Research on the Chemical Composition of Khat

Braenden, O. J.

At its 24th session, the Commission on Narcotic Drugs requested that the United Nations Narcotics Laboratory should carry out research on the chemical composition of khat, such research being fundamental for the subsequent evaluation of the effects on health and society caused by the chewing of khat.

Early literature on the chemistry of khat gives no information on the degree of freshness of the material used. This is an important factor because, in practice, khat is used only when fresh. Until recently the only well-characterized component of khat was cathine ((+)-norpseudoephedrine). The stimulating effects obtained from the chewing of khat were associated exclusively with the presence of cathine, but this could not be substantiated because of marked differences between the activities of fresh material and cathine.

The UN Laboratory therefore made an intensive study of the chemical composition of khat, using fresh material. Staff members visited Kenya, Madagascar, and the Yemen Arab Republic where they purchased fresh khat and immediately extracted this with suitable solvents. At the same time, khat material was freeze dried.

Thin layer and gas chromatographic analysis of extracts showed the presence of a number of nitrogen-containing components that were previously unknown in the plant. These compounds were separated into two major groups: the phenylalkylsmine derivatives and the weakly basic alkaloids.

A study of the phenylalkylamine fraction showed that, in fresh or well-preserved khat material, cathine was only a minor component. However, in each sample, a new compound was found and its chemical structure was established as (-)-α-aminopropiophenone. As this compound had not previously been reported in nature, it was tentatively assigned the designation "cathinone". Cathinone base is very unstable and essily under es decomposition reactions leading to the formation of a "dimer" (3,6-dimethyl-2,5-diphenylpyrazine) and possibly smaller fragments such as benzaldehyde and ethylamine. Further decomposition may lead to 1-phenyl-1,2-propanedione. Both the "dimer" and the latter compound have been isolated from khat

extracts. The absolute configuration of cathinone was established by Schorno and Steinegger 1978. The UN laboratory also synthesized racemic cathinone using the method of Gabriel 1908, with some modifications. From this, the optically active isomers and the "dimer" were prepared. Other minor compounds were also identified in the amine fraction.

The fraction containing the weakly basic alkaloids was found to have a very complex composition. More than forty alkaloids have so far been detected in khat by thin layer chromatography. Some of the major components in this group were isolated. Structures were proposed for eleven alkaloids and further structures are being established. In this work, the UN Laboratory collaborated closely with Professor L. Crombie and his group at the University of Nottingham, where considerable work has been done in this field (Baxter et al. 1976, Crombie et al. 1978). With two exceptions, all the alkaloids thus far isolated from khat have had a common hydroxylated sesquiterpene skeleton (euonyminol) which is esterified with various acids. The common name "cathedulin" was proposed for this class of alkaloids.

In November 1978, the UN Laboratory convened a group of experts to review present knowledge of the botany and chemistry of khat and to prepare guidelines for future research in these fields. The report of this group includes an annex listing all the substances that have been isolated from khat together with their structural formulae. The UN Laboratory is now concentrating its attention on the preparation of adequate amounts of certain khat components for the pharmacological studies being carried out under the auspices of the World Health Organization.

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AUTHOR

Olav J. Braenden, Cand.pharm., Ph.D.,
Director, United Nations Narcotics Laboratory
Palais des Nations
CH-1211 Geneva 10, Switzerland