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CENTRAL AND PERIPHERAL ACTIVITIES OF CANNABIS SATIVA L. AND ITS CONSTITUENTS

E. Formukong, A.T. Evans, E.M. Williamson and F.J. Evans, Dept. of Pharmacognosy, The School of Pharmacy, University of London WC1N 1AX, U.K.

Cannabis herb has reputed analgesic activity (Gill et al 1970) and may be used for its medicinal rather than its social properties as a drug. Its cataleptic effects are believed to be related to its social use in man. The central activity and antiphlogistic activities may be concerned with effects on arachidonate metabolism. Cannabis constituents have been shown to both stimulate and inhibit PG release in vitro (Barrett et al 1985). This communication describes the actions of Cannabis and its constituents which may be responsible for these effects.

TABLE 1

Substance	Inhibition of PBQ writhing ED_{50}	Inhibition of erythema % inhibition*
Asprin	15.85 $mgkg^{-1}$	n/a
Trifluoperazine	n/a	50
Petroleum extract	12.60 $\mu gkgm^{-1}$	83
Ethanol extract	44.60 $\mu gkgm^{-1}$	92
Tetrahydrocannabinol	>25 $mgkgm^{-1}$	100
Cannabinol	>25 $mgkgm^{-1}$	25
Cannabidiol	41.6 $\mu gkgm^{-1}$	92
Cannabigerol	1.26 $mgkgm^{-1}$	33
Olivetol	0.63 $mgkgm^{-1}$	62
Cannflavin	0.63 $mgkgm^{-1}$	82

n/a = not applicable; * $^{1}\Delta$-THC and trifluoroperazine 1mg per animal, all other substances 100 µg/5 µl per animal.

Using the ring test (Pertwee 1972) for assessment of cataleptic activity $^{1}\Delta$-THC demonstrated activity with an ED_{50} of 6.9 $mgkgm^{-1}$. Related cannabinoids and other constituents were inactive in this test up to a dose of 100$mgkgm^{-1}$. A petroleum Cannabis extract (Cannabinoid extract) and an alcoholic extract (Cannabinoid free), prepared by the method of Fairbairn and Pickens (1979) were also inactive in this test. The petroleum extract contained 2%w/w $^{1}\Delta$-THC as measured by GLC analysis and should have exhibited some central activity. We have recently shown (Evans et al 1986) that constituents of Cannabis have complex and often conflicting actions on the enzymes of arachidonate metabolism

It is possible that in a complex mixture as occurs in cannabis the non-active compounds may moderate or antagonise the central activity of $^{1}\Delta$-THC. These same extracts and constituents were tested topically on mice skin for their ability to inhibit phorbol ester induced erythema (Table 1) by the method of Williamson and Evans (1981). With the exception of Cannabigerol and Cannabinol these substances were more potent in this system than trifluoperazine, a known phorbol ester antagonist. Analgesic activities (Table 1) were measured by the suppression of phenylbenzoquinone induced writhing in the mouse. Neither $^{1}\Delta$-THC nor cannabinol were active in this system in doses of up to 25 $mgkgm^{-1}$, whilst cannabigerol was toxic at doses of 4$mgkgm^{-1}$. The remaining constituents and extracts of Cannabis were considerably more potent than Asprin. The central effects of the cannabinoids can be distinguished from the analgesic activities on a structural basis in that $^{1}\Delta$-THC was active in the cataleptic test whilst cannabidiol was not. The opposite was the case when tested for their analgesic activity. Cannabis possesses pharmacological properties not related to the content of $^{1}\Delta$-THC, but which are dependent upon other substances from the plant.

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