

**Flower of paradise (Khat: *Catha edulis*): Psychosocial, health and sports perspectives.**

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**SUMMARY**

Flower of paradise (*Catha edulis*: khat), a controversial, religion and psychosocial plant grown in the countries around East to southern African and Arabian Peninsula (around the red sea). The spectrum of khat actions has been postulated to lie between amphetamines and caffeine, therefore, khat and its principal active constituents (cathinone & cathine) are categorized as amphetamine-type substances/stimulant (ATS).

Presently, khat is not under international control, but, the two substances that are usually present in khat; cathinone and cathine were placed group as schedule I and IV ATS respectively. The morality and legality of khat usage by the general populace varies from country to country. However, the World Antidoping Agency and International Olympic Committee has place a limit of 5µg/ml urinary cathine level in sports competition. This partial ban might not be unconnected to cathinone-cathine, ATS action.

Though, many studies seem to support the negative effects of chronic khat usage on human health. However, longitudinal and quantitative data on health issues seem scanty. By and large, the need clearly exist for longitudinal and qualitative investigations on the effects of khat chewing on humans, before a conclusive statement could be established.

**Keywords:** khat; *Catha edulis*; flower of paradise,

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**Introduction**

Khat with the botanical name *Catha edulis* Forsk belongs to the family of plant Celastraceae(moonseed).It is an evergreen tree which grows at high altitudes extending from East to southern

African as well as Afghanistan, Yemen and Madagascar [1,2].The earliest scientific report concerning khat was in the eighteenth century by the botanist Peter Forskal [3, 4].The chewing of khat leaves is common in certain countries of East Africa and the Arabian peninsula. It is

known by various names, ForA example “Mirra” and has many spellings [3, 5].

Historically, khat has been used for medical purposes [6]; as well as as aphrodisiac [1,7]; though it was also used for recreational purposes[2]. It is most used for its stimulant effects[3]. The chewing of khat leaves has a deep rooted socio– cultural tradition (kalix & Braenden, 1985). It is usually chewed in company [2, 5], but may be used by individual to enhance their working capacity [2,5,8]. The principal features of the “khat experience” are described as increased level of alertness, ability to concentrate, confidence, friendliness, contentment and flow of ideas [2]. Khat contains the alkaloids norephedrin,cathine and cathinone. Norephedrin and cathine do not contribute significantly to the phyclostimulant action, however, they probably of importance for the sympathomemetic effects on the autonomic nervous system. The constituent that is mainly responsible for the stimulant qualities and the dependence producing effects of khat is cathinone. Cashinone has a similar mechanism of action as amphetamine therefore it must be considered as a natural amphetamine [9–11].

Cardiovascnar effects of khat chewing occur within 15 to 30 minutes after ingestion, the effects include tachycardia palpitations, and increased systolic and diastolic blood pressure. These effects can persist up to 4 hour after the onset of chewing [12–15].

**Fig 1. Fresh Khat leaves**



Clinical studies have linked khat chewing and diseases in different organ system. Khat chewing has been suggested in modifying the circadian rhythm in acute myocardial infarction [16–18]. Also, reports have linked khat chewing and its constituents to systemic hypertension and increased heart rate [9,12,19,20]. These clinical findings were concomitant to the level of cathinone in the blood [12]. khat chewing has been reported to be associated with acute myocardial infarction [21,16].

Khat causes hyperthermia and reduces body weight by decreasing appetite.Khat chewing increases plasma leptin concentration particularly in individual that chew about 400gramme of khat leaves, it also increases plasma level of nonesterified fatty acid, it reduces plasma level of triglycerol while plasma cholesterol were not affected [22,23] on the contrary khat chewing does not affect plasma triglycerides, total cholesterol and low density lipoprotein cholesterol so also plasma malondialdehyde (MDA) [23].

There seems to be a general agreement that khat chewing does not affect serum glucose in healthy individual [5,24]. However the effect of khat chewing on diabetic patients is unclear and equivocal. Hayman et

al,[25] reported a blood glucose reduction following khat consumption; while Saif-Ali et al.[24] reported a contrary notion that khat increases blood glucose level during khat session in diabetic individual.

#### **Historical background and Botanical specification.**

Khat: Kingdom, Plantae; class, Magnoliopsida; order, Celastrales; family, Celastraceae; genus, *Catha*, species, *C. edulis*. The origin of khat are often argued many believe that it originated from Ethiopia from where it spread to the hillsides of East Africa and Yemen [26–28]. Others believe that it originated in Yemen before spreading to Ethiopia and nearby countries [29, 30,31]. From Ethiopia and Yemen the tree spread to Kenya Somalia, Malawi, Uganda, Tanzania, Arabia, Congo, Madagascar, Zimbabwe, Zambia and South Africa, is also been found in Afghanistan & Turkistan [32].

Khat has been grown for use as a stimulant for centuries in the horn of Africa and Arabian peninsula. The chewing of khat predates the use of coffee. The khat plant is known by a variety of names, such as qat in Yemen, chat in Ethiopia, jaad in Somalia and miraa in Kenya and Tanzania [2]; it is also known as marungi, catha, cat, cot, qat, gaad, African salad, tohai, bushmans tea, flower of paradise, four of paradise, Abyssinian tea, African tea, Arabian tea, chafta, chat, ciat, crafta, djimma, ikwa, ischott, iubulu, kaad, kafta, kat, khat, la salade, liss, liruti, mairongi, mandoma, maonj, marongi, mbugula mabwe, mdimamadzi, meongi, mfeike, mhulu, mira, miraa, mirungi, miungi, mlonge, m'mke, msabukinga, masbukinja, msuruti, msuvuti, msekera, muholo, muhulu, muirungi, mulungi, muraa, musitate, mutsawari, mutsawhari, mutsawhri, mwandama, mzenge, nangungwe, ol meraa, ol nerra,

qat, quat, salahin, seri, Somali tea, tohai, tohat, tsad, tschad, tschat, tshut, tumayot, waifo, warfi, Kus-es-Salahin, warfo. In most western literature it is referred to as khat [27,32].

The shrub khat (*Catha edulis* Forsk) has a slender trunk with smooth, thin bark. The lanceolate shaped leaves are between 0.5 to 10cm long and 0.5 to 5cm wide. Young leaves are reddish green, later turning to yellow green (fig 1). In areas with frost, the shrub grows to higher than 1.5 meters, but in places with more rainfall like highlands of Ethiopia and areas near the equator. Khat trees can reach 20meters [2,30], khat can also survive in droughts where other crops have failed. Khat is a perennial, propagated by grafting; it grows at altitude of 1500–2000 meters. Leaves are faintly aromatic with an astringent, slightly sweet taste. Trees are grown for 3–4 years before leaves are harvested. A healthy tree yields for about 50years. Khat is not affected by any known disease. The tap root grows to a depth of 3 meters or more [30,31].

#### **Chemistry and pharmacokinetics of khat.**

The environment and climate conditions determine the chemical profile of khat leaves. In the Yemen Arab Republic, about 44 different types of khat exist, originating from different geographic areas of the country [10,30]. Its taste varies from one kind to another and depends on the tannic acid content. Khat leaves have an astringent taste and have an aromatic odour. The young leaves are slightly sweet [33]. Many different compounds are found in khat, including alkaloids, terpenoids, flavonoids, sterols, glycosides, tannins, amino acids, vitamins and minerals [8,27].

The phenylalkylamines and the cathedulins are the major alkaloids. The cathedulins are based on a poly-hydroxylated sesquiterpene skeleton and are basically polyester of euonyminol. Recently 62 different cathedulins were characterized from fresh khat leaves [34]. The khat phenylalkylamines comprise cathinone [s-(−) cathinone] which is considered as the primary constituent of khat. And two diastereoisomers cathine [1S,2S -(+) – norpseudo-ephedrine or (+) norsendoephodrine] and norephedrine [1R,2S -(−)-norephedrine] which are the secondary constituents. These compounds are structurally related to amphetamine and noradrenaline. Cathinone is mainly found in the young leaves and shoots. During maturation, cathinone is metabolised to cathine [ (+)-norpseudoephedrine in a ratio approximately 4:1] [33,35]. Other phenylalkylamine alkaloids in khat leaves are the phenylpentanylamines meru cathimone, pseudomerucathine and merucathine. These seem to contribute less to the stimulant effect of khat [36,37].

Cathinone is unstable and undergoes decomposition reactions after harvesting and during drying or extraction of the plant [36,37]. Decomposition leads to a “dimmer” (3,6-dimethyl-2,5-diphenylpyrazine) and possibly to small fragments. Both the dimmer and phenyl propanedione have been isolated from khat extracts [38]. As cathinone is presumably the main psychoactive component of khat, this explains why fresh leaves are preferred and why khat is wrapped up in banana leaves (fig 2) to preserve freshness [33].

The pleasure derived from khat chewing is attributed to the euphoric actions of s-(−)-cathinone, a sympathomimetic amine with properties similar to amphetamine [39]. The euphoric effect of khat starts after

about 1 hour of chewing. Blood levels of cathinone start to rise within 1 hour and peak plasma levels are obtained within 1.5–3.5 hours after the onset of chewing [20]. During khat chewing most of the alkaloids were extracted into the saliva, since only 10% of the original content was found in the leaf residues. It is concluded that the buccal mucosa plays a major role in the absorption of all the three alkaloids. The stomach and/or the small intestine receive the swallowed juice and are probably the second phase of absorption. Chewing and masticating the material effectively liberating the alkaloids from the leaves and allowing rapid absorption into the systemic circulation. On average, peak plasma levels were obtained after 2.3 hours for cathinone, 2.6 hours for cathine and 2.8 hours for norephedrine [14].

#### **Socio-cultural and religion perspectives**

Khat chewing has a deep rooted socio-cultural tradition, its pleasure inducing and stimulation effects seem to have a strong influence on the social and cultural life of the communities who indulge in it [8,40]. Khat is predominantly consumed in a social setting. The habit in Yemen is socially sanctioned and even prestigious; such sessions are a form of social interaction and status competition. They are governed by subtle rules while being under certain circumstances of almost ritual importance it has been suggested that the function of khat in the context is to provide a pretext for a gathering of high social significance rather than to provide pleasurable effects for the individual. Indeed because of its stimulating and euphorogenic properties, khat is certainly an appropriate tool for enhancing social interaction [40]. In other countries other than Yemen it is consumed in much less rigidly defined context,

frequently by individuals, who are a lone. Therefore, it can be assumed that in those countries the psychological benefits of its consumption are of secondary

**Fig 2. A bundle of khat wrapped up in banana leaves.**



importance and that rather it is the pharmacological action that induces the use of this plant. This is also borne out by the fact that khat use tends to be compulsive in certain individuals and the cost of the euphorogenic effect of the leaf is addiction [40,41]. A study conducted in Butajira, Ethiopia where khat usage is legal, result showed that 80% of chewers used khat to gain a good level of concentration for prayer, facilitate contact with God and prevent them from crime. [42].

Muslim religion, smoking and low income and high educational level showed strong association with daily khat consumption [43, 44]. The Moslem faith of the Yemenites forbids intoxicants other than those prescribed for medical reasons. However, the Koran mentions only alcohol, perhaps because use of khat did not become widespread until after occupation by the Ottoman Turks in –the sixteenth century. To some Muslims, Khat is known as "the flower of paradise.". Other countries in the Middle East impose heavy penalties equivalent to those for opium or cannabis on

anyone who carries or uses khat. This is not so in Yemen, where even religious leaders may practice the habit. This may be because, in contrast to opium and cannabis, khat produces milder antisocial behavior and is more akin to amphetamine– or caffeine–type substances. In the town of Bohmensaka, South Africa the consumption of this product has been noted to date back as late as the 1500's. Tribes would chew on these at festivals and large gatherings. Khat was a delicacy to the natives and was customary to their nature.

### **Moral and Legality of Khat usage**

Khat is not under international control at present, but, two substances that are usually present in khat, cathine and cathinone are, since in the early 1980s all amphetamine–like substances were placed group wise under international control. [33] Cathinone was included in Schedule I of the UN Convention on Psychotropic Substances in 1988 and cathine was included in Schedule III of this Convention [39] then. Presently cathinone still remain schedule I and cathine as schedule IV [45, 46]. However, the legality of khat usage by the general populace varies from country to country [9, 11, 12, 47, 48].

Many people around the Red Sea, including parts of Ethiopia, Kenya, Somalia Zimbabwe, Tanzania, Uganda, Malawi and South Africa [49] as well as Yemen use khat and its use is not illegal. However nowhere else it is as wide spread as it is in Yemen [31]. In Islamic countries like Yemen Republic and Somalia, as among the Muslim members of Ethiopia and Kenya, khat is the drug of choice and is legal, for unlike alcohol, it's use violates no precise proscription of the Koran[40].

Khat is banned on religious grounds and economic grounds in some other Muslim Countries such as Saudi Arabia [11,50]. In some other Countries the penalties are equivalent to those for opium or cannabis for any one that carries or uses it. This is not so in Yemen, where even religious leader's practice this habit. This may be because, in contrast to opium and Cannabis, it produces milder antisocial behavior and more akin to amphetamine or Caffeine type substance [51]. In Ethiopia and neighboring countries it is commonly used in social gatherings as much as alcohol is used in western countries [40]. Khat trade and use is not illegal in the UK, and it is known that there is a market and distribution network for the drug and that in certain locations the use of this plant is substantial also that an attempt to cultivate it in a country at moderate climate for personal use has been reported in literature[48]. The position of the European countries with regard to khat is not uniform [52]. It is prohibited in France, Switzerland and Sweden while it is tolerated in the UK and Netherlands. Outside Europe, it is illegal in the USA and Canada [9,11,12]. Indeed, the case of this plant is an equivocal one and the international law on this issue is currently ambiguous [40].

### **Health perspective**

Khat has a psychological, medical, social and economic effect on human beings. Cathinone is structurally and functionally closely similar to amphetamine and releases catecholamine from pre-synaptic storage sites resulting in CNS stimulation and a variety of peripheral sympathomimetic effect such as tachycardia and hypertension. Khat use affects cardiovascular, digestive, respiratory, endocrine, and genito-urinary systems. In

addition, it affects the nervous system and can induce paranoid psychosis and hypomanic illness with grandiose delusions [41]. The effects on the nervous system resemble those of amphetamine with differences being quantitative rather than qualitative[27,36,40,53,54].

Cathinone contents in this plant may be partially or totally responsible for the reproductive toxicity in human and in experimental animals [55,56]. This effect appears to be a decrease in semen output, sperm count, motility and an increase in the number of abnormal sperms. It has been found that khat decreases fertility through this mechanism, which is reversible by withdrawal of its usage [40,57]. Khat affect pregnant women by reducing maternal daily food intake and mean birth weight of the offspring. Low birth weight is a contributing risk factor for both prenatal and infant mortality among khat chewers during pregnancy. It can affect fetal growth during pregnancy through placental insufficiency, which could be explained by the high blood pressure registered among these women [40].

A common effect of khat use is insomnia, a condition that the users sometimes try to overcome with sedatives or alcohol. Furthermore, it has a pronounced anorectic effect. In clinical terms, khat can be said to induce a state of mild euphoria and excitement, often accompanied by loquacity or even logorrhea. In some cases it can progress to a stage of hypomania. Toxic psychosis may also result from its consumption, and a number of such cases have been described in the literature [58,59].

Most reports are of cases of psychosis and suggest a low incidence. The impression of low incidence may reflect the fact that in countries where it is most used, health facilities are lacking and people are managed at home by their family. Other studies [60] reported that adverse effects are dose-related. However, khat is considered to precipitate a psychotic illness in those who are already predisposed.

Khat may induce "Moderate but often persistent psychic dependence" the withdrawal symptoms after prolonged usage seem to be limited. However, to lethargy, mild depression, slight trembling and recurrent bad dreams [54]. Intoxication with khat is self-limiting, but chronic consumption can lead to impairment of mental health, possibly contributing to personality disorders and 'mental deterioration' [8].

CNS tolerance is not usual in khat users probably due to the physical limits on the amount that can be chewed. Mydriasis occurs as a sympathomimetic effect of khat, which also induce hyperthermia and causes dryness of the mouth[40].

At the cardiovascular level there may be arrhythmias and moderate increase in blood pressure which can be chronic upon long term use [54]. It can also cause acute cardiovascular problems problem in elderly people [61]. There is exaggerated cardiovascular response to physical effort under the effect of khat [62]. Cathinone has vasoconstrictor activity [63]. The effect was unlikely to be due to an indirect action by release of noradrenaline from sympathetic nerve endings or due to a direct action on  $\alpha_1$ -adrenoreceptors. (-)-Cathinone is able to potentiate noradrenaline-evoked contractions of the rat right ventricle [64] and to inhibit the uptake of noradrenaline into ventricular slices by a

mechanism involving competitive blockade of the noradrenaline transporter [65]. The vasoconstrictor activity of cathinone explains the increase in blood pressure seen in humans [9] and in animals [66], and might be related to the increased incidence of myocardial infarction occurring during khat sessions[30], and associated with heavy khat chewing [16].

Khat induces a fall in average and maximum urine flow rate in healthy men [36,67]. The urinary effects are probably mediated through stimulation of  $\alpha_1$ -adrenergic receptors by cathinone. This is indicated by the complete blockage of this effect by indoramin, a selective antagonist of  $\alpha_1$ -adrenergic receptors [67].Khat chewing has no clinically significant effect on gal bladder motility [68].

As a consequence of its mode of consumption khat affects the oral cavity and the digestive tract [52]. A high frequency of periodontal disease, oral keratotic lesions at the site of chewing, plasma cell gingivitis (allergic reaction to khat) [69] has been suggested as well as gastritis [6] and chronic recurrent subluxation and dislocation of the temporomandibular joint [70].Epidemiological studies, however, have yielded conflicting results. Several studies indicated no such detrimental effects of khat chewing and suggested beneficial effects on the periodontium [71,72]. Another study could not show a significant role of khat chewing and suggested bad oral hygiene as a major factor in periodontal disease [73]. No significant association could be found between khat chewing and oral leukoplakia in a Kenyan study [74]. In the study[36], the authors concluded that khat chewing does not seem to increase the colonization of gingival plaque and that, in stead, khat chewing might induce a microbial profile

compatible with gingival health [4]. The tannins present in khat leaves are held responsible for the gastritis that has been observed [54,75]. Studies have linked khat chewing with various cancer diseases of the oral cavity. [71,75,76,77,78,79].

In the Kenyan region, subjective investigation indicated that the use is reported among the Meru tribe for the treatment of erectile dysfunction, malaria, influenza, vomiting and headache [33].

### **Sports and recreation perspectives**

Over four thousand years, people have been using substances to improve their physical performance and appearance. Descriptions of athletes ingesting special foods to enhance their performance dated back to ancient Greece [80–83]. The search for methods to improve athletic achievement such as manipulation of diet, various drugs and the use of “miracle” foods can be considered wholesome as long as they are used to supplement rather than to supplant and they constitute no health hazard to the athletes and finally they are not illegal or banned by sanctioning sports bodies [82,84].

Cathine, a secondary constituent and one of the major final by-products of khat metabolism is categorized as a stimulant and is presently banned by the IOC and WADA. However, the ban on cathine is not absolute as it is in amphetamine, the IOC and WADA allow urinary concentration of Cathine up to 5 micrograms per milliliter [85–87]. Twenty-four-year-old Kenya bantamweight boxer, David Munyasia was disqualified from the 2004 Athens Olympic (Greece), after testing positive for cathine. The boxer admitted to chewing an African weed or bangi, khat which contains the banned stimulant, nor-pseudoephedrine (cathine) [88].

Historically, khat has been used for recreational purposes [2]. It is most used for its stimulant effects [3]. Khat may be used by individuals to enhance their working capacity [2,5,8,89]. It produces excitation and increased activity [8,19]. Khat also increases metabolic rate and oxygen consumption and has an analgesic effect via activation of monoaminergic pathways mediating nociception [8,19,90,91,92].

Khat may influence athletic performance by reducing the perceived effort of exercise via its analgesic effect. Conner, et al. [93] investigated the analgesic effect of khat, amphetamine and ibuprofen in mice. After intragastric administration of the drugs, analgesia was measured relative to water-injected control using hot plate, tail flick and abdominal constriction test. At the highest dose examined (amphetamine 18 mg/kg, ibuprofen 90 mg/kg & khat extract 180 mg/kg). All three substances produced analgesia. They concluded that khat like amphetamine and ibuprofen can relieve pain.

In recent years many reports [14,46,94] have been published on neuropharmacology, metabolic and biochemical changes of *Catha edulis*. Little is known about its exercise and sports performance effect. Also the few reports [5,19,86,95] on the ergogenic effect of khat on exercise and sports performance has been subjective and unclear and mostly on animals. However, WADA, IOC and other international sports organizations have placed a limit on cathine, one of the constituents of khat. Reason for this partial ban might not be unconnected to the fact that cathinone, a major constituent of khat which is finally metabolized to cathine has an amphetamine-like action. But the ethical line of cheating in sport is being scrutinized more



closely than whether a cultural incident of khat chewing is being handled appropriately.

### Conclusion

In recent time, Khat is probably the most controversial plants in all ramifications. Khat chewing has a deep rooted religion and socio-cultural tradition; also the legality of khat varies from country to country. Therefore the ethical or morality of khat chewing seems ambiguous, equivocal and unclear. Ironically, the IOC and WADA and other international sport organizations has placed a limit to khat-cathine usage in sports performance. Their reason for this partial ban might not be unconnected to cathinone-cathine amphetamine like action and effect. By and large, there is paucity of information in literature regarding ergogenic effect of khat and its derivatives on human performance. Although, literature seems to support the negative effects of chronic khat usage on human health. However, longitudinal studies and quantitative data on health issues seem scanty.

### Recommendation

Based on the present review, the followings are hereby recommended

- (1) The need for both qualitative and quantitative studies investigating the effect of khat chewing on human body system and functions clearly exist.
- (2) Studies to investigate both acute and chronic khat chewing on human system.
- (3) Well design studies using fresh young khat leaf chewing on sports and exercise performance, with respect to WADA and IOC doping limit are needed.

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