INHIBITION OF PROSTAGLANDIN-E_2 PRODUCTION BY A TETRAHYDROCANNABINOL-FREE EXTRACT OF CANNABIS SATIVA L.

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Extracts of Cannabis herb are noted for their analgesic and anti-inflammatory properties (Gill et al 1970) but work involved with pure tetrahydrocannabinol (THC) and other cannabinoids is controversial in that Sofia et al (1973) reported analgesic activity of Δ^9-THC in the rat tail flick test whilst Dewey et al (1972) observed these effects only at high dose levels of THC which produced central activity. Fairbairn and Pickens (1981) showed that the cataleptic effect of THC could be reduced by cyclo-oxygenase inhibitors and also by an ethanol extract of Cannabis sativa L. This observation provided the first indications that the well-known anti-prostaglandin effects of Cannabis, such as anti-inflammatory and analgesic action may not be due to the THC content of the herb. These results led us to investigate Cannabis extracts for their ability to inhibit prostaglandin (PG) production in vitro. Powdered cannabis herb was extracted exhaustively with petroleum spirit and then further extracted with ethanol. The ethanol extract was shown by analytical thin-layer chromatography (TLC) to be free of THC. The inhibition of PG-E_2 production by the ethanol extract was assessed using isolated synovial cells. Plastic adherent human synovial cells from rheumatoid arthritis patients undergoing synovectomy were used as described by Dayer et al (1976). Tetradecanoylphorbolacetate (TPA, 10 μg/ml) was incubated with the cells in DMEM and 10% heat inactivated foetal calf serum. Extracts and fractions were added in ethanol (20 μl/ml) and following incubation the PGE_2 content of the supernatant fluid was measured by radio-immune assay.

The TPA-induced production of PGE_2 by synovial cells was found to be inhibited by the cannabis extract with an IC-50 equivalent of 2 μg /dry weight of original herb. In the same system aspirin exhibited an IC-50 of 1·5 μg/ml, indomethacin, 3.5 μg/ml and dexamethasone, 0.5 μg/ml. The cannabis extract was purified by preparative-TLC using silica gel as adsorbent and developing with chloroform:ethanol (100:15). The band of R_f 0.45 to 0.69 was removed and eluted with ethanol. This fraction produced a 90% inhibition of TPA-induced PGE_2 production in synovial cells at a dose of 8μg/ml. Further purification of this fraction was carried out as before using cyclohexane:butanone:ethanol (70:25:5) as solvent. The residue recovered from the zone of R_f 0.38 produced a 90% inhibition of PGE_2 production at a dose of 0.7 μg/ml. This residue consisted of a number of compounds and its chemical nature is unknown at the present time. Nevertheless we have demonstrated for the first time that an extract of Cannabis sativa L. inhibits PGE_2 production in vitro and that this activity cannot be attributed to THC. The anti-prostaglandin agent of Cannabis is stable during TLC separations and could possibly be responsible for the anti-inflammatory and analgesic actions of Cannabis herb noted by other workers.

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