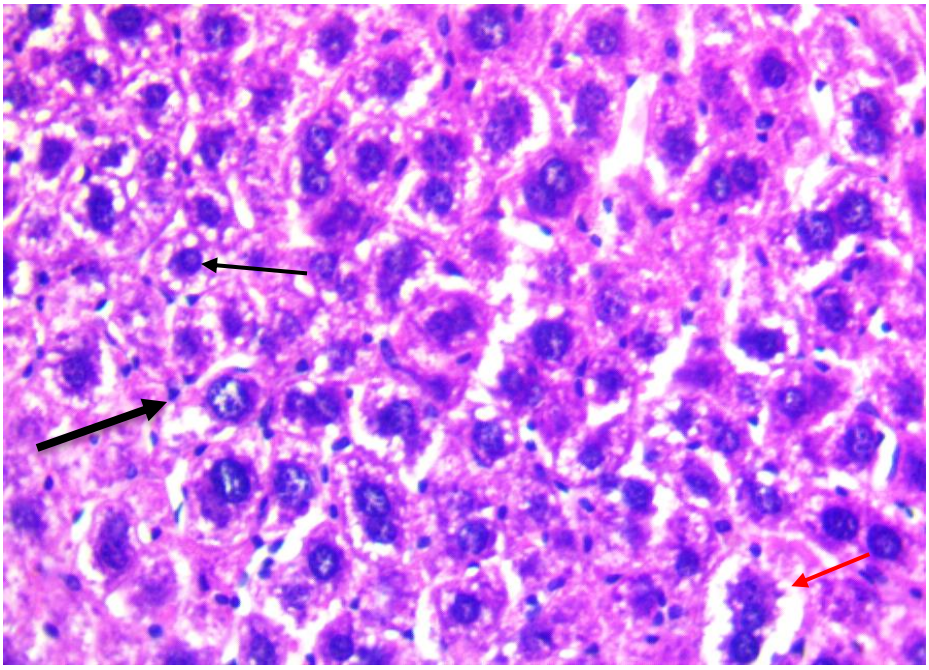


Figure. 6-G. Photomicrograph of liver section treatment C3 showing microvesides (arrows), hepatocytes with hydropic degeneration. (Red arrows), and high number of kupffer cells (small arrows) (H&E X400)

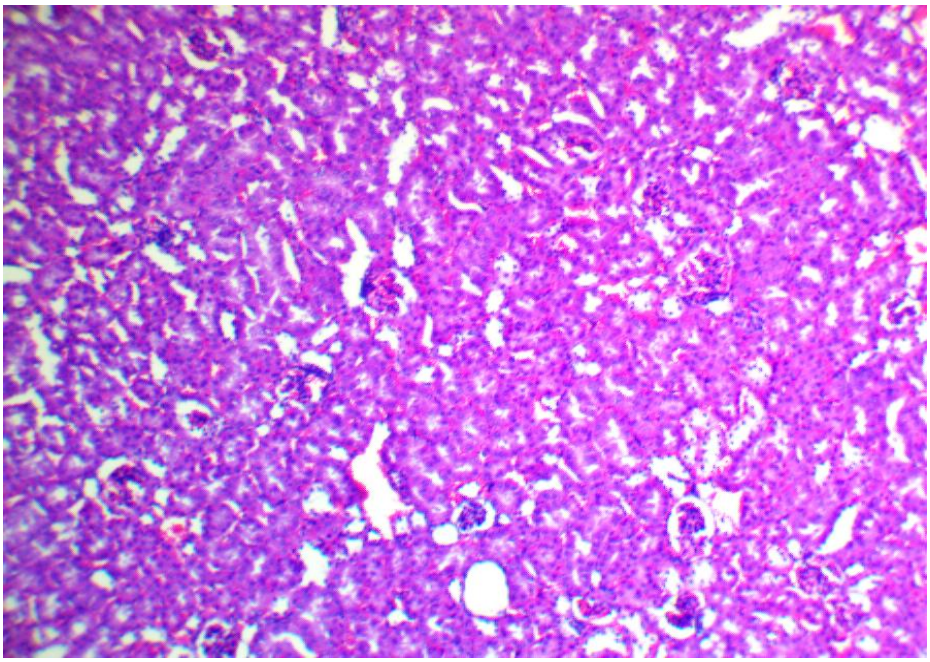


Figure .7-A. Hematoxylin-eosin stained section in a kidney of control male mice.

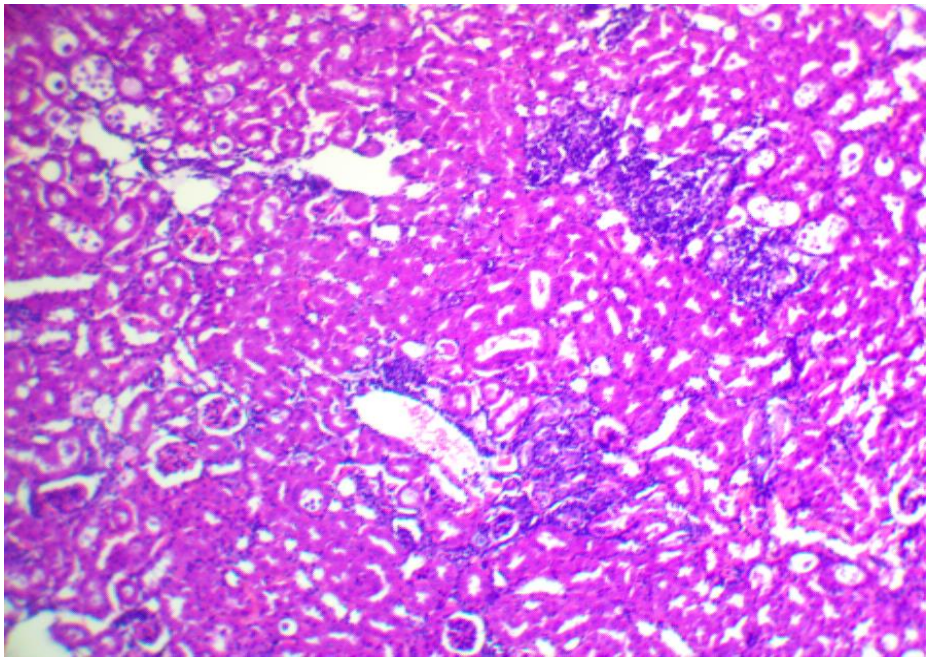


Figure.7-B. Section of a kidney from a mice in the aqueous extract treatment C1 Showing focal areas of cellular infiltration between renal tubules. H&EX10

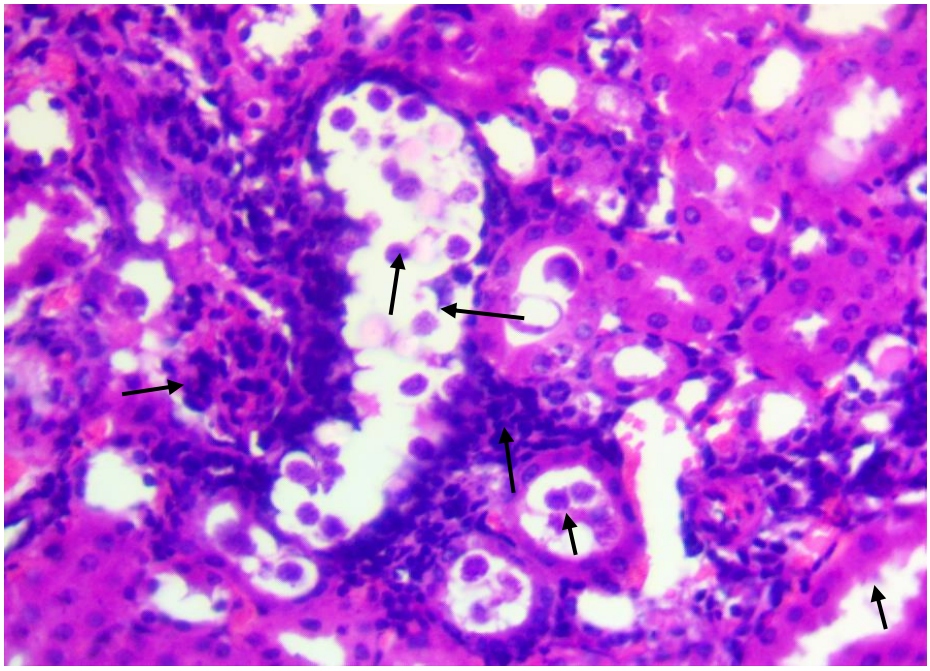


Figure.7- C- Photomicrograph of kidney cortex treatment C1 .Note the Irregular dilation of tubules (arrows), and heavy cellular infiltration association with tubules and glomerular (short arrow)(H&EX400)

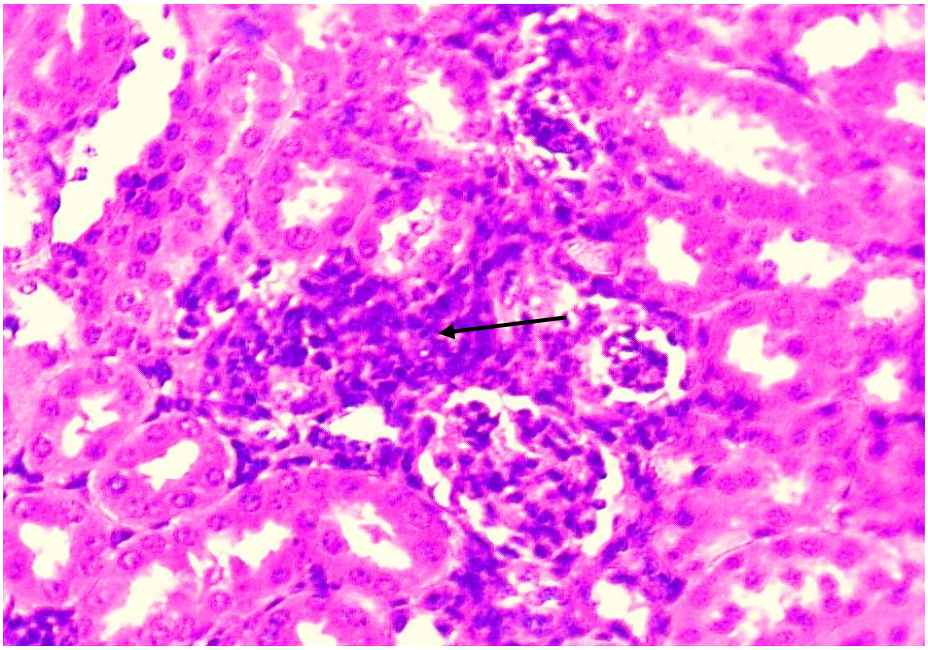


Figure.7-D. Photomicrograph of renal cortex treatment C2 showing the glomeruli Obscured by inflammatory cells (arrow) diffuse cellular in filtration between renal Tubules for kidney (H&E) X400

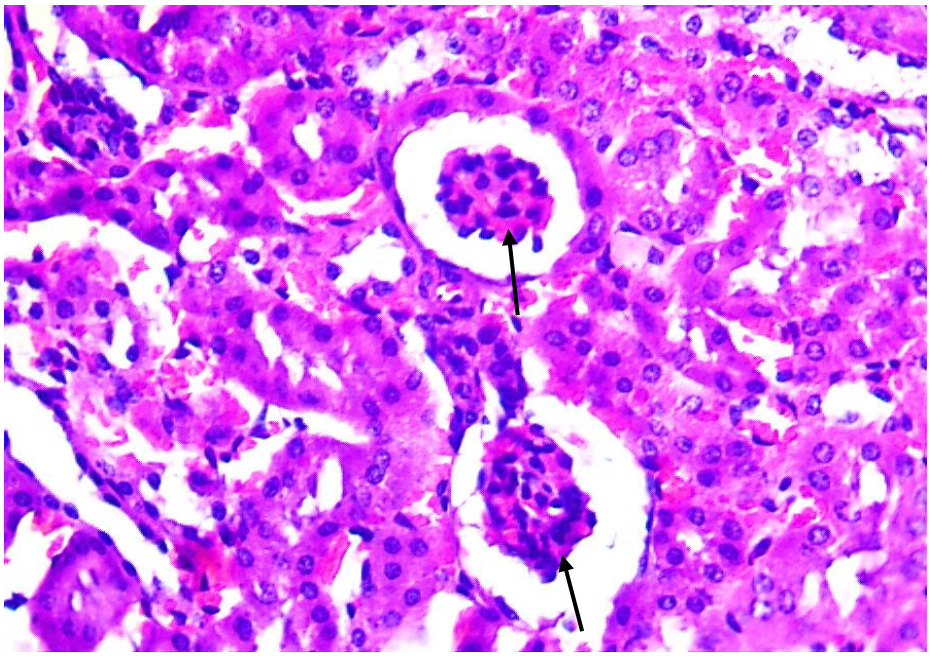


Figure.7-E. Photomicrograph of renal cortex of treatment C3, showing two central Renal corpuscle for kidney its glomeruli (black arrow) shurnked with dilated urinary space (H&EX400).

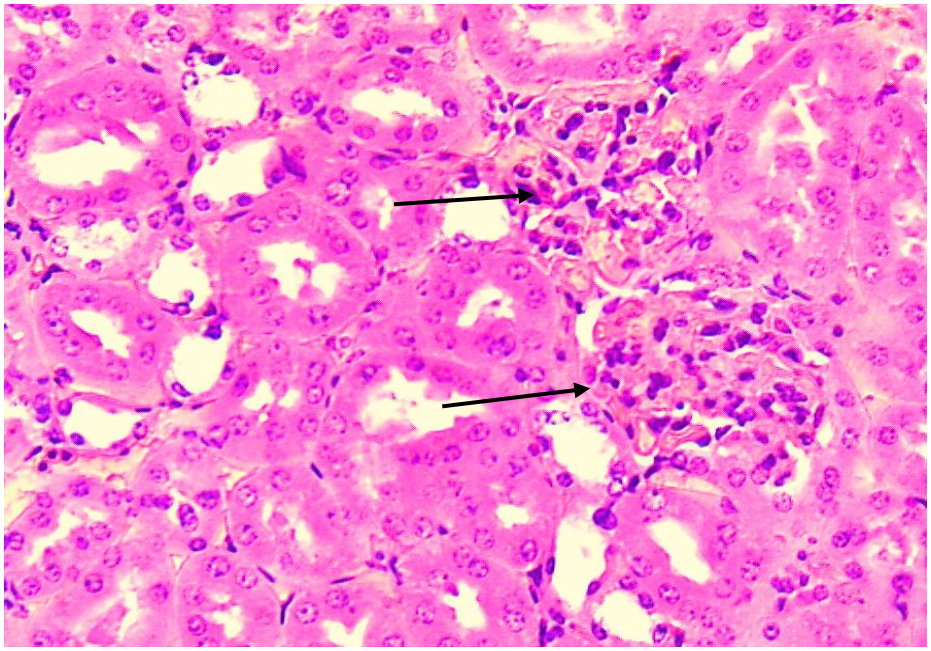


Figure.10-F.Photomicrograph of the kidney cortex treatment C3 showing the glomeruli completely obsaured by inflammtory cells Foring foreign body –like granuloma (arrows). (H&EX400)

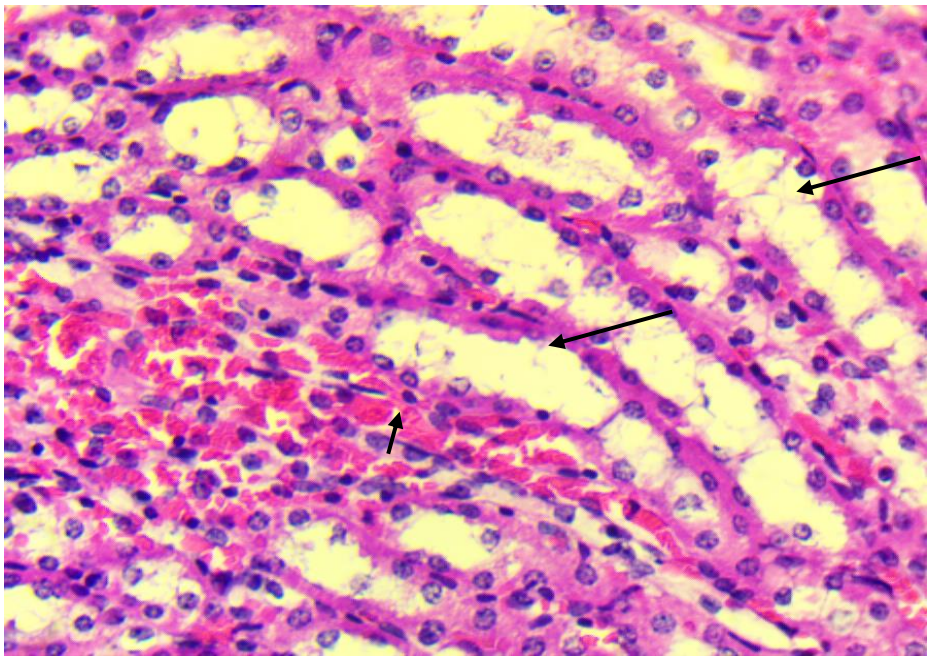


Figure. 10-G. Photomicrograph of renal medulla of treatment C3 showing cloudy Swelling (arrows) and large hemorrhage arras for kidney (small arrows). (H&EX400).

D I S C U SS I O N.

Datura stramonium leaves aqueous crude extract were administered to males of the treatment group under the same above-mentioned laboratory conditions. Therefore, contents of the crude aqueous extract, collectively, should have stood behind the recorded changes in physical activity and behavior.

These contents should also be considered responsible for the observed deviation from normal that have been exhibited by other investigated selected parameters. Absence of mortalities in both control and extract treatment groups of animals confirmed the availability of sufficient survival requirements.

The toxicity of *D. stramonium* leaf extract was clearly observed in male mice that were exposed through oral doses. Symptoms of intoxication were easily detected. However, no mortality was detected in the higher used dose 200mg/kg. This result came in support of Antov *et al* (1991) who observed several signs of symptoms but no mortality .The toxic responses observed in the treated male mice has also supported by Bouzid et al (2002) who described similar symptoms of *D.stramonium* toxicity in humans.

The result of the toxicity obtained in this may indicate that *D. stramonium* is slightly toxic, however, in reality that is not might be the case when looking to previous anthers who pointed the degree of this plant toxicity.

Therefore, the lake of mortality even in the higher used dose 200mg/kg leaf extract can be explained (1) most previous works were with the active ingredients of the plant, Atropine and scolopolamine, whereas, our study was on the crud extract of the plant. (2) The efficiency of the extraction could have been poor of greeting good percentage of the plant active ingredient. (3) No organic solvent used in the extraction because the intention were on the whole plant constituents which mostly used in the case of medication or poisoning and that synergism or antagonisms could happen in the two cases.

Furthermore, survival of the extract treatment male mice could be invested to point out to the employed tolerable non -lethal dose of the crude aqueous extract though it was repeated 4 times over 40 days weekly.

In this study the Initial and final body weight means of the control and extract treated male, Swiss albino mice dose not seems to have any significant difference between the two groups.

D.Stramonium is known to contain highly toxic tropane alkaloids, including the pharmacologically active compounds atropine and scopolamine (Desachy et al., 1997).

In the subchronic toxicity study in males rats given the alkaloids intraperitonealy, and, the changes in body weight was used as an indicator of adverse effects of the drugs and no change in weight gains were observed in the treated rats as compared to the controls. (El Hilaly et al., 2004). Furthermore Gidado et al. (2007) have noted no change in body weight of seeds *D. stramonium* treated rat.

No significant change in other relative organ weight. The results obtained in this study, then, confirm the finding of the above mentioned authers.

The results of the present study show alterations in haematological parameters associated with the subchronic and intra peritoneal exposure to alkaloids (atropine and scopolamine) in rats. Although the exact moment in which these alterations took place was not established; it was observed that a decreased number of red blood cells (RBC), hemoglobin concentrations and hematocrit value usually occur after 4 weeks of alkaloids exposure.

These hematological alterations suggest possible dehydration (Dugan et al., 1989). This is consistent with the known pharmacological action of atropine in

producing thirst and dryness of the mouth (Dugan et al., 1989). Also, there may be a relationship between RBC, HCT HBC and increased activity of transaminases especially the ALT. In the 120 day chronic experiment the rats treated with synthetic alkaloids, did not show reduction in body - weight gain but showed a decrease in the relative weight of liver. This observation on body growth and relative organ weight is not consistent with studies by Dugan et al. (1989) in which the male rats fed Jimson weed at 0.5% in the diet decreased body weight and increased the relative weight of liver. The toxicity of seeds of *D. stramonium* may be due to alkaloids but also to other components present in the seeds of plant. This chronic experiment produced high levels of transaminases. This is an indication of organ damage (El Hilaly et al., 2004). The increase or decrease in relative organ weights results when organ weights change without change in body weights are often indicative of underling disease or damage of such organs (Udem et al., 2009).

The significant change in the relative organ weight in association with the increased activities of the transaminases indicate organ damage.

This is not a good sign changes in the relative organ weight of the liver may affect the metabolic processes such as detoxification, biotransformation, and synthesis of serum proteins that take place in the liver.

Thus Adekomi (2010) stated the section of the liver and kidneys obtained from the treatment group in rats has disrupted histological organization compared with the control group. Some of the deleterious effects seen in the section of the liver obtained from the treatment group include degeneration and disruption of the hepatocytes, degeneration of the cells lining the bile ducts and occlusion of the central portal vein.

With these histological abnormalities, the anatomical, physiological and biochemical functions of the liver could be compromised. It is known that the hepatocytes play a vital role in the proper functioning of the liver as the hepatocytes are the main functional cells of the liver. The hepatocytes frequently contain glycogen and maintain a steady level of blood glucose. This is one of the main sources of energy for use by the body (Stevens and Lowe, 2005; Junqueira and Carneiro, 2003).

A compromise in the integrity of the hepatocytes could lead to improper functioning of the liver. The tubular structure of the renal cortex of the animals in the treatment group exposed to the smoke extract of *D.stramonium* leaf showed disruption in the histological make up of the organ. Varying degrees of vacuolation were also seen in the proximal convoluted tubules which may compromise the functional integrity of the brush border. These characteristics may lead to the retention of waste products of metabolism. Persistence of such abnormalities results into loss of the sensitive homeostatic functions of the kidneys (Stevens and Lowe, 2005). Kidneys are also the targets involved in unavoidable side effects of so many drugs (Mackinnon et al., 2003). Renal damage has been reported as a side effect to the administration of many medications

The effect of *D.stramonium* on kidney organ including renal tubules, cortex and heavy cellular infiltrations of glomerular were observed and this confirm the study of (Chang *et al*., 2001., Ono *et al*., 1998). Such damages should reach a minimal accepted extent, as a side effect, at the end of experimentations aimed at determining the extent of toxicity under specified conditions of frequency and duration of treatment.

All parts of the plant are toxic because of their high tropane alkaloid level. The approximate content of atropine and scopolamine per blossom is 0.20 and 0.65 mg, respectively. Since the recommended therapeutic dose of atropine and scopolamine is 0.5 mg for the average adult, it is evident that ingestion of as little as 10 flowers can cause death Diker *et al* (2007).

The toxic effects appear 5-15 min after ingestion and may persist for days. They are typical for atropine intoxication and are expressed as an anticholinergic syndrome with central signs such as anxiety, agitation, disorientation, hallucinations, delirium, coma, respiratory failure, and death. Peripheral signs include tachycardia, dry mouth, mydriasis, hyperthermia, urinary retention, and hypertension followed by hypotension. While the peripheral signs appear at lower doses, the central signs develop with dosage escalation.

The threshold dosage for poisoning is lower than that of many other hallucinogens or members of the same family, such as Belladonna and Deadly nightshade. Poisoning sequelae may vary from blurry vision to depression and loss of short-term memory lasting for several weeks, as well as to coma and death. Treatment consists of decontamination and supportive therapy, i.e., fluid replacement, gastric lavage, and activated charcoal cathartics that may be given even 24 h after ingestion since the anticholinergic effect reduces gastrointestinal peristalsis Diker *et al* (2007) .

C O N C LU S I O N.

The weekly oral administration of non-lethal dose of *Datura stramonium* leaves aqueous extract have been well tolerated by the male Swiss albino mice as judged by the mild transient neurotoxicity symptoms. Nevertheless, negative impact have been observed on the body weight gain and on the some vital organs physiology and histology.

From the present study it is clear that the doses used in the acute toxicity study did not reveal in any degree of mortalities although stress symptoms were reported.

In the prolonged toxicity studies and at the designed 0.36, 0.7, 4 mg /kg concentration, no significant changes in body weight between control and treatment were found, on the other hand ,the blood parameter namely RBC, WBC ,HB, HCT, MCT and PLT did not reveal much changes, however C2 has reported relatively high values compared with control.

Histological finding did not reveal adverse effects on the liver whereas, kidney seems more effects.

Result of the present investigation has pointed out the necessity for systematic series of trials leading to the establishment of facts and solid information about the commonly used folk medication of this plant.

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