

(de Stevens, 1965). It is therefore of fundamental interest that an analogous change in the molecular structure of etorphine results in a compound which, although less potent, retains powerful analgesic properties whilst showing altered pharmacological characteristics. The evidence obtained from five laboratory species indicating that in compound II there is dissociation of analgesic and respiratory depressant properties, justifies extension of these studies to man.

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Pharmacological activity of cannabis according to the sex of the plant

SIR,—It is an old tradition, probably originating in India, that the female plants of *Cannabis sativa* contained more activity than male plants (Walton, 1938). In Brazil some planters used to cut the terminal buds to induce more expanded branches, richer foliage and, consequently, more extractable material. According to a popular belief this *castration* of the pistillate plants must be performed only by men (Doria, 1916). By cultivating marihuana near our laboratories (Valle & Hyppolito, 1964) we were able to gather separately the male and female plants, and to prepare a powder of the leaves and flowering tops, and to store the samples by sex under the same conditions. It was possible, then, to reinvestigate whether there existed a difference of activity between the two kinds of powder.

Leaves and flowering tops were separated from other parts of the plant, dried at room temperature (20–24°), powdered and distributed according to the sex of the plant in dark ampoules, 5 g each, closed under nitrogen and kept in the refrigerator (4°). The crude resin to be assayed was obtained: (a) after 4–6 hr Soxhlet extraction with light petroleum (b.p. 50–80°), the extracts being treated with activated charcoal, filtered and evaporated under reduced pressure; (b) by extracting the powders at room temperature with the same solvent, the charcoal treatment being omitted before filtration. In both instances the residue

was taken up in acetone and the solution kept overnight at 4° to separate wax constituents. After acetone evaporation the crude resin was dissolved in ethanol and the stock solutions (10 mg/ml) used in the assays. These were made on rabbits using the abolition of the blink reflex (Valle, Souza & Hyppolito, 1966) and by a test based on toxicity to the fish *Lebistes reticulatus* (Valle, Baratella & others, 1967).

The average yield of powder from male and female plants excluding fruits, stem, branches and roots was respectively 11 and 15%. This is not unusual since it is known that at maturity the male plants are more slender and with less foliage than the female ones. Comparative bioassays of the crude resins based on the abolition of the rabbit blink reflex showed that male and female cannabis preparations exhibited practically the same degree of activity, the mean difference not being significant (Table 1). The same was true using the test on the fish.

TABLE 1. COMPARATIVE BIOASSAY OF MALE AND FEMALE CANNABIS CRUDE RESINS BASED ON THE ABOLITION OF THE RABBIT BLINK REFLEX*

Groups	Number of injected animals	Body weight kg (average and limits)	Preparations from	Test solution†	Threshold dosage mg/kg \pm s.d.‡
I	6	2.33 (1.5 - 2.9)	male plants	0.5 mg/ml	0.83 \pm 0.30
II	6	2.46 (1.9 - 3.2)	female plants	0.5 mg/ml	0.75 \pm 0.31

* Repeated intravenous injections (0.2 ml/kg each) at 10 min intervals enough to abolish blink reflex or both eyes.

† Ethanol stock solution (10 mg/ml) diluted in saline plus polysorbate 80 before using.

‡ Mean difference not significant ($t = 0.445 < 2.228$, $n = 10$, $p = 0.05$).

Although Bouquet (1938) recorded a pharmacological difference in favour of the female cannabis, Houghton & Hamilton (1908), among others, had previously pointed out that staminate and pistillate plants exhibited very similar amounts of activity. We too, by different methods of assay have concluded that cannabis female plants, despite yielding higher amounts of starting drug material, do not exhibit more activity, on a weight basis, than the male plants.

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