

HYPERMOTILITY OF THE AMPHETAMINE TYPE INDUCED BY A CONSTITUENT OF KHAT LEAVES

PETER KALIX

Département de Pharmacologie de l'Université, Rue Ecole-de-Médecine 20,
CH 1211 Genève 4, Switzerland

Khat leaves, widely used as a stimulant in East Africa and the Arab Peninsula, contain the alkaloid, (–)-cathinone. The effects of this substance on the locomotor activity of rats were compared to those of (+)-amphetamine. Both substances were found to induce a similar degree of hypermotility. Furthermore, the effect of (–)-cathinone on the locomotor behaviour of hypophysectomized rats was analogous to that reported for (+)-amphetamine in such animals. The results support the claim that the symptoms caused by the chewing of khat are amphetamine-like.

Introduction For many centuries, fresh leaves of the khat shrub (*Catha edulis*, Celastraceae) have been chewed by people in East Africa and the Arab peninsula in order to alleviate the sensations of hunger and fatigue. However, in recent years, due to the availability of air transport, the habit has spread beyond the areas of cultivation of the plant. Since the resulting socio-economic phenomena were seen as detrimental both to the individual and to the community, the World Health Organization became concerned with the problem (WHO Technical Report, 1964) and the United Nations Narcotics Laboratory has made studies (UN Documents, 1974–77) and collaborated in others (Baxter, Crombie, Simmond & Whiting, 1976; Schorno & Steinegger, 1979) with the purpose of identifying and isolating the active constituents of the plant.

Khat leaves contain several alkaloids that belong to the phenylalkylamine group (Halbach, 1972) of which (–)-cathinone is considered the most active. (–)-Cathinone, or S-(–)- α -amino-propionophenone, is a compound that is different from (+)-amphetamine only in that the methylene group in the α -position of the side chain is substituted by a carbonyl group. The substance was recently synthesized by the UN Narcotics Laboratory (UN Document, 1978) and shown to be identical to the alkaloid extracted from khat (Schorno & Steinegger, 1979). A direct comparison with amphetamine has thus become possible and preliminary observations (J. Knoll, personal communication) suggest that the two substances are pharmacologically quite similar. Since the behavioural effects

caused by the chewing of khat resemble those of amphetamine (Halbach, 1972), it seemed of interest to compare the effects of these two substances on locomotor activity in an animal model.

Methods The experiments were performed on female Wistar rats weighing 200 to 240 g and obtained from Iffa-Credo, Lyon, France. Some of them had been hypophysectomized under light ether anaesthesia through the transauricular route 3 to 6 weeks before the experiments. The animals were housed in a temperature controlled room with food and water provided *ad libitum*. The room was lighted from 17 h 00 min to 07 h 00 min; the experiments illustrated in Figure 1 were performed during the dark period. For these experiments the animals were placed individually in a locomotor activity cage of the Ugo Basile type that was connected to a printing counter which cumulated the number of impulses for consecutive 4 min periods. (–)-Cathinone hydrochloride and (+)-amphetamine sulphate, dissolved in 0.3 ml saline, were injected intraperitoneally. Each animal was used for only one experiment.

Results An injection of 25 mg/kg (–)-cathinone hydrochloride was found to result in a rapid and strong stimulation of the locomotor activity of rats. It also induced an increased sensitivity to audiogenic stimulation as well as periods of compulsive gnawing. When the dose was reduced to 10 mg/kg, the latter effect disappeared, but a quite high level of motor activity persisted. Quantification of the hypermotility induced by (–)-cathinone revealed that the effect of a given quantity of (+)-amphetamine, as determined in parallel experiments, could be reproduced by an only three times greater dose of (–)-cathinone (Figure 1a). The effect of (–)-cathinone lasted longer than that of (+)-amphetamine, i.e. approximately 5 h.

Recent studies (Benakis, 1978) of the effects of (+)-amphetamine on hypophysectomized rats revealed a specific modification of the hypermotility

pattern as compared with normal rats, i.e. a slow onset of the stimulatory effect followed by a rapid rise to a much higher level of stimulation. In the present study, similar experiments were carried out on hypophysectomized rats to test the effect of (–)-cathinone. The results showed a modification of locomotor activity that was very similar to that described for (+)-amphetamine. As shown in Figure 1b, there was no noteworthy effect during the first hour, after which the stimulation level rose rapidly to twice that of

unhypophysectomized rats and remained at that high level for approximately 2 h.

Discussion The three essential findings of the present study are that (–)-cathinone causes modification of the locomotor behaviour of rats that are quite similar to those induced by (+)-amphetamine, that the potency of (–)-cathinone in this respect is comparable to that of (+)-amphetamine and that the loco-

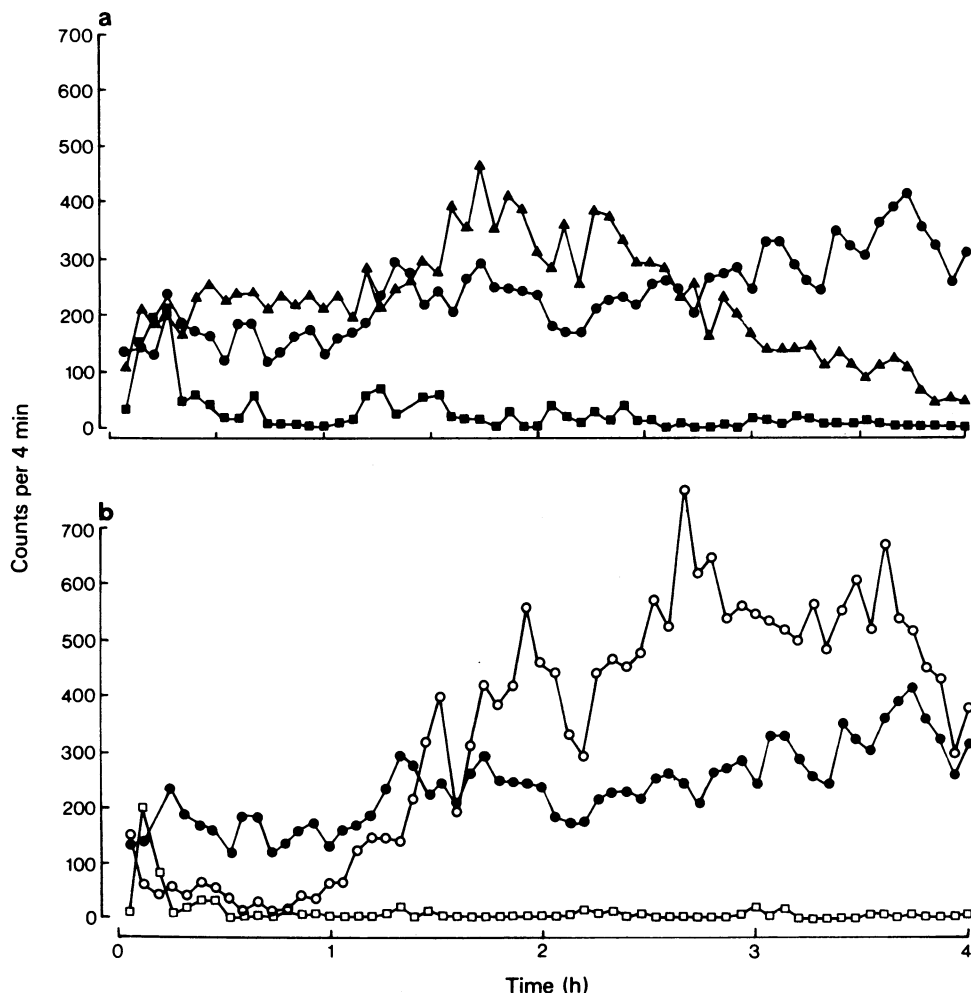


Figure 1 (a) Effect of (–)-cathinone hydrochloride (●) and (+)-amphetamine sulphate (▲) on locomotor activity of rats. Injections were made at zero time; the control animals (■) received saline. The doses administered were 10 mg/kg (–)-cathinone hydrochloride and 5 mg/kg (+)-amphetamine sulphate, corresponding, respectively, to 8.33 mg/kg and 2.87 mg/kg of the free base. The points indicate the number of impulses counted for 4 min periods and represent average values for 3 (■) or 4 (●, ▲) experiments. (b) Effect of (–)-cathinone hydrochloride (10 mg/kg) on hypophysectomized (○) and on 'normal' rats (●), (curve taken from a). Hypophysectomized control animals (□) received saline injections. The points indicate the number of impulses counted for 4 min periods and represent average values for 3 (□) or 4 (○, ●) experiments.

motor behaviour of hypophysectomized rats after injection of (–)-cathinone is analogous to that induced by (+)-amphetamine in such animals. Although the effect of the khat alkaloid on other behavioural parameters remains to be evaluated, the results clearly support the claim that the effects of the chewing of khat are amphetamine-like.

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