

# Acute Toxic Effects of AB-CHMINACA on Lung, Heart and Liver: An Experimental Pilot Study

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## Abstract

**Background:** Synthetic cannabinoid (SCs) substances are intended for drug addiction while they cannot be easily detected on a regular drug screen. The danger of these substances is not only being undetected, but also their health effects are not well studied and cannot be predicted. This is one of the recent major health problems that threaten populations around the world. **Aim of the study:** This study is an experimental study to detect the toxic effect of acute exposure to a synthetic cannabinoid substance "AB-CHMINACA" clinically and histopathologically in different organs in adult male albino rats. **Material and methods:** AB-CHMINACA was tested for dissolution in different solvents to choose the best vehicle. Doses were selected according to "Guidance on dose level selection for regulatory general toxicology studies for pharmaceuticals". Animals were injected intraperitoneal and after 24 hours, animals were sacrificed and the lung, heart, and liver were examined for histopathological changes. **Results:** AB-CHMINACA dissolves best in organic solvents like ethanol and DMSO. The most suitable vehicle for intraperitoneal injection of animals was ethanol-saline. After injection, animals showed CNS manifestations; depression or excitation followed by depression according to the dose. Histopathological examination of the lung, heart, and liver tissues showed generalized congestion, hemorrhage, inflammatory cell infiltration and degeneration, which increased by increasing the dose. **Conclusion:** AB-CHMINACA has toxic histopathological effects on the lung, heart, and liver on single-dose exposure even with minimal clinical manifestations. These effects are dose-related.

## Key words

AB-CHMINACA, Synthetic Cannabinoids, Experimental Study, Lung, Heart, Liver

## Introduction

Cannabis or Marijuana is the most widely used drug of abuse worldwide. The active substance of cannabis is Delta-9 Tetrahydrocannabinol ( $\Delta^9$ -THC). Because Marijuana use is banned or even limited to prescriptions in most countries, new synthetic drugs were synthesized to mimic the effect of  $\Delta^9$ -THC with different chemical structures to avoid being detected in regular drug screens (Banister et al., 2015).

In 2004, herbal blends emerged for recreational purposes. Four years later, these drugs were identified as synthetic cannabinoids (SCs) (JWH-018 and CP47,497-C8). In 2009 these drugs were banned so other drugs have emerged and since then the circle of banning and emergence of new drugs is endless. According to a study in 2018, there are nearly 200 different types of synthetic cannabinoid drugs sold for recreational purposes. It was marketed as herbal blends for many years, then other forms emerged as C-liquids (for electronic cigarettes), pure powder or even

cannabis plant blended with synthetic cannabinoids (Hermanns-Clausen et al., 2018).

AB-CHMINACA is an indazole-based synthetic cannabinoid substance. Its pharmacological actions are quite similar to THC. (Wiley et al., 2015). AB-CHMINACA was first discovered by Pfizer in 2009. It was a trial to find a cannabinoid receptor agonist that has the therapeutic effects of cannabis without the other harmful effects. However, these trials showed harmful effects and the project was aborted at that level (Buchler et al., 2009). Later in 2013, AB-CHMINACA was detected as a substance of abuse in the illicit drug market with some cases of acute intoxication at the emergency department in different countries (Uchiyama et al., 2014).

According to a retrospective study in Australia reviewing the cases of death from synthetic cannabinoids, it was found that AB-CHMINACA was the most commonly used member of the synthetic cannabinoid family. Also, it was found that the most common manner of death was acute intoxication (Darke et al., 2019).

In Egypt, a cross sectional study at the poison control center of Ain-Shams University hospital, reported around 500 cases of acute intoxication from SCs between 2018 and 2019. The majority of these cases were due to Strox consumption, nearly 350 cases (Hashem et al., 2021). Sobh and Sobh, (2020) reported that strox is a mixture of different synthetic cannabinoids and AB-CHMINACA was reported to be one of the substances involved in this mixture. Regarding legislation, the Egyptian Ministry of Health and Population added AB-CHMINACA to schedule I substances by the act no, 440 for the year 2018 (Sobh and Sobh, 2020).

The present study is an experimental study to evaluate the acute toxic effects of AB-CHMINACA in adult male albino rats.

## Patients and Methods

### Material

AB-CHMINACA was purchased from Cayman chemicals in a solid formulation. Absolute ethanol and Dimethyl sulfoxide (DMSO) were purchased from Diachem chemicals. Normal saline was purchased from Egypt Otsuka Pharmaceutical Co., S.A.E., and castor oil from Nefertari, Egypt. Haematoxylin and Eosin were purchased from Fisher Scientific. The used light microscope was Leica DM500 Microscope with ICC50 attached camera system.

### Methods

Animals, the experimental procedure was conducted following the guidelines of the care and use of laboratory animals approved by the Ethical Committee of Sohag University. The study was conducted on adult male healthy albino rats weighing  $250 \pm 20$  g. They were housed in laboratory conditions for 1 week before experimentation. Animals were housed maximally 5 rats/cage in a temperature-controlled room ( $22 \pm 2$  °C) with 12–12 h dark-light cycles. Animals were fed with standard pellet feed and water.

Dissolution and determination of best vehicle: Solubility of AB-CHMINACA was tested in different vehicles as follows: Ethanol, saline, castor oil, water, deionized water, a mix of ethanol and deionized water at a ratio of 1:9, a mix of ethanol and saline at a ratio of 1:9, a mix of ethanol, castor oil and saline in a ratio of 1:1:18, and a mix of ethanol and gum acacia 2% solution in normal saline in a ratio of 1:9.

Acute toxicity study: The used protocol for dose selection was "Guidance on dose level selection for regulatory general toxicology studies for pharmaceuticals" (Robinson et al., 2009). The guidance suggested the first doses for studying the toxicity of a new substance by using half-log intervals 3, 10, 30, 100, 300, and 1000 mg/kg. These doses should be given in ascending manner on different days and different animal groups with observing the clinical signs on animals. If severe morbid signs appeared at any dose level, the animals should be euthanized, and further higher doses should be stopped.

Severe morbid signs that are mentioned in the cited guidance are those set by the Federation of European Laboratory Animal Science Associations (FELSA). Endpoint signs reported by FELSA for testing toxicity in rodents are classified into mild, moderate, and severe. At moderate signs, the dosing should be stopped or lowered. When severe signs are noticed, euthanasia is recommended. These signs include labored respiration, prostration, and unresponsiveness to stimuli.

In the present study, the recommended doses were administered via intraperitoneal (i.p) to different groups of adult male albino rats according to the guidance that was mentioned before. Further increasing of doses was stopped after severe morbid signs had appeared. The used concentration of the vehicle did not exceed the maximal safe dose for intraperitoneal injection. The total injection volume did not exceed the allowed level for intraperitoneal injection in rodents (5 ml/kg) (Gad et al., 2006).

The sample size was the minimum for a pilot exploratory study (three per each dose group) with the recommended sample size calculation for experimental studies reported by Charan and Kantharia, (2013). Animals were sacrificed within 24 hours according to guidelines of the scientific ethics committee of the Faculty of Medicine, Sohag University. Animals were euthanized under anesthesia with inhalation of light ether. Necropsy was done for all animals and the lung, heart, and liver were dissected for histopathological tissue preparation and examination under light microscope.

## Results

Dissolution: Dissolution in different vehicles was assessed by naked eye examination as the formation of a homogenous solution. Different vehicles were tested with different concentrations. AB-CHMINACA did not dissolve in water. It dissolved well in organic solvents as DMSO and ethanol. However, it dissolved in DMSO better than ethanol. In castor oil, it showed partial dissolution. The results are shown table (1).

Adding deionized water or saline to dilute the organic solvent had different results according to the concentration. The most suitable vehicle was found to be ethanol: saline 1:9. The substance is first dissolved completely in ethanol then gradual addition of saline. The final solution was an opaque homogenous solution. This was up to 1mg of AB-CHMINACA in 1 ml solution, more addition of saline or shaking of the solution led to precipitation of AB-CHMINACA on the wall of the tube. The solution precipitated and the precipitation time decreased with increasing the concentration, so it should be freshly prepared before administration. Concentrations higher than 1 mg/ml need a surfactant to dissolve. It was found that adding a surfactant as Gum acacia enhanced more dilution with saline without precipitation.

Clinical observation: AB-CHMINACA was administered i.p in ascending doses of logs, 3, 10, 30..., 1000 mg/kg and the clinical effects on rats were observed. These observations are summarized in table (2). The lowest dose, 3mg/kg, led to locomotor depression in rats and calmness. The next dose of 10 mg/kg led to stimulation in the form of hyperactivity for few minutes then depression. Some animals showed splay legs, catalepsy, and respiratory distress. At the dose of 30 mg/kg, animals showed severe morbid signs, so the study was stopped at this dose level. Signs of sever morbidity included respiratory depression and distress in the form of bluish coloration of the mouth, tachypnea, and irregular respiration sever respiratory distress with bluish discoloration. Most of the animals in this group showed no mobility, no response to stimuli, and splay legs. Other signs were noticed in some animals like ptosis and urinary retention. The onset of signs in all groups was very rapid, within few minutes. The duration increased with increasing the dose, ranging between few minutes in the lowest dose to several hours in the largest dose. At the end of the 24 hours, the animals regained normal activity, with no reported death.

The final animal groups were as follow (3 animals each):

**Group 1** (Negative control): Animals were on a regular diet.

**Group 2** (Positive control): Animals received vehicle only (ethanol: saline 1:9).

**Group 3:** was divided into 3 subgroups:

**Group 3a:** Animals received 3 mg/kg as a single dose by i.p injection.

**Group 3b:** Animals received 10 mg/kg as a single dose by i.p injection.

**Group 3c:** Animals received 30 mg/kg as a single dose by i.p injection.

Histopathological examination: Hx & E- stained sections from lung, heart and liver of all animal groups were examined under the light microscope.

**The lung** (figure 1): H&E-stained sections from the negative and positive control groups (groups 1 and 2 respectively) showed normal lung tissue formed of bronchi, bronchioles, alveolar ducts, alveolar sacs, interalveolar septa and vessels. Examination of lung sections from the 3 mg/kg treated group (group 3a) showed slight thickening in the interalveolar septum and congestion in blood vessels. Also, there was minimal cellular infiltration around the bronchioles. More prominent changes were observed on examination of the 10 mg/kg treated group (group 3b). There was more increase in the thickness of interalveolar septa, more

congestion of blood vessels, and increased peribronchial cellular infiltration. However, pathological changes in the 30 mg/kg treated group (group 3c) were much more severe. There was severe thickening in the interalveolar septa with vascular congestion, interstitial hemorrhage and cellular infiltration leading to marked narrowing and distortion of the alveolar sacs. Some alveoli showed desquamation of the epithelial lining. Also, there were multiple foci of inflammatory cell infiltration and peribronchial inflammation.

**The heart** (figure 2): Histological sections from the negative and positive control groups showed branching, cylindrical and parallel muscle fibers with central vesicular nuclei and deep acidophilic sarcoplasm with clear transverse striations. The interstitial tissue was more or less normal. Group 3a showed the picture of apoptosis in some cardiac muscle fibers in the form of pyknotic nuclei and acidophilic cytoplasm. The number of apoptotic cells increased in the 3b group cardiac tissue sections. Also, there was an increase in the interstitial tissue thickness with areas of hemorrhage and cellular infiltration. In group 3c the damage was more severe. There was a loss of architecture and splitting, loss of striations, loss of nuclei and segmental degeneration. There were pyknotic nuclei in other fibers, wavy sarcolemma and myofibril. The interstitial tissue showed hemorrhage and congestion.

**The liver** (figure 3): Hepatic tissue obtained from the negative and positive control groups stained by H&E showed normal architecture of hepatic lobules. The central and portal veins were of average normal diameter. Hepatocytes were arranged in tightly packed cords radiating from the central vein and separated by intrahepatic sinusoids. Hepatocytes showed no pathologic changes. Unlike the control groups, liver sections that were obtained from group 3a showed dilated and congested central and portal veins. Hepatocytes were normal while the normal cords of cells were separated by dilated intrahepatic sinusoids. While group 3b showed the same dilatation and congestion, hepatocytes showed swelling and vacuolation of hydropic degeneration. On examination of stained hepatic tissue obtained from group 3c, it showed disturbed liver architecture, and hepatic cell cords were widely separated due to dilatation of intrahepatic sinusoids. Portal vein and central vein were severely dilated and congested. Most hepatocytes showed hydropic degeneration. Hepatocytes with enlarged nuclei (nucleomegally) were noticed in all treated groups, and the number of these cells increased with increasing the dose.

Table (1): Showing solubility of AB-CHMINACA in different vehicle substances.

Substance	Solubility	Solubility
DMSO	++++	15 mg/ml
Ethanol	+++	10 mg/ml
Ethanol: saline-gum acacia (1:9)	+++	10 mg/ml
Ethanol: saline: castor oil (1:1:18)	++	3 mg/ml
Ethanol & saline (1:9)	+	1 mg/ml
Castor oil	+	1 mg/ml
Water/saline	-	0 mg/ml

Table (2): Showing the signs observed in rats after i.p administration of AB-CHMINACA in the treated groups.

Dose	Signs (Number of affected animals)	Onset	Duration
3 mg/kg	locomotor depression (3/3)	5 min	14 min
10 mg/kg	Hyperactivity (3/3) Depression (3/3) splay legs (2/3) catalepsy (1/3) respiratory distress (2/3)	5 min	2 hours
30 mg/kg	no mobility, no response to stimuli (3/3) splay legs (3/3) respiratory depression (2/3) respiratory distress (3/3) ptosis (3/3) urinary retention (1/3)	5 min	8 hours

Figure 1:

Lung tissue by Hx &amp; E X100

A: Negative control

B: Positive control

C: 3mg/kg

D: 10 mg/kg

E: 30mg/kg.

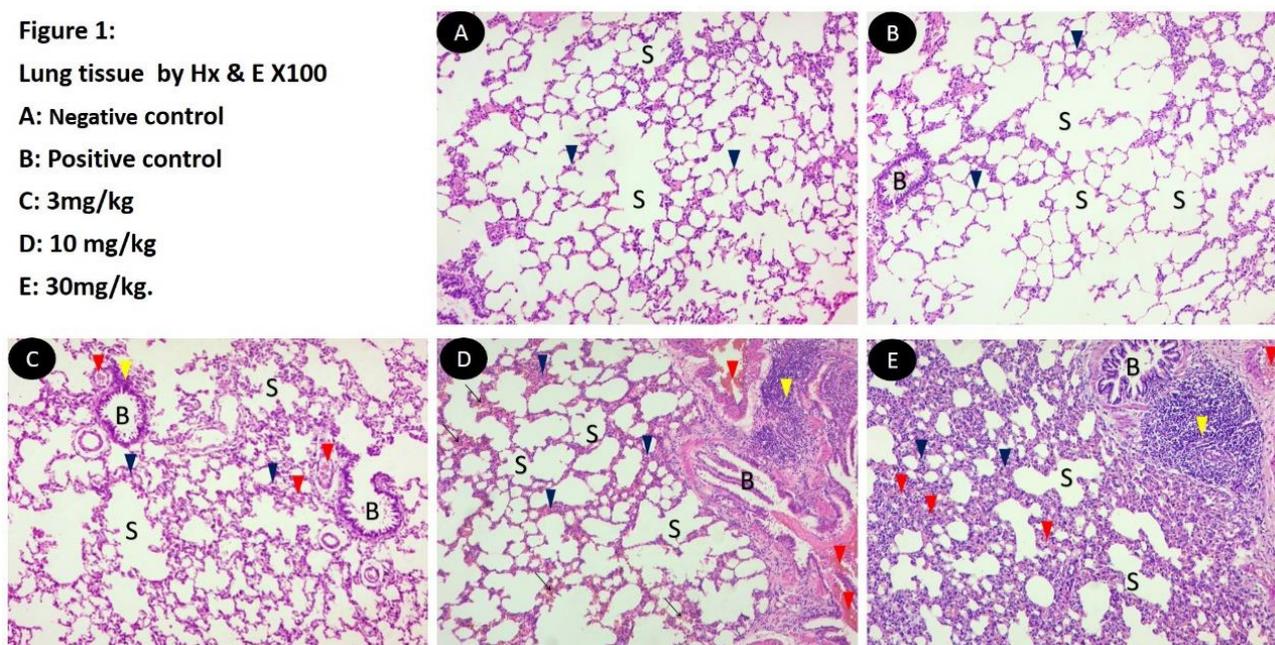


Figure 1: Photomicrograph of lung tissue by Hx & E. (A and B): normal lung architecture in the form of normal alveolar sac (S), thin interalveolar septa (blue arrowheads), and normal bronchioles (B). (C): congested blood vessels (red arrowheads) and slightly thickened interalveolar septa with minimal cellular infiltration around the bronchioles (yellow arrowheads). (D): narrow distorted alveolar sac and alveoli (S), increased thickness of the interalveolar septa (blue arrowheads), dilated and congested blood vessels (red arrowheads), and massive cellular infiltration around the bronchioles (yellow arrowheads). (E): marked thickening of interalveolar septa (lung consolidation) with more narrow and distorted alveolar sacs (S), congestion (red arrowheads), and massive cellular infiltration (yellow arrowheads) around the bronchioles (B). (Magnification x100).

**Figure 2:**

Heart tissue by Hx &amp; E X400

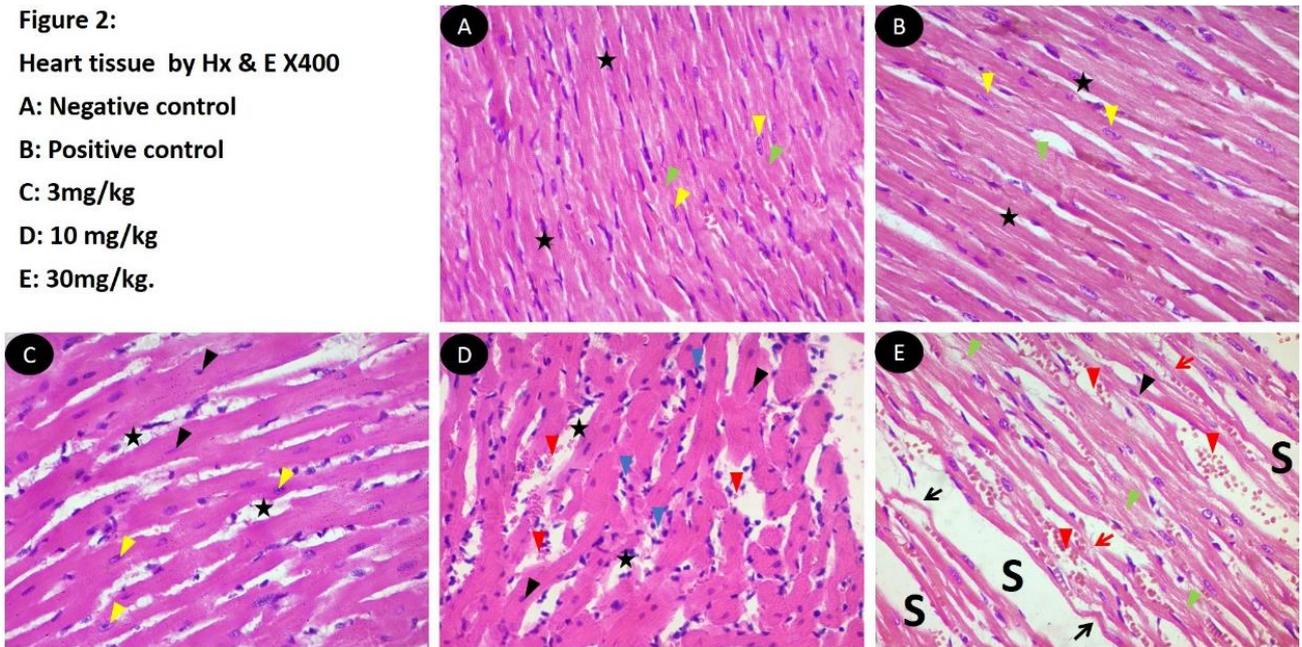
A: Negative control

B: Positive control

C: 3mg/kg

D: 10 mg/kg

E: 30mg/kg.



**Figure 2: Photomicrograph of cardiac tissue by Hx & E. (A and B):** branching, cylindrical and parallel muscle fibers, Central vesicular nuclei (yellow arrowhead), deep acidophilic sarcoplasm with clear transverse striations. The interstitial tissue is normal. **(C):** muscle fibers with few pyknotic nuclei (black arrowhead) and acidophilic sarcoplasm. There is increased interstitial tissue (black asterisk). **(D):** pyknotic nuclei (black arrowhead) with acidophilic sarcoplasm. Increased interstitial tissue (black asterisk). Interstitial hemorrhage (red arrowhead) and cellular infiltration (blue arrowhead). **(E):** loss of architecture of some fibers Splitting (S), loss of striations (green arrowhead), loss of nuclei, and segmental degeneration (red arrow). pyknotic nuclei in other fibers (black arrowhead), wavy sarcolemma, and myofibril (black arrow). Interstitial hemorrhage and congestion (red arrowhead). (Magnification x400).

**Figure 3:**

Liver tissue by Hx &amp; E X200

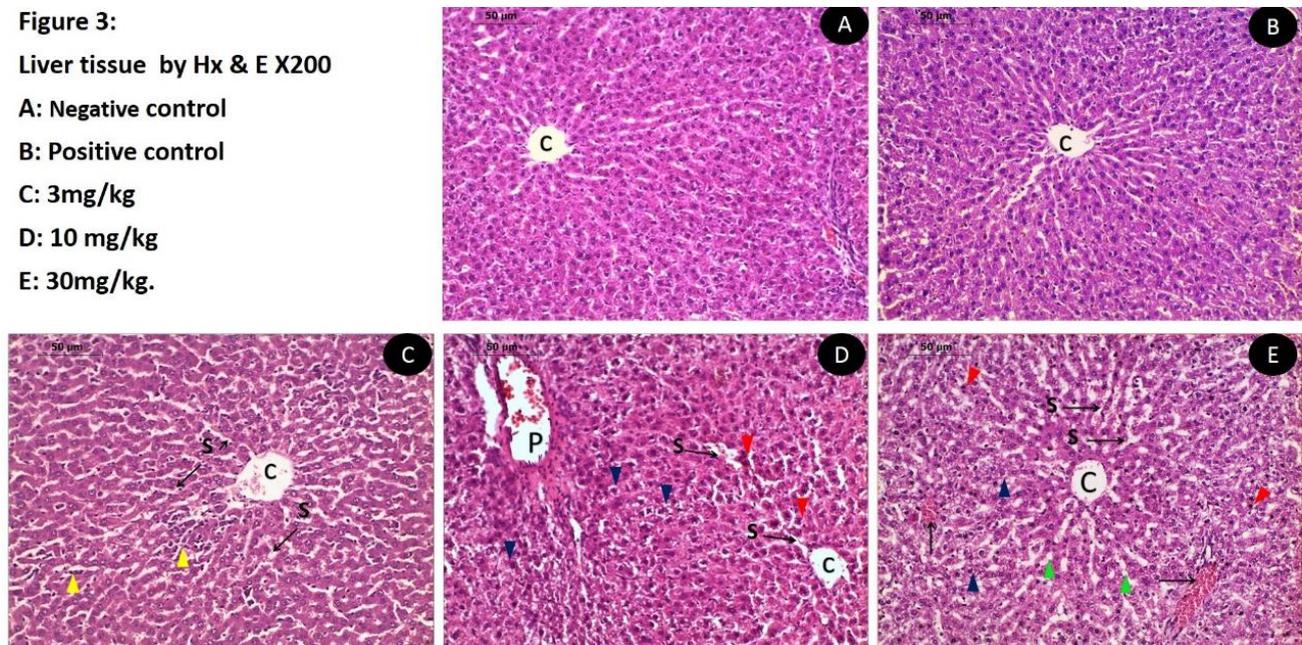
A: Negative control

B: Positive control

C: 3mg/kg

D: 10 mg/kg

E: 30mg/kg.



**Figure 3: Photomicrograph of liver tissue by Hx & E. (A and B):** normal hepatic architecture in the form of centrally located central vein (C) and radiating from it, cords of hepatocytes surrounded by portal area (P) at each pole. **(C):** dilated central vein (C) and intrahepatic sinusoids (S) and abundant Kupffer cells (yellow arrow). **(D):** dilated and congested central vein (C), portal vein (P), and sinusoids (S). Hepatocytes show hydropic degeneration (blue arrow) and apoptotic changes (red arrow). **(E):** dilation and congestion of central vein (C), portal vein (P), and sinusoids (S). Hepatocytes show hydropic (blue arrow) and fatty degeneration (green arrow). (Magnification x200).

## Discussion

Strox, voodoo, Spice, K2 and others, are famous trade names for new psychoactive substances. They are now a big health problem that threatens all different populations. Since their appearance in the illicit drug market, they are growing very fast, and now hundreds of substances are present worldwide. Although many emergency cases are present each year from acute intoxication, the health effects of these substances cannot be predicted. They are different from person to person and from substance to another (Mills et al., 2015). Less is known about the toxicological effects of NPS. The toxic dose, clinical effects and systemic and organ response to these substances are considered obscure to this moment (Zapata et al., 2021).

In the present study, the chosen vehicle was ethanol : saline at a ratio of 1:9 for IP injection in mice.

Wiley et al. (2015) used a surfactant added to the ethanol: saline solution to deliver AB-CHMINACA to mice. They used ethanol: cremophore: saline at a ratio of 1:1:18 for IP injection. Marshall et al. (2014) used ethanol diluted with Tween 80 and normal saline in a concentration of 8% and 92% respectively for IP injection of SC substances in mice.

Ito et al. (2019) used DMSO for the dissolution of 5F-AMB (a new synthetic cannabinoid substance). Similar to the present study, the solution was diluted with normal saline at a ratio of 1:9 respectively for IP injection in mice.

The present study showed motor depression and catalepsy in treated animals. Also, tachypnea and respiratory distress were observed. The severity of signs increased with increasing the dose.

Searching the literature there were no available data about the tolerated dose or the toxic dose of AB-CHMINACA. Some animal studies were carried out to observe the behavioral effects in mice. They used different doses of AB-CHMINACA with a maximum of 3 mg/kg for i.p. injection. Wiley et al. (2015), Lefever et al. (2017), and Wiley et al. (2019) all used doses ranged between 0.03 mg/kg and 3 mg/kg. All these studies showed full THC substitution by AB-CHMINACA and produced the tetrad effect (decreased motor activity, decreased temperature, catalepsy, and antinociception which means decrease the sensation to painful stimuli).

Most of the studies reporting toxic effects of SCs are case studies of ER patients with recent consumption of SC substances. The most-reported system affections are CNS, gastrointestinal, and cardiopulmonary. Acute renal toxicity and acute hepatotoxicity were also reported at a lower rate as a complication of acute toxicity. Case studies give attention to the clinical symptoms and leading causes of death without paying attention to specific organ pathology. Organized animal studies evaluating the histopathological toxic effects on different body organs are scarce (Solimini et al., 2017).

The present study involved histological examination of sections from lung, heart, and liver of control and treated animal groups. H&E- stained section from lungs of treated animal groups showed

congestion, interstitial hemorrhage, and consolidation. Examination of the heart tissue showed congestion with hemorrhage and apoptosis of cells in large doses. While liver sections of treated animal groups showed congestion and dilatation. Hepatocytes showed hydropic degeneration and nucleomegaly. The effects increased with increasing the dose.

On reviewing the available literature there was no published experimental study revealing the histopathological effects of SC on body organs. However, many studies were found exploring the toxicological effects and the leading cause of death in human cases of acute intoxication. Some of them reported postmortem histological analysis of different body organs.

Darke et al., (2019) had conducted a statistical analysis of various parameters in all cases of SCs intoxication in Australia that are reported between 2000 and 2017. AB-CHMINACA intoxication represented the largest percentage of other SC substances, more than one-third of cases. In about 70 percent of cases, the leading causes of death were due to cardiovascular complications.

Going in harmony, Paul et al., (2018) reported two cases of death due to SC intoxication one of them confirmed to be due to AB-CHMINACA intoxication. Both were reported to be chronic abusers several months before death. An autopsy was done for both cases. Results obtained from the case of AB-CHMINACA intoxication showed cardiorespiratory affection. The heart was enlarged and myopathic. Histological examination showed hypertrophy of the cardiac cells and contraction band necrosis. Gross examination of the lungs showed diffuse edema with associated pleural effusion. Histological examination revealed edema and congestion of the lung tissue.

Similar findings were reported by Ivanov et al. (2019). He reported a case of death from SC use. The deceased was a chronic abuser who consumed a large amount the day before death. Analysis was done to detect and quantify the level of the involved substances in blood samples from the deceased. Histopathological examination was carried out for lungs, heart, brain, and spleen. Sections from lung tissue showed lung edema and huge infiltration with macrophages. The alveolar epithelium showed degeneration and desquamation. PAS-stained sections showed hyaline degeneration. The author concluded that it is a picture of early-stage ARDS. While microscopic examination of sections from the heart tissue showed preserved cardiac cells with dilatation and congestion of the vessels.

In another case reported by Maeda et al. (2018), the final diagnosis of the cause of death was non-cardiogenic pulmonary edema from SC consumption. The deceased was an adult male who was found dead in his office and beside him, a package of an herbal mixture which was confirmed to contain a mix of SC substances. the main active substance in this mixture was identified to be AB-CHMINACA. An autopsy showed edema of the lungs. Histological examination detected froths in the alveoli supporting rapidly

progressing edema. The cardiac assessment concluded that the lung edema was non-cardiogenic.

Although hepatic affection is not a common presentation of SC intoxication, there are confirmed cases of fulminant hepatic failure and liver affection after smoking SC. However, there was no histopathological assessment in these cases.

Sheikh et al. (2014) reported a case of acute hepatic failure after consumption of SC substance. The case developed hyperbilirubinemia, an increase in INR, shooting liver enzymes, and coma. However, the case improved with supportive treatment. Similar findings were described by Armenian et al. (2018) who reported three cases with hepatic affection from SC use and the cases had been improved with supportive treatment.

Histopathological changes can be explained by oxidative stress in tissues causing cell apoptosis. Athanasiou et al. (2007), studied the effect of THC, endocannabinoids and synthetic cannabinoids on mitochondrial function. The study was carried out on in vitro cells. synthetic cannabinoids and THC showed marked effect on mitochondrial respiratory enzymes. There was lower rate of O<sub>2</sub> consumption in the cell with higher levels of hydrogen peroxide. This effect is due to direct toxic effect and not related to CB1 or CB2 receptors.

## Conclusion

AB-CHMINACA is a toxic substance in multiple body organs. The most prominent feature is generalized congestion. Other features as apoptosis, hemorrhage, and cellular infiltration are dose-related. Histopathological effects can develop even at a small dose.

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## التأثيرات السمية الحادة لـ AB-CHMINACA على الرئة والقلب والكبد: دراسة تجريبية

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### الملخص العربي

**الخلفية:** القنبات المصنعة تم إختراعها للإستخدام كمواد مخدرة تعطي تأثير مشابه لمخدر الحشيش بينما لا يمكن إكتشافها بسهولة بواسطة الإختبارات الحالية لتعاطي المخدرات. و لا يقتصر خطر هذه المواد على صعوبة إكتشافها بالتحاليل المعتادة، ولكن أيضًا أثارها الصحية ليست مدروسة جيدًا ولا يمكن التنبؤ بها. هذه واحدة من المشاكل الصحية الرئيسية الأخيرة التي تهدد السكان في جميع أنحاء العالم. **هدف الدراسة:** هذه الدراسة عبارة عن دراسة تجريبية للكشف عن التأثير السام للتعرض الحاد لمادة من مجموعة القنبات المصنعة "AB-CHMINACA" على أنسجة الرئة و القلب و الكبد في ذكور الجرذان البيضاء البالغة. **المواد وطريقة البحث:** تم اختبار AB-CHMINACA للذويان في مذبذبات مختلفة لاختيار المذيب الأنسب للحقن. تم اختيار الجرعات وفقًا لـ "إرشادات بشأن اختيار مستوى الجرعة لدراسات السموم للمستحضرات الصيدلانية". تم حقن الحيوانات داخل الغشاء البريتوني وبعد ٢٤ ساعة، تم تشريح الحيوانات وفحص الرئة والقلب والكبد لدراسة التغيرات النسيجية. **النتائج:** AB-CHMINACA يذوب بشكل أفضل في المذيبات العضوية مثل الإيثانول و ثنائي ميثيل سلفوكسيد. تم إختيار الإيثانول المخفف محلل الملح كوسيلة للحقن داخل الغشاء البريتوني للحيوانات. بعد الحقن، أظهرت الحيوانات تأثير ملحوظ على الجهاز العصبي المركزي. كانت الأعراض في صورة تثبيط أو إستتارة يتبعها تثبيط حسب الجرعة. أظهر فحص أنسجة الرئة والقلب والكبد احتقانًا عامًا ونزيفًا وتجمع لخلايا الالتهاب الحاد كما تبين زيادة في شدة التأثير على الأنسجة بزيادة الجرعة الدوائية. **الخلاصة:** AB-CHMINACA له تأثيرات سامة على أنسجة الرئة والقلب والكبد عند التعرض لجرعة واحدة حتى مع الحد الأدنى من المظاهر السريرية. هذه التأثيرات تزداد بزيادة الجرعة.

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