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Stability, transfer and absorption of cannabinoid constituents of cannabis (hashish) during smoking

The cannabinoids of a hashish preparation were determined qualitatively and quantitatively.

A group of Cannabis smokers using this preparation obtained a 14—20 % transfer of the cannabinoids present in the hashish cigarette to the respiratory system. These results agree with experiments using tobacco cigarettes impregnated with pure cannabinoids, showing a 14—29 % transfer with the main stream smoke. While cigarette smoking made only 14—20 % of the cannabinoid constituents of hashish available to the smoker, this figure was increased to about 45 for pipe smoking. The experienced cannabis smokers using deep inhalations absorbed over 80 % of the cannabinoids in the main stream smoke.

There is no difference in the transfer of cannabinoids using the deep inhalation technique, when compared to normal superficial smoking.

Except for decarboxylation of cannabinoid acids, there is no substantial difference between the major cannabinoids of the smoke as compared to the drug itself. That the smoking process causes only limited changes in the cannabinoid fraction was also shown by smoking pure Δ^1 -tetrahydrocannabinol, cannabidiol, cannabinol and cannabidiolic acid.

The present results indicated that to achieve a "normal biological high" by smoking, the absorbed dose of Δ^1 -tetrahydrocannabinol was in the range of 3—5 mg for the tested persons.

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Marihuana components in smoke and identification of Δ^9 -THC and two of its metabolites in rats

Cigarettes impregnated with various preparations of Δ^9 -tetrahydrocannabinol (Δ^9 -THC) and cannabidiol were artificially smoked, and the smoke was analyzed by means of gas chromatography and a combination of gas chromatography and mass spectrometry. Retention of the two test substances in smoke was 21 to 23 % of the starting amount. The ratio of

Δ^9 -THC to cannabidiol in smoke is different from that in starting material. It is suggested that these differences are the result of partial cyclization of the cannabidiol to Δ^9 -THC. An increase in the percentage of cannabinol in smoke is the result of a partial dehydrogenation of Δ^9 -THC or cannabidiol. No evidence for the isomerization of Δ^9 -THC to Δ^8 -THC or for the formation of new pyrolyzed products was found.

In another study two metabolites of Δ^9 -THC were found, following i.p. injection of this substance into rats. Extracts of rat urine, blood, bile and feces were analyzed by means of gas chromatography, mass spectrometry and mass fragmentography. In urine and in feces unchanged Δ^9 -THC was found. After glucuronidase treatment of feces, cannabinol (CBN) and an equal amount of Δ^9 -THC was also found. Dihydroxy- Δ^9 -THC was identified in urine and feces. Diacetyl- Δ^9 -THC was isolated from bile.

1. F. Mikes, A. Hofmann and P. G. Waser. *Biochem. Pharmac.* In press
2. F. Mikes and P. G. Waser. *Science* 172, 1158 (1971)

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Changing concepts of cannabis pharmacology

A number of widely held ideas about the pharmacology of cannabis must be abandoned in the light of recent research findings. These include: (1) its classification as a sedative, (2) the absence of tolerance and withdrawal effects, (3) the notion of reverse tolerance, (4) its ability to dilate the pupils, and (5) produce hypoglycemia, (6) the development of conjunctival infection as a result of the irritant effects of the smoke. These and other long held beliefs about cannabis are now in question since the intensive, scientific study of the drug began a few years ago.

Information about the botany, chemistry, physiology and psychology of *Cannabis sativa* is rapidly accumulating. Still, answers to certain critical questions are not at hand. The quite unknown possibilities of its carcinogenetic potential, and long term psychic adverse effects cannot be estimated today. We do have some preliminary impressions about the escalation theory that cannabis leads to heroin taking and about the nature of the amotivational syndrome.

It is surprising that so little is known of this plant which has been used for millenia. Many of our beliefs are based upon folk lore. Many fables about marihuana will have to be demolished before we arrive at a clear, impartial understanding of cannabis.