

Original Research Article

Screening of alpha-fetoprotein, C-reactive protein and gamma-glutamyl transferase among Khat chewers

Alariqi Reem^{1*}, Al-Awar Mohammed Sadeq², Rachad Alnamer³, Mazen Almehmadi⁴, Aisha Mane'a¹, Maram Hazza¹

¹Faculty of Medical Sciences, Medical Laboratory Department, Al-Razi University, Sana'a, ²Faculty of Medical Sciences, Physiology and Histopathology Department, Al-Razi University, Sana'a, Yemen, ³Faculty of Medicine and Health Science, Pharmacy Section, Al-Razi University, Sana'a, Yemen, ⁴Department of Clinical Laboratory Sciences, College of Applied Medical Sciences, Taif University, P.O. Box 11099, Taif 21944, Saudi Arabia

*For correspondence: **Email:** r.alariqi@alraziuni.edu.ye; **Tel:** 0967-777632182

Sent for review: 18 April 2025

Revised accepted: 22 August 2025

Abstract

Purpose: To evaluate the possible effects of Khat and its active ingredient, cathine, on the hepatic production of alpha-fetoprotein (AFP), C-reactive protein (CRP) and gamma-glutamyl transferase (GGT) levels among khat chewers.

Methods: The study is a descriptive study among khat chewers in Sana'a, Yemen. The serum levels of AFP, GGT and CRP were evaluated in 70 chronic khat chewers comprising 57 males (81 %) and 13 females (19 %). Serum CRP levels were determined using a commercial latex-enhanced turbidimetric immunological assay kit. On the other hand, serum AFP concentrations were quantified using ELISA kits, while serum γ -glutamyltransferase (GGT) was determined using the Roche Cobas c501 analytical system.

Results: Three of the 70 participants in the study had elevated AFP levels, with an overall prevalence of 4 %, while GGT was elevated in 13 (19 %) of the participants. In contrast, CRP levels were normal in all participants. However, cathine had no significant effects on serum levels of AFP, GGT and CRP in long-time chewers of khat.

Conclusion: These data demonstrate that cathine has no significant effect on several liver-derived proteins such as AFP, GGT and CRP, in those who chew khat for a long time.

Keywords: Khat, Cathinone, Alpha-fetoprotein, CRP, GGT

This is an Open Access article that uses a funding model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>) and the Budapest Open Access Initiative (<http://www.budapestopenaccessinitiative.org/read>), which permit unrestricted use, distribution, and reproduction in any medium, provided the original work is properly credited.

Tropical Journal of Pharmaceutical Research is indexed by Scopus, Chemical Abstracts, Embase, Index Copernicus, EBSCO, African Index Medicus, JournalSeek, Directory of Open Access Journals (DOAJ), African Journal Online, Bioline International, Open-J-Gate and Pharmacy Abstracts

INTRODUCTION

For centuries, many people in Eastern Africa and the Arabian Peninsula (Yemen, Ethiopia, Somalia, Kenya, Saudi Arabia, South Africa, and Madagascar) have been chewing fresh leaves and branches of *Catha edulis*, generally identified as khat, for its stimulating effect [1]. The majority of Yemenis chew khat leaves daily as a social habit. A few years ago, most khat

chewers were guys. However, the number of women and children who chew khat has increased. During wedding celebrations and funerals, people consume khat [2]. The main psychoactive compound in *C. edulis* is cathinone, a β -keto analogue of amphetamine. It shares both the stimulant properties of amphetamines and a similar phenethylamine structure.

The amount of cathinone in khat leaves, which varies depending on the region in which it is grown, determines its market worth and potency [3]. In addition, the WHO has designated khat as an abuse substance because it is associated with detrimental health outcomes. Moreover, the cardiovascular system is primarily affected by khat, as evidenced by elevated heart rate, elevated blood pressure and a high risk of myocardial infarction. Khat increases the risk of stroke, and it causes stress, sadness, hallucinations, insomnia, poor oral hygiene, dental caries, periodontitis, increased ulceration of the oral mucosa, gingival recession and bleeding [4]. It has been hypothesized that the liver is particularly susceptible to the adverse effects of khat [5]. Chewing khat raises the possibility of hepatotoxicity and liver cirrhosis, and the habit causes hemorrhoids, constipation, gastritis and appetite loss. Ultimately, khat chewing results in low-birth-weight infants, poor micturition and low sperm motility and counts in khat-chewing males. Although there is a link between khat consumption and liver damage, the exact mechanism is unknown. Several researchers postulate that khat might cause an autoimmune reaction in vulnerable people and have demonstrated khat-related liver damage that resembles autoimmune hepatitis [6]. The present study was carried out to evaluate the possible effects of khat and its bioactive component, cathine, on serum concentrations of AFP, GGT, and CRP among Yemeni khat chewers.

METHODS

Study participants and collection of samples

The present study was conducted on 70 subjects who chewed khat daily in Sana'a, Yemen. After a full explanation of the objective of the study, each participant provided written informed consent and completed a questionnaire on socio-demographic data through interview. Participants were considered eligible if aged ≥ 18 years (through self-declaration) and free of obvious acute or chronic illnesses. Most khat chewers declared using khat for about 6 h daily. Blood samples were drawn via the antecubital vein into vials without heparin or EDTA, for biochemical determination of AFP, GGT and CRP. Following a 10-minute centrifugation, the serum samples obtained were kept at -20°C until analysis.

Ethics statement

The ethical approval for this study was obtained from the Ethics Committee (Al-Razi University) under approval number (01/FMHS/2004). All

procedures performed in this study comply with the ethical standards of the institution or the National Ethics Committee's Ethical Standards, the 1964 Helsinki Declaration, and its later amendments or comparable ethical standards [7].

Determination of CRP

Serum CRP levels were determined using a commercial latex-enhanced turbidimetric immunological assay kit (Agappe, India). The assay method has linearity up to 200 mg/L.

Determination of α -fetoprotein

The serum concentrations of α -fetoprotein were quantified using ELISA kits from Snibe, China, with a reference range of 0 – 5.8 IU/mL.

Determination of GGT

The serum quantitative determination of γ -glutamyltransferase (GGT) was done using the Cobas 501 systems (Roche, Switzerland). This is a kinetic (Rate-A) reaction, with detection limited to (8 - 50) U/L.

Statistical analysis

Version 7.2 of the Epi-Info program was used for the data analysis. The frequency distribution of each variable was determined using univariate analysis. Bivariate analysis was employed to identify independent determinants of higher GGT levels among khat chewers. The variables linked to higher GGT levels were chosen using the odds ratio (OR) at a 95 % confidence interval.

RESULTS

Socio-demographics of participants

A total of seventy (70) participants were included in this study. Majority of the participants were males (81 %) and more than half (64 %) of them were aged thirty or more. A total of 60 participants (86 %) were from urban areas, while 10 (14 %) were from rural areas. Two (2) of the 70 participants (3 %) had primary school education, 30 participants (43 %) were educated up to secondary school level, while 21 subjects (30 %) had education up to the tertiary school level. While most participants (77 %) chewed khat for over 6 h daily, with a mean duration of 7.5 h per session, twenty-nine percent (29 %) of the participants smoked. These demographic data are shown in Table 1.

Table 1: Demographic and behavioral characteristics of participants

Characteristic	Number	Percentage (%)
Sex		
Male	57	81
Female	13	19
Age		
<20 years	8	11
20-30 years	20	29
≥30 years	42	60
Residence		
Rural	10	14
Urban	60	86
Educational level		
Illiterate	9	13
Can read and write	8	11
Primary	2	3
Secondary	30	43
Tertiary and above	21	30
Duration of khat chewing session (hours)		
<6 hours	16	23
>6 hours	54	77
Smoking		
Yes	20	29
No	50	71

Table 2: Serum AFP, GGT and CRP levels among participants

Test	Normal		Abnormal (Elevated)	
	N	%	N	%
alpha-fetoprotein (AFP)	67	96	3	4
Gamma-Glutamyl Transferase (GGT)	57	81	13	19
C-Reactive Protein	70	100	0	0

Percentage of elevated AFP, GGT and CRP levels among Participants

Serum AFP was elevated in 3 (4 %) of the 70 participants in this study, while serum GGT was elevated in 13 (19 %) of the participants. However, serum CRP level was normal in all participants. These results are presented in Table 2.

Bivariate analysis

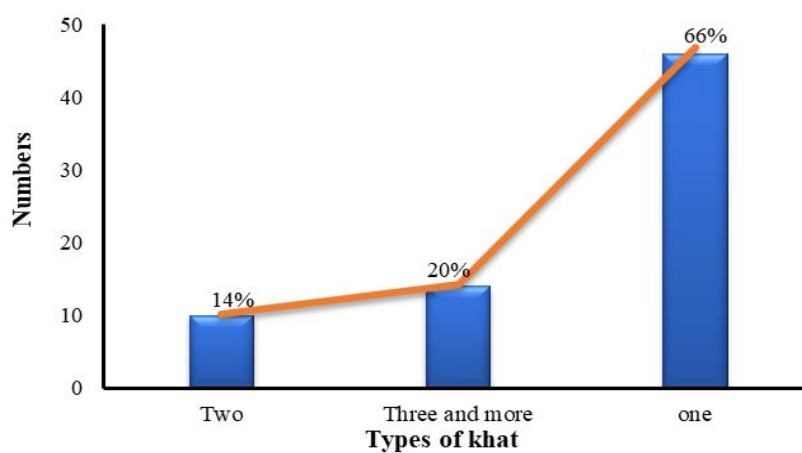
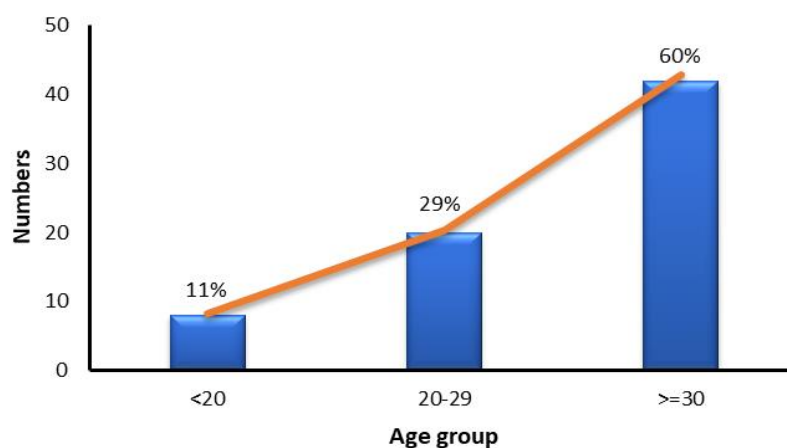
Bivariate analysis was used to identify factors independently associated with elevated GGT levels in khat chewers. The results obtained indicate that there was no significant correlation between increased risk of elevated GGT and sex, age, residential area, daily duration of khat chewing, khat washing, or smoking (Table 3). Majority of the participants (66 %) usually chewed one type of khat, 20 % of the subjects chewed three or more khat types, while 14 % of the participants chewed two types of khat. These data are shown in Figure 1. Figure 2 shows the distribution of subjects according to age groups. Half of the participants (50 %) were aged 30 years or more, 29 % of the subjects were in the age group of 20 - 29 years, whereas 11 % of

participants were below 20 years of age. Analysis of the educational level showed that, whereas 3 % of the participants had only primary education, 43 % had secondary school education, 30 % of participants were educated up to the tertiary level, while 13 % of the subjects were illiterate. Conversely, only 11 % of the subjects could read and write. These results are shown in Figure 3.

This study was aimed at determining the impact of *C. edulis* on liver alpha-fetoprotein, C-reactive protein, and γ-glutamyl transferase in khat chewers. Khat is similar in composition to amphetamine and studies have shown a strong link between excessive amphetamine consumption, particularly methylenedioxymethamphetamine (MDMA: "ecstasy") and specific types of clinically noticeable liver injury [8]. Moreover, biochemical and histopathological data from animal studies have indicated that *C. edulis* is toxic [9]. Findings from previous studies demonstrate that all consumption levels of *C. edulis* leaves investigated resulted in significant increases in plasma levels of AST, ALT and ALP throughout the treatment [9].

Table 3: Bivariate examination of variables related to elevated GGT among khat chewers in Sana'a, Yemen

Variable	GGT		OR (95% CI)
	Elevated N (%)	Normal N (%)	
Sex			
Male	11(19%)	9(81%)	0.76 (0.14-3.9)
Female	2(85%)	11(15%)	
Age group			
<30 years	1(4%)	27(96%)	0.09 (0.01-0.76)
≥30 years	12(29%)	30(71%)	
Residence			
Rural	2(20%)	8(80%)	1.1 (0.2-5.9)
Urban	11(18%)	49(82%)	
Hours of khat chewing per day			
<6 hours	3(19%)	13(81%)	1 (0.2-4.2)
≥6 hours	10(19%)	44(81%)	
Washing Khat			
No	3(15%)	17(85%)	1.4 (0.3-5.7)
Yes	10(20%)	40(80%)	
Smoking			
Yes	8 (40%)	12(60%)	0.1 (0.04-0.6)
No	5 (10%)	45(90%)	

**Figure 1:** Distribution of participants according to the type of khat**Figure 2:** Distribution of participants by age group

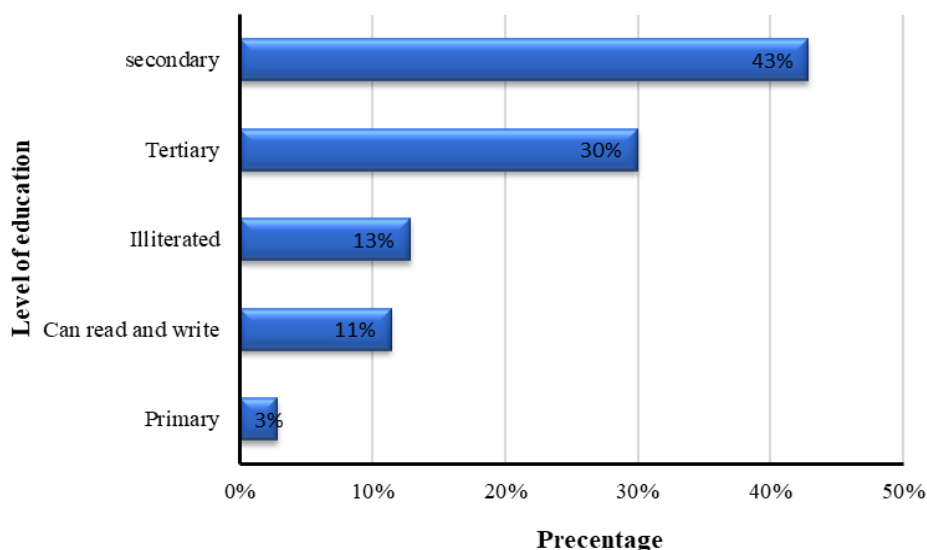


Figure 3: Distribution of participants by level of education

DISCUSSION

It is well known that CRP is elevated in patients with a history of drug abuse and previous results reveal that CRP levels were considerably higher in amphetamine users [13]. Other findings indicate that CRP levels are higher in opiate-dependent patients, both independently and after controlling for age. Moreover, it has been suggested that opiate addiction-induced elevations in CRP and immunological activation may be responsible for accentuated age-related multi-system coronary and chronic atherosclerosis, both of which have been well documented in opiate dependency [14,15]. Thus, in the present study, CRP levels were determined in khat chewers. However, the results showed no elevated CRP levels in the khat chewers investigated.

Furthermore, a study conducted in Baghdad revealed significant differences in liver function indices (GGT, AST, ALT, and ALP) between amphetamine addicts/abusers and controls [16]. Several studies have also reported liver injury in amphetamine abusers [17,18]. However, the present descriptive study showed no significant increases in serum levels of AFP, CRP, and GGT in subjects who chewed khat for durations ranging from 6 to 10 h daily.

CONCLUSION

The results of this investigation demonstrate that catechin has no significant effect on liver proteins such as AFP, GGT, and CRP in people who chew khat for a long time. However, there is a need to validate this finding using additional

randomized controlled research with a larger sample size.

DECLARATIONS

Acknowledgment/Funding

The authors extend their appreciation to Taif University, Saudi Arabia, for supporting this work through project number TU-DSPP-2024-02. The research was funded by Taif University, Saudi Arabia, Project No. (TU-DSPP-2024-02).

Ethics approval

Ethical approval for this study was obtained from the Ethics Committee (Al-Razi University) under approval number (01/FMHS/2004).

Use of Artificial intelligence/Large language models

We also declare that we did not use Generative artificial intelligence (AI) and AI-assisted technologies in writing the manuscript.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Conflict of interest

No conflict of interest is associated with this work.

Contribution of authors

We declare that this work was done by the author(s) named in this article, and all liabilities pertaining to claims relating to the content of this article will be borne by the authors. Alariqi Reem made a substantial contribution to the concept or design of the article or the acquisition. Alariqi Reem drafted the article or revised it critically for important intellectual content. Rachad Alnamer and Al-Awar Mohammed Sadeq approved the version to be published. Mazen Almeahmadi, Aisha Mane'a and Maram Hazza analysed or interpreted the data for the article.

REFERENCES

1. Al Shubbar MD. *Understanding Khat: Its sociocultural and health implications in Saudi Arabia*. *Cureus* 2024; 16(3): e56657. DOI: 10.7759/cureus.56657
2. Al-Motarreb A, AL-Suwaidi J. *Khat chewing and cardiovascular disease*. *Heart Views* 2022; 23(2): 103–107
3. Soares J, Costa VM, Bastos MDL, Carvalho F, Capela JP. *An updated review on synthetic cathinones*. *Arch Toxicol* 2021; 95(9): 2895-2940. DOI: 10.1007/s00204-021-03097-1.
4. Abdelwahab S, Sidahmed H, Alfaifi H, Albadawi D, Alzahrani A. *Mechanistic insight into the cholinergic, muscarinic and antagonistic effects of Khat (Catha edulis) on native nicotinic acetylcholine receptors*. *Trop J Pharm Res* 2024; 23(12): 1991-1999
5. Andrade RJ, Aithal GP, Boer YSD, Liberal R, Gerbes A, Regev A, Piccoli BTB, Schramm C, Kleiner DE, Martin ED. *Nomenclature, diagnosis and management of drug-induced autoimmune-like hepatitis (DI-ALH): An expert opinion meeting report*. *J Hepatol* 2023; 79(3): 853-866. DOI: 10.1016/j.jhep.2023.05.012.
6. Abdelwahab SI, Taha MME, Moni SSS, Alnajai MM, Jerah AA, Farasani A, Abdullah SM, Aljahdali LA, Oraibi O, Alfaifi HA. *Impact of fresh khat extract on proinflammatory cytokines and hepatic and renal responses*. *Med Sci Monit* 2024; 30: e946108. DOI: 10.12659/MSM.946108.
7. World Medical Association. *World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects*. *JAMA* 2013; 310(20): 2191-2194. DOI: 10.1001/jama.2013.281053.
8. Alharbi S, Aldubayan MA, Alhowail AH, Almogbel YS, Emara AM. *Co-abuse of amphetamine and alcohol harms the kidneys and liver*. *Sci Rep* 2024; 14(1): 23400. DOI: 10.1038/s41598-024-23400.
9. Al-Habori M, Al-Aghbari A, Al-Mamary M, Baker M. *Toxicological evaluation of Catha edulis leaves: a long-term feeding experiment in animals*. *J Ethnopharmacol* 2002; 83(3): 209-217. DOI: 10.1016/S0378-8741(02)00231-5.
10. Riyaz S, Imran M, Gleeson D, Karajeh MA. *Khat (Catha edulis) as a possible cause of autoimmune hepatitis*. *World J Hepatol* 2014; 6(3): 150-154.
11. Roelandt P, George C, d'Heygere F, Aerts R, Monbaliu D, Laleman W, Cassiman D, Verslype C, Steenbergen WV, Pirenne J. *Acute liver failure secondary to khat (Catha edulis)-induced necrotic hepatitis requiring liver transplantation: case report*. *Transplant Proc* 2011; 43(9): 3493-3495. DOI: 10.1016/S0378-8741(02)00231-5.
12. Yildiz H, Komuta M, Monsalve C, Starkel P, Lefebvre C. *To chew or not to chew: that's the question*. *Acta Clin Belg* 2016; 71(3): 187-189. DOI: 10.1080/17843286.2016.1163577.
13. Al-Rafiah A, Magadmi R, Al-Kaabi A, Alsomali N. *Parkinson's disease-related biomarkers that may appear in amphetamine abusers*. *Biomed Res Int* 2021; 2021: 3081891. DOI: 10.1155/2021/3081891.
14. Tanrikulu AB, Kaya H, Çatak Z. *Elevated C-reactive protein/albumin ratio in patients with methamphetamine use disorder*. *Int J Psychiatry Clin Pract* 2023; 27(4): 351-358. DOI: 10.1080/13651501.2023.2190921.
15. Reece AS. *High-sensitivity CRP in opiate addiction: relative and age-dependent elevations*. *Cardiovasc Toxicol* 2012; 12(2):149-157. DOI: 10.1007/s12012-012-9167-3.
16. Mohammed NS, Ali ZQ, Mohamed AS, Sazan Abdulwahab Mirza SA. *The impact of methamphetamine on liver injury in Iraqi male addicts*. *Toxicol Rep* 2024; 13: 101806.
17. Roy DN, Goswami R. *Drugs of abuse and addiction: A slippery slope toward liver injury*. *Chem Biol Interact* 2016; 5: 255: 92-105. DOI: 10.1016/j.cbi.2015.12.001.
18. Silva DDD, Carmo H, Lynch A, Silva E. *An insight into the hepatocellular death induced by amphetamines, individually and in combination: the involvement of necrosis and apoptosis*. *Arch Toxicol* 2013; 87(12): 2165-2185. DOI: 10.1007/s00204-013-1078-4.