

Khat and synthetic cathinones: Emerging drugs of abuse with dental implications



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The rising global availability of the stimulant and euphoric substances, khat and synthetic cathinones, has become a cause for concern in many countries, including the United States. Both substances are illegal in United States, although this has not deterred their use. Besides central nervous system effects, these drugs also cause sympathomimetic and orodental adverse effects, similar to those of amphetamine. Although synthetic cathinones are stronger than khat in most cases, the latter additionally contains tannins, which have astringent effects on tissues components, including those in the oral cavity. Recognizing the use prevalence and reported orodental adverse effects of khat and synthetic cathinones, dental practitioners should be more familiar with these substances to optimally treat and educate their patients abusing them. This paper reviews the pharmacology and adverse effects of khat and synthetic cathinones, along with the extent of their use in United States, with particular emphasis on dental implications. (Oral Surg Oral Med Oral Pathol Oral Radiol 2018;125:140–146)

Khat is an evergreen shrub widely grown in parts of Eastern Africa and southwestern Arabian Peninsula.¹⁻⁵ Its fresh leaves are typically chewed for their stimulant and euphoric effects, and the habit of chewing khat in these regions is regarded a deep-rooted practice, especially among members of the Muslim community.¹⁻³ The majority of khat chewers are adult males, who usually participate in khat group sessions almost every day for a number of years.¹⁻³

There has been an increase in regional khat consumption during the past several decades, and the availability of khat has also expanded to many other places.¹⁻⁵ The World Health Organization and others have estimated that more than 20 million people chew khat on a regular basis worldwide.⁶⁻⁸ This new development has been facilitated by increased number of immigrants from khat-producing areas and by improved methods of khat transportation and distribution.^{1,9,10}

It has been determined that khat leaves contain more than 40 different compounds; contain 3 phenylalkylamine alkaloids (identified as cathinone, cathine and norephedrine); and have stimulant, euphoric, and sympathomimetic effects, among others.^{11,12} Of these, cathinone is the most efficacious, contributing to nearly all of the central nervous system (CNS) effects of khat, for which it is primarily consumed. Unrelated to the alkaloids, khat leaves also contain another group of bioactive compounds known as *tannins*, which possess astringent effects.^{8,13} Both the alkaloid and tannin components have been reported to contribute to the orodental adverse effects associated with khat chewing.

On the basis of the structure of khat's cathinone, analogues have been synthesized since the 1920s, following

the lead of Europe.¹⁴⁻²⁰ These are a group of recreational drugs that only came to the attention of U.S. authorities in 2010 under the popular name “bath salts.”^{14-16,18-23} Because of strict regulations, these products are largely synthesized in underground laboratories and made available to users on illicit markets. Apart from having similar actions as the natural cathinone, these drugs also share most of the pharmacologic/toxicologic properties of amphetamine and related compounds. To date, more than 40 different chemicals have been identified as synthetic cathinones in the United States, and many of them are used as cheap substitutes for other more widely abused and tightly regulated stimulants. In addition to CNS stimulation and euphoria, synthetic cathinones also induce multiple additional effects, including sympathomimetic and orodental adverse reactions.^{14,15,19,20,22-24}

Among the synthetic cathinones identified so far, some are more commonly used than others, and these include mephedrone, methylone, methcathinone, 3,4-methylenedioxypropylvalerone, naphyrone, butylone, pentadron, 4-fluoromethcathinone, pyrovalerone, and methedrone.^{14,15,21} These drugs are synthesized in the form of a white or brown crystal-like powder and sold to consumers usually in small plastic or foil packages of 200 to 500 mg, labeled as “bath salt” accompanied by the phrase “not for human use.”^{18,19,23} In some cases, products sold are concealed with some other deceptive labels, such as “plant food,” “jewelry cleaner,” “insect repellent,” and “phone screen cleaner,” together with appealing brand names to make them even more attractive. Besides the powder form, products are also available in other

Statement of Clinical Relevance

Khat and synthetic cathinones are emerging drugs of abuse that cause multiple central and peripheral adverse effects with considerable dental implications of which oral health care professionals need to be aware.

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formulations, such tablets and capsules. With improved synthesis and marketing efficiencies, there appears to be a recent trend toward a rapid increase in availability of synthetic cathinones in many parts of the world, including in North America, Europe, and Asia.^{18,19,21,23}

Given the potential health risks associated with the abuse of khat and synthetic cathinones, the increasing availability of these substances has become a cause for growing concern. This paper reviews the pharmacology and adverse effects of khat and synthetic cathinones, with particular emphasis on dental implications, along with the legality and extent of their abuse in the United States. Because previous reviews on khat and synthetic cathinones in relation to oral health were very limited in both quantity and scope, the current work was intended to provide a more comprehensive and updated information based on the literature from credible sources.

PHARMACOLOGY AND ADVERSE EFFECTS OF KHAT AND SYNTHETIC CATHINONES

Among the 3 types of psychoactive alkaloids in khat, cathinone has been reported to be the most active as a stimulant, euphoric, and sympathomimetic substance, acting like amphetamine, although to a lesser extent.^{6,18,21,24} Its mechanisms of action as a stimulant and a euphoric compound are mainly related to enhancement of neuronal release of dopamine and norepinephrine, and inhibition of the metabolizing enzyme, monoamine oxidase.^{5,6,25-27} Through both mechanisms, synaptic concentrations of the monoamines are increased, resulting in enhanced activity. There are also reports indicating augmented release of serotonin by cathinone, but the significance of this is not clear. Apart from these effects, norepinephrine accumulation in peripheral adrenergic synapses causes

increased responses of different target tissues, more notably the cardiovascular system.^{5,6,25-27}

It has been reported that largely on the basis of the above mechanisms, khat/cathinone causes both acute (short-term) and chronic (long-term) central, peripheral, and oral adverse effects, depending on the amount used and the duration of use. These effects are a reflection of augmented CNS and sympathomimetic responses linked to levels of synaptic neurotransmitters.

Tannins present in khat leaves are a group of polyphenolic biomolecules that form complexes with different macromolecules, especially proteins, potentially affecting functions of tissues that they come in contact with.^{13,28,29} Therefore, besides the effects of the phenylalkylamine alkaloids, khat chewing produces additional adverse effects on tissues in the oral cavity, the gastrointestinal (GI) system, and the liver as a result of the release of tannins.^{13,28,30,31}

The specific effects manifested in different parts of the body as a consequence of khat chewing are summarized in Table I. It is evident that at least part of the actions of khat mediated via CNS stimulation, peripheral sympathetic activation and the astringent effects of tannins contribute to the development of the orodental conditions listed.^{5,12,13,24,27,28,31,32} Furthermore, it has been reported that the physical impact of forceful and persistent khat chewing, per se, can be an additional factor contributing to orodental disorders.^{6,14,31} As mentioned earlier and reported previously, it is predictable that the magnitude and/or nature of the orodental effects induced can vary with the amount of khat chewed and the duration of the chewing habit.^{12,13,26,28,30-34} The different orodental effects of khat chewing reported include dry mouth/xerostomia, bruxism, caries, periodontal diseases, tooth/occlusal wear,

Table I. Reported orodental and systemic effects of khat chewing*

<i>Orodental manifestations of khat chewing</i> ^{13,26,28,30-32}	<i>Systemic effects of khat chewing, some with potential influences on dental management</i> ^{2,5,6,8,11,12,14,25-27,33-37}	
	<i>Short-term/intermediate effects</i>	<i>Long-term effects</i>
<ul style="list-style-type: none"> • Dry mouth/xerostomia • Caries • Periodontal disease/lesions and gingival recession at site of chewing • Mucosal white lesions and/or dark pigmentation • Oral trauma, ulcers and burning sensation • Bruxism • Occlusal wear • Difficulty in opening mouth/trismus • Difficulty in swallowing • Temporomandibular joint dislocation • Oral mucosal keratosis, cancer 	<ul style="list-style-type: none"> • Mild euphoria and excitement • Alertness and relief of fatigue • Insomnia • Improved ability to communicate and talkativeness • Dizziness, lethargy, depression, headache (migraine) • Fine tremor post khat session • Psychotic reactions at high doses • Irritability • Hallucinations, mostly at end of khat session • Inability to concentrate • Anorexia • Tachycardia, vasoconstriction, increased blood pressure • Hyperthermia, perspiration, tachypnea, polydipsia • Impotence, libido change (mostly in men) • Mydriasis, blurred vision • Constipation • Hyperglycemia (inconsistent) 	<ul style="list-style-type: none"> • Gastrointestinal disorders, including stomach ulcers, inflammation, constipation, increased risk of upper gastrointestinal tumors, hemorrhoids • Malnutrition and weight loss • Psychosis, depressive reactions, impaired cognitive functioning • Increased cardiovascular disorders, myocardial infarction, heart attack, cerebral hemorrhage • Liver cirrhosis, fibrosis • Pulmonary edema, bronchitis • Impaired male sexual function, impotence

*The nature and intensity of effects can vary with amount and duration of khat chewed.

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