The green leaf: Khat and potentiality of dependence

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ABSTRACT

Khat leaves originate Yemen and East Africa and are chewed socially for their psychoactive properties. The main constituents of khat, cathinone and cathine, are illegal substances in USA and most of Europe, including the UK. Concern over cathinone’s potential abuse, there were case study reports, anecdotal observations, reviews of the literature and researches report on a possible association between khat use and the occurrence of potential dependence. Despite that reports of khat-induced dependence are not supported with robust scientific studies, and evidence for a causal relationship is lacking. This is based on the similarity in the structure of cathinone "the major psychoactive ingredient in khat" and amphetamine. These studies have drawn a parallel between khat and other illicit substances, particularly amphetamine. Provoking calls for its prohibition. This raises alarm may possibly encourage to strict classifications of khat as an illegal or dangerous substance. Contrary to this view, there is an emerging consensus among some international health agencies that khat has a low abuse potential and the evidence of harms associated with the use of khat is insufficient to justify control and it would be inappropriate and disproportionate to classify khat under the Misuse of Drugs Act 1971. This paper will analyse and address the question of the potentiality of khat dependence in terms of data gathered during an extensive field study of khat use.

Keywords: Khat, Qat, cathinone, dependence, addiction, Yemeni drug use.

Background

The use of drugs or natural psychoactive substances seems to be an almost universal phenomenon. Khat (Catha edulis) evergreen shrub of the family Celastraceae (Kennedy, 1987). Khat leaves have been chewed for centuries for their mildly stimulating properties as part of their social life and cultural heritage. Chewing fresh leaves of the Khat (Catha edulis), represents a widespread habit with a deep-rooted sociocultural tradition in Yemen (Numan, 2004). It is said to enhance social interaction, playing a role in ceremonies such as weddings births, marriages, and funerals. The major psychoactive ingredient is cathinone. Cathinone has pharmacological properties (WHO, 1980; Kalix, 1980; Zelger and Carlini, 1980) and effects similar to amphetamine (Knoll, 1979; Kalix and Khan, 1984). Khat is now an international article of trade and consumed in the cities of Western Europe and North America. The general attitude to consider khat use as a drug addiction, like those widespread substances in the West, reflects something of an exaggeration stem from the ignorance about the nature of real social life in Yemen.

The major psychoactive ingredient is the phenylalkylamine...
Cathinone and cathine are the main chemical constituents of khat. When isolated in pure form, from synthetic compounds, both substances are stable and are controlled under the Misuse of Drugs Act 1971. This is in direct contrast to the unstable nature of cathinone, which quickly degrades to cathine, as found in the fresh khat plant. Depending on the country, the status of khat and cathinone varies amongst the countries in which khat has been historically used are Yemen, Saudi Arabia, Ethiopia, Eritrea, Somalia, Djibouti, Kenya and Uganda. With the exception of Eritrea and Saudi Arabia (where khat is now prohibited), there is a legal trade in the commodity in these regions, where khat chewing is part of the social and cultural fabric in all these countries. Khat is now an international article of trade and consumed in North America, European cities where there are Yemeni, Ethiopian and Somali communities. In Canada, consumption is confined to members of the immigrant communities from eastern Africa and the Arabian Peninsula. Internationally, during the 1940s and 1950s, a series of khat banning laws were enacted in Kenya, Yemen, Djibouti and Somalia (Anderson and Carrier, 2011). In 1957, the United Nations Commission on Narcotic Drugs was asked to take up the question and make recommendations on whether khat should be internationally classified as an illegal drug. In 1964, Committee on Addiction Producing Drugs studied
available information on the medical aspects of habitual chewing of khat leaves (WHO, 1964). The committee was of the opinion that the problems associated with khat and with amphetamines should be considered in the same light. It was also noted that the problems with khat were confined to only a few countries in one region of the world (WHO, 1964). World Health Organization Expert Committee on Dependence producing Drugs' Fourteenth Report noted, "the view that the abuse of this substance is a regional problem and may best be controlled at that level" (WHO, 1965). For this reason, khat was not scheduled under the Single Convention on Narcotic Drugs. A study commissioned by the UN produced a report in 1975 that determined cathinone to be the active ingredient that gives fresh khat its potency. Previously, cathine, which is basically ephedrine, was believed to be the main active ingredient. Since, in the early 1980s, all amphetamine-like substances were placed as a group under international control, cathinone and cathine were – based on a 1985 recommendation of the WHO Expert Committee (22nd report, TRS 729) - added to the list of controlled substances of the 1971 UN Convention on Psychotropic Substances, respectively to Schedule I and III (Axel et al., 2012). In 1986 the United Nations finally added cathinone, but not the khat plant, to its list of substances that should be regulated. In fact, the United Nations Office on Drugs and Crime is quite explicit that the khat plant is a stimulant "not subject to international control" (UNODC, 1996; Gebissa, 2010). Cathinone was included in Schedule I of the UN Convention on Psychotropic Substances in 1988; it was placed among those substances subject to the most stringent international restrictions. And cathine was included in Schedule III of this Convention; much less restrictive legal category (ACMD, 2013). In 2002, a critical review on whether the plant itself needed to be placed under international control (WHO, 2003). But, WHO concluded in 2006 that scheduling was not required: “The Committee reviewed the data on khat and determined that the potential for abuse and dependence is low (WHO, 2006a). The level of abuse and threat to public health is not significant enough to warrant international control. Therefore, the Committee did not recommend the scheduling of khat. The Committee recognized that social and some health problems result from the excessive use of khat and suggested that national educational campaigns should be adopted to discourage use that may lead to these adverse consequences”. This conclusion of the WHO Expert Committee blocked the option of bringing khat under UN control, clearly to the frustration of the International Narcotics Control Board (INCB, 2006), and a strong recommendation by the INCB that khat should be brought under international control (Axel et al., 2012). In Britain, Advisory Council on the Misuse of Drugs (ACMD, 2005) believes that it would be inappropriate to classify khat under the Misuse of Drugs Act 1971 and that the evidence of harm resulting from khat use is not sufficient to recommend its control. Following a review by the Advisory Council on the Misuse of Drugs (ACMD, 2010), a recommendation was made to reclassify synthetic cathinones as a Class B drug, culminating in a UK ban in 2010. Khat, however, despite being mostly banned in Europe due to its 1% cathinone content, has until recently remained legal in the UK. Although the governmentally commissioned ACMD report (ACMD, 2013) found insufficient evidence for the ban, the government has reclassified khat as a Class C drug. Class C is the lowest classification in the Misuse of Drugs Act; however, the drugs listed are still considered by the Home Office to hold significant health and societal risks (Alice, 2016). Cathinone and cathine are illegal substances in most of Europe, including the UK, which reclassified khat as a Class C drug in June 2014 (Alice, 2016). Khat is illegal in the United States of America, cathinone is a Schedule I drug (the same as heroin and cocaine), and cathine is a Schedule IV drug (ACMD, 2005; Gebissa, 2012). Khat’s alkaloids (cathine, cathinone) restricted under Federal Law, effectively prohibiting khat, but legal status varies under State law.

With regard to specific national legislations, in 1981, following publicity given to investigations by the WHO, Finland, Germany and New Zealand legislated against khat. Norway and Sweden acted in 1989, followed by Italy in 1990, and Denmark and Ireland in 1993. None of these countries conducted studies into khat consumption or potential harms studies before legislating. Thus decisions appear not to be driven by evidence. The UK’s Advisory Council on the Misuse of Drugs recently reviewed evidence pertaining to khat harms and reported its findings in January 2013. As with its 2005 review, it recommended that khat should not be controlled in the UK (ACMD, 2013; ACMD, 2005).

Despite such widely reported concerns of such harms related to khat e.g. possible association between khat use and the occurrence of medical, mental disorders and social harms, but no robust evidence has been found which demonstrates a causal link between khat consumption and any of the harms indicated. However, there is a general lack of quality studies that consider the harms of khat to support the controls imposed (ACMD, 2013). It appears that decisions to control khat are likely not to have been based on robust evidence of either physical or societal harms, but other factors.

The general attitude to consider khat use as a drug addiction, like those widespread substances in the West, reflects something of an exaggeration stem from the ignorance about the nature of real social life in Yemen. In this paper, a systematic review of literature to clarify whether or not potential tolerance capacity, psychic and physical dependence are caused by khat or rather associated with its use.
RESULTS

Early theories of drug dependence, for example, placed major emphasis on the physical effects of withdrawal as a factor of drug dependence (Himmelsbach, 1943) and tolerance (Edwards and Gross, 1976). Nahas (1981) defined drug dependence/addiction as “A state, psychic and sometimes also physical, resulting from the interaction between a living organism and a drug, characterized by behaviour and other responses that always include compulsion to take the drug on a continuous or periodic basis in order to experience its psychic effects, and sometimes to avoid the discomfort of its absence”.

In this regard, there were contradictory reports on a possible association between khat use and the occurrence of and potential tolerance capacity, psychic and physical dependence.

With respect to potentiality of dependence, (Eddy et al., 1965) reported traditional consumption by chewing characterized by moderate but often persistent, psychic dependence, lack of physical dependence and absence of tolerance, in contrast to the marked tolerance observed with amphetamine abuse (Kennedy, 1987); Laurent, (1962a; 1962b) noted that physical dependence does not occur after prolonged administration of khat. WHO (1980) reported “no evidence that khat produces physical dependence. Kennedy (1987) in his extensive study reported ‘a mild form of physiological dependence dose result from extremely heavy use’. Withdrawal symptoms after prolonged use are mild and may consist of lethargy, mild depression, slight trembling and recurrent bad dreams (Kalix, 1988), but these symptoms are mild and resolve in short time (Kalix, 1990), while Halbach (1972); Luqman and Danowski, (1976); WHO (1980) reported that symptoms of withdrawal interpreted as rebound phenomena rather than the expression of a true physical dependence as a specific abstinence.

The potential for khat chewing to create tolerance is disputed (Eddy, 1965; Lemordant, 1966; Luqman and Danowski, 1976; Kennedy, 1980; WHO, 1980; Kalix and Braenden, 1985; Giannini et al., 1986; Nencini et al., 1986; Kennedy et al., 1987; Kalix, 1988; Petal, 2000; WHO (ECDD) 2006). While no tolerance to khat chewing is reported, this could be due to the physical limits on the amount that can be chewed rather than to an inherent property. Tolerance is difficult to evaluate because chewing sets an upper limit to the amount of khat that can be consumed (WHO, 2006b). Halbach (1972) in his study suggested that tolerance to khat practically does not occur, as generally stated and confirmed by Laurent (1962a; 1962b); Lemordant (1966). Halbach (1972) interpreted the absence of an appreciable tolerance to khat may be the result of an intrinsic property of khat or of the physical limits on the amount that can be chewed and, hence, the amount of active principle absorbed.

A certain degree of tolerance seems to develop to the increases in blood pressure, heart rate, respiratory rate and body temperature, and to the insomnia (Kalix and Braenden, 1985; Kalix, 1990; Luqman and Danowski, 1976; Nencini et al., 1986). Nencini et al. (1984) reported that a certain degree of tolerance may develop due to sympathetic effect of khat. But in his study there no mention of any monitoring of a control group of non-chewers in identical condition. These finding cannot therefore be taken as evidence of tolerance. The interesting in his study indicate that no evidence of withdrawal symptoms, and khat consumption being non-addictive than addictive. Whilst, the WHO (1980); Halbach (1972); Kalix (1988) reported no tolerance to khat chewing, this could be due to the physical limits on the amount that can be chewed rather than to an inherent property. Contrary, Petal (2000) stated that tolerance develops with daily regular use and this strongly suggests development of psychic or physical dependence or both in the user.

DISCUSSION

Khat dependence

Reports of prevalence of dependence vary considerably. The issue of physiological and/or psychological dependency is also difficult to clearly ascertain and the literature provides variable conclusions (Laurent 1962a, 1962b; Eddy, 1965; Lemordant, 1966; Halbach, 1972; WHO, 1980; Halbach (1972); Luqman and Danowski (1976); Kennedy et al. (1980); Kalix (1983b); Nencini et al. (1984); Kalix 1985; Giannini et al. (1987); Kalix (1987); Kennedy (1987). Pantelis, 1989; Giannini et al., 1992; Griffiths et al., 1997; Alem and Shibre, 1997; Pennings et al., 2008; Kassim, 2010; Kassim, 2012; Numan, 2012; ACMD, 2013).

Reported outcome

In fact, there are very few reports on khat dependence and habitual users do not show serious problems when stopping use (WHO, 2006). 2 Cases (a 20-yr-old woman and a 26-yr-old man) with khat dependence have been described in the literature (Giannini et al., 1992). In one study, 0.6% of khat chewers reported to take khat because of dependence to prevent withdrawal symptoms (Alem and Shiber, 1997); Griffiths et al., (1997) have shown dependence of 6% of khat chewers self administering on a daily basis. Khat has a psychological dependence effect that can be measured by the SDS, even in low doses and with irregular use (Maged, 2016); Kassim et al. (2010) found that 51 percent of respondents scored 6 or more on a severity of dependence scale.
(SDS) for khat, suggesting probable psychological dependence. Whilst Griffiths et al. (2010) study scoring 207 Somalis in the UK on an SDS found scores were skewed towards the lower end of the scale, 70% of chewers scored under six. In a small study, Colzato et al. (2011a) found that all khat chewers (n=20) met more than four of the seven criteria that define addiction. Othieno (2000) reported that no signs of khat dependence were found in a survey held in Kenya among outpatients attending rural and urban health centres, and habitual users do not show serious problems when stopping use (ACMD, 2013).

However, in these studies the diagnosis of dependence was not validated through structured clinical interview (ACMD, 2013). The Severity of Dependence Scale (SDS) (Gossop et al., 1995) was initially developed to measure psychological dependence upon different drugs (heroin, cocaine and amphetamine) and not specifically developed for khat. It must be emphasised that the SDS has not been validated in this population or for this drug, and interpreting these findings requires caution.

Surprisingly, some study authors use scale clinical case reports and surveys or obtained their results from a small number of individuals which are not considered to be representative of the wider population of interest. Others generalized their results that might have been nonconforming and at increased risk of harm, were considered to be equal to all khat chewers. ACMD (2013) stated that "Not all research designs are structured such that the methodology applied is equal in terms of the potential risk of error and possible bias in their results". The quality of the available literature was considered to be generally poor so as to preclude meta-analysis. The most satisfactory evaluation of khat in this respect is presented in the WHO Document of 1964, ACMD (2005, 2013); ECDD (2006b); Halbach (1972); Kennedy (1987); Penning et al. (2008) and UK reviews on khat, such as those conducted by Warfa et al. (2007); Feyissa and Kelly (2008); Anderson (2011), and their respective colleagues have reached similar conclusions (ACMD, 2013).

**Potential tolerance capacity**

**Reported outcome**

In this regard, there were contradictory reports on a possible association between khat use and the occurrence of potential tolerance capacity, some literature pointed to absence of tolerance (Laurent, 1962a, 1962b; Eddy, 1965; Lemordant, 1966; Halbach 1972; WHO, 1980), or a certain degree of tolerance (Nencini, 1984; Kalix, 1985; Pantelis, 1989). Tolerance has been suggested as developing following prolonged hours of khat chewing over several days (Odenwald, 2006); Eddy et al. (1965) has argued that the physical size and texture of khat bundle will naturally limit intake and thus prevent tolerance. Tolerance is difficult to evaluate because chewing sets an upper limit to the amount of khat that can be consumed (WHO, 2006b); Halbach (1972) in his study suggested that tolerance to khat practically does not occur, as generally stated and confirmed by Laurent (1962a; 1962b); Lemordant (1966); Halbach (1972) interpreted the absence of an appreciable tolerance to khat may be the result of an intrinsic property of khat or of the physical limits on the amount that can be chewed and, hence, the amount of active principle absorbed. NIDA, (2007; 2011) noted that unclear whether khat to cause tolerance.

**Physiological and psychological dependency and withdrawal symptoms**

**Reported outcome**

The issue of khat and physiological and/or psychological dependency is also difficult to clearly ascertain and the research provides variable conclusions. Also, there was no consensus of opinion with regard to khat physical dependence and/or withdrawal symptoms. Physical dependence does not occur after prolonged administration of khat (Laurent, 1962a; 1962b) and lack withdrawal symptoms (Eddy,1965; Halbach, 1972; Luqman and Danwiski, 1976); Kennedy (1987) reported a mild physical dependence. Unfortunately, most scientific literature repeats this statement and ignores what Kennedy stated ‘true physiological dependence appears to be relatively unimportant in overall Yemen picture, in terms of Kennedy’. NIDA (2007, 2011) reported it's unclear whether khat to cause physical dependency or withdrawal.

Regarding to psychic dependence, a moderate persistence psychic dependence (Eddy, 1965; Halbach, 1972; Luqman and Danwiski, 1976; WHO, 1980; Kalix, 1988; Petal, 2000). Others reported psychological rather than any physical dependence (Nahas, 1981). Symptoms of withdrawal interpreted as rebound phenomena rather than the expression of a true physical dependence as a specific abstinence (Halbach, 1972); Luqman and Danwiski (1976); WHO (1980). While, no definite physical withdrawal syndrome indicating dependence associated with the cessation of khat use (ACMD, 2013; Balint et al., 2009; Giannini et al., 1986; Patel, 2008; Pennings et al., 2008).

Other scholars have reported that khat use may be compulsive (Kalix, 1987), craving (Penning, 2008), craving and compulsive (Kassim, 2010).

Despite use of the above terms (tolerance, physiological and/or psychological dependency, physical dependence and/or withdrawal symptoms or withdrawal
psychological dependency is often cited as a key problem. Review of international literature relating to khat’s dependence potential. The significance of khat chewing cannot be realized or understood in terms, unless knowing the social, cultural and ritual tradition that urge the individuals participate in khat sittings in eastern Africa, the Arabian Peninsula and immigrant communities from these countries to the West. In simple words, the review found a general lack of strong evidence linking the use of khat and potentiality of dependence. The evidence on a possible association between khat use and the occurrence of potential tolerance capacity is confounding, contradictory and inconclusive. Physiological and/or psychological dependency is often cited as a key problem among khat chewers but no clear causal link emerges from the literature, although heavy, frequent khat chewing. Most studies; case reports, quantitative, literature, and reviews on khat are confounding, contradictory and inconclusive.

Review of international literature relating to khat’s dependence potential

During the last six decades, there has been an increase in reviews of the literature and researches on the negative medical, mental, social harms of khat use and potentiality dependence. The literatures are not just inconclusive, but also contradictory (ACMD, 2005; Warfa, 2007; Pennings 2008; Anderson, 2011; Gebissa 2012, Numan 2012; ACMD, 2013). This variation was not limited to the scholars in this field, but it extended to corridors of international bodies, such as WHO Expert Committee on Drug Dependence (ECDD, 2006), International Narcotics Control Board (INCB, 2006), US drug enforcement agencies (http://www.justice.gov/dea/concern/khat.html) and UK Advisory Council on the Misuse of Drugs (ACMD2005, 2013).

US Drug Enforcement Agencies report that the adverse effects of khat chewing and encourage stricter classifications of khat as an illegal or dangerous substance (http://www.justice.gov/dea/concern/khat.html). This is the consensus of International Narcotics Control Board [80] opinion with regard to khat. Some countries have applied the scheduling of cathine and cathinone as a reason to prohibit khat. Thus decisions appear not to be driven by evidence, i.e., no review of harms has been conducted; none of these countries conducted studies into khat consumption or potential harms studies before legislating. However, the ACMD (2013) did not find evidence that these decisions were based on a thorough assessment into khat use or its potential harms. 18 years later of UN Convention on Psychotropic Substances in 1988, at the 34th meeting of the WHO Expert Committee on Drug Dependence (ECDD) in most recent critical review by the World Health Organization (WHO, 2006a) there is inconsistent data regarding the dependence potential of khat. For that reason, the ECDD recommended in 2006 that the potential for abuse and dependence of khat is low. WHO experts had to date found insufficient evidence of adverse effects from abuse to justify scheduling, and urged the commission to ignore the INCB recommendations in their report; i.e., the level of abuse and threat to public health is not significantly enough to warrant international control. Therefore, the Committee did not recommend scheduling of khat (WHO, 2006; IDPC, 2007; Pennings, 2008). This conclusion, a non-scheduled substance (khat) has generated tensions between International Narcotics Control Board (INCB) and the World Health Organization (WHO); and a strong recommendation by the INCB that khat should be brought under international control (Axel et al., 2012). In a wide-coverage for “risk assessment of khat use in the Netherlands, a review based on adverse health effects, prevalence, criminal involvement and public order” by CAM (Coordination point Assessment and Monitoring new drugs) to assess the overall risk of khat in the Netherlands, Pennings (2008) came recently to a similar conclusion of Kennedy (1987) three decades before: “the abuse potential of khat is low and khat dependence is low. Mild craving and tolerance to khat effects exists but there is no definite withdrawal syndrome. There is no strong, and even contradictory, evidence for a causal relation between khat use and psychiatric morbidity”. In Australia, the primary finding of the Fitzgerald review (2009) was that there was little evidence to support direct
causal links between psychiatric illness or criminality and khat use. Further it was found that ‘there is an emerging consensus among international health authorities that Khat has low abuse potential’ (Fitzgerald 2009). The UK's Advisory Council on the Misuse of Drugs (ACMD) (2013) recently reviewed evidence pertaining to khat harms and reported its findings in January 2013. In comprehensive summary the ACMD considers that the harms of khat does not reach the level required for classification. The ACMD (2013) considers that the evidence of harms associated with the use of khat is insufficient to justify control and it would be inappropriate and disproportionate to classify khat under the Misuse of Drugs Act 1971. As with its 2005 review (2005), it recommended that khat should not be controlled in the UK. Therefore, the ACMD recommend that the status of khat is not changed. The ACMD echoes the view of the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA, 2011) that — knowledge gaps in this area remain considerable and little is known about the social or health consequences of khat use. Although the governmentally commissioned ACMD report (ACMD, 2013) found insufficient evidence for the ban, the government has reclassified khat as a Class C drug. Class C is the lowest classification in the Misuse of Drugs Act; however, the drugs listed are still considered by the Home Office to hold significant health and societal risks (Alice Caulfield (2016).

Briefly, it is true that khat is closely related both structurally and pharmacologically to amphetamine, but the contextual conditions of use and perhaps the more favourable unwanted effect profile render the substance less deleterious. Second, the use of khat happens in companies or under working conditions (khat sitting) where it serves sociability, community feeling, increase of physical and mental capacities, to reduce fatigue etc. and not the aggressive behavioral patterns as it happens with amphetamine-like drugs under "disco" conditions. Third, what regarding to medical harms even with the literature is not just inconclusive, but also contradictory (Numan, 2012); the effects observed are mild and the evidence for an association very thin. Forth, the debates on khat, often by focusing on the anecdotal observations, empirical studies and case reports often fail to understand that khat has been part of social life and traditional (Yemeni) middle-class social life is structured such as the "khat sitting" is an integral part of it. Sixth, as with any substance, the range of harms and the development of dependence is a complex interaction between properties of the individual conditions (such as genetic factors, personality, psychological and physical health), drug (psychopharmacological effects, dose, route of administration), and socio-cultural factors, including environmental factors (such as drug availability and price), social conditions (including unemployment, crime, family breakdown, poverty, educational problems and lack of integration into host societies (Anderson, 2011; ACMD, 2013) and established rules or patterns of use within a cultural group.

Finally, Khat do not inevitably be made up of pure feeling or sensations of pleasure like the “high” or the “rush” due to typical of amphetamine or of inhaled crack (cocaine base) but can take milder forms of hedonia, such as relief of tension, reduction of fatigue, increased arousal, or improvement of performance. These positive sensations can explain why khat is used, but not necessarily why it can produce the behavioural repertoire characteristic of dependence.

CONCLUSION

Cathinone is a close relative of amphetamine and contextual factors render khat only slightly stimulant. Khat sitting (session) promotes reward stemming from social contacts; it is an important medium for social communication. The potentiality of dependence (potential tolerance capacity, physiological and/or psychological dependency, withdrawal symptoms) is not fully evidence-based and cannot be abbreviated in technical terms. Most studies; case reports, quantitative, literature, and reviews are confounding, contradictory and inconclusive. The review found a general lack of strong evidence linking the use of khat and potentiality of dependence. Because of the ambiguous reports of its medical and social harms, as well as the confusions in the evidence regarding its dependence, attempts to place it on lists of dangerous and banned drugs failed.

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