

The Chemistry of Khat and Adverse Effect of Khat Chewing

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Abstract

The leaves of khat shrub have a stimulating effect, and the chewing of this material has been practiced for many centuries in certain areas of East Africa and Arabian Peninsula. Khat is widely consumed among the youth of Ethiopia; especially among high school, College and University students as well as drivers. The active ingredient of khat responsible for its psycho stimulant effect is an alkaloid chemical known as cathinone, which is structurally and chemically similar to d-amphetamine, and cathine, a milder form of cathinone. Cathinone is a highly potent stimulant, which produces central nervous system stimulation analogous to the effect of amphetamine. The major effects of khat chewing include those on the gastro-intestinal system and on the nervous system. The negative effects of khat also include increased blood pressure, tachycardia, insomnia, anorexia, constipation, urine retention, irritability and impaired sexual potency in men. This review highlights the chemistry of khat, the health, social and economical aspects of khat chewing particularly in Ethiopia.

Keywords: Khat; Phenylpentenylamines; Phenylpropylamines; Gastrointestinal tract

1. Introduction

Catha edulis, commonly known as khat, qat, chat or miraa, [1] is a shrub or small to medium sized evergreen tree that belongs to the Celastraceae family. It is cultivated as a bush or small tree, mainly in Yemen and East African Countries [2,3]. Some oral traditions claim that khat originated from Yemen, however the literature indicates that khat originated from Ethiopia, specifically in Hararghe with a gradual expansion to different parts of Ethiopia, Yemen [4] and other parts of the world such as Somalia, Sudan, South Africa and Madagascar, Afghanistan and Turkestan [5].

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The shrub grows to a height of 6 meters and the leaves are leathery, glossy, brownish green, with serrated edges, arranged in an alternate fashion on straight branches. The chewing of the young shoots and fresh leaves of *Catha edulis* Forsk, variously referred to as khat, chat, Abyssinian tea, are used for their psychoactive properties [6,3].

The leaves of chat have an aromatic odour. The taste is astringent and slightly sweet. The plant is seedless and hardy, growing in a variety of climates and soils. Khat can be grown in droughts where other crops have failed and also at high altitudes. Khat is harvested throughout the year. Planting is staggered to obtain a continuous supply [7].



Figure 1: A young khat shrub [8,9]

In Ethiopia, khat chewing has deep rooted history as early as fourteenth century and is commonly used for social and religious purposes. Furthermore, it considered as a recreational substance. Recently, khat chewing becomes a common practice among high school, College and University students [10]. Occupational groups such as motor vehicle drivers, truck drivers, who chew khat during long distance driving, to keep awake, also use it under a variety of other conditions. A significant number of students chew khat to be alert and wakeful especially during examination periods. There is also specific usage of khat by the special sections of the community: craftsmen and farmers use khat to reduce physical fatigue and traditional healers to heal ailments [11].

For instance, in Dire Dawa high school 18.4% of students chewed khat. In a similar manner other sections of the community; such as, laborers, truck drivers, craftsmen, teachers and farmers have chewed khat in order to reduce fatigue, increase performance and to suppress appetite. In Jimma town 37.8% of the communities reported khat chewing practice [4]. As stated in [4], Khat chewing has major effect on the gastro-intestinal system, central nervous system, cardiovascular system and urinary system. Central nervous system effects of khat chewing are alertness, dependence, tolerance, anxiety, depression, delusion and insomnia. Gastro-intestinal system effects of khat chewing are dental problem, stomach ulcer, constipation, oral and esophageal cancer. On cardiovascular system habitual use of khat causes hypertension, arrhythmia, myocardial infarction, stroke and death.

Chewing is the most common mode of administration although a small number of users use dried leaves to make drinks and an equally small number smoke it. The traditional way to consume khat is to pick a few leaves of a young shoot and chew them slowly. Once the leaves are pulped, they are kept in the side of the cheek and the mouth is filled with fresh leaves. The user then chews slowly and intermittently to release the active components of khat that are then swallowed with saliva, periodically ingesting fresh leaves [12].

The bud of khat contains the chemical called cathinone and cathine. Cathinone is more lipids soluble than cathine and it can easily cross the brain blood barrier and enter in the central nervous system that is responsible for adverse effect on the body. Similarly, it has amphetamine like structure and causes similar effect on the body. Khat is chewed daily by a high proportion of adult population for its Central Nervous System stimulant effect. Furthermore, it is widely masticated among youth Ethiopians, especially high school, college and university students [13].

The chemical properties of khat are now well documented; the active agent responsible for the physical and mental effects observed when juice of the leaves is chewed is cathinone or alpha aminopropiophenone. When the leaves, which contain the psychoactive substance, cathinone are chewed and the juice is ingested, it produces stimulation of the central nervous system in man analogous to the stimulation produced by amphetamine [14,15]. Many different compounds are found in khat including alkaloids, terpenoids, flavonoids, sterols, glycosides, tannins, amino acids, vitamins and minerals [6,16,17,18].

Khat chewing nowadays has become an epidemic over East Africa especially in Ethiopia, Somali and southern Arab from the old to young, male and female, urban and rural settings [19]. Moreover, many adolescents have low knowledge towards adverse effects of khat chewing as indicated in literature [20]. Though khat chewing has become a common practice among high school, college and university students in Ethiopia, few studies have assessed the prevalence and associated factors. The consumption of Khat can cause various physiological and socio-economic impacts, which have put a control on its use by several countries. This review paper clearly discusses the chemistry of chat (khat Edulis Tree) and its consequences on human health.

2. Chemical Composition of Khat

Khat contains a lot of chemical components that may have different effect on the body system. Many of them are alkaloids, terpenoids, flavonoids, sterols, glycosides, tannins, amino acids, vitamins and minerals [9]. The major active ingredients in khat leaf were identified as the phenylalkylamine (-)-alpha aminopropiophenone named as cathinone (psychostimulant component of khat) [21] and cathine (nor-pseudo-ephedrine). Cathinone is a psycho stimulant; it has the same basic configuration as amphetamine as shown in figure.2) [22].

The cathedulins are based on a poly-hydroxylated sesquiterpene skeleton and are basically polyesters of euonyminol. Recently, 62 different cathedulins from fresh khat leaves were characterized [8,23]. The khat phenylalkylamines comprise cathinone [(S-(-)-cathinone) and the two diastereoisomers cathine (1S,2S-(+)-norpseudoephedrine or (+)-norpseudoephedrine) and norephedrine (1R,2S-(-)-norephedrine)]. These compounds are structurally related to amphetamine and noradrenaline (norepinephrine) as shown in (figure 3). The plant

contains the (-)-enantiomer of cathinone only; the (+)-enantiomer is not found. Thus, the naturally occurring S-(-)-cathinone has the same absolute configuration as S-(+)-amphetamine [8,24,25,26]. Cathinone is found mainly in the young leaves and shoots. During maturation, cathinone is metabolized to cathine, and (-)-norephedrine. The leaves contain these two substances in a ratio of approximately 4:1 [18].

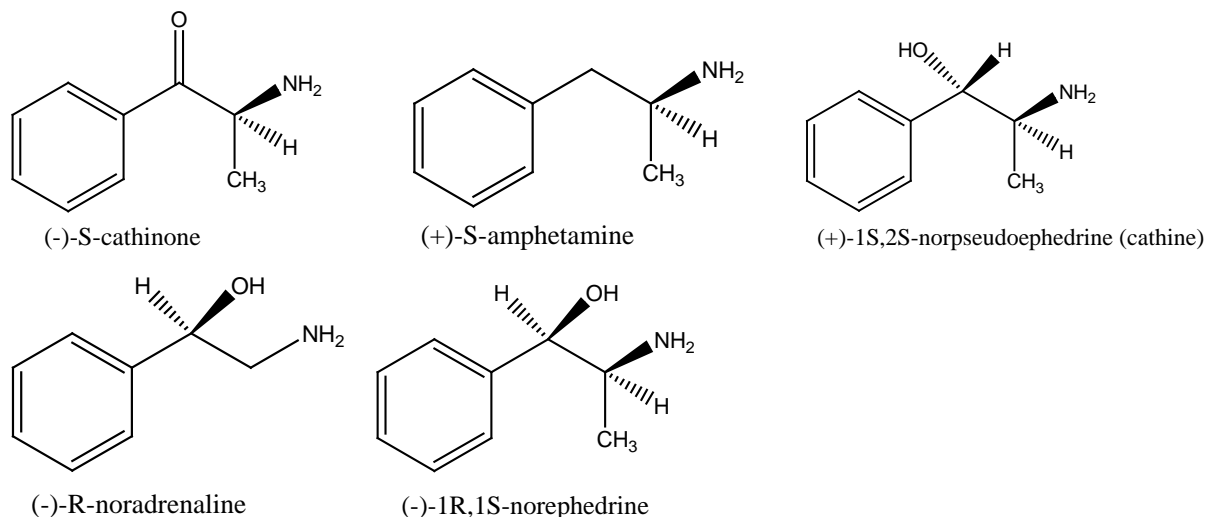


Figure 2: Chemical structure of the phenylpropylamine alkaloid from khat (*Catha edulis* Forsk) cathinone, norephedrine, norpseudoephedrine (cathine) compared with amine and noradrenaline [27]

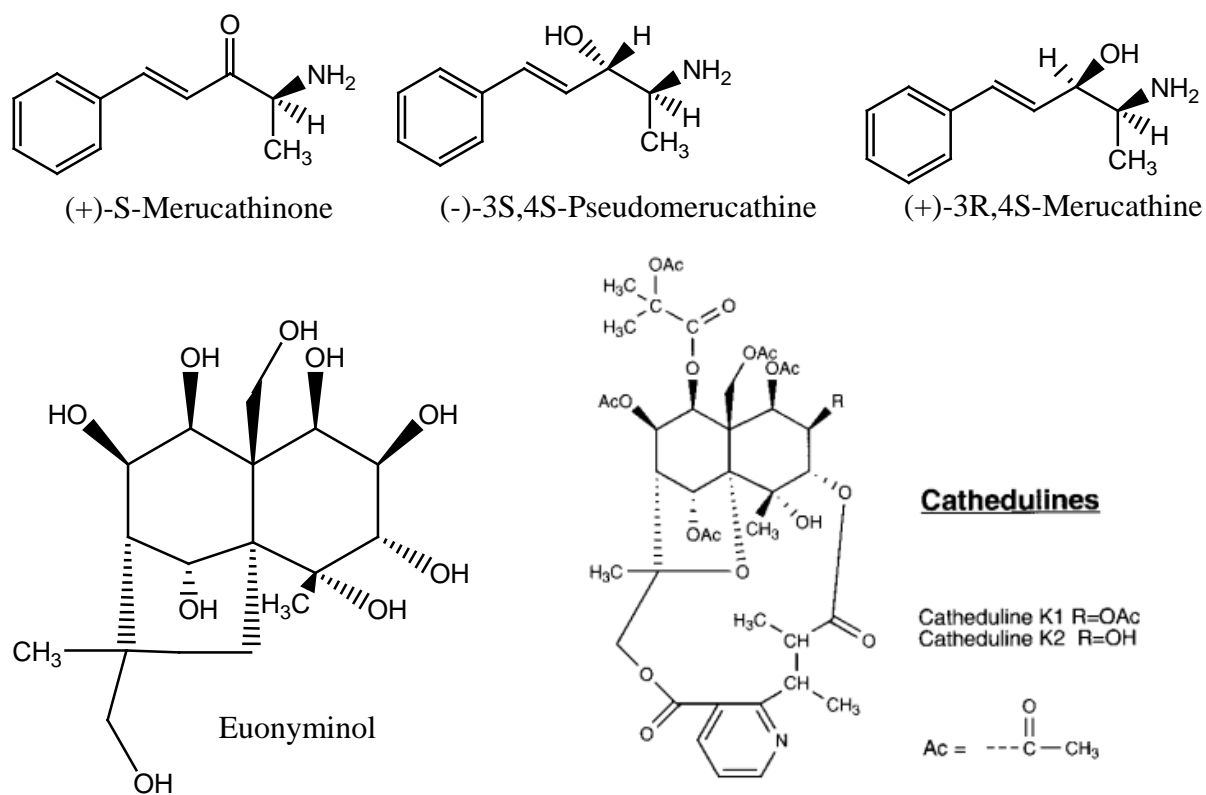


Figure 3: Chemical structure of the phenylpentenylamine and catheduline alkaloids from khat (*Catha edulis* Forsk) [27].

3. Health Hazards related to chat chewing

Over the years epidemiological and case control studies have indicated a clear association between long-term khat use and cardiovascular, respiratory, gastrointestinal, obstetric, metabolic, endocrine, and nervous system dysfunction [12]. Besides, the habit of khat chewing reinforces the development of other habits like cigarette smoking, and alcohol intake, leads to unnecessary expenses and wastes productive time of citizens.

The appetite suppressant effects of chewing leaves of the khat plant (*Catha edulis*) have been reported for several centuries. The predominant active ingredients of *C. edulis* are cathinone (1- α -aminopropiophenone) and cathine (D-nor-pseudoephedrine). These compounds share similarities with amphetamine, with up to 90% being absorbed during chewing, predominantly via the oral mucosa. Amphetamine-like compounds affect appetite centrally, by acting in the hypothalamus. Apart from its central effect, cathinone enhances sympathomimetic activity leading to a delay in gastric emptying [28].

Table 1: Reported and suggested adverse effects of khat in man

System	Adverse effects
Cardiovascular system	tachycardia, palpitations, hypertension, arrhythmias, vasoconstriction, myocard infarction, cerebral hemorrhage, pulmonary edema
Respiratory system	tachypnoea, bronchitis
Gastrointestinal system	dry mouth, polydipsia, dental caries, periodontal disease, chronic gastritis, constipation, hemorrhoids, paralytic ileus, weight loss, duodenal ulcer, upper gastro-intestinal malignancy
Hepatobiliary system	fibrosis, cirrhosis
Genitourinary system	urinary retention, spermatorrhoea, spermatozoa malformations, impotence, libido change
Obstetric effects	low birth weight, stillbirths, impaired lactation
Metabolic and endocrine effects	hyperthermia, perspiration, hyperglycaemia
Ocular effects	blurred vision, mydriasis
Central nervous system	dizziness, impaired cognitive functioning, fine tremor, insomnia, headaches
Psychiatric effects	lethargy, irritability, anorexia, psychotic reactions, depressive reactions, hypnagogic, hallucinations

Adapted from [6].

In addition, several studies revealed that cathinone, which is an active ingredient of khat increases heart rate, arterial blood pressure, HIV exposure, endocrine, genito-urinary systems and respiratory rate transiently. It also improves cerebral blood flow, mental alertness and increases energy [29,30]. In relation to this effect, regular

khat chewing is thought to be a predisposing factor for gastritis and peptic ulcer disease, mental illness (nervous system), cardiac arrhythmia, tooth decay and constipation [18,31]. Generally, the negative somatic consequences associated with khat use include: mucosal problems, hypertension, cardiovascular complications, duodenal ulcers, sexual dysfunction, hepatotoxicity and reduced birth weight of infants born to khat chewing mothers [32].

3.1. *Effects of khat chewing on the urinary bladder*

Khat induces a fall in average and maximum urine flow rate in healthy men. The urinary effects are probably mediated through stimulation of alpha1-adrenergic receptors by cathinone. This is indicated by the complete blockage of this effect by indoramin, a selective antagonist of alpha1-adrenergic receptors [27,33].

3.2. *Effects of khat chewing associated with dental problems*

Some researchers reported that long-term khat chewing caused stomatitis followed by secondary infection. These might be related to mechanical strain on the cheek and other oral tissues as well as chemical irritation of the mucosal surfaces. A high rate of periodontal diseases and low rate of dental caries has been observed among male Yemeni khat chewers [7].

According to Alsharabi [34], khat chewing caused many lesions to the supporting structures of the teeth, namely gingivitis, periodontal pocket formation, gingival recession, tooth mobility and tooth mortality. Khat chewing caused clicking or pain in the temporo-mandibular joints. This effect leads to attrition and staining of teeth and cervical caries, particularly among crystallized sugar consumers. Due to continuous mechanical friction and/or the chemical content, khat chewing caused white lesions on the buccal and gingival mucosa.

3.3. *Effects of khat chewing associated with gastrointestinal tract*

The digestive tract is mainly affected by the presence of tannins in this plant. Gastritis and constipation are some of the main complaints of its users; loss of appetite is also a characteristic of khat [35]. Khat chewing has also been reported to be a risk factor for duodenal ulcer formation. Delay to intestinal absorption contributes to some degree to malnutrition and may lead to liver cirrhosis. Tannins and norpseudoephedrine contribute to malnutrition and constipation, the most common medical complaint of the khat user [27].

3.4. *Effects of khat chewing associated with elevated diastolic blood pressure*

Khat typically is ingested while chewing the leaves. After ingesting Khat, the chewer experiences an immediate increase in blood pressure and heart rate. Various reasons have been given for chewing Khat. Most chewers used Khat to gain good level of concentration for prayer. Some chewers reported that Khat intake results in increased energy levels and alertness, enhances imaginative ability and the capacity to associate ideas, and improves the ability to communicate [35].

In a pharmacokinetic study, diastolic and systolic blood pressures were elevated for about 3 hours after chewing [26]. Khat chewing induces small and transient rises in blood pressure and heart rate. Cathinone (0.5 mg base/kg of body weight) has similar effects coinciding with the presence of cathinone in blood plasma. These effects could be blocked by the beta1-adrenoreceptor blocker atenolol, but not by the alpha1-adrenoreceptor blocker indoramin, indicating mediation through stimulation of beta1-adrenoreceptors [36].

3.5. Khat and reproductive health

There are suspected effects of khat on various reproductive health parameters such as fertility, pregnancy, and infant and child survival. Intrauterine growth retardation, low foetal birth weight and infant mortality are some of the most important reproductive health problems affecting most developing countries. Khat chewing during pregnancy is on the increase among women of reproductive age and questions have been raised on the potential effects of khat on foetal development [37].

Table 2: Possible effects of khat on various aspects of reproduction.

Reproductive organ/function	Khat extract	Effects
Semen volume	Cathinone	Reduced
Sperm motility	Cathinone	Reduced
Sperm count	Cathinone	Reduced
Abnormal sperm	Cathinone	Increased
Utero-placental blood flow	Cathine	Reduced
Post implantation losses	Methanolic khat extract	Increased
Maternal weight gain	Cathine & Methanolic khat extract	Reduced
Placental vascular resistance	Cathine	Increased
Maternal blood pressure	Cathine	Increased
Maternal myoendometrial blood flow	Cathine	Reduced
Sex organs size	Cathine	Reduced
Plasma testosterone	Cathino	Reduced
Fertility	Methanolic khat extract	Reduced
Potency	Cathinone	Reduced
Maternal milk production	Methanolic khat extract	Reduced

Adapted from [38].

Khat is genotoxic and has teratogenic effects on the foetus if regularly consumed by pregnant mothers. Since low birth weight is a well-established risk factor for both perinatal and young infant death, khat chewing during pregnancy may be one of the factors contributing to infant mortality in communities where khat is

commonly chewed. Khat consumption affects the potency of male sexuality by affecting spermatogenesis and plasma testosterone concentration. However, the precise mechanisms by which khat may affect the male reproductive physiology have not been elucidated [38]. Long-term and regular consumption of khat may also lead to progressive and diminished sex performance, and this suggests chronic consumption of khat may be the cause of sexual impotence [39].

4. Socio-Economic Hazards

4.1. Social

Khat chewing is a common habit in East Africa, South Saudi Arabia and among Yemenis. This habit involves picking tender leaves of Khat, putting them into one side of the mouth, chewing for a while and storing the chewed leaves in the same side of the mouth. Khat contains alkaloids of the phenylpropylamine type of which the main psychoactive constituent is S-(-)-aminopropiophenone (cathinone), [37]. People chew Khat to get psycho-stimulation effect in the form of euphoria and excitement resulting from the cathinone contents.

The guests are welcomed and carefully seated according to their social position. They then begin to masticate the leaves thoroughly one at a time while they engage in discussions and social interactions. During these sessions, the leaves and the bark of the plant are chewed slowly over several hours and the juice of the masticated leaves but not the residue is swallowed [7].

Khat chewing may obviously have attractive psychomotor-and rewarding effects such as euphoria, enhanced self-confidence and self-esteem, feeling of calm, peace and friendliness towards strangers, heightened sense of awareness, increased attention and concentration, increased energy, reduction of depression and physical fatigue the primary reasons for its regular use in Yemeni society are entirely different and this difference can be extended also to the majority of Arabian countries [22].

Among the various consequences of khat use are absenteeism and decreased productivity that frequently lead to unemployment. Furthermore, the purchase of khat puts a strain on family income and the detrimental social effects of the khat habit are felt within the family. The interaction with the father is adversely affected, since he is irritable and quarrelsome while under the effect of the drug or silent and withdrawn when the effect was worn off. Through its effect on the male reproductive system, the drug leads to progressive estrangement between husband and wife [40].

The evidence shows that the use of khat is associated with several social effects—both positive and negative. On the positive side, it serves as an employment opportunity and source of income for those involved in the cultivation and in the chain of the marketing process. It also serves as an export commodity for countries in which it is cultivated. On the other hand, it has been shown to be deleterious in terms of being a factor in family disharmony and breakdown, diverting household and individual income, resulting in delay and absenteeism from work and threatening food security.

4.2. Economic

Prior to the expansion of the Khat trade, coffee was the biggest crop in Yemen. Yemeni coffee trade peaked in the 17th and 18th centuries, but began to decline as a result of the competition of coffee production in Indonesia, South America, and East Africa. Now, as a result of national and regional demand, Khat is replacing coffee crops.

In Ethiopia, khat is widely grown not only for local use but also for export, which provides millions of United States dollars per year to the national economy [40]. So, Khat is Ethiopia's fastest growing export. In Ethiopia, over 93,000 hectares is devoted to Khat production, the second largest crop in terms of land area (coffee is first). Though Khat cultivation has taken over arable land because of its value, as a crop it is non-nutritious and unproductive". Khat is also cited as part of the problem for the economies of Ethiopia, Yemen, Djibouti and others, partly because, as statistics suggest, nearly every family spends one third of its disposable income on Khat [41].

In Djibouti, khat consumption is committed to be a luxurious habit since the material cannot be grown in the country and has to be imported. Mainly because of its availability, about 90% of men and 10% of women uses khat, either daily or occasionally. It is estimated that about 1/3 of all wages is spent on the purchase of khat [18].

The employment opportunity created through the cultivation of khat is very high in that large numbers of people are involved in growing, harvesting, sorting, packing, transporting, loading and unloading the commodity. The wood of the plant is commonly used for fuel and due to its resistance to termite is used in the construction of houses and fencing. It is also used for making rafters, handles of farm tools (hammers and chisels) and handles of household articles such as pots and pans, rolling pins, and to make forks, combs, spoons and for rulers [42].

5. Conclusion

The habit of chewing Khat leaves (*Catha edulis*) is widespread in certain areas of east Africa especially in Ethiopia. Some studies have shown that Khat contains chemicals which are active brain stimulant. It has pleasurable central stimulant properties, which are commonly believed to improve the capacity for work and counteract fatigue. There are concerns about health hazards related to the consumption of Khat. Intoxication with khat is self-limiting but chronic consumption can cause certain health disturbances such as sexual violence, HIV exposure, digestive tract problems, periodontitis and elevated blood pressure, in the user and also lead to social and economic damage to the individual and the community. Hence strong measures need to be taken for creating a greater awareness among the most common users as poor peoples, taxi and auto drivers, school students, college students and public in general.

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