Δ^1-Tetrahydrocannabinol and adrenergic mechanisms

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Δ^1-Tetrahydrocannabinol (THC) has been shown in the past to possess several cardiovascular actions in both animals and man (Graham & Li, 1973; Davies, Weatherstone, Graham & Griffiths, 1974; Marshall, unpublished observations). The basic pharmacological mechanisms underlying these actions are complex and have not yet been fully eludicated.

Using isotope studies Graham, Lewis & Li (1974a) have shown that Δ^1THC in doses ranging from 1.1×10^{-7} M to 1.4×10^{-5} M inhibited the uptake of ^{3}H-l-noradrenaline (NA) into the isolated, perfused rat heart, the ID_{50} value being 1.4×10^{-5} M. These workers (1974b) also found that in rat vasa deferentia, the amount of ^{3}H-l-NA released spontaneously or as a result of transmural electrical stimulation was reduced in the presence of Δ^1-THC in similar concentrations to the above. The reduction was dose-dependent. Rat vasa pre-incubated with ^{3}H-Δ^1-THC released significantly more tritium into the bath fluid in a given period of time when stimulated than not stimulated. Pretreatment of rats with 6-hydroxydopamine (6-OHDA) in a dose which destroys adrenergic nerves (Furness, Campbell, Gillard, Malmfors, Cobb & Burnstock, 1970) abolished this difference, suggesting that the release of Δ^1-THC from the stimulated vas deferens came, at least in part, from the adrenergic nerve. Further evidence that Δ^1-THC is taken up into the adrenergic neurone has recently been obtained by Egan, Graham & Lewis (unpublished observations). These workers have shown that the isolated rat vas deferens incubated for varying times with ^{3}H-Δ^1-THC retained significantly more tritium prior to treatment of the animals with 6-OHDA than afterwards.

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Ultracryotomy for high resolution drug-localization studies

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The usefulness of high resolution autoradiographic drug-localization studies is severely limited by the ability of most drugs to diffuse from the receptor sites during lengthy preparative procedures. To overcome this disadvantage, work is in progress to obtain ultra-thin (ca. 100 nm) sections of fresh, unprotected, unfixed, unstained tissue which is rapidly frozen using a variety of quenching agents.

Evidence is presented that sections are cut (and not formed by fracturing) using glass or diamond knives at temperatures as low as -125°C, using a Huxley Mark II ultramicrotome with a cryo-attachment (Cambridge Instruments). Sections are picked up on carbon coated grids and transferred to the coating unit where they are allowed to warm up to room temperature under vacuum. They may or may not be top-coated with a layer of carbon before examination in a Philips 300 electron microscope.

Electron micrographs of liver sections prepared as above are displayed, together with micrographs illustrating artifacts arising from overlaying sections by carbon evaporation, allowing sections to warm up in air, and ice-crystal formation.

A new technique utilizing contact adhesive for applying photographic emulsion to frozen-cut sections is reported.

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