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Medical Faculty of the Palacký University, Olomouc, Czechoslovakia
Institute of Hygiene and Epidemiology
Director: Prof. MUDr. RNDr. PhMr. Z. Krejčí, CSc.

THE PRESENT STATE OF KNOWLEDGE IN THE CHEMISTRY OF SUBSTANCES OF CANNABIS SATIVA L.

III. TERPENOID SUBSTANCES

L. HANUŠ

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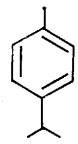
Terpenes represent an ample group of organic compounds, very spread in plants. They are a substantial component of volatile oils, aromatic substances of different parts of plants, mainly in flowers, fruits and leaves, but also in stalks and roots. They could be obtained from plants by distillation with steam, by pressing of extraction with convenable solvents. The molecules of terpenes are somposed of two or more variously placed isoprene units of the summary formula $(C_5H_8)_n$.

The first study on volatile oils in Cannabis sativa L. was published in 1880 by *Valente*[13] in Italy and 15 years later by *Vignolo*.[14] In 1896, *Wood* et al.[15] investigated the volatile fractions obtained from hemp plants, growing in Etawah, province Uttar Pradesh in India, and they described the isolation of terpene ($C_{10}H_{16}$, b. p. 170-175°), probably myrcene, and of sesquiterpene ($C_{15}H_{24}$, b. p. 258-259°). Many years later, *Simonsen* and *Todd*[10] studied an ethereal oil obtained from Egyptian hashish. They found that its lower boiling fraction contained mainly p-cymene (I) with an admixture of small amount of l-methyl--4-isopropenylbenzene (II) and other non-identified optically active substance. The higher boiling fraction of the oil contained mostly humulene (α-caryophyllene) (III).

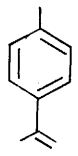
Dutt[3] later found in hemp the presence of p-cymene, myrcene (IV), limonene (V) and caryophyllene, together with non-identified sesquiterpenes and sesquiterpenic alcohols. He also described the presence of a compound, named p-cymedene (b. p. 179-180°, 2-bromodibromide, m. p. 187-189°), in Indian hemp.

Farmillo[4] published a method of gas chromatography with steam of volatile, so-called „terpenic fraction" of fresh green hemp.



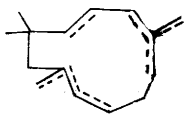
I

p-cymene
$C_{10}H_{14}$, m. w. 134,21
oil



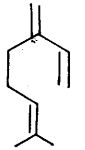
II

1-methyl-4-isopropenyl benzene
$C_{10}H_{12}$, m. w. 132,20



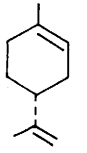
III

α - caryophyllene (humulene)



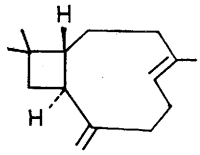
IV

myrcene
$C_{10}H_{16}$, m. w. 136
oil



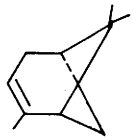
V

limonene
$C_{10}H_{16}$, m. w. 136
oil



VI

β - caryophyllene
$C_{15}H_{24}$, m. w. 204,36
oil



VII

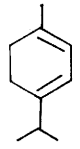
α - pinene
$C_{10}H_{16}$, m. w. 136, oil
l - $[\alpha]_D$ — 47,2°
d - $[\alpha]_D$ + 48,3°

VIII

camphene
$C_{10}H_{16}$, m. w. 136
l - m. p. 42—52°
$[\alpha]^{17}_D$ −52°— −94°

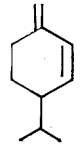
IX

β - pinene
$C_{10}H_{16}$, m. w. 136
oil, $[\alpha]_D$ −22°



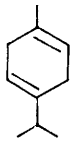
X

α - terpinene
$C_{10}H_{16}$, m. w. 136, oil



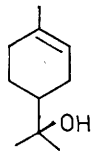
XI

β - phellandrene
$C_{10}H_{16}$, m. w. 136



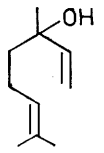
XII

γ - terpinene
$C_{10}H_{16}$, m. w. 136, oil



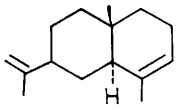
XIX

α - terpineol
$C_{10}H_{18}O$, m. w. 154



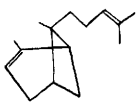
XIII

linalool
$C_{10}H_{18}O$, m. w. 154



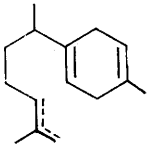
XX

α - selinene
$C_{15}H_{24}$, m. w. 204, oil



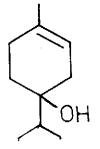
XVI

α - trans-bergamotene
$C_{15}H_{24}$, m. w. 204



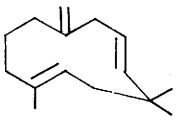
XXI

β - curcumene
$C_{15}H_{24}$, m. w. 204
$[\alpha]_{5461}$ $-48{,}2°$



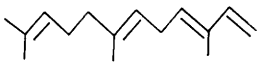
XVII

terpinene-4-ol
$C_{10}H_{18}O$, m. w. 154
d - oil, $[\alpha]^{11}_D$ $+24{,}5°$



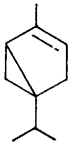
XXIII

β - humulene
$C_{15}H_{24}$, m. w. 204



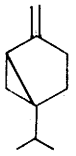
XVIII

farnesene
$C_{15}H_{24}$, m. w. 204, oil



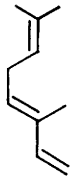
XXIV

α - thujene
$C_{10}H_{16}$, m. w. 136



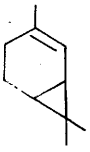
XXV

sabinene
$C_{10}H_{16}$, m. w. 136
l - oil, $[\alpha]^{16}_D$ −42,5°



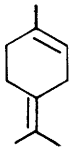
XXX

trans - β - ocimene
$C_{10}H_{16}$, m. w. 136



XXVI

Δ^4 - carene
$C_{10}H_{16}$, m. w. 136
oil, $[\alpha]^{30}_D$ +62,2°

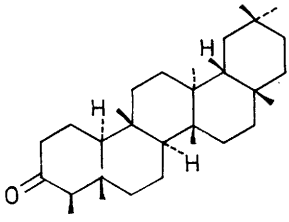


XXXI

terpinolene
$C_{10}H_{16}$, m. w. 136, oil

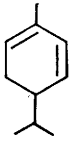
XXVII

Δ^3 - carene
$C_{10}H_{16}$, m. w. 136
oil, $[\alpha]^{30}_D$ +7,69°



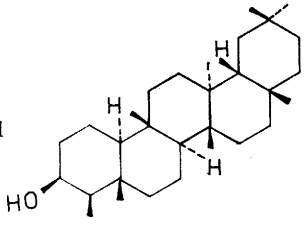
XXXII

friedelin
$C_{30}H_{50}O$, m. w. 426,73 white needles, m. p. 252,5—254,5°
$[\alpha]^{30}_D$ −23,9° (c 1.0, $CHCl_3$)



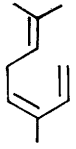
XXVIII

α - phellandrene
$C_{10}H_{16}$, m. w. 136, oil



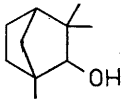
XXXIII

epifriedelanol
$C_{30}H_{52}O$, m. w. 428,74
white plates, m. p. 274,5—277°
$[\alpha]^{31}_D$ +18,9° (c 1.0, $CHCl_3$)



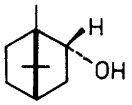
XXIX

cis - β - ocimene
$C_{10}H_{16}$, m. w. 136, oil



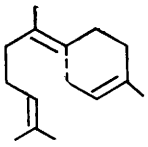
XXXV

fenchyl alcohol
$C_{10}H_{18}O$, m. w. 154
m. p. 45°; $[\alpha]_D$ +10,36° (EtOH)



XXXVI

(−) - borneol
$C_{10}H_{18}O$, m. w. 154
m. p. 208°; $[\alpha]^{20}_D$ +37,44° (EtOH)

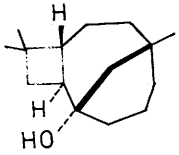


XXXVII

bisabolene
$C_{15}H_{24}$, m. w. 204, oil

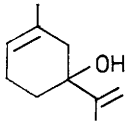
XXXVIII

(+) - longifolene
$C_{15}H_{24}$, m. w. 204
oil, $[\alpha]_D$ +42,73°



XLI

α - caryophyllene alcohol
(caryolan-1-ol)



XLII

m-mentha- - 1.8(9) - dien-5-ol
$C_{10}H_{16}O$, m. w. 152

Martin et al.,[8] after steam distillation of fresh male and female hemp plants (0,05-0,11% of oil), discovered on gas chromatography the presence of myrcene (IV), limonene (V) and α- and β-caryophyllene (III, VI). The results are described by *Farmillo*.[5]

Farmillo et al.[6] found approx. 13 % of α-caryophyllene, 0,8-7,0 % of myrcene and 1-9 % of limonene in hemp cultivated in Canada.

Nigam et al.[9] described the identification of new substances in volatile oil of marihuana. The ethereal oil obtained by hydrodistillation of freshly reaped Indian hemp contained these substances: α-pinene (VII), camphene (VIII), β-pinene (IX), α-terpinene (X), β-phellandrene (XI), γ-terpinene (XII), linalool (XIII), trans-linalool oxyde (XIV), sabinene hydrate (XV), α-bergamotene (XVI), terpinene-4-ol (XVII), β-farnesene (XVIII), α-terpineol (XIX), α-selinene (XX), curcumene (XXI) and caryophyllene oxyde (XXII). There was also discovered the presence of trace amounts of two alcohols and α, β-nonsaturated ketone.

Bercht et al.[2] stated the presence of new volatile constituents of hemp - α-thujene (XXIV), sabinene (XXV), Δ^4-carene (XXVI), Δ^3-carene (XXVII), α-phellandrene (XXVIII), cis-ocimene (XXIX), trans-ocimene (XXX) and terpinolene (XXXI) by hydrodistillation of a monoterpenoid hydrocarbonic fraction of an ethereal oil from Dutch and Turkish hemp and by subsequent gas chromatography. Apart from the above mentioned constituents, a rang of substances, previously described, was identified (I, IV, V, VII-XII).

The first isolation of higher terpenes from roots of Cannabis sativa L. was performed by *Slatkin* et al.[11] They isolated pentacyclic triterpene ketone, friedelin (XXXII), and its corresponding β-alcohol, epifriedelanol (XXXIII) from the ethanol extract of hemp roots.

In 1973, *Hood* et al.[7] performed new analyses with the help of gas chromatography and they found for the first time 2-methyl-2-heptene-6-one (XXXIV), fenchyl alcohol (XXXV), borneole (XXXVI) and β-bisabolene (XXXVII) as constituents of marihuana. Besides the new substances, they detected many others, already found terpenoids.

The classification and identification of some new substances in ethereal oil of Cannabis sativa L. were described by *Stahl* and *Kunde*[12]. Using spectral methods, they revealed the presence of longifolene (XXXVIII), humulenepoxyd - I and- II (XXXIX, XL), caryophyllenol - I (XLI) and m-mentha-1.8(9)-dien-5-ol (XLII).

At the present time, there appeared a new type of the substance on the black market. It is called „dark green oil" and its odour is typical for hashish, but it is less strong than hashish. As *Bercht* et al.[1] mention, its content of terpenes is lower, when compared to the normal hashish. The monoterpenes are almost absent and the amount of sesquiterpenes is very low. With the help of a combination of gas chromotography and mass spectrometry, it was determined about 11 sesquiterpenes of M^+ m/e 204. Their amount does not exceed 15 % of the total mixture.

SUMMARY

The study presents a survey (up to 1973) of natural terpenoid substances isolated from hemp (Cannabis sativa L.), of its products hashish and marihuana and of their structures with known physical characteristics.

СОВРЕМЕННОЕ СОСТОЯНИЕ ЗНАНИЙ ХИМИИ СУБСТАНЦИЙ ВСТРЕЧАЮЩИХСЯ В CANNABIS SATIVA L. III. ТЕРПЕНОЫДНЫЕ ВЕЩЕСТВА

Резюме

Дан литературный обзор (до 1973 г.) природных терпеноыдных субстанций изолированных из конопли (Cannabis sativa L.) и ее продуктов гашиша и маригуаны с их конституцией и известными физикальными характеристиками.

SOUČASNÝ STAV ZNALOSTÍ CHEMIE OBSAHOVÝCH LÁTEK *CANNABIS SATIVA* L. III. TERPENOIDNÍ LÁTKY

Souhrn

Podán literární přehled (do r. 1973) přírodních terpenoidních látek isolovaných z konopí (*Cannabis sativa* L.) a jeho produktů hašiše a marihuany s jejich konstitucemi a známými fyzikálními charakteristikami.

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