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The Possible Abuse of *Catha edulis* and its Associated Health and Socio-economic Impacts

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ABSTRACT

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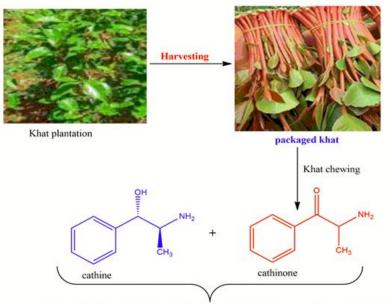
KEYWORDS

cessation strategies, cathinone, medical problems, pharmacology, khat chewing

economic times, drug abuse has increased significantly. Currently, control measures aimed at curbing drug abuse have been applied by various authorities with little success. This paper focuses specifically on one of the emerging drug substances that have been ignored for centuries - Catha edulis. The consumption of khat (Catha edulis) is mainly through chewing of young fresh shoots, sprinkling dry crushed leaves of khat on already prepared food, smoking, and boiling dried khat leaves in water to form Abyssinian tea. The use of khat has spread to many communities of the world such as the United States of America, Canada, the United Kingdom, and the Netherlands. This has been brought about by a high number of immigrants notably from East Africa and the Middle East, improved road and air transport networks, and improved preservation methods. Chronic and excessive use of khat may result in serious medical concerns among khat users. The medical effects of khat depends on the amount and potency of the chemical cathinone and cathine that is taken in or being absorbed. This work, therefore, reviews the current knowledge on the health effects of khat, social benefits, and possible negative impacts of khat use. Moreover, this work also clearly outlines cessation strategies towards curbing chronic khat abuse, withdrawal symptoms, and pharmacology. It also identifies and recognizes the role of government authorities, non-governmental institutions, and society in addressing the medical problems associated with the consumption of khat.

With increasing stress levels, disease burden and harsh





GRAPHICAL ABSTRACT

psyco-stimulants and causes of illneses - liver failure, mental disorders, and cardio problems Desitues, internet has become a reliable source of

Introduction

Presently, there is an exponential growing habit in drug abuse among various communities worldwide largely associated with immeasurable physiological outcomes such as low intelligent quotient (IQ) among the young children, psychiatric effects, and impairment or disabilities [1]. Studies have shown that some of the major effects of drug abuse include loss of income, unemployment, poor interpersonal relationships, disabled individuals unable to fulfill their expectations, which may result in death as a result of chronic or acute ailments [2]. Some of the social problems associated with drug abuse are murder, suicide, child abuse, traffic accidents, sexual assaults, and violence [3]. Anincrease in drug abuse has presented significant challenge among communities, global economy and human health [4]. Khat is one of the most established drugs that have been abused globally despite stringent measures put in place by government authorities. not controlled Khat is bv international law, nor has it been systematically included in the list of illegal drugs monitored in the European Union (EU); however; the current primary source of information on khat use in Europe is the early-warning system set up to document new and emerging drugs [5, 6].

information giving birth to "internet-khat trade" which has gained mounting popularity across the world [7].

Generally, khat is an evergreen shrub that is planted and commonly grows in the native Eastern through the southern parts of Africa and in the Arabian Peninsula [8-10]. It is mainly chewed [11-13] because of its stimulating properties [12, 14, 15] and euphoric effects [8, 16, 17] caused by the psychoactive chemical cathinone [12, 18, 19]. This chemical has a close chemical resemblance to amphetamine hence the similarity in its stimulating properties [20]. Particularly, it triggersthe central nervous stimulations leading to the produce of catecholamine [20] from the terminals of the sympathetic nerves [21] which results in hyperactivity, euphoria, and anxiety [22, 23]-the motivating basis for its widespread consumption [24, 25]. Depending on the origin of khat and the country where it is grown, this shrub is known by several names including chat, quad, qat, cat, mairungi, catha, and Jaad [9, 26, 27]. Khat chewing is regarded as a tradition and a social habit in areas where it is used intensively[13, 28-30]. Additionally, it is widely usedfor recreational purposes [18, 27], psychological pleasure[17, 20], religious purposes [31-33] and recognized for its

medical purposes [27, 34]. For instance, processed khat roots and leaves are recognized in Ethiopia to treat cough, influenza and asthma [35]. Besides, khat intrusion is used to treat boils [35] and premature ejaculation in the recent past [36]. Fresh leaves of the khat shrub (*Catha edulis*) are chewed for their euphoric characteristics in East Africa mainly Kenya, Ethiopia and Somalia, and parts of the Middle East, including Yemen and Saudi Arabia [37]. Historically, khat cultivation originated from Ethiopia and was imported and distributed to other African countries, Yemen, and across the world [11]. This is due to connectivity of road and air transportation networks considered as a great business opportunity as demand for khat chewing has increased significantly [38-40] thus causing production rates to go up [17]. Furthermore, it has been spread by immigrants as they traveled across the world [16, 41-43] and improved preservation methods [12] hence it is among the most profitable trade commodities [44]. This has made khat producing countries, and khat farmers earn very high profits through khat exports resulting in elevated khat useboth locally and internationally [45].

Currently, it is estimated that more than 10 million people across the world consume khat daily with its use largely in East African countries and Southwestern Arabia [11, 46-48]. It is estimated that about 10 million people across the world consume khat daily with its use largely in East African countries and Southwestern Arabia [11, 46, 47] although consumption intensity varies among countries [49]. Daily chewing of fresh khat leaves is a popular event in East African countries and the Arabian Peninsula, starting in the afternoon until late in the night [5]. A khat chewer is estimated to chew 50 - 200g of fresh khat daily [50, 51] - thee quivalent of 5mg amphetamine oral dosage [18] leading to a high intake of alkaloid chemicals [50]. It has been documented that cathinone concentrations vary among different types of khat with estimates

ranging from 78-343mg/100g of fresh khat leaves. Cathine and norephedrine concentrations depend on the freshness of the khat shrub and the conversion rates of cathinone [8] with an average of 120 mg and 8 mg each per 100g of fresh leaves, respectively [32, 52]. Khat leaves are leathery in texture with serrated edges [53], brownish-green leaves arranged alternately along its branches [54] as shown in Figure. 1. The leaves are slightly wide, have a highly polished appearance and at most 10 cm long [35]. Additionally, they have an aromatic odor with an astringent taste [55, 56] arising from tannins contents [57] that encourages people to consume it [56].



Fig. 1 Fresh young khat shrub

Khat users and guitters reported that their initiation into khat consumption was at a the tender age of about 12 years mainly through imitation and peer pressure [30]. various studies have revealed that khat chewing is associated with gender [58], alcohol drinking, and cigarette smoking [11]. It is also noted that religion mostly among Muslims has played a key role in the consumption of khat [32, 40] in addition to availability of khat leftovers for persons with no cash [59], high wealth index and residential places [24] are indicators to this practice [13]. Besides,the background ofplays a role in psychoactive substance abuse [60, 61].Khat chewing is associated with increased energy and cognitive abilities [32], boosts self-esteem and enhances excitement [60], improves alertness, and reduces hunger [27, 52]. It is further attributed to better academic performance

among students, enhances concentration during reading, and examination preparations [58]. It has been observed to improve work rates and enhances socialization [40], inculcates flow of ideas [34], and improves imaginative abilities [62]. Despite the aforementioned benefits of khat use, acute, chronic, and a high dose of khat [63] especially chewing may result in serious health problems [12, 15, 42] as well social and economic effects [11, 19] - all attributed to psychoactive action of khat [13]. The health problems are ascribed to the more potent cathinone component in khat [9, 16]. Toxicity due to pesticides left on leaf surfaces during their application [35], and possible pollution by heavy metals in khat products after long accumulation in the body is a new concern [64]. Hence these medical concerns worry khat consumers and drug abuse enforcing agencies [65, 66].

It is important to note that there is anabundant body of knowledge available with respect to the effects of acute and chronic khat dosing in animal models but research on the behavioral and cognitive effects of khat in human subjects is scarce in literature [67]. Although less addictive than other drugs widely abused, the World Health Organization (WHO)has already classified khat as a possible drug substance prone to abuse[11, 65], with dependence ranging from mild to moderate [9, 23]. It has also been found that other illnesses that result include dental caries[20, 51], oral cancer [68, 69], urinary retention, blurred vision, and impotence [9]. Khat chewing habit results in risky sexual behaviors [60, 70] that might enhance HIV/AIDS and sexually transmitted infections, psychiatric disorders, decreased work input, poor academic performance, and crimes [70, 71]. The indirect results include unemployment [68] and unhealthy family living conditions [72]. Khat use may also have negative effects on various body organs[16], for example, it compromises the reproductive health system where it leads to low birth weights through its teratogenic and genotoxic effects associated with cathinone chemical [73]. Moreover, it leads to decreased amount of food taken daily by pregnant women [72] which may affect neonate development which may in turn result in anemia, and extreme cases can cause the death of an infant [74]. Besides, high dose of khat preferably more than 500g/week for a short period of time (one month) has the ability to significantly decrease sperm quality, testosterone levels [36], and in some cases contributed to male infertility as demonstrated in a research done on baboons [75, 76]. High doses of cathinone component when administered reduces sexual performance and diminished sexual motivation as witnessed in rats [36]. Moreover, men also suffer sexual impotence despite high libido levels [76]. This practice also exposes khat users to stroke and ultimately death [16, 30].

It is important to recognize that khat chewing practice seriously undermines the efforts in development economic and social advancement[19, 77, 78] largely because of the psychotropic characteristics of khat [17] which is a precursor for time wastage[19, 77] and absenteeism from work continuous and decreased productivity [9, 33]. Furthermore, it leads to negligence of family basic needs occasioned by the diversion of budgetary allocation of funds to khat consumption[66]. This ultimately results infamily conflicts and violence [19, 77], financial constraints [33], and the likelihood ofcriminal behaviors [77].Consumption of khatmay also lead to divorce, which is attributed to decreased sexual activities [79, 80]. The first documented account of chewing leaves of khat which appeared more than seven centuries ago described khat leaves as a cure for depression and melancholy, and indicated their efficacy in easing hunger and fatigue particularly on social occasions [81].

Whereas numerous research findings have focused on the negative impacts of khat use prevalence, the challenges associated with khat

use remain poorly understood. The harmful constituent of khat has not been adequately defined. However, khat wood is useful in the construction such as building domestic structures [82] thereby improving social life. There are scarce literature findings on the potential socio-economic benefits of using khat. It is important to note that a few review articles have been published on the effects of khat usage [83-88]hence this present paperis very important in articulating issues of concern on khat cessation strategies, the role of the government and other institutions in minimizing khat usage. This review paper provides a comprehensive review on the pharmacology and chemistry of khat, the symptoms of khat use, social and economic impacts. Khat use is also very important in positively identifying the cultural background of a people such as Somalian, Ethiopian or Yemenis communities living outside their country of origin.

Methods of khat ingestion

Khat is ingested through different administration methods. These include chewing fresh young leaves and shoots [52] - the most common method of khat consumption used by the majority of khat community [11, 89]. Other procedures include boiling dried khat leaves in water to form Abyssinian tea [32, 90], sprinkling dry crushed leaves of khat on already prepared food, and khat smoking [91, 92]. A khat chewer normally puts fresh leaves and/or the barks of the plant into the mouth [21], and retains them on one side while chewing slowly. The extract is then swallowed [43] and the residues spat out [27]. The new fresh leaves or barks of khat are added consistently once the boluses in the mouth get dry [57]. The psychoactive alkaloid chemicals in the extract are absorbed through the stomach and buccal mucosa [27], and the small intestines [90]. After ingestion, the khat chewer experiences

increased heart rate and intermittent blood pressure levels [28].

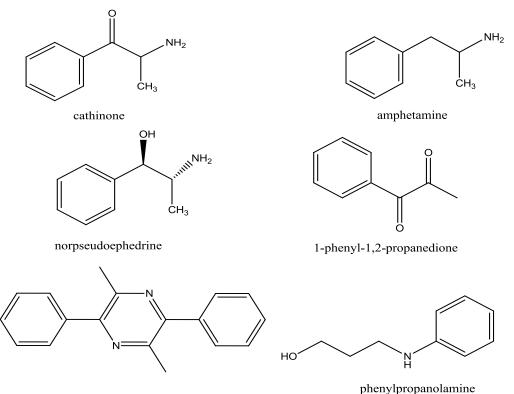
The analysis of cathinone levels presented in Table 1 was determined spectrophotometrically in the Biochemistry Department of Sana'a University, College of sciences, Yemen. This table gives the distribution of cathinone and tannic acid levels in khat grown in various regions in Yemen. It is evident from Table 1 that cathinone is high for khat types,Nehmi, Hori, Harazi, Sawti, Serafi, Dula'ee, Rade'ee, Ghorbani, and Matari regions. These cathinone levels correspond to the concentration of tannic acid in the same regions.

The chemistry and pharmacology of khat

Literature reports that khat consists of many different compounds [15, 91]. The pleasure resulting from khat chewing is credited to the euphoric nature of its chemical, cathinone, a sympathomimetic alkaloid with properties understood to be similar to those of amphetamine [93]. Cathinone is similar in structure and pharmacological activity to amphetamine in affecting the central nervous system (CNS) [94]. The extent of pharmacological actions of khat depends on the khat type [35]. Previous research has shown that fresh leaves of khat contain more than 40 chemicals [9, 32] including alkaloid chemicals, sterols, tannins, amino acids, terpenoids, minerals, vitamins [46], ascorbic acid [95], flavonoids [96], carbohydrates, glycosides and metals [15], depending non-toxic on environmental and climatic conditions where khat is grown [97].Cathinone is the main active alkaloid responsible for pharmacological effects 28] together with other alkaloids [18, norephedrine and cathine [12, 98]. Cathinone is more potent than cathine hence estimated to be at 7-10 times more [98]. Moreover, it has a close chemical resemblance with amphetamine hence exhibits similar properties (Fig. 2) [20].

S/No.	Khat type	Conc. of cathinone (mg/100g)	Conc. of tannic acid (mg/g)
1	Nehmi	342.8	<u>9.69</u>
2	Hori	337	9.71
3	Harazi	326.1	9.59
4	Sawti	323.55	9.35
5	Serafi	256.6	7.45
6	Dula'ee (upper)	255.3	7.46
7	Dula'ee (lower)	235.8	7.04
8	Rada'ee	220.6	6.83
9	Ghorbani	206.9	5.94
10	Matari	206.6	6.43
11	Shar'abi	191.3	5.53
12	Sharo'ee	187	5.52
13	Habashi	182.9	5.46
14	Bani Heshaish	180.6	5.19
15	Mashwani	176.6	5.35
16	Samawee	170.5	4.98
17	Bukhari	170.5	5.17
18	Mulahi	169.7	5.21
19	Mabra'ee	169.2	5.09
20	Najri	167.9	4.94
21	Sabri	167.3	4.96
22	Khawlani	164.4	4.8
23	Hajwee	163.4	9.38
24	Shagi	162	0.82
25	Sa'di	158.3	4.92
26	Khattabi	158.2	4.79
27	Baladi	148.8	4.56
28	Abbasi	148.5	4.52
29	Harami	148.3	4.61
30	Jayshani	147.3	4.75
31	Sharafi	135.8	4.18
32	Dehla	127.4	4.01
33	Hamdani	123.4	3.72
34	Kotobi	122.2	3.77
35	Wadi Dhar	115.3	3.45
36	Adnani	109.5	6.2
37	Ofashi	109.4	6.86
38	Saifi	77.7	4.84

Table 1. Concentrations of cathinone and tannic acid in fresh khat leaves obtainedfrom different regions of Yemen [37].



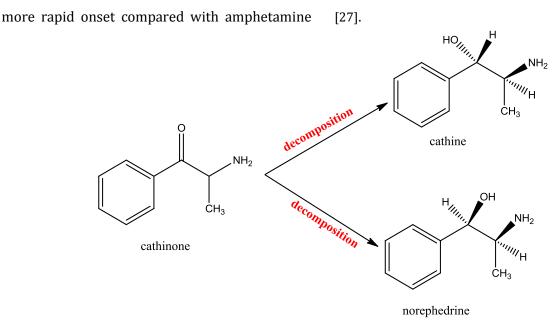
3,6-dimethyl-2,5-diphenylpyrazine

Fig. 2 The major chemicals found in khat

Cathinone is a very unstable molecule and decomposes to norephedrine [87] and cathine after harvesting [27] or exposure to sunlightas proposed in scheme 1, hence leading to decreased stimulating properties over time [27, 99]. Therefore there is the need to wrap fresh khat leaves using banana leaves to preserve its freshness and slow down the degradation process [27, 80]. Some of cathinone transformation products including norpseudoephedrine, norephedrine, 3,6dimethyl-2,5-diphenylpyrazine, and 1-phenyl-1,2-propanedione, have been isolated and characterized _ Fig. 2 [100]. Generally, norpseudoephedrine is a psychostimulant drug of the amphetamine family [20]. Like cathine, Lnorpseudoephedrine acts as a releasing agent of norepinephrine ($EC_{50} = 30$ nM) and to a lesser extent of dopamine ($EC_{50} = 294 \text{ nM}$) [101]. Previously, phenylpropanolamine (cf. Fig. 2), another chemical of khat was isolated and

characterized although this chemical was found to be no-psychoactive [102]. It is proposed that cathinone is a biosynthetic precursor of cathine and norephedrine in khat leaves [103]. Oral administration of this plant and its active constituents, cathine and cathione on model experimental animals, has shown evidence of stimulating effects on the adrenocortical function which has associated with significant decrease in adrenal cholesterol, ascorbic acid, glycogen, and enhance increase in adrenal phosphorylase activityin addition to the increased level of urinary 17-hydroxycorticosteroids and plasma free fatty acids [104].

Seizures associated with khat use are increasing among the European Union (EU) members, and significantly more synthetic derivatives of the pharmacologically active ingredients of khat (cathine and cathinone) are now available on the market [5, 6]. However, it is believed that cathinone has a shorter half-life and exhibits



Scheme 1 Degradation of cathinone to cathine and norephedrine

Hence through hepatic metabolism in the liver, it generates norephedrine [105] which can be detected and excreted in urine [90]. Equally, it suppresses the chewer's appetite [34] and decreases the body weight of the consumer [106]. The presence of flavonoid components actively leads to toxic effects after consuming khat [57]. Tannins and cathinone components both contribute to constipation medical problems [20, 21], duodenal ulcers, esophagitis and liver failure [6, 22]. Thepsychoactive effects of cathinone are similar to those of amphetamine[34]. Cathinone is predicted to be one-third as potent as amphetamine and 10 times more potent than cathine and norephedrine [103, 107]. It has been hypothesized in literature that khat leaves contain two reductases that catalyze the conversion of cathine and norephedrine, respectively, although further experimentation is required to verify or reject this assumption – in any case, the enzymatic activity possibly accounts for the rapid disappearance of cathinone from young leaves and the accumulation of the diastereomeric alcohols, cathine and norephedrine (cf. scheme 1) in mature leaves [103].

Withdrawal symptoms of khat

The results when one stops chewing khat completely or reduced consumption intervalsare dealt with here [9]. These symptomsinclude craving after reducing the amount of khat consumed and heightened appetite [66], feeling heat mostly in the legs, and undesirable nightmares [108]. It has also been witnessed that the majority of khat users experiencemild depression and sometimes sedation [52], irritability, hypersomnia and feeling fatigued, insomnia, slight tremor, the urge to chew khat, and headacheas shown in Figure 2 [9]. These symptoms are experienced by temporary and permanent khat quitters after cessation hence widely reported in the literature [66]. Figure 3 shows withdrawal symptoms and their levels percentage among university undergraduate students [9, 52]. It has been evaluated previously that cathinone leads to elevated mean diastolic blood pressure and increased risk of acute myocardial infarction, associated with prolonged chewing for instance greater than 6 hours per day [6]. This is a precursor for cardiac arrest and other heart diseases including thrombosis.

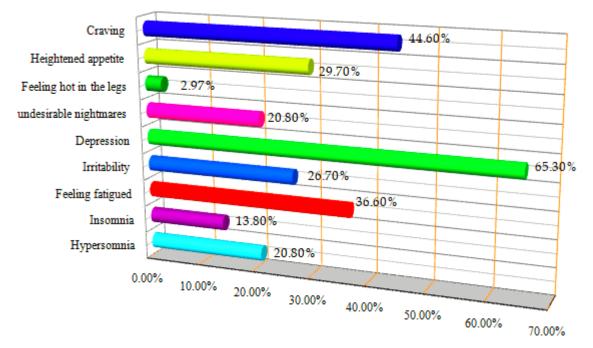


Fig. 3 Withdrawal symptoms among undergraduate university students at the University of Jimma – Ethiopia [9].

The literature findings indicate that the abuse of khat is a precursor of withdrawal symptoms that have negatively affected the social life of the user. As presented in Figure 3, the leading withdrawal symptom among the university students is depression which accounts for 65.30% of khat abusers. This correlates with the results of 53.6% of khat users in Jazan University among undergraduate students in April 2018 with a response rate of 90.1% - depression emerging as the prevalent withdrawal symptom [109]. Generally, depression is a psychological disorder that destabilizes the mental health of a person. This symptom can develops due to dependency associated with chronic khat use [110] as also witnessed among Somali refugees [111]. From Figure 3, it is clearly a predominant condition that leads to poor academic performance among university students [109]. Consumption of khatis presently recognized by WHO hence it has set an action plan to address and prevent its occurrence khat abuse and its related health outcomes [109]. The severity of other withdrawal symptoms such as insomnia, hypersomnia, irritability, feeling

fatigued, felling hot in the legs and heightened appetite affect the individual and the society at varying intensities [112].

Notably, withdrawal symptoms such as tremor may last longer after the last ingestion [113]. β_2 adrenoceptors stimulations based in the muscle tissues are triggered by khat alkaloids thatresult in tremor and trembling withdrawal symptoms [113]. Cathinone's amphetamine-like effects and additionally gastric emptying delay after chewing khat leaves may result in reduced food intake and consequently loss of appetite [114]. The insomnia symptom may make a khat chewer susceptible to psychosis and other mental disorders [115]. Nonetheless, continued khat usage has been encouraged to avoid unpleasant khat withdrawal symptoms by some khat chewers [76].

Khat cessation strategies

These primarilydepend strategies on an individual's responsibility, society, and government efforts. For instance, healthcare professionals should encourage khat chewers to quit while educating the khat chewing

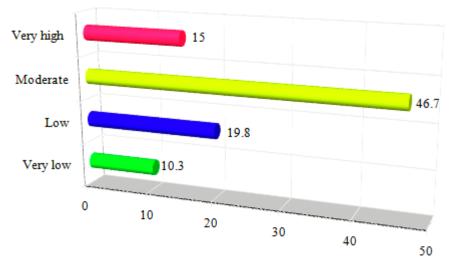
community on the medical problems caused by khat consumers [79, 116]. Accordingly, the government should create jobs for the millions of unemployed youths to avert this practice [79]. Additionally, it should impose high taxation on khat related activities to increase prices of khat hence becoming expensive for khat chewers to acquire thereby decreasing khat consumption rates [117]. Sensitization of the community preferably bv non-governmental and governmental institutions is vital to the negative effects of khat use in trying to encourage them to create teaching environments that will mainly spur educating targeted youths about khat impacts and offer them solutions [33]. The creation of awareness programs on the negative impacts of khat consumption should be embraced by various institutions including institutions, non-governmental learning organizations, and other stakeholders in trying to curb this practice [10, 118]. Fig. 4 shows the level of awareness among students on drug abuse in high schools[119]. Ministry of Education officials across the world should inculcate psychoactive and substance abuse related topics to the education curriculum at all levels to create awareness and discourage drug abuse [120]. Besides, in secondary schools, counseling services should be offered professionally to help students quit this practice and educate and mentor non-users on the negative impacts of khat consumption and possible cognitive threats to their academic performance [23, 119]. Equally important is the strengthening of peer-based education programs for mentoring students to be responsible to their well-being [49].Most importantly mass media such as newspapers, radio, and televisions can be used to communicate or create awareness on the negative impacts of khat use [69] and encourage khat cessation programs use such as rehabilitation counselling and services. Prevalence and appreciation be accorded to khat quitters who need to be molded and used to educate active and potential users on the negative effects that accompany the consumption of khat [116].

Psychoactive and cardiovascular problems

Typical khat chewing which is the main and primary use of khat increases chances of cardiovascular disease [29] and even mortality [28]. Cardiovascular activities are triggered by the amphetamine-like monoamine alkaloid cathinone [21] and cathine components in khat [121]. These lead to health concerns such as heart illnesses for example heart failure which can be fatal [42], hypertension which results from regular and excessive intake of khat [13, 28]sometimes stroke [73] vasomotor effects [121] and cardiogenic shock [122]. This depends on the concentrations of alkaloid chemicals in blood plasma [121]. It has been confirmed from studies that particularly the cathinone component in khat increases blood pressure in both animals and humans [28].

Social impacts of khat use

Here we present a case study of northeastern Kenyaand Ethiopia - an observation which can be replicated elsewhere among the khat consuming communities. Khat chewing is a more popular practice that commonly happens in homes and popularly in khat cafes [123], restaurants [90] workplaces, and cars [117]. Additionally, it commonly happens in social gatherings (khat sessions) [27, 90], that lasts for 3 - 7 hours daily [124] and averagely in 2.95 days weekly [108]. During these sessions, the participants maintain physical contact while engaging in discussions [95] for example in wedding parties and funerals [29]. Sometimes, these sessions are important in solving some conflicts within the society and act as mediation where participants get involved in political discussions [66]. Khat use is habitually used more by males than females for socialization [17, 28, 44] with similar trends among university students [19, 125].



Percentage level (%)

Fig. 4 Level of awareness on substance abuse in school high school a case of Machakos, Kenya [119].

This is because of cultural and social influence that gives males more credit and prevalence over females [23]. The prime ages for this practiceare 25-29years [99]. It is reported that this practice increases with age [69, 70] where it is maximum at 30-34 years for all khat chewers [69]. Figure 5 shows the prevalence of khat consumption among males and females according tohealth reports in northeastern Kenya [99, 126]. Generally, khat is harvested early in the morning and sold as bundles of twigs, stems, and leaves to the market by late morning, and mostly wrapped in banana leaves to preserve its freshness and prevent decomposition of unstable important compounds such as cathinone in it [55, 91]. It has also emerged khat chewing is done mostly in the afternoon and sometimes in the morning [29]as a pastime activity [43]. It is commonly accompanied by soft drinks [34] that are usually sweet to counter khat's bitter taste [90].

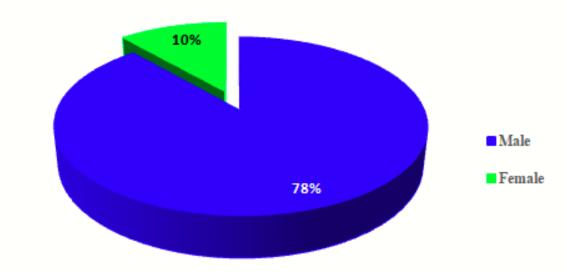


Fig. 5 Khat use characteristics among the Somali male and female population of northeastern Kenya [126]

This is associated with the fact that this practice progressively dries oral mucosa during chewing [127]. Sometimes cigarette smoking can be done concurrently [90]or with alcohol and peanuts [68]. After these khat sessions, chewers leavefeel exhausted [128]. Khat chewing is largely considered a Muslim habit [17] as it is perceived to heighten concentration especially for prayer [30] and during fasting seasons [47]. Preference for khat chewing is more in males than in females in all segments of the society [29, 80]. Table 2 shows information of studies conducted on the risk behavior khatchewing in areas where khat is intensely used (Ethiopia and Saudi Arabia). Khat chewing practice is preferred by some people because it is a sexual stimulant when it is administered in mild doses [30] but in large doses it decreases sperm count and sexual performance as witnessed in rats [30].

Table 2. Distribution of khat use in Ethiopia and Saudi Arabia

nce

Economic impacts of khat

The main native khat production zones include for example Ethiopia, Yemen and Kenya [24]. In these countries, the economic potential of khat growing has been significantly important to farmers and traders who depend on it [17] as well as offering a wide range of employment opportunities [129]. Therefore, it is a highly valued cash crop in areas where it is grown in terms of good returns it gives [99], more reliable and superior to harsh climatic conditions such as drought [73]. Therefore, farmers prefer it by avoiding production risks attached to food crops [66, 128] also claiming concerns with existing climatic conditions [129]. Khat farmers can employ different farming methods such as application of fertilizers, practicing irrigation, use of composite manure [64], traditional methods of controlling pests and application of pesticides [35] all aimed at boosting the yield of khat [64]. This is important in matching the ever increasing demands of khat globally [64]. This has led to unhealthy competition for available scarce fertile land and water between khat and other much stable food crops [44], resulting in the loss of traditional systems of farming and knowledge

[130]. It is reported by khat chewers that they could spend as much as two-thirds of their basic salaries to meet their needs [99]and in extreme cases all their earnings on khat and even they had to borrow from their relatives and friends [30].Sometimes they fail to return to work during khat sessions at lunchtime leading to a reasonable decrease in overall production [131]. Persons who have high income and slightly higher advantage economically are more likely to be engaged in khat chewing and other psychoactive substances compared to those who are not [120]. In khat production areas, political leaders have encouraged farmers to invest khat growing as it contributes considerably to economic empowerment hence directly improving livelihoods [59]. Khat is considered 'black' gold in the Arab states and has the economic influence as that of oil [59]. Moreover, khat is abundantly available in Ethiopia and is a highly valued export commodity in the country [20].

Government officials and her employees are key consumers who advocate full legislation and support [123]. Politicians for example, in Ethiopia consume it during engagements in political rallies and meetings to shore up political support [123]. The sale and consumption of khat are legal in some countries, such as Ethiopia, Kenya, Somalia and Yemen basically for economic productivity of khat [132]. In many khat samples there exists a good correlation between the amount of cathinone (fresh leaves), the chief CNS-active compound, and the pricing of khat[107]. The prevalence of khat use in East Africa is highly variable (between 15.9% and 90%), but it has become a worldwide issue because of migration. Currently, khat is illegal in the USA, Canada, and many European countries [6]. However, in some EU countries for instance UK, khat possession and use are situated in a socalled "legal grey area [5]." Currently, a bunch of 200g can be easily purchased in the UK for only £3.00 [133], and more recently khat can be

bought online. Therefore, the incidence of khat use in the UK (78% of Somalis in the UK live in London) is nearly as high as in the country of origin [134]. Although the use of insecticides and possibly fertilizers leads to better branches of leaf growth and better economic output, there are concerns relating to the safety to humans [37]. This is because of the possible toxicity of heavy metals such as lead (Pb) and cadmium (Cd) mainly arising from synthetic insecticides and soil environments on which khat is grown [48]. The contamination of khat products by heavy metals and insecticides results in human poisoning and subsequent adverse health problems [64]. Serious health concerns arise at elevated levels of heavy metals [48].

Conclusion

This study has demonstrated that the alkaloid cathinone is the most addictive component in the abuse of khat. Together with other alkaloids norephedrine and cathine, they may cause serious mental health problems such as depression and psychosis as well as negative reproductive health concerns. For instance, high dose of khat preferably more than 500g per week has the ability to significantly decrease sperm quality and testosterone levels. One major driving force towards khat consumption is religious practices and social gatherings during weddings and cultural events. Khat use has also penetrated academic institutions where there is a significant rise in khat use among the student population mainly because it is believed to enhance academic performance. Arguably, consumption of khat commonly chewing of khat is a practice that is currently widespread globally from native khat production zones. It is preferred its psychoactive because of stimulation properties used for religious purposes mostly among the Muslims during prayer and fasting seasons, for socialization as well as for recreational purposes. Traditionally, it was used for medical purposes for the treatment of headaches as well as common colds and relieving

khat has substantiated fatigue. In sum, advantages economically and contributes to the well-being of social life through family conflict resolution, and enhances soil fertility by adding nutrients to it. However, WHO has classified khat as a drug of abuse although with less addictive tendencies. Developed countries consider it as a drug and sponsor campaigns against its existence and use. Chronic and longtime khat use affects the social structure, causes adverse health effects, and affects the economic status of the society. Based on the findings of this review, it is important that those in authority make more effortstotake necessary measures aimed at restricting khat use. Moreover, it is worth noting that identifying predictors for khat chewing practice among the most vulnerable groups of the society is vital, and will act as an input to program planners and policy makers to design an effective strategy in taking appropriate interventions towards khat abuse.

Declarations

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Consent for publication

This article has the consent of all the authors

Availability of data and materials

N/A

Competing interests

The authors have no competing interests

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