TPM Vol. 32, No. S7, 2025
ISSN: 1972-6325
https://www.tpmap.org/

ASSOCIATION BETWEEN KHAT CHEWING AND CORONARY ARTERY DISEASE

ABDULRAHMAN S. ALRADAEI
FACULTY OF MEDICINE, UNIVERSITY OF CYBERJAYA, MALAYSIA. EMAIL: dr.aboodsaad111@gmail.com

HESHAM A. ALFAKIH
LECTURER OF CARDIOLOGY DEPARTMENT, FACULTY OF MEDICINE, SANA'A UNIVERSITY, YEMEN.
EMAIL: Hisham900090@gmail.com

MUHAMED T. OSMAN
ASSOCIATE PROFESSOR, FACULTY OF MEDICINE, UNIVERSITY OF CYBERJAYA (UOC), PERSIARAN BESTARI, CYBER 11, 63000 CYBERJAYA, SELANGOR DARUL EHSAN, MALAYSIA. EMAIL: dr.osman@cyberjaya.edu.my

ABSTRACT
Cathinone, cathine, and norephedrine are the main active ingredients in khat. The main active ingredient in khat leaves, catehinone, shares structural and functional characteristics with amphetamine. Khat use is a risk factor for the start of AMI on its own. Khat users were typically older men, more likely to present late, had higher heart rates, had a higher Killip class when admitted, had a higher risk of ST-segment-elevation myocardial infarction, and were less likely to have a history of coronary artery disease or cardiovascular risk factors. Khat users were at higher risk for ventricular arrhythmia, stroke, cardiogenic shock, recurrent myocardial ischaemia, and mortality.
Keywords: Khat Chewing, Coronary Artery Disease, Yemen

INTRODUCTION

Known for its sympathomimetic and euphoric effects, khat, also known as Catha edulis, is an indigenous plant that grows in Yemen, Ethiopia, and East Africa. Individuals frequently chew it for its euphoric benefits, which takes place due to its stimulant amphetamine-like properties linked to Cathinone, a phenylethylamine found in fresh leaves. Although it is generally regarded as a safe medicine, it is associated with many cardiovascular diseases. [1]

Cathinone and cathine stand as the primary plant components. These molecules exhibit a structural relation to amphetamine, noradrenaline, as well as ecstasy (3,4-methylenedioxymethamphetamine). [2]

Khat use remains associated with heart rate and blood pressure increase, greater risks for cardiovascular and cerebrovascular diseases, as well as elevated mortality among individuals developing acute coronary syndrome (ACS). Additionally, chewing khat has a dose-response relationship and is a risk factor for myocardial infarction on its own. [3]

Abuse of amphetamines has been shown to have a substantial correlation with AMI; in Texas, it accounts for 0.2% of AMIs linked to amphetamine use. In recent years, khat chewing has evolved, with many individuals extending their chewing sessions at the evening, sometimes until midnight, which is linked to an altered circadian rhythm of AMI presentation. [4]

SEARCH METHODOLOGY

We produced this review article following a meticulous investigation as well as evaluation of the diverse studies performed on the relationship between khat chewing and coronary artery disease. The main database utilized for the search is PubMed, supplemented by Scopus, Google Scholar, as well as research acquired from other databases and sources. The timeframe for the publishing of articles eligible for review is the last 14 years. Articles that failed to provide a definitive and exact conclusion, as well as those with questionable findings, were eliminated.

Khat

In some regions, the evergreen plant known as khat (Catha edulis) is cultivated. Chewing on its fresh green leaves and buds for many hours each day results in a psychostimulant effect that boosts alertness, decreases weariness, and promotes productivity. Khat leaves and buds include methcathinone, cathine, and cathinone, which are known to have an effect and structure similar to amphetamines. [5]

Khat chewing represents a socially ingrained practice, governing the Yemeni population lives. Their food, sleep schedule, job leave, familial responsibilities, financial constraints, interpersonal interactions, as well as societal engagements remain correlated with the khat problem. [6]

Khat chewing has incapacitated societal productivity while producing several social, economic, as well as health-related issues. It exhibits a significant impact on the cardiovascular system. Khat consumption represents a primary obstacle facing Yemen modernization. [6]

Cultivation, Harvesting, and Consumption

Khat is cultivated throughout the central and western highland regions of Yemen, where the majority of the country's population resides. In this region, the most well-known varieties of Yemeni khat are commonly cultivated. The coastal and desert regions are unsuitable for cultivating khat due to climatic conditions. Khat cultivation in Ethiopia predominantly takes place at middle altitudes in almost all highlands, with elevations ranging from 1500 to 2100 meters, and the area allocated to khat cultivation has significantly expanded. Khat cultivation is also common in Kenya, particularly in the North Eastern Province. [7]

Khat harvesting typically takes place in the early morning, where khat pickers, often producers and vendors, pack the twigs and the fragile, reddish-green leaves into little or big bundles after cutting them together. On the same day, these bundles are then sent to the market to be sold to customers.

Delaying the sale until the next day, however, results in reduced quality and price, as the psychoactive cathinone is converted to the less active cathine, which accounts for khat users' preference for fresh leaves and twigs. [8]

Khat sessions typically begin between 1 and 2 PM daily, when men assemble in a designated area known as Majlis or Diwan and initiate the process of selecting and chewing fresh khat leaves and twigs on one side to facilitate juice absorption via the oral mucosa, or through the digestive system after swallowing the leaves, which have been thoroughly chewed, with fresh leaves and twigs periodically added to achieve a euphoric state. On average, khat consumers typically consumed between 200 and 500 grams of khat per day. [9]

Chemical Composition of Khat:

Cathinone, namely (S)-2-amino-l-phenyl-l-propanone, and cathine (norpseudoephedrine) are the main active ingredients in khat. [10] The khat plant only contains the left-handed cathinone enantiomer. Consequently, S- (−)-cathinone and S- (+)-amphetamine have the same absolute configuration. The juvenile development of plants is the main source of cathinone. During maturity, catehinone is changed into (-)-norephedrine and cathine [(+)-norpseudoephedrine]. The ratio of (+)-norpseudoephedrine to (−)-norephedrine in the leaves is 4:1.11. The leaves of khat contain a number of phenylalkylamine alkaloids, including merucathine, pseudomerucathine, and meucathinone. These substances appear to have less influence on khat's invigorating effects. [10]

The chemical composition and biological impact of cathinone are analogous to those of amphetamine, and it is primarily responsible for the pharmacological consequences of khat consumption. Studies have shown that khat extract and cathinone interfere with the production of ribonucleic acid (RNA), deoxyribonucleic acid (DNA), and proteins in dividing cells, leading to reduced cell growth and potentially impairing spermatogenesis. Cathine has also been linked to the moderate central nervous system stimulatory effects that are characteristic of khat consumption. Additionally, the psychoactive monoamine alkaloid cathinone, namely (S)-2-amino-1-phenyl-1-propanone, which induces euphoric effects, is present in immature khat shoots and fresh leaves. [11]

Alkaloids, flavonoids, sterols, and more than 40 other alkaloids, glycosides, tannins, and terpenoids are among the many chemical substances found in khat leaves. Chemically speaking, the leaves are high in calcium, iron, niacin, and vitamin C. Khat has a psychoactive substance called cathinone that can activate the central nervous system. Khat is a non-narcotic, physiologically active drug that can become addictive and have serious negative effects on the central nervous system that are similar to those of amphetamine. [11]

Khat Phytochemistry

In 1930, Wolves discovered norpseudoephedrine, also known as cathine, in the leaves of khat, and this alkaloid was considered the primary active compound of khat until the 1960s. Following Brücke's statement in 1941 that the quantity of this alkaloid was insufficient to explain the symptoms experienced by khat users, further investigation of the plant's chemistry was undertaken, resulting in the first isolation of cathinone. [9, 12] The stimulating effects of this 'natural amphetamine' are mainly caused by cathinone, one of the most prevalent alkaloids found in fresh leaves of Catha edulis. After harvesting, catehinone decomposes into cathine and norephedrine due to its relative instability. The drying of the leaves increases the process's efficacy. Only recently harvested leaves are completely effective. Fresh khat typically contains between 36 and 343 milligrams of cathinone, as well as between 83 and 120 milligrams of cathine and between 8 and 47 milligrams of norephedrine per 100 grams of leaves. [13]

These substances have structural and physiological similarities to noradrenaline and amphetamine, suggesting that they can affect the central and peripheral nervous systems. [10]

Phenylalkylamine alkaloids including phenylpentenylamines, merucathinone, pseudomerucathine, and merucathine, as well as cathedulin alkaloids, have been found in khat leaves, albeit at relatively low concentrations. The chemical composition of khat leaves is influenced by environmental factors, climatic conditions, and the methods of cultivation and harvesting used. Alkaloids, terpenoids, glycosides, and other unique chemical compounds are found in fresh khat leaves, along with certain amino acids like tryptophan, glutamic acid, and threonine, a number of vitamins like ascorbic acid, thiamine, and riboflavin, necessary elements like iron, manganese, and zinc, and hazardous metals like lead and cadmium. [11]

Khat Legality

While cathine was designated as a Schedule IV drug in 1988, cathinone has been a Schedule I substance since 1993 under the Controlled Substances Act. The plant itself is exempt from controlled substances lists, leading to difficulties in determining its legal status, which can vary significantly between different countries. The khat plant can be categorized under Schedule I when its cathinone content is detectable. [13]

Khat is progressively being categorised as a restricted drug by nations all over the world. Many nations in Europe, Asia, and North America have laws governing khat. The practice is still legal in the majority of East African nations. Coffee has been overtaken as Ethiopia's most important export. In the last twenty years, the area given over to khat cultivation has risen by 160%, resulting in the annual production of hundreds of millions of kilograms of khat. [13]

Khat Toxicodynamic

Khat's primary psychoactive and sympathomimetic effects are attributed to cathinone and cathine. The primary chemical that causes khat's early effects on the central nervous system (CNS) is catehinone. A beta-keto derivative of amphetamine, catehinone has stimulant properties similar to those of amphetamine in the central nervous system. [14]

Amphetamine derivatives are classified as 'β-phenylethylamines', a group of substances that share structural similarities with the neurotransmitters noradrenaline and dopamine, which are both catecholamine substances. The sympathomimetic effects of amphetamine derivatives are explained by their structural resemblance to noradrenaline. Furthermore, amphetamine has ephedrine-like characteristics, and it shares a metabolite with cathinone, norephedrine. Monoamine reuptake transporters are competitively inhibited by amphetamine derivatives. Additionally, amphetamine works as a monoamine releaser on the central nervous system, affecting serotonin, noradrenaline, and dopamine while also causing the peripheral sympathetic nervous system to release adrenaline. [15]

Monoamine oxidase (MAO) inhibition and monoamine reuptake inhibition are linked to this pathway, which eventually raises synaptic monoamine levels. In fact, cathinone has sympathomimetic and CNS stimulant qualities that are comparable to those of other synthetic and naturally occurring sympathomimetic and CNS stimulant compounds like cocaine and amphetamines. [16]

Early research revealed that cathinone can trigger the release of dopamine in the CNS, similar to amphetamine, and also limit the activity of MAO, particularly MAO-B, which in turn contributes to decreased dopamine breakdown and increased synaptic accumulation. [17] The stimulation of dopaminergic pathways in certain brain regions has been linked to the euphoric effects of khat. [18]

Prevalence of khat consumption

In societies like Djibouti, khat consumption is strongly linked to men, which ultimately holds back the country's economic and social progress. Regular khat users have been found to experience issues related to oral hygiene, including dental caries. [19] Notably, approximately 90% of its population regularly consume khat. [20] Khat use is widespread in Ethiopia, particularly among university students at a rate of 23.22%. The issue has been of concern due to factors like family oral habits, alcohol consumption, and social influence from peers. [21] The lifetime prevalence of chewing khat was observed to be 33.2% in the Jazan area of Saudi Arabia. [20] Kenya has a very high rate of khat usage, mostly due to the crop's legal tolerance, which encourages its export and boosts the country's economy. [22]

The high incidence of khat use can be linked to variables like place of residence and gender. [23] In locations like Kisenyi, Uganda, factors including family history of khat use and the availability of the substance are found to influence the prevalence of khat use. The social norms and cultural diversity in areas where khat is used significantly influence its prevalence. [24]

Khat consumption in Kenya is widespread, reportedly because it enables users to stay active, stimulates their brain function, and alleviates stress. Because of the city's long history of khat farming and use, khat has been a long-standing habit in Harar, and its effects are especially apparent when compared to other parts of Ethiopia. [25]

In eastern Africa, including Ethiopia, the prevalence of khat abuse is becoming a major public health concern, with a notable lifetime rate of khat chewing, particularly among women, who are associated with certain sociodemographic risk factors. [26]

Systemic Effects of Catha edulis (Khat) on Humans

Long-term khat use may have negative consequences on the central nervous system, systemic blood pressure, urinary system, and mental health, according to research findings. Cathinone, the psychostimulant component of khat, is mostly responsible for causing addiction. Prolonged use of khat can result in cognitive and mental problems, including headaches, insomnia, difficulty concentrating, migraines, fine tremors, and coordination issues. [27]

Research has demonstrated that khat chewing can lead to anorexia and insomnia, resulting in impaired work performance the following day. Physical and psychological dependency, euphoria, schizophrenia, hallucinations, moderate sadness, increased alertness, dizziness, anxiety, and psychosis are just a few of the documented psychological consequences of khat. Manic psychosis and paranoid or schizophrenia spectrum illness were the two primary types of psychosis that were mostly caused by chronic khat usage. [28] Khat-induced psychosis usually does not necessitate the use of antipsychotics, and instead full recovery typically occurs following khat withdrawal. [28, 29]

High diastolic blood pressure is also a negative consequence of cathinone, resulting from peripheral vasoconstriction caused by heightened sympathetic nerve activity. Long-term use of khat can lead to chronic elevated blood pressure. Consequently, this population has a significantly higher rate of acute coronary vasospasm and myocardial infarction. [27]

In comparison to a control group, khat abusers have urological problems, including a lower maximal urine flow rate. This might be because cathinone interacts with α1-adrenergic receptors in the neck of the bladder to produce sympathomimetic effects. Regular khat users were shown to have a higher risk of mouth cancer, according to a study findings. [30]

It is proposed that the habit of chewing khat may be a significant contributing factor in individuals with squamous cell carcinoma. A substantial body of evidence in medical literature confirms the link between khat chewing and progressive liver damage. Prolonged consumption of khat has been shown to lead to hepatitis, fibrosis, and cirrhosis. [13]

- **Khat Leaves' Constituent**

The primary alkaloids found in khat leaves include cathinone, pseudoephedrine (also known as cathine), and norephedrine. The highest levels of these amines were found in the young leaves, which explains why they were selected from khat by users seeking their potent effects. [31]

Cathinone represents an amphetamine component, inducing endogenous catecholamines' release from both peripheral as well as central neurons. Cathinone is a naturally produced amphetamine. [32]

- **Cathinone effect**

Cathinone is the most potent constituent of khat leaves, functioning as a central nervous system stimulant. Cathinone works in a similar way to amphetamine by indirectly stimulating sympathetic nerve terminals to release catecholamines. This action on blood vessels is localized and not mediated by the release of noradrenaline or the activation of α-adrenoceptors. [33]

This is likely mediated by the newly discovered trace amine-associated receptors. Cathinone exhibits both direct as well as indirect effects on blood vessels, inducing dose-dependent vasoconstriction within aortic ring preparations, demonstrating greater potency in comparison to noradrenaline at higher dosages. [34]

Factors contributing to the use of khat

In Islam, differing interpretations exist regarding khat's permissibility, as a substantial quantity view it as forbidden, whereas others define it as merely discouraged or even permissible. In contrast to the overall religious ban on the grounds of its effects on physical and mental well-being, a substantial number of khat users do not perceive its consumption as being religiously forbidden. The evidence is particularly apparent in countries like Yemen and Somalia. In Saudi Arabia, the Muftis, typically regarded as scholars, are in complete agreement that khat is banned. A portion of khat consumers in Saudi Arabia may hold varying viewpoints. [35]

Khat's affordability and relatively low price are significant reasons for its widespread use, particularly among individuals with lower incomes who view it as a budget-friendly form of entertainment. The open sale of khat leaves in Yemen's marketplaces and stores has led to the commercialisation of khat and made its usage more socially accepted, and because Yemen shares a border with Saudi Arabia, khat is likely to be readily available in southern Saudi Arabia compared to other areas in the country. [35]

Acute effects of khat use

The onset of khat's effects typically occurs within a 30 to 60 minute period after chewing. A khat chewing session usually lasts for 3 to 6 hours, with users consuming 100 to 500 grams of leaves throughout this time frame. [36]

Extracting the desired effects from khat leaves involves swallowing the juices, however, this process is notably time-consuming due to cathinone concentrations averaging approximately 1 mg/g/leaf. As a result, regular users have reported experiencing physical dependency symptoms including tolerance and withdrawal, however overdoses from khat have not been reported. [36]

The user often displays "mirquaan" during the first phase, which is defined by emotions of joy, enthusiasm, verbosity, and a quick flow of thoughts. After this, users have a steady comedown that leads to feelings of restlessness, anger, and depression before entering a more secluded phase.

Following consumption of khat, a typical increase in breathing rate is frequently noted along with excessive body heat and enlarged pupils. [36]

Chewing khat has been associated with increased systolic and diastolic blood pressure and an increase in heart rate. [36]

Research shows that changes in plasma cathinone levels during and after chewing are strongly associated with peak effects on heart rate and blood pressure, suggesting that cathinone is the main chemical responsible for these cardiovascular effects.

Studies conducted among non-chronic khat consumers have found that blood pressure and heart rate take a considerable amount of time to normalise after chewing, whereas this was not evident in chronic users, suggesting that they may develop a tolerance to khat's sympathomimetic effect with prolonged use. Khat users have also shown blunted responses to stress in terms of blood pressure. [36]

Khat effect on the cardiovascular system

It has been found khat chewing causes hypertension.[37] Chewing khat leads to an elevated heart rate. Wabe et al. attributed this finding to the vasoconstrictor effects of cathinone, a consequence that may persist in habitual khat users. [38] Furthermore, a study [37] found that cathinone exhibits positive inotropic and chronotropic effects on isolated atria. Chewing khat can lead to a higher likelihood of experiencing an acute myocardial infarction (AMI). The coronary vasospasm effect of khat was explained by its contribution to thrombus formation, which in turn results from catecholamine-mediated platelet aggregation. Coronary vasospasm occurs due to cathinone's amphetamine-like effects, which boost irritability and nervousness following khat use. This, combined with the elevated heart rate, heightens the heart muscle's oxygen demand and triggers catecholamine-induced platelet aggregation, ultimately leading to coronary vasospasm. [39]

Khat and Coronary Artery Disease

Coronary artery disease has a higher rate of occurrence among people who use khat, as opposed to those who do not. A meta-analysis and thorough review of another study's findings suggested that using khat increases the likelihood of experiencing stroke, MI, and heart failure. The exact methods through which khat and cathinone impact the cardiovascular system are unclear; nonetheless, it is proposed that they could trigger a coronary artery spasm. [40] Research indicates that consuming khat can lead to narrowing of the coronary and aortic arteries, which in turn contributes to the formation of atherosclerosis. [41]

Khat use adversely affects the cardiovascular system. Tension, sleeplessness, anorexia, as well as reduced physical activity remain linked to khat chewing, thus adversely affecting the cardiovascular system. [41]

Khat enhances the tendency towards consuming more cigarettes throughout the session. Additionally, it is linked to heightened risks for passive smoking during "khat parties" as well as social interactions. These variables increase the risk of khat use resulting in the development of coronary artery disease, particularly AMI. In a case-control study, khat consumption was significantly higher among individuals in the AMI case group compared to controls, showing a dose-response correlation. Excessive khat users have a 39-fold increased risk of AMI. Research discovered that khat use is a separate, dose-dependent risk factor for myocardial infarction. [42]

Khat consumption leads to increased heart rate and hypertension throughout its duration, thereby disrupting the body's natural circadian rhythm in patients presenting with AMI. Increased oxygen demand, along with peripheral and coronary vasoconstriction, can also trigger AMI. The incidence of AMI within the khat effective time frame (2 PM to midnight) was 59% for individuals who chewed khat, as opposed to 34% for non-khat chewers presenting during the same period. [43]

Amphetamine usage has been shown to induce AMI. Additionally, cathinone is recognized as a natural amphetamine. Consequently, the misuse of both could result in coronary vasoconstriction, leading to AMI. A laboratory investigation was conducted utilizing the isolated The Langendorff heart preparation, obtained from guinea pigs, showed that cathinone caused coronary vasoconstriction and resulted in negative inotropic effects. [44]

Separate laboratory research was conducted on pigs' coronary arteries. Cathinone caused a narrowing of the blood vessels within the left anterior descending coronary artery of a pig. The effect was not caused by an indirect sympathomimetic pathway involving α1-adrenoceptors and the endothelium. Instead, cathinone, the primary component of khat leaves, causes direct vasoconstriction in the coronary arteries. Studies employing clinical and angiographic techniques have identified coronary vasospasm as the main cause of AMI, and factors influencing the increased frequency of heart attacks among individuals who chew khat. [45]

Individuals who use khat and subsequently develop Acute Coronary Syndromes typically experience more severe outcomes. Individuals who use khat are at a higher risk of death, suffer from recurring heart attacks, heart failure, abnormal heart rhythms, and stroke compared to those who do not use khat. The effectiveness of aspirin and thrombolytic therapy in AMI was reduced among individuals who chew khat, as demonstrated by two separate studies (unpublished data). Additional research is needed to confirm the effects of khat chewing on blood clotting and its potential to dissolve clots. [46]

Cathinone causes substantial narrowing of coronary blood vessels along with a considerable weakening effect on heart muscle contraction, suggesting that coronary constriction contributes to the onset of AMI. Amphetamine shows vasoconstrictive properties through the stimulation of sympathetic neurons to release noradrenaline, and it may also play a role in the onset of AMI. [47]

Because catecholamines induce platelets to clump together, they temporarily block the coronary arteries. This blockage is made worse by catecholamines increasing the oxygen demand on the heart. Abuse of amphetamines increases the risk of AMI and can also result in cerebral haemorrhage, pulmonary heart disease, chronic cardiomyopathy, and necrotising vasculitis. The development of congenital cardiac disease is linked to catechinone. [48]

In Yemen, Al-Motarreb et al. [49] carried out hospital-based case-control research with 100 patients who experienced AMI and 100 age and sex-matched control subjects. Acute myocardial infarction patients were much more likely to consume khat; heavy users were 39 times more likely to experience an AMI.

CONCLUSION:

khat use poses significant cardiovascular risks, particularly in older male individuals, who tend to present with more severe symptoms and complications. The stimulant properties of cathinone, along with the higher likelihood of developing AMI, ventricular arrhythmia, stroke, and other severe outcomes, underscore the need for heightened awareness and management of khat-related health risks. The absence of a history of traditional cardiovascular risk factors in many users highlights the unique dangers associated with khat consumption, emphasizing the importance of further research and targeted interventions to mitigate these risks.

Highlights:

1- **Active Ingredients in Khat**: The main active ingredients in khat are cathinone, cathine, and norephedrine, with cathinone being structurally and functionally similar to amphetamine.

2- **Increased Risk for AMI and Complications**: Khat use is a significant risk factor for the onset of acute myocardial infarction (AMI) and is associated with higher risks of ventricular arrhythmia, stroke, cardiogenic shock, and mortality.

3- **Demographics and Clinical Presentation**: Khat users, typically older men, present later for medical treatment, have higher heart rates and Killip class upon admission, and are more likely to experience ST-segment-elevation myocardial infarction despite having fewer coronary artery disease risk factors.

REFERENCE:

Jayed D, Al-Huthi MA, Al-Zandani A, Al-Shuki S, Al-Dholae M, Salah MK. Khat Chewing Induce Transient Elevation of Blood Pressure: By Using 24-Hour Ambulatory Blood Pressure Monitoring, in Yemen Republic. *Open Access J*. 2023;10(6):1-12.

2. Mega TA, Dabe NE. Khat (Catha Edulis) as a risk factor for cardiovascular disorders: systematic review and meta-analysis. *Open J Cardiovasc Surg*. 2017;11:146.

3. Alsanosy R, Mahfouz MS, Arishi AM, et al. Risk of acute coronary syndrome and relationship with the use of khat and tobacco products in the Jazan region, Saudi Arabia: A prospective case-control study. *Tob Induc Dis* 2024;22(3):1-14.

4. Akasaki Y, Ohishi M. Cerebrovascular and cardiovascular diseases caused by drugs of abuse. *Hyperten Res*. 2020;43(25):363-371.

5. Alshoabi SA, Hamid AM, Gameraddin MB, et al. Risks of khat chewing on the cardiovascular, nervous, gastrointestinal, and genitourinary systems: A narrative review. *J Family Med Prim Care*. Jan 2022;11(1):32-36. doi:10.4103/jfmpc.jfmpc_1254_21

6. Gudata ZG. Khat Consumption and Household Economies. *Handbook of Substance Misuse and Addictions: From Biology to Public Health*. Springer; 2022:1717-1737.

7. Cochrane L, O'Regan D. Legal harvest and illegal trade: Trends, challenges, and options in khat production in Ethiopia. *Int J Drug Policy*. Apr 2016;30:27-34. doi:10.1016/j.drugpo.2016.02.009

8. Yi R, Zhao S, Lam G, Sandhu J, Loganathan D, Morrissey B. Detection and elimination profile of cathinone in equine after norephedrine (Propalin®) administration using a validated liquid chromatography-tandem mass spectrometry method. *Anal Bioanal Chem*. Dec 2013;405(30):9711-22. doi:10.1007/s00216-013-7073-0

9. Badedi M, Darraj H, Hummadi A, et al. Khat Chewing and Type 2 Diabetes Mellitus. *Diabetes Metab Syndr Obes*. 2020;13:307-312. doi:10.2147/dmso.S240680

10. Pendl E, Pauritsch U, Kollroser M, Schmid MG. Determination of cathinone and cathine in Khat plant material by LC-MS/MS: Fresh vs. dried leaves. *Forensic Sci Int*. Feb 2021;319:15-30. doi:10.1016/j.forsciint.2020.110658

11. Al-Maweri SA, Warnakulasuriya S, Samran A. Khat (Catha edulis) and its oral health effects: An updated review. *J Investig Clin Dent*. Feb 2018;9(1):15-30. doi:10.1111/jicd.12288

12. Patel NB. Khat (Catha edulis Forsk) - And now there are three. *Brain Res Bull*. Feb 2019;145:92-96. doi:10.1016/j.brainresbull.2018.07.014

13. Orlien SMS, Sandven I, Berhe NB, et al. Khat chewing increases the risk for developing chronic liver disease: A hospital-based case-control study. *Hepatology*. Jul 2018;68(1):248-257. doi:10.1002/hep.29809

14. Ji Kwon N, Han E. A review of drug abuse in recently reported cases of driving under the influence of drugs (DUID) in Asia, USA, and Europe. *Forensic Sci Int*. Sep 2019;302:30-70. doi:10.1016/j.forsciint.2019.06.012

15. Cho S, Han E. Association of breastfeeding duration with dyslipidemia in women aged over 20 years: Korea National Health and Nutrition Examination Survey 2010-2014. *J Clin Lipidol*. Mar-Apr 2018;12(2):437-446. doi:10.1016/j.jacl.2018.01.009

16. Darroudi S, Saberi-Karimian M, Tayefi M, et al. Prevalence of combined and noncombined dyslipidemia in an Iranian population. *J Clin Lab Anal*. Oct 2018;32(8):15-25. doi:10.1002/jcla.22579

17. Khan MA, Hashim MJ, Mustafa H, et al. Global Epidemiology of Ischemic Heart Disease: Results from the Global Burden of Disease Study. *Cureus*. Jul 23 2020;12(7):30-55. doi:10.7759/cureus.9349
18. Soliman GA. Dietary Fiber, Atherosclerosis, and Cardiovascular Disease. *Nutrients*. May 23 2019;11(5)doi:10.3390/nu11051155
19. Bennani A, Mohamed S. Effect of Khat consumption on oral health: study carried out in Djibouti City. *Oral Health Dental Sci*. 2021;5(1):1-8.
20. Al-Maweri SA, Warnakulasuriya S, Samran A. Khat (Catha edulis) and its oral health effects: An updated review. *JICD*. 2018;9(1):15-30.
21. Gebrie A, Alebel A, Zegeye A, Tesfaye B. Prevalence and predictors of khat chewing among Ethiopian university students: A systematic review and meta-analysis. *PLoS One*. 2018;13(4):19-35. doi:10.1371/journal.pone.0195718
22. Ongeri L, Kirui F, Muniu E, et al. Khat use and psychotic symptoms in a rural Khat growing population in Kenya: a household survey. *BMC psychiatry*. 2019;19:1-10.
23. Ageely HM. Prevalence of Khat chewing in college and secondary (high) school students of Jazan region, Saudi Arabia. *HRJ*. 2009;6:1-7.
24. Sadeq-Ali A-M, AlAkhali M. Oral hygiene and periodontal health status among khat chewers. A case-control study. *J Clin Exp Dent*. 2017;9(5):15-30.
25. Gudata ZG, Cochrane L, Imana G. An assessment of khat consumption habit and its linkage to household economies and work culture: The case of Harar city. *PLoS One*. 2019;14(11):30-50. doi:10.1371/journal.pone.0224606
26. Yitayih Y, van Os J. Prevalence and determinants of chewing khat among women in Ethiopia: data from Ethiopian demographic and health survey 2016. *BMC Psychiatry*. Mar 4 2021;21(1):30-70. doi:10.1186/s12888-021-03136-y
27. Alzahrani MA, Alsahli MA, Alarifi FF, et al. A Narrative Review of the Toxic Effects on Male Reproductive and Sexual Health of Chewing the Psychostimulant, Catha edulis (Khat). *Med Sci Monit*. Apr 1 2023;29:55. doi:10.12659/msm.939455
28. Atnafie SA, Muluneh NY, Getahun KA, Woredekal AT, Kahaliw W. Depression, Anxiety, Stress, and Associated Factors among Khat Chewers in Amhara Region, Northwest Ethiopia. *Depress Res Treat*. 2020;2020:15-30. doi:10.1155/2020/7934892
29. Abou-Elhamd AS, Sumayli S, Steger K, Ali AKM, Zayed AE. Effect of Khat (Catha edulis Forsk) extract on testicular maturation in pre-pubertal and pubertal rats: A morphological and biochemical study. *Anat Histol Embryol*. Mar 2021;50(2):271-283. doi:10.1111/ahe.12626
30. Al-Maweri SA, Warnakulasuriya S, Samran A. Khat (Catha edulis) and its oral health effects: An updated review. *J Investig Clin Dent*. Feb 2018;9(1):-15-30. doi:10.1111/jicd.12288
31. Kiros T. Non-alkaloidal compounds from khat (Catha edulis) leaves. *Biol Med Natural Prod Chem*. 2020;9(2):81-89.
32. Al Shubbar MD. Understanding Khat: Its Sociocultural and Health Implications in Saudi Arabia. *Cureus*. 2024;16(3)
33. Poyatos L, Pérez-Mañá C, Hladun O, et al. Pharmacological effects of methylone and MDMA in humans. *Front pharmacol*. 2023;14(5):112.
34. Patel NB. Khat—a natural source of cathinone. *Synthetic Cathinones: Novel Addictive and Stimulatory Psychoactive Substances*. 2018:25-40.
35. Al Shubbar MD. Understanding Khat: Its Sociocultural and Health Implications in Saudi Arabia. *Cureus*. Mar 2024;16(3):657. doi:10.7759/cureus.56657
36. Ahmed S, Minami H, Rasmussen A. A systematic review of treatments for problematic khat use. *Subst Use Misuse*. 2020;55(4):590-601.
37. Geta TG, Woldeamanuel GG, Hailemariam BZ, Bedada DT. Association of Chronic Khat Chewing with Blood Pressure and Predictors of Hypertension Among Adults in Gurage Zone, Southern Ethiopia: A Comparative Study. *Integr Blood Press Control*. 2019;12:33-42. doi:10.2147/ibpc.S234671
38. Wabe NT. Chemistry, pharmacology, and toxicology of khat (catha edulis forsk): a review. *Addict Health*. Summer-Autumn 2011;3(3-4):137-49.
39. Ali WM, Zubaid M, Al-Motarreb A, et al. Association of khat chewing with increased risk of stroke and death in patients presenting with acute coronary syndrome. *Mayo Clin Proc*. Nov 2010;85(11):974-80. doi:10.4065/mcp.2010.0398
40. Costa VM, Grando LGR, Milandri E, et al. Natural sympathomimetic drugs: From pharmacology to toxicology. *Biomolecules*. 2022;12(12):1793.
41. Köprülü D, Ahmed SA, Hassan MS, et al. The severity and complexity of coronary artery disease in Khat user somali patients: a study in a PCI-Capable Tertiary Center in Somalia. *Res rep clin cardiol*. 2023;18:85-90.

42. Negesa Bulto L. *Cardiovascular risk behaviour and health literacy among patients with cardiovascular disease in Ethiopia*. 2021.
43. Hussen AA, Hussien FM, Yusuf N, Ahmed AY, Hassen HY. Case report: khat chewing and acute myocardial infarction in two young men without underlying risk factors. *Am J Trop Med Hyg*. 2021;105(44):890.
44. James S, Sintim E, Mtewa AG. Pesticides and disease causing contaminants in Khat and Khat products. *Cannabis and Khat in Drug Discovery*. Elsevier; 2024:647-660.
45. Al-Motarreb A, Al-Suwaidi J. Khat Chewing and Cardiovascular Disease. *Heart Views*. Apr-Jun 2022;23(2):103-107. doi:10.4103/heartviews.heartviews_88_21
46. Alhaithmi AS, Aman KS, Ben Mohamed Alsaadi M. Acute Coronary Syndrome with Normal or Near-Normal Coronary Angiography: Prevalence and Clinical Outcomes among Yemeni Patients. *Med J Cairo Univ*. 2021;89(7):1101-1110.
47. Bereda G. Catha Edulis Forsk and its adverse effects on health: current and ongoing factuality. *Ann Clin Med Case Rep*. 2021;7(13):1-10.
48. Navya P. *Platelet Aggregometric Study in Patients with Acute Coronary Syndrome*. Rajiv Gandhi University of Health Sciences (India); 2018.
49. Al-Motarreb A, Briancon S, Al-Jaber N, et al. Khat chewing is a risk factor for acute myocardial infarction: a case-control study. *Br J Clin Pharmacol*. May 2005;59(5):574-81. doi:10.1111/j.1365-2125.2005.02358.x