MYRISTICA FRAGRANS (NUTMEG)

Introduction

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The idea of publicly discussing as a psychotropic agent a commonly available household spice such as nutmeg (*Myristica fragrans*) presents many questions and problems. There is a paramount concern about promoting unscientific experimentation and abuse by the laity, but this seems to be easily preventable by simultaneously enumerating the toxic effects of nutmeg, which are quite unpleasant. One might question the need for study of an additional candidate drug for an already overstocked field, ask how such a discussion could yield new insights into mental processes and possible therapeutic gains from the investigations.

Myristicin (3-methoxy-4, 5-methylenedioxy allyl benzene), the largest component in the volatile oil fraction, has been implicated as the hallucinogenically active agent in nutmeg. If so, it is chemically unique in lacking a nitrogen atom. Its chemical similarity to mescaline (3,4,5-trimethoxy phenylethylamine) is also striking.

The Chemistry and Psychopharmacology of Nutmeg and of Several Related Phenylisopropylamines

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A complete chemical analysis of the volatile fraction of the nutmeg seed (*Myristica fragrans*) is reported, as is a proposed mechanism of the participation of several of these components in the psychotomimetic intoxication resulting from the ingestion of nutmeg.

Chemical analysis of the oil was achieved by the combined procedures of fractional distillation and preparative gas-liquid chromatography. The presence and proportions of the principal aromatic components (myristicin, elemicin, and safrole) is reported for a number of different samples of both nutmeg and mace representing several sources. Several previously unreported hydrocarbons were found (sabinene, γ-terpenoline, and toluene), but some chemicals (cineole, camphor, citronellol, citronellal, and *d*-borneol) which have previously been reported present in oil of nutmeg were not detected in any of the samples investigated.

In the evaluation of those compounds present which might be responsible for the psychoactivity of nutmeg, attention was focused on the aromatic fraction, because several of the compounds therein have ring-substituents identical both in nature and in position to those of known psychotomimetics. The three major constituents (myristicin, elemicin, and safrole) occur together in nature only in nutmeg. A hypothetical addition of ammonia to the olefinic side chain of each would result in the formation of 3-methoxy-4,5-methylenedioxyamphetamine (MMDA), 3,4,5-trimethoxyamphetamine (TMA), and 3,4-methylenedioxyamphetamine (MDA), respectively. All three of these phenylisopropylamines are known to be more potent psychotomimetics in man than mescaline, and their combined action provides a quantitatively acceptable explanation of the activity of nutmeg. The qualitative aspects of the natural intoxication can be accounted for by the hallucinogenic syndrome of each of the several synthetic bases mentioned.

A complete series of all the possible methoxy- and methylenedioxyphenylisopropylamines (substituted amphetamines) was prepared, displaying substitution patterns identical with all known essential oils. The synthetic routes and physical properties of these "natural" amphetamines are shown. Also recorded are the levels effecting human intoxication insofar as these are known.

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