

The presumed neurotoxic effects of *Catha edulis* – an exotic plant now available in the United Kingdom

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SUMMARY Bilateral optic atrophy is reported in two patients who, although they were long-standing users of the leaves of *Catha edulis*, had chewed larger quantities than usual. Since the leaves of this plant are used widely throughout its native area as the source of a mildly stimulant narcotic, the effect in these cases may be an idiosyncratic reaction to an unusually large dose.

Case 1

A 32-year-old Somali male had worked as a medical assistant in Somalia. After returning from a medical expedition in a remote area of the country he described a period of abnormally large ingestion of a local leaf known as khat, though he had chewed smaller quantities since childhood.

The patient had spent three days relaxing with two friends and chewing khat. The quantity used was considerably more than was usual either for the patient or generally. He obtained little sleep during these three days but after this slept almost continuously for 36 hours. Before sleeping he had noticed a slight blurring of vision, but he attributed this to fatigue. On waking, the visual disturbance had increased, and the description of symptoms suggested bilateral scotomas. These symptoms increased over the next three days and had apparently remained static since then. Both eyes were affected equally.

The patient suffered no pain and was certain that he had not been subjected to any trauma. There was no history of exposure to any neural toxin other than tobacco and alcohol. Alcohol intake was minimal, amounting to an occasional drink of commercial gin, and he had had none for at least seven days before the visual symptoms appeared. He was a moderate smoker of good quality commercial cigarettes. Diet had remained normal throughout the period. One of the other participants in the khat session had also suffered some visual defect, but he remained in Somalia when the patient came to Britain and has since perished in an air raid.

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The patient was a tall, well-nourished negro male. Right visual acuity was hand movements and left was counting fingers, both eccentrically at half a metre. He was virtually emmetropic, and refraction did not improve his vision. Anterior segment examination of each eye was normal, and intraocular pressures were 14 mmHg in each eye. There was no demonstrable afferent pupil defect, and although pupillary light reflexes were sluggish on each side they were symmetrical.

Gross bilateral optic atrophy was present, with pigmentary anomalies at each disc, but no elevation. Blood vessels and retina appeared normal, save for an obvious paucity of retinal nerve fibres in the papillomacular bundle on each side on red-free ophthalmoscopic examination.

Vision field examination was difficult, but with large targets bilateral central scotomas, breaking out into the periphery, were demonstrated. The patient's mobility and behaviour were consistent with this form of visual field defect. Routine haematology scan, VDRL and the fluorescent treponema antibody absorption tests were normal, save for a band of HbA on electrophoresis. Fluorescein angiography was normal apart from gross lack of perfusion in the small vessels of both optic discs. There was a reduction of the electroretinogram (ERG) on flash stimulation. Skull radiography was normal. Since the patient suddenly decided to return to Somalia, a visual evoked response and further neurological examination were not performed. There is no prospect of follow-up.

Case 2

This patient was a 27-year-old Arab who had lived

most of his life in a small Yemeni community in South Wales. He attended casualty accompanied by his brother, complaining of decreased vision in each eye. He first noticed blurring of vision three months earlier, and it had become worse over a period of approximately one week. Since then his vision had remained static.

His visual acuities were 6/36 left and 6/60 right eye, and he had no significant refractive error. Anterior segment examination was normal and intraocular pressures were 11 mmHg in each eye. Pupillary light reflexes were grossly normal, if rather sluggish. Retinal vessels were normal, but there was a reduction in nerve fibres of the papillomacular bundle in each eye on red-free ophthalmoscopic examination. Both discs were atrophic. Visual fields showed central scotomas. Routine blood scan and skull x-rays were normal.

The patient neither smoked or drank alcohol and he had had no serious illness. He took no drugs, but he and his brother admitted chewing imported khat leaves since childhood within the family group. On inquiry the patient said that during the week preceding the onset of visual symptoms he had been staying with friends. These friends had a large quantity of fresh khat leaves, and during this week he had used a much larger quantity than ever before.

An outpatient appointment was made for further investigations, but unfortunately he failed to attend and efforts to trace him were unsuccessful.

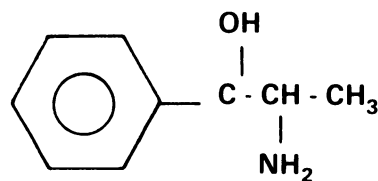
Discussion

Catha edulis Forsk., or khat, is a member of the family Gelastraceae and has been grown for centuries in parts of eastern Africa and southern Arabia. The fleshy, pinnate leaves are chewed by millions of inhabitants of these countries for the drug's ability to produce euphoria, combat fatigue, and as part of social gatherings.¹ Khat grows at 3000 to 6000 feet (900–1800 m) above sea level and reaches a height of 20 feet (6 m). It is a thirsty plant but can survive drought, and the leaves can be harvested throughout the year. The plant is seedless, and this may explain its limited distribution.²

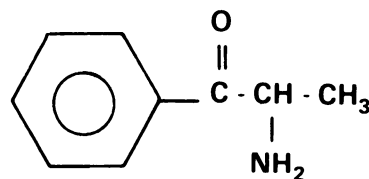
Extensive thin-layer and gas-liquid chromatographic analyses of the fresh leaves of the khat plant have isolated three major compounds: cathine ((+) norpseudoephedrine or phenylpropanolamine), cathinone ((-) alpha-aminopropiophenone), and (-) norephedrine.^{3,4} Fig. 1 shows the similarity in chemical structure between cathine, cathinone, and amphetamine.⁵ In addition there are vitamins, minerals, and considerable quantities of tannins. Cathine was identified in 1930, and for a long time it was considered to be the only active stimulant in

khat.⁶ Cathinone was isolated in 1975. It is a ketone congener of cathine, and it is now believed that it is the main active principle responsible for khat's stimulant properties.

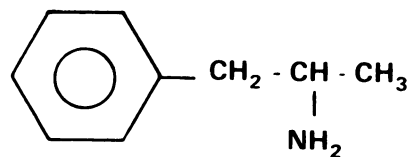
Khat induces amphetamine-like sympathomimetic and central stimulant effects in users. The pharmacological effects include mydriasis, pseudoexophthalmos, tachycardia, extra systoles, hypertension, conjunctival congestion, headaches, and increased respiration. Anorexia and insomnia are also common in habitual users. It has been reported that the central artery pressure is increased up to three times the usual value after khat use.⁷ Chewing khat leaves has been shown to cause a reduction of intraocular pressure in both normal and glaucomatous patients in two or three hours.^{8,9}



cathine [(+) - norpseudoephedrine]



cathinone [(-) - α - aminopropiophenone]



amphetamine

Fig. 1 Structural formulae.

Schizophrenic behaviour has been observed during and after khat use, like the schizophrenia and paranoia following chronic amphetamine absorption.¹ A mania-like psychosis was reported in an Arab student in the USA after he had been seen to chew 24 leaves of a houseplant. The plant was later identified as khat.⁵ A similar case of khat-induced schizophreniform psychosis has been reported in a member of a Yemeni community in Liverpool, and there are small Yemeni groups in several South Wales seaports. These have sustained the khat habit and have taught succeeding generations to use it. It is imported regularly by air and stored in domestic deep-freezers without loss of activity.¹⁰

There are no previous reports of khat-induced optic atrophy in the ophthalmological literature, but there was a report of optic neuritis in two khat addicts in Somalia in which vision and optic disc oedema improved after withdrawal of khat.¹¹

The two patients described in this report had an unusually high intake over several days. Thereafter they suffered bilateral and rapidly progressive visual deterioration which remained apparently unchanged. Since diet, alcohol, or tobacco intake were unlikely to be causative, it appears likely that this neurotoxic reaction was a direct result of ingestion of an unusually high dose of khat alkaloids. The reduced ERG in case 1 suggests some retinal toxicity and not merely a toxic optic neuropathy.

Since khat has been used so extensively for many centuries, such reactions must be rare. However, as the plant is now available in the United Kingdom, it should be considered in cases of optic nerve disease in patients of African or Arabian origins.

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