The distribution of ^{3}H-$\Delta^{1(6)}$-THC after intravenous administration is characterized by a moderate to low level of radioactivity in the blood up to and including 24 h after administration. High levels of radioactivity are found in the liver, bile, intestinal contents, and urinary bladder. Except these, only the myocardium, lung, spleen, and adrenal cortex showed a level of radioactivity exceeding that of the blood. The radioactivity in the spleen is found mainly in the border zone between the red and white pulp, and was fairly constant at a moderate level during the whole study. The activity in the liver and lung also show a long duration. The activity in the grey matter of the CNS is somewhat higher than in the white matter, being in all parts lower than in the blood. The compound $\Delta^{1(6)}$-THC and/or its metabolites pass into the foetus to a low concentration not exceeding that of the maternal blood.

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Studies on the interaction of $\triangle^{9}$-tetrahydrocannabinol with plasma lipoproteins

The major classes of lipoprotein (LP), the very low density LP (VLDL) containing chylomicra, the low density LP (LDL) and high density LP (HDL) as well as non LP protein containing both albumin and globulin can be isolated by rate zonal flotation in the ultracentrifuge using a two step procedure in a continuous gradient constructed with sodium bromide. Fractionation of human and rat plasma by this procedure after addition of ^{14}C-THC (10 μg/ml) showed that 60—70 % of the drug is associated with LP. Ammonium sulfate fractionation of the non LP protein fraction indicated that the remainder of the drug is associated with the albumin. In human plasma, LDL is the major LP component; in rat, HDL predominates; the distribution of THC in LP fractions reflects this difference. Percent of drug in fraction: Human plasma: VLDL, 11; LDL, 34; HDL, 18. Rat plasma: VLDL, 27; LDL, 13; HDL, 29. Enrichment of human plasma with LDL fraction to 1.5 times the normal concentration increases the percentage of the drug in LP from 63 to 77 % and that in the LDL fraction from 34 to 58 %. In both species the distribution of THC in LP fractions appears related to the content of neutral lipid (triglyceride, free and esterified cholesterol) rather than that of phospholipid or protein. The rapid accumulation of THC in tissues after intravenous administration suggested that the drug is not strongly bound in plasma.

Previous studies from this laboratory (*Pharmacologist* 13, 296, 1971), have demonstrated that THC is rapidly taken up by the isolated perfused liver where it is localized in nuclei and microsomes. A less striking redistribution of THC can be shown using liver homogenates. After equilibration of liver homogenates (0.5—1.0 g liver) with plasma (4 ml) containing THC (10 μg/ml) 40—60 % of the drug is found in the particulate components. These findings further emphasize the importance of the intense lipid solubility of THC in determining its interactions with biological material.

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Binding of Δ^1-tetrahydrocannabinol and 7-hydroxy-Δ^1-tetrahydrocannabinol to human plasma proteins

The binding of tritium-labelled Δ^1-tetrahydrocannabinol to human plasma proteins was studied *in vitro* with different electrophoretic techniques.

Δ^1-Tetrahydrocannabinol was found to be associated to 80—95 % with lipoproteins. The metabolite (^{14}C)-7-hydroxy-Δ^1-tetrahydrocannabinol formed in rat liver was shown by agarose-gel electrophoresis to be extensively bound to the albumin fraction of human plasma.