

Medical aspects of the chewing of khat leaves

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The khat plant (Catha edulis) is produced in certain areas of East Africa and the Arabian peninsula, and the leaves are chewed for their stimulating effect. Fresh material, which is preferred by users, contains a substance that is rapidly converted to (+)-norpseudoephedrine. As a consequence of the traditional means of consumption, intoxication with khat is self-limiting but chronic consumption can cause certain disturbances to the health of the user and may also lead to social and economic damage to the individual and the community.

In 1935 the Advisory Committee of the League of Nations on the Traffic in Opium and Other Dangerous Drugs was confronted with the problem of khat, having before it two technical studies on the subject.² Neither of those reports proved or disproved clearly that the harmful effects were of an extent that would warrant international intervention. While no further action was taken by the international narcotics control authorities, the cultivation, sale, and use of khat were prohibited in British Somaliland (now part of Somalia) in 1921 and again in 1939 (*East Afr. med. J.*, 1945), and in Kenya in 1934 (Kenya Department of Agriculture, 1947).

The problem of khat was taken up again by the UN Commission on Narcotic Drugs in 1956.³ After having weighed the need for immediate action against the need for a prior investigation of the harmful character of khat, the Commission on Narcotic Drugs decided to postpone further consideration of any measures to be taken until the World Health Organization had studied the medical aspects of the habitual chewing of khat leaves. From the evidence available it became clear that the isolation of the active ingredient(s) should be undertaken before further experimental and clinical research into the pharmacodynamics of khat was carried out.

BOTANY, ECOLOGY AND CONSUMPTION

Details about the khat plant as a whole, and the circumstances and conditions of its consumption, will be referred to only in so far as they have a bearing on the effects in man.

Comprehensive data on the botany of the khat plant (*Catha edulis* Forsk.), which belongs to the family Celastraceae, are to be found in recent publications by Paris & Moyse (1957, 1958) as well as in a general survey (United Nations, 1956). Details about the ecology of khat and production statistics are given by Brooke (1960). It is noteworthy that the amounts of khat exported from Ethiopia and Yemen and the quantities imported by Aden (Southern Yemen) and French Somaliland (now the Territory of the Afars and Issas) have multiplied several times since 1947. This is partly the result of rapid transport by air, which is essential for the preservation of the fresh material. Kenya is less important than Ethiopia and Yemen as a khat-producing and exporting country. The fact that khat leaves can be harvested practically throughout the year has economic, sociocultural, and medical significance.

A wealth of information on the ways in which khat is consumed is available in the ancient literature. This material is of particular interest for sociocultural studies but these are outside the scope of the present report, which is concerned with the active ingredients and their biological action. Particular emphasis is given to the psychopharmacological effects of khat as the basis for an explanation of the overall effects of the whole plant on man.

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² League of Nations document O.C. 1617 (3 February 1936).

³ UN Commission on Narcotic Drugs (1956) UN document E/2891, paragraphs 16, 17, 24.

CHEMICAL CONSTITUENTS

Alkaloids of the phenylalkylamine (amphetamine) type

Among the first to find an alkaloidal fraction in the khat plant were Flückiger & Gerok (1887), who called it "katin", and Mosso (1891), who demonstrated that it had a stimulating effect on the frog's heart and caused dilatation of the frog's pupil. The first crystallized salts of this material were isolated by Beitter (1901). Stockman (1913) described two more fractions of an alkaloidal nature—namely, cathinine and cathidine. Only cathinine was obtained in a crystallized form as the sulfate. Neither could subsequently be identified as an individual substance different from cathine (as katin is now called), but both have been, and still are, referred to in many reports. Possibly one of them corresponds to (—)-ephedrine, which was isolated from khat leaves by Ristić & Thomas (1962) and chromatographically identified without any indication of the yield.

Wolfes (1930) succeeded in identifying cathine as (+)-norpseudoephedrine. This phenylalkylamine derivative had been isolated by Smith (1928) and Nagai & Kanao (1929) from the plant *Ephedra*, the biological effects of which are in many respects similar to those of khat. Subsequently, (+)-norpseudoephedrine was isolated by Paris & Moyse (1957), Alles et al. (1960), and Winterfeld & Bernsmann (1960), and identified with the synthetic compound.

Karawya et al. (1968) and Elkies et al. (1968) isolated from both fresh and dried khat leaves 5 alkaloidal fractions, designated as cathine, cathinine, cathidine, eduline, and ephedrine. Of these, cathine was identified as (+)-norpseudoephedrine; cathinine was very similar and, being present in larger amounts in fresh leaves, possibly a precursor. Cathidine was isolated in minute quantities and was impossible to identify. The fraction designated eduline was identified by the formation of an ether-soluble oxalate as distinct from the ether-insoluble oxalates of the other fractions. The content of cathine in dried material (leaves and tender twigs) of *C. edulis* has been determined by various methods of isolation and identification, as shown in Table 1.

Until a few years ago it was generally held that cathine was the only alkaloid of this type present in dried plant material of *C. edulis* and was not accompanied by any of its stereoisomers, by

Table 1. Cathine content of dried khat leaves of various origins

Country of origin	Cathine content (%)	Authors
Tanganyika	0.18	Paris & Moyse (1957)
Ethiopia	0.1	Alles et al. (1960)
Ethiopia	0.18 (total alkaloids)	Lemordant (1959)
Egypt	0.11 (total alkaloids)	Elkies et al. (1968)

ephedrine or its isomers, by other substances of a phenylalkylamine structure, or by other extractable bases in amounts that could account for the specific biological effects of khat. While Alles et al. (1960) and Hofmann et al. (1955) were satisfied that an estimate based on these effects seemed to confirm that cathine was the sole specific agent, Brücke (1941) had earlier concluded, from the comparatively small stimulating effect produced by cathine in mice and man, that the fresh plant contained a substance with a more powerful stimulating action. This conclusion was corroborated by the preference shown (and the higher prices paid) by khat consumers for the fresh material on account of its considerably greater central effects compared with the withered or dried plant, or preparations (infusions, decoctions, smoke) obtained from the latter. There was nothing to indicate whether cathine was a biotransformation product of the unknown substance in the fresh plant or whether they were chemically different substances.

A further search for a specific substance in the fresh plant having greater activity than cathine was then undertaken, the biological activity being checked throughout the chemical isolation. Since the subjective effects of the fresh and dried plant material are identical, the sought-for substance was likely to be similar chemically to cathine and therefore present in the basic fraction. Using the locomotor activity of mice as a biological test, and taking special precautions, Brilla (1962) and Friebe & Brilla (1963) succeeded in isolating another alkaloid from fresh leaves. It was obtained as the monooxalate in crystallized form. Following the experience of khat consumers that the leaves maintain their potency for about 4 days after harvesting, the plant material obtained from Ethiopia was not older than 3–5 days when it was freeze-dried

and processed. This precaution, and the care taken to avoid precipitating the free base, probably permitted the isolation of an alkaloid that differed from (+)-norpseudoephedrine in respect of its optical rotation and melting point, and had a similar, but stronger, locomotor effect in mice. A comparison of the new alkaloid with (+)-norpseudoephedrine is shown in the following tabulation.

	(+)-norpseudoephedrine (monooxalate)	new alkaloid (monooxalate)
α_D^{21}	+33°	+3.5°
melting range (°C)	168–170	145–150

Differences between (+)-norpseudoephedrine and the new alkaloid exist also with regard to their chemical stability. While the locomotor effect in mice of (+)-norpseudoephedrine was not changed by boiling for 60 min in aqueous solution at pH 11.5, the new alkaloid completely lost its locomotor effect when treated in the same way, and a change in colour and odour indicated chemical decomposition. While infrared spectrophotometry and paper chromatography did not permit a differentiation to be made between the new alkaloid and (+)-norpseudoephedrine, the difference between them was clearly shown by proton-resonance analysis, indicating that they differed in the molecular structure of the side chain attached to the phenyl group (H. Friebe, personal communication). The authors considered the new substance to be a labile precursor of cathine. It is not known whether the living plant contains both cathine and this precursor or only the latter and it is, therefore, not yet possible to relate the effects of the whole plant to those of the active principle(s) in a quantitative way.

Aminoacids

Winterfeld & Bernsmann (1960), using a freeze-dried hydrochloric acid extract of fresh khat leaves as starting material, separated and identified the following amino acids by means of ion-exchange and paper chromatography: asparaginic acid, threonine, serine, glutaminic acid, proline, glycine, alanine, valine, leucine, isoleucine, phenylalanine, tyrosine, α -aminobutyric acid, histidine, tryptophan, ornithine, and arginine. Choline was found by Alles et al. (1960) to the extent of about 0.05 % in the dried plant. Phenylalanine was shown by Leete

(1958) to be an intermediate in the biogenesis of cathine.

Tannins

C. edulis contains considerable amounts of tannins. While dry samples from Tanganyika (Paris & Moyse, 1958) and Yemen (El Sissi & Abd Alla, 1966) yielded approximately 14 %, similar samples from Ethiopia contained only about half that amount (Alles et al., 1960; Lemordant, 1959). The methods of estimation were, however, different.

Vitamins, minerals, etc.

The ascorbic acid content of khat is high; according to Mustard (1952) and the Nutrition Survey, Ethiopia (1959) 100 g of fresh leaves and sprouts contain 130–160 mg. The following tabulation derived from the Nutrition Survey, Ethiopia (1959) report gives the contents of minerals and other vitamins in 100 g of a mixture of fresh leaves and a small amount of tender stem.

ash	1.6%
fibre	2.7%
protein	5.2%
niacin	14.8 mg
thiamine	<0.05 mg
riboflavin	<0.05 mg
β -carotene	1.8 mg
calcium	290 mg
iron	18.5 mg

Alles et al. (1960) showed that it also contains a significant amount of magnesium.

Dulcitol was isolated from dry leaves by Ploccvier (1949) and El Sissi & Abd Alla (1966), while Alles et al. (1960) found reducing sugars (probably mainly galactose) to a total amount of 1.4 %. El Sissi & Abd Alla (1966) isolated the flavonols kaempferol, quercetin, and myricetin.

PHARMACOLOGY

Considering the nature and content of the various substances known to be present in khat, it is evident that compounds of the amphetamine type and the tannins are those that are particularly relevant to the effects of consumption of khat observed in man. The amounts of amino acids, choline, and minerals present in khat can not be expected to cause noticeable effects. The vitamins, especially the large amount of vitamin C, could

be expected to exert an influence only in cases of vitamin deficiency. Considering the quantities in which it is commonly consumed, the nutritional value of khat must be considered to be very low or insignificant.

The effects of khat extracts on small animals that were observed by some early investigators (Chevalier, 1911; Stockman, 1913) were of a sympathomimetic nature. This was corroborated when Wolfes (1930) identified cathine as (+)-norpseudoephedrine and when Friebel & Brilla (1963) found that the probable precursor of the latter had a similar chemical composition. For a comparison of the qualitative effects of khat with those of the pure substances referred to above, it is irrelevant, at this stage of our knowledge, whether the plant originally contains both substances or only the precursor. Their effects are qualitatively similar to the effects produced by both fresh and dried khat leaves.

The pharmacodynamics of (+)-norpseudoephedrine have been studied by Brücke (1941), Hofmann et al. (1955), Alles et al. (1960), Brilla (1962), and Friebel & Brilla (1963). Its peripheral and central effects were qualitatively identical to those of many amphetamine-like substances, and the difference between their optical isomers (i.e., the dextrorotatory form having stronger central stimulant or locomotor effects) was also the same. In mice, the locomotor stimulating effect of racemic norpseudoephedrine was found to be one-sixth that of (+)-methamphetamine, but higher than that of caffeine (Hofmann et al., 1955), whereas (+)-norpseudoephedrine was 10 times less potent than (+)-amphetamine in that respect (Fairchild & Alles, 1967). Van Rossum & Van Koppen (1968) found this ratio in rats to be of the same order of magnitude, while the biological half-life of (+)-norpseudoephedrine was about twice that of (+)-amphetamine.

These findings correspond well with observations made in human subjects; the subjective responses in man to (+)-norpseudoephedrine ranged from those produced by methamphetamine to those produced by caffeine (Hofmann et al., 1955). Alles et al. (1960) found in experiments with self-administration that after doses of 20 mg of (+)-norpseudoephedrine the subjective effects were minimal, but were more evident after doses of 40 or 60 mg (the latter dose perhaps being comparable with 10 mg of amphetamine sulfate).

Friebel & Brilla (1963) have shown that the locomotor effect in mice of the congener of cathine obtained from fresh leaves exceeds that of (+)-norpseudoephedrine, difference being statistically significant. They observed also qualitative differences in the dose-response curves, indicating that the substance isolated from fresh leaves loses its activity, *in vitro* as well as *in vivo*, more rapidly than (+)-norpseudoephedrine does. These differences could not be accounted for by differences in absorption since they were not influenced by changes in the route of administration (oral, subcutaneous, intravenous). Friebel & Brilla (*op. cit.*) also showed that the locomotor effects of the substance in mice was significantly less than that of (+)-amphetamine, when given in equimolar amounts.

Thus it is evident that khat and pure amphetamine-like substances produce similar clinical effects, their differences being due to slight pharmacodynamic differences between the stimulating principles, to certain constituents (mainly tannins) of the plant, and to differences in dosage, administration, and the circumstances, mostly environmental, under which the drugs are consumed.

The synthetic racemates of both the enantiomorphs, i.e., (+)-*cis*-norephedrine and (+)-*trans*-norpseudoephedrine, have been introduced as sympathomimetics for therapeutic purposes; the latter, which is racemic cathine, is also used as a central stimulant and anorectic agent.

CLINICAL EFFECTS

Descriptions of the clinical effects of khat have been given by Tanret (1933), Petrie & Seal (1943), Heisch (1945), Greenway (1947), Peters (1952), Hodgkinson (1962), Laurent (1962a, 1962b), Guedel (1965), Le Bras & Frétilière (1965), and El Guindy (1971). It is noteworthy that the effects produced by khat are described, almost completely, in ancient manuscripts, mostly of Arabic origin.

Somatic effects

Cardiovascular effects appear rapidly after the absorption of the active ingredients of khat; they consist of transient conjunctival and facial congestion, tachycardia and palpitations, sometimes with extrasystoles, and increased blood pressure to a level depending on the quantity of active material absorbed. Bradycardia and impairment of regulatory functions have also been observed.

Migraine, cerebral haemorrhage, myocardial insufficiency and infarct, and pulmonary oedema have been described after the intake of khat, particularly in older and predisposed individuals. The assumption that hypertension in young persons without other apparent etiology is due to the chronic intake of khat is supported by the observation that spontaneous regression occurs after consumption ceases.

Raymond-Hamet (1965) showed that an aqueous extract of khat leaves increases adrenaline-induced hypertension and renal vasoconstriction in the dog. The comparison by Rose & Tragisch (1963) of the circulatory responses to ephedrine with those to (+)-norpseudoephedrine in man are of interest inasmuch as the latter is an active constituent of khat. Schmidt & Klinger (1963) found that in rats (+)- and (—)-norpseudoephedrine were stronger circulatory and respiratory stimulants than ephedrine, and there was no difference between the stereoisomers.

An increase in respiration after the ingestion of khat can be interpreted as the result of stimulation of the respiratory centre and of bronchodilatation brought about by a peripheral sympathomimetic effect. Regulatory mechanisms against hyperthermia may also be involved.

Hyperthermia and sweating commonly occur in subjects soon after the chewing of khat begins. Since increased perspiration cannot be the result of a sympathomimetic agent, it must be interpreted as a consequence of the hyperthermia, and it is often enhanced by the high environmental temperatures that habitual khat chewers often prefer, and that are then artificially created. Hyperthermia is a well-known effect of amphetamines (Belenkii & Vitolina, 1961) and has been the cause of death when such drugs have been taken to increase athletic performance (Bernheim & Cox, 1967). Said (1968) observed hyperthermia after an extract of dried khat leaves was administered subcutaneously in rabbits.

Mydriasis is common in khat consumers. The regularity with which it is mentioned in publications coincides with the fact that dilatation of the pupil is a rather sensitive reaction for sympathomimetic substances. Lasting effects consequent upon chronic khat-induced mydriasis do not seem to have been observed. Racemic norpseudoephedrine has been used therapeutically for its mydriatic effect. Le Bras & Frétilière (1965) reported

decrease of the intra-ocular pressure after the chewing of khat which resembled that caused by amphetamines.

Stomatitis, oesophagitis, and gastritis are often encountered in chronic khat consumers and are probably due mainly to the presence of strongly astringent tannins in khat. Rosenzweig & Smith (1966) observed an exceptionally high rate of periodontal disease in Yemeni males who chewed khat. If malnutrition is present as a consequence of the habitual chewing of khat it may enhance these local inflammatory processes. A hypotonic or atonic stomach may well be the result of the sympathomimetic action of cathine and its precursor. Although it has not been proved experimentally, this effect can be inferred from the fact that ephedrine inhibits peristalsis and delays the emptying time of the stomach (Van Liere et al., 1936).

A common symptom in khat chewers is constipation. It is easy to understand that this is a result of the astringent effects of tannins, appreciable amounts of which are ingested, and of the sympathomimetic effect of the khat alkaloids. The causative connexion between khat and constipation is illustrated by the observation that when a ban was imposed on khat in Aden in 1957 the sales of laxatives decreased by 90% but returned to the original level soon after the ban was lifted. Meteorism and paralytic ileus are well known sequelae of khat chewing; usually there is spontaneous remission. The immediate relief given by physostigmine is evidence of their sympathotonic origin (Laurent, 1962a, 1962b). The inhibition of micturition that occurs in khat eaters is similar.

Petrie & Seal (1943) suspected that cirrhosis of the liver resulted from a heavy intake of khat, possibly in conjunction with other factors, such as an over-consumption of proteins alternating with periods of starvation.¹ This view has not so far been confirmed but it is plausible in view of the well-known hepatotoxic effects of tannic acid (Barnes & Rossiter, 1943).

Said (1968) described hyperglycaemia following the subcutaneous administration in rabbits of an extract of dried khat leaves. No change of the blood sugar level was found in man after the ingestion of khat (Le Bras & Frétilière, 1965); a functional hypoglycaemia was, however, prevented

¹ Young, K. D., Government Hospital Hargeisa, personal communication, 1959.

by the (+)-norpseudoephedrine (Hofmann et al., 1955).

Anorexia is a concomitant of khat chewing. Loss of appetite is a characteristic effect of amphetamine substances and synthetic (+)-norpseudoephedrine is used therapeutically for this purpose in single doses of 10 mg up to 4 times a day (Fischer, 1958). The mechanism of anorexigenic sympathomimetic drugs is not clear. Besides a possible direct effect on the hypothalamic "hunger" centre (Verzar, 1955; Andersson & Larsson, 1961), psychological processes such as a diversion of attention to food, could interfere with the feeling of hunger. Although direct gastric effects of khat do not appear to be involved in the suppression of hunger, gastritis and other troubles of the alimentary tract could very well be contributory factors. Nevertheless, anorexia is only one factor in the vicious circle: khat–destitution–hunger–khat–anorexia–malnutrition–digestive troubles–anorexia, etc.

Another currently observed symptom resulting from the interplay of physiological and psychological khat-induced changes is anaphrodisia. While this effect is also, but not regularly, observed following the administration of other amphetamine-like substances (Hill, 1947; Bonhoff & Lewrenz, 1954), it is mentioned in almost all ancient and recent reports on khat. Initially increased libido, probably of psychic origin, is sometimes reported. Most of the reports mention the occurrence of spermatorrhoea and subsequent impotence as a typical effect of the chronic use of khat. Loewe (1938) and Jaffe & Ellis (1958) observed analogous effects of amphetamine in mice. The increase in diuresis that is often reported appears to be the result of a high intake of fluids together with khat.

Psychic effects

The effects looked for in the main by khat chewers are psychic in nature and can be included in the category of central stimulation. The effects of khat are, at least for the observer, in the same class as those produced by amphetamine-like substances or caffeine (coffee). The differences between them are probably due to the special way in which khat is consumed, although the rapid onset of many of the psychic, as well as the organic, reactions to khat indicate a rather rapid absorption of the sympathomimetic agent. This question has not been systematically investigated, but the considerable capacity of the oral mucosa

to absorb a wide range of substances should be remembered.

Central stimulation by khat can manifest itself in euphoria, increased alertness, the enhancement and facilitation of associations, logorrhoea, hyperactivity, excitement, aggressiveness, anxiety, and hypomanic and manic behaviour. Insomnia almost always follows. All these symptoms are also produced by various substances of the amphetamine group. For a proper judgement of the severity of the effects produced by khat in comparison with those produced by amphetamines, the question of psychotic reactions resulting from intoxication should be examined. Amphetamine psychosis is a well-defined clinical state and has been described in great detail by Bonhoff & Lewrenz (1954), Connell (1958), Askevold (1959), and Hampton (1961). This syndrome occurred in epidemic-like proportions following the nonmedical use of amphetamines in Japan (WHO Expert Committee on Drugs Liable to Produce Addiction, 1956; Tatetsu, 1960).

Amphetamine psychosis resulting from intoxication (but not from withdrawal) is a paranoid reaction with delusions, auditory and visual hallucinations, acute anxiety, and ideas of superiority or persecution as the main features. It occurs after chronic use as well as after the administration of single doses of amphetamine, metamphetamine, and phenmetrazine, to name the more common substances of this class; the symptoms usually occur after large doses that exceed by many times the therapeutic dosage. Before the amphetamine etiology was known, such psychotic episodes were often, and are still, diagnosed as schizophrenia.

Whereas this type of toxic psychosis is characteristic of an excessive intake of amphetamines, it seems to occur much less frequently in areas where khat is consumed, even if consumption is heavy. In fact, personal inquiries in Harrar and Dire-Daua (Ethiopia), Djibouti, Somalia, Kenya, Aden, and the Yemen in 1959 gave the impression that toxic psychosis in khat consumers was very seldom, if ever, diagnosed in these areas. Cases like those reported by Carothers (1945) and Laurent (1962a, 1962b) seem to be rare. The former stated that in one of three cases he saw khat chewing had aggravated a preexisting psychosis. The latter compared the state of delirium occurring after the consumption of large quantities of khat with an amphetamine-induced psychosis, and added that in

such cases khat appeared to exaggerate natural tendencies and morbid predispositions. Margetts (personal communication, 1960) concluded from many years' experience in Kenya that khat taken in excess rarely causes toxic psychosis, but may precipitate the onset of a "functional" psychosis in a predisposed individual.

It is concluded that in relation to the amounts of amphetamines and khat consumed, and in relation to the numbers of users, a psychotoxic reaction is much less frequently produced by khat than by amphetamines, and the reaction is less severe when it does occur.

The rarity of khat-induced psychosis, as reflected by the scarcity of relevant observations and reports, can best be explained by the fact that the way in which khat is consumed does not permit the plasma level of the active sympathomimetic principle to rise high enough for a toxic psychosis to be produced.

With a very few exceptions, such as the self-experiments made by Alles et al. (1960) and trials carried out by Hodgkinson (1962), the effects of khat on man have been studied under the circumstances of ordinary use, i.e., with the addition of various beverages in large amounts. Thus, the stimulating, sedative, or diuretic effects, as the case may be, of water, coffee, tea, beer, and cola beverages, etc., are likely to enhance, or interfere with, the action of khat as such. The effects of simultaneous, and sometimes excessive, smoking, mainly of cigarettes, may also influence the symptoms produced by khat.

Tolerance to amphetamine and its derivatives (manifested through the tendency for users to increase the dose during prolonged periods of use in order to obtain the desired effects) can develop rapidly and to a high level. Individuals whose physical condition is apparently normal in spite of a daily consumption of 10 or more times the therapeutic dose of amphetamine, metamphetamine, or phenmetrazine, are not rare. On the other hand, tolerance to khat practically does not occur, as generally stated and recently confirmed by Laurent (1962a, 1962b) and Lemordant (1966). If it does occur the doses are increased only very slowly. 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.

Physical dependence, in the sense in which this is understood by Eddy et al. (1965) for drugs of the morphine or barbiturate types, does not occur after prolonged administration of amphetamine-like substances or khat. This is the consensus of opinion with regard to amphetamines (Leake, (1958) as well as to khat; for the latter, confirmation was provided most recently by Laurent (1962a, 1962b). Mental depression, sedation, or hypotension, which are sometimes observed after the withdrawal of both amphetamines and khat, are to be interpreted as rebound phenomena (or a reestablishment of the condition that initiated the use of the drugs) rather than as a specific abstinence syndrome.

Psychic dependence and craving are far more difficult to measure than an abstinence syndrome as a manifestation of physical dependence. A craving for amphetamines does not generally reach the level that is often observed with morphine-like drugs. In general, khat seems to behave in this respect like amphetamines, but its effect may be smaller. Reports from some areas that, traditionally, women do not use khat to the same extent as men (if at all) may throw some light on the relatively lower level of psychic dependence on khat in comparison with amphetamines.

For an appraisal of the status of khat in relation to the drugs that are subject to international control because of their harmfulness to both the individual and society, the principles established by the WHO Expert Committee on Drug Dependence (1969) for the initiation of control measures should be taken into account. Questions of tolerance to, and dependence on, khat arising under the prevailing conditions of its use should be assessed, particularly in comparison with other widely used and abused drugs with a central stimulant effect.

CONCLUSIONS

Although khat contains, in addition to amphetamine-like substances, various other compounds that produce medical effects, it can be considered as a drug of the amphetamine type.

As a consequence of the traditional mode of consumption, the dosage of khat is self-limited; such a limitation does not exist for drugs of the amphetamine type that are available in a chemically pure form for oral or parenteral administration. Hence, toxic psychosis as a result of excessive

use is much less frequent with khat than with amphetamines.

Besides certain disturbances to the health of the individual, the chronic consumption of khat can cause social and economic damage to both the individual and the community including the loss of working time, over-spending, and the possibility of subsequent malnutrition and the aggravation of disease. These features lead to a differentiation

between drug dependence of the amphetamine type and that of the khat type, as proposed by the WHO Expert Committee on Dependence-Producing Drugs (1965).

For a more detailed assessment of the effects of khat in comparison with other types of commonly used psychostimulants such as coffee, a complete analysis of the genuine active substance in the khat plant would be of great value.

RÉSUMÉ

ASPECTS MÉDICAUX DE LA MASTICATION DE FEUILLES DE KHAT

La présente enquête tire sa source des discussions de la Commission des Stupéfiants des Nations Unies sur les éventuels effets nocifs de l'usage chronique du khat. Le khat est constitué par les feuilles et les tiges tendres d'un arbuste, *Catha edulis*, de la famille des Célastracées, cultivé en Ethiopie, au Kenya et au Yémen, et est consommé par mastication dans diverses régions d'Afrique orientale et de la péninsule arabique. On trouve dans d'anciennes publications une description détaillée de ses effets, mais ceux-ci n'ont fait l'objet d'une étude poussée qu'après l'isolement et l'identification des principes actifs de la plante, la (+)-norpseudoéphédrine (cathine) et un précurseur biologique de structure chimique et de propriétés similaires, mais plus actif.

L'action de la cathine et de son précurseur est de type amphétaminique, avec excitation du système nerveux central et répercussions sympathicomimétiques périphériques. Parmi les principaux effets de la consommation de khat sur l'organisme, il faut citer: l'augmentation de la pression sanguine, la tachycardie, l'accélération du rythme respiratoire, l'hyperthermie, la mydriase, la

constipation, l'anorexie et la spermatorrhée. Du point de vue psychique, on peut observer de l'euphorie, de l'hyperactivité, de la logorrhée, de l'hypomanie, de l'anxiété, de l'anaphrodisie et de l'insomnie. Contrairement aux amphétamines, le khat suscite rarement des épisodes psychotiques toxiques de quelque importance, ce qui peut s'expliquer par les modalités de sa consommation.

Le khat contient des quantités appréciables de tanins, qui sont probablement la cause principale de la constipation, de la stomatite et de la gastrite. Sa teneur en acide ascorbique est élevée, mais les autres constituants (vitamines, sucres, sels minéraux, protéines) sont présents en faibles quantités et n'ont qu'un rôle physiologique et nutritionnel insignifiant.

Outre ses inconvénients éventuels pour la santé du consommateur, l'usage chronique du khat peut avoir des conséquences sociales et économiques: perte d'heures de travail, dépenses exagérées, malnutrition et réceptivité accrue aux maladies.

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