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ظهور التهاب الكبد المناعي بنسبة عالية عند المريض اليمني المتعاطى للقات

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## Autoimmune hepatitis have higher frequencies in Yemen's patient's who chewing khat

#### Abstract.

The khat tree is a common plant that grows in Yemen and East Africa (East and West Harge regions in Ethiopia) and has many health, social and economic damages. Because of the lack of awareness in this field and the lack of research, we find that this phenomenon is difficult to control, and we find that people who consume khat suffer from many serious health problems and may lead to death. One of these risks is the harmful effects of consuming khat on the human liver. This paper presents the damage that the khat tree causes to humans and that it is a major cause of hepatitis and autoimmune liver disease as autoantibodies to ANA and ASMA have been shown in patients without chronic liver. disease. Clinical examinations. blood and urine tests, and abdominal ultrasound were conducted for a group of 420 patients between the ages of 18-45 years from different cities of Taiz, Al-Turbah, Lahi and their villages in the Republic of Yemen. The immunosuppressant drug prednisalone Keywords: Khat, Autoantibodies,

**Keywords:** Khat, Autoantibodies, autoimmune hepatitis, ANA, ASMA.

(0.5 mg/kg/day), Ursochol 250 mg (10 mg/kg/day) and Livbest tab (2 tablets twice daily) have been suggested and given excellent results for all patients. After the treatment, according to the duration suggested in the research, three weeks and continuing for one month in order for all the enzymes of the liver to become normal. After that, treatment stopped completely and abstained for three months consuming khat, where the percentage of complete recovery was 315 out of 420, except for 80 cases with a weak rise in liver enzymes and 20 cases where an anti-smooth muscle antibody (ASMA) remained positive without symptoms and 5 cases of antinuclear antibodies (ANA) positive without symptoms. Through the results, it became clear that the treatments proposed in the research have a good effect in treating such cases and can be stopped after a liver function improves as long as khat chewing is abstained.

## ظهور التهاب الكبد المناعى بنسبة عالية عند المريض اليمنى المتعاطى للقات

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#### ملخص البحث:

شجرة القات نبات شائع ينمو في اليمن وشرق إفريقيا (مناطق شرق وغرب هارج في إثيوبيا) وله العديد من الأضرار الصحية والاجتماعية والاقتصادية. وبسبب قلة الوعى في هذا المجال وقلة البحث نجد صعوبة السيطرة على هذه الظاهرة ونجد أن من يستهلك القات يعانون من مشاكل صحية كثيرة خطيرة وقد تؤدي إلى الوفاة. ومن هذه المخاطر الآثار الضارة لتعاطى القات على كبد الإنسان. يعرض هذا البحث الضرر الذي تسببه شجرة القات للإنسان وأنه سبب رئيسى لالتهاب الكبد وأمراض الكبد المناعية الذاتية حيث تم عرض الأجسام المضادة الذاتية لـ ANA و ASMA في المرضى الذين الا يعانون من أمراض الكبد المزمنة. تم إجراء الفحوصات السريرية واختبارات الدم والبول والموجات فوق الصوتية للبطن لمجموعة من 420 مريضاً تتراوح أعمارهم بين 18-45 سنة من مختلف مدن تعز والتربة ولحج وقراهم في الجمهورية اليمنية. تم اقتراح عقار بريدنيسالون المثبط للمناعة (0.5 مجم / كجم

الطبقة الوسطى للشريان السباتي الاضطرابات بالأشعة التلفزيونية

/ يوم) و Ursochol 250 مجم / كجم / كجم / يوم) وعلامة التبويب Livbest (قرصان مرتين يوميًا) وتم إعطاؤهما نتائج ممتازة لجميع المرضى. بعد العلاج وحسب المدة المقترحة في البحث ثلاثة أسابيع وتستمر لمدة شهر حتى تصبح جميع إنزيمات الكبد طبيعية. بعد ذلك توقف العلاج نهائيا وامتنع عن تناول القات لمدة ثلاثة أشهر حيث كانت نسبة الشفاء تناول القات لمدة ثلاثة أشهر حيث كانت نسبة الشفاء التام 315 من 420 باستثناء 80 حالة مع ارتفاع ضعيف في إنزيمات الكبد و 20 حالة فيها اجسام مضادة مناعية. (ASMA) بقيت إيجابية بدون أعراض و 5 حالات من الأجسام المضادة المناعية الفرض و 5 حالات من الأجسام المضادة المناعية الضح أن العلاجات المقترحة في البحث لها تأثير جيد وظائف الكبد طالما امتنع عن مضغ القات.

الكلمات المفتاحية: القات ، الأجسام المضادة . ASMA, ANA .

#### 1. Introduction

Khat (scientific name: Catha edulis) is a monophyletic genus of evergreen shrubs of the family Euonymous (Celastraceae) and is a common plant that grows in East Africa (East and West Harge regions of Ethiopia) and Yemen. Khat contains minoamine, an alkaloid called cathinone, which is similar to amphetamine, and is a central nervous system stimulant, causing feelings of excitement and euphoria. Khat is chewed as a social custom that dates back thousands of years, such as the use of coca leaf in South America and betel nut in Asia. Khat is an integral part of society. It is eaten during family gatherings in homes or cafes (instead of coffee) or after work as a way to relax, and students also use it while preparing for exams. The leaves are placed in the mouth and chewed vigorously with the teeth, then the leaves are moved through the tongue above the cheek, where the process continues for three hours or more and while you speak. Khat has many health problems that affect, in the short or long term, human health and may lead to death in many cases in the societies that consume khat, due to the lack of awareness in the community about the damage and risk of khat, and also due to the small amount of research in this field. It is important that the communities that consume khat, as well as the workers in the Ministry of Health who are supervising their care, are more aware of the risks and physiological and psychological effects of khat and the diseases that lead to death. There are studies on the effects of khat on the psychological state of its users [1], as khat contains compounds similar to amphetamine and cathinone, which affect the nervous system in the brain, and this may lead to psychotic states [2-5]. As in some studies, it appears that consuming khat leads to insomnia, distress, depression and lack of concentration [7-6]. Also, consuming khat for 3-4 hours leads to an increase in heart rate and blood pressure due to indirect activity [9,8]. Khat also leads to esophagitis, gastritis, and ulceration of the oral mucosa, which may develop into cancer [10-13] due to the presence of tannins in khat leaves. The short- and longterm physical effects of khat consumption are well described according to the respective physiological systems [14,15,16,17] and summarized in Figure 1. Sources [19,18] presented the effect of khat on the liver, as long-term khat users can develop complications from acute and chronic liver disease, which in the case of chronic khat use may lead to hepatitis and cirrhosis. Study [20] presents the relationship of khat with hepatomegaly and hepatotoxicity in male and female SD rats, and nephrotoxicity only in SD female rats.

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#### Mukhtar Abdullah Al-Nahary

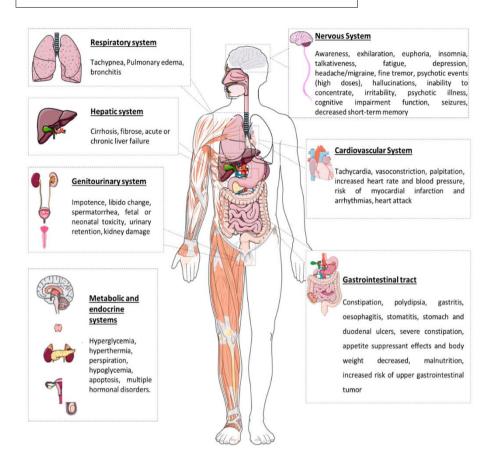


Figure 1. Common adverse effects of khat abuse.

It is important that the communities that consume khat and the Ministry of Health workers who supervise their care are more aware of the risks and physiological and psychological effects of khat and the diseases that lead to death.

The importance of the research is that it exposes the danger of consuming khat to human health, especially the liver, which is an important organ in the body, and neglecting it may lead to serious diseases, which leads to death.

This paper presents that khat is a major cause of hepatitis and autoimmune liver disease as autoantibodies to ANA and ASMA have been shown in patients without chronic liver disease. These symptoms appeared through clinical examinations, blood and urine investigations, and abdominal ultrasound for a group of 420 patients

between the ages of 18-45 years from different cities of Taiz, Al-Turbah, Lahj and their villages in the Republic of Yemen. The immunosuppressive drug prednisalone (0.5 mg/kg/day), Ursochol 250 mg (10 mg/kg/day) and liver support Livbest Tab (2 tablets twice daily) have been proposed and have given excellent results after treatment and khat abstinence for three months. In future work, we propose to study the relationship of khat with heart diseases and diseases of the gallbladder, and pancreas.

The rest of this paper was arranged as follows: In the next section we discussed the methodology used in the research to study patients' cases, diagnosis and treatment, while the third section presented the results of the method used during the treatment period. Finally, the fifth section presented the conclusion of this paper.

## 2. Methodology

In this section, we will present the method used to diagnose and treat patients who chew khat and suffer from liver disease. The proposed method is explained in the following steps: data collection for patients, medical examinations (clinical examination, blood investigation, urine examination and an abdominal ultrasound) and treatment plan.

#### 2.1 Data collection

The research was conducted on a group of 420 patients consuming khat, aged between 18 and 45 years, from different cities of Taiz, Al-Turbah, Lahj and their villages in the Republic of Yemen.

#### 2.2 Medical Examination

The research includes a clinical examination, blood investigation (clinical, biochemical and serological), urine examination, and an abdominal ultrasound.

### A. clinical examination

By clinical examination, most patients have abdominal pain, yellowish discoloration of eyes, general fatigue, loss of appetite, pallor and dark urine.

#### B. Blood Test

The blood was examined for 420 patients who chewed khat, and the number of patients with anemia reached 100, while 320 patients did not suffer. As for the eosinophilia in blood test, 370 patients out of 420 showed elevation. While the biochemical blood investigations (GPT, GOT, and Bilirubin (direct / Indirect)) was high in all patients and the Serum albumin test of 350 patients was normal, and 70 patients were slightly decresed. Viruses A, B, and C, as well as tests for schistosomiasis, were negative for all patients.

Finally, the results of the autoimmune Antibodies tests for ANA were positive for 170 patients, and the ASMA tests were positive for 180 patients, while the results of 50 patients were positive for both ANA and ASMA tests together, and the results for 20 patients were negative.

### C. Abdominal ultrasound

By testing the patients using the abdominal ultrasound, the results showed fatty liver for 30 patients and 100 patients with mild periportal fibrosis, while 150 patients had splenomegaly and 320 patients had hepatomegaly.

## **D.** Urine analysis

On the urine test, high R.B.S, Urobilinogen were observed in 100 patients.

#### 2.3 Treatment

The immunosuppressant drug Prednisalone (0.5 mg/kg/day), ursochol 250 mg (10 mg/kg/day) and Livbest tab (2 tablets twice daily) were suggested for all patients and their health conditions were monitored.

#### 3. Results

After giving all the patients taking khat the suggested drug treatments, an excellent response was observed in the patients and an improvement in their health condition. The results showed a decline in all symptoms and a decrease in liver enzymes in 280 patients during the first week. It was also noted that symptoms also decreased completely in 380 patients during the next two weeks, and when treatment was continued for one month, symptoms decreased completely in 420 patients else as seen as figure 2. It was found that the liver enzymes became normal in all patients after the completion of treatment for one month.

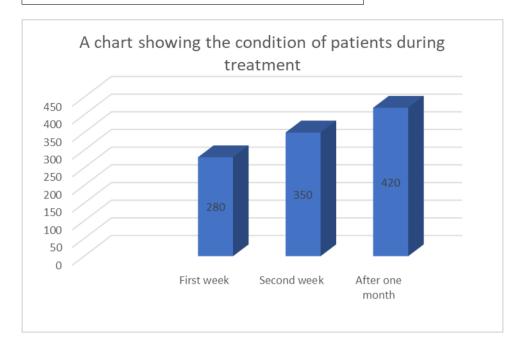


Figure 2. A diagram of the treatment plan and timetable

After that, it was suggested to stop the treatments and prevent the patient from consuming khat for a period of 3 months to consider the effect of khat disappear. Clinical examination, blood and urine investigations, and abdominal ultrasound were done for all treated patients and the results were normal for 315 out of 420 except for 80 patients with slight elevation in liver enzymes, 20 patients remaining ASMA positive without symptoms and 5 ANA positives without symptoms. The figure 3. illustrates the status of patients after treatment for three months and refrain from chewing Khat.

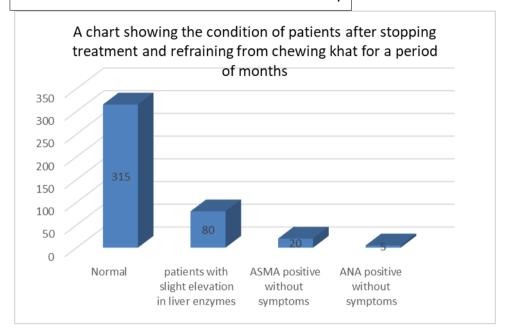


Figure 3. A diagram of the patients' condition after stopping treatment for three months and refraining from chewing khat.

#### 4. Conclusion

This paper aims to identify the damages of khat and the diseases it causes to the body as a whole and to the liver in particular as ANA and ASMA autoantibodies were shown to patients without chronic liver disease. After the results of the tests for the 420 patients who were diagnosed, it can be said that khat causes hepatitis and its symptoms are completely similar to the symptoms of hepatitis for any other causes. It was also found that khat causes aberrations in the immune system. In the research, the immunosuppressive drug Prednisalone (0.5 mg/kg/day), Ursochol 250 mg (10 mg/kg/day) and Livbest tab (2 tablets twice daily) were suggested and they gave excellent results. After using the treatment according to the duration proposed in the research, as well as abstaining for three months from chewing khat, where the percentage of complete recovery was 315 out of 420, except for 80 cases with a weak rise in liver enzymes and 20 cases where ASMA remained positive without symptoms and 5 cases of ANA positive without symptoms. Through the results, it became clear that the drug treatments proposed in the research have a good effect in treating such cases and can be stopped when liver function improves as long as khat chewing is stopped.

## Reference

- 1. Pehek EA, Schechter MD, Yamamoto BK. Effects of cathinone and amphetamine on the neurochemistry of dopamine in vivo. Neuropharmacology29(12):1171-6, 1990.
- 2. Giannini A, Castellani S. A manic-like psychosis due tockhat. J Toxicol Clin Toxicol, 19(5):455-9, 1982.
- Critchlow S, Seifert R. Khat induced paranoid psychosis. Br J Psychiatry;150;247-9, 1987.
- 4. McLaren P. Khat psychosis. Br J Psychiatry 1987;150:712-3.
- 5. Yousef G, Huq Z, Lambert T. Khat chewing as a cause of psychosis. Bri J Hosp Med (Lond),54(7):322-6, 1995.
- 6. Kalix P. Catha edulis, a plant that has amphetamine effects. Pharm World Sci, 18(2):69-73, 1996.
- 7. Al-Motarreb A, Baker K, Broadley KJ. Khat: Pharmacological and medical aspects and its social use in Yemen. PhytotherapyRes,16(5):403-13, 2002a.
- 8.Toennes, S.W.; Harder, S.; Schramm, M.; Niess, C.; Kauert, G.F. Pharmacokinetics of cathinone, cathine and norephedrine after the chewing of khat leaves. Br. J. Clin. Pharmacol, 56, 125-130, 2003.
- 9. Widler, P.; Mathys, K.; Brenneisen, R.; Kalix, P.; Fisch, H.-U. Pharmacodynamics and pharmacokinetics of khat: A controlled study. Clin. Pharmacol. Ther 55, 556-562, 1994.
- 10.Gunaid AA, Sumairi AA, Shidrawi RG, Al-Hanaki A, Al-Haimi M, Al-Absi S, Al-Huribi MA, Qirbi AA, Al-Awlagi S, El-Guneid AM, Shousha S, Murray-Lyon IM. Oesophageal and gastric carcinoma in the Republic of Yemen. British Journal of Cancer, 71: 409-410, 1995.
- 11. Benson PB, Mcdermott W, editors: Cecil-Loeb Textbook of Medicine, Philadelphia, W. B. Saunders Co, 107-149. 13, 1971.
- 12. Heymann TD, Bhupulan A, Zuriekat NEK, Bomanji J, Drinkwater C, Giles P. Murray-Lyon IM. Khat chewing delays gastric emptying of a semi-solid meal. Aliment Pharmacol Ther, 9: 81-83, 1995.
- 13. Hill, C.M.; Gibson, A. The oral and dental effects of q'at chewing. Oral. Surg. Oral. Med. Oral. Pathol, 63, 433-436, 1987.
- 14. Abebe, W. Khat: A Substance of Growing Abuse with Adverse Drug Interaction Risks. J. Natl. Med Assoc, 110, 624-634., 2018.
- 15. Valente, M.J.; de Pinho, P.G.; Bastos, M.D.L.; Carvalho, F.; Carvalho, M. Khat and synthetic cathinones: A review. Arch. Toxicol, 88, 15-45, 2014.

- 16. Engidawork, E. Pharmacological and Toxicological Effects of Catha edulisF. (Khat). Phytotherapy Res, 31, 1019-1028,2017.
- 17. Ahmed, A.M. Effect of Khat on the Heart and Blood Vessels. Heart Views, 5, 54-57, 2004.
- Chapman, M.H.; Kajihara, M.; Borges, G.; O\_Beirne, J.; Patch, D.; Dhillon, A.P.; Crozier, A.; Morgan, M.Y. Severe, Acute Liver Injury and Khat Leaves. N. Engl. J. Med, 362, 1642-1644, 2010.
- 19. Stuyt, R.J.L.; Willems, S.M.; Wagtmans, M.J.; Van Hoek, B. Chewing khat and chronic liver disease. Liver Int, 31, 434-436, 2011.
- 20. Abdulsamad Alsalahi, Mahmood Ameen Abdulla, Mohammed Al-Mamary, Mohamed Ibrahim Noordin, Siddig Ibrahim Abdelwahab, Aied M. Alabsi, Abdrabuh Shwter, Mohammed A. Alshawsh, "Toxicological Features of Catha edulis (Khat) on Livers and Kidneys of Male and Female Sprague-Dawley Rats: A Subchronic Study", Evidence-Based Complementary and Alternative Medicine, vol. 2012, Article
  - ID 829401, 11 pages, 2012. https://doi.org/10.1155/2012/829401, 2012.