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An inhalation aerosol of Δ^9-tetrahydrocannabinol

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The most common method of Δ^9-tetrahydrocannabinol [Δ^9-THC] administration is by smoking marijuana leaf. This route achieves a rapid and reproducible absorption as reflected by consistent increases in pulse, psychotropic effects and bronchodilation. However, during smoking, other pyrolysed products are inhaled which may be bronchial irritants and possibly even carcinogens. Hence a study of Δ^9-THC aerosols was instigated to see if it is an advantageous method of administration.

Formulations of Δ^9-THC are difficult to prepare because of water insolubility and also because of the tacky [sticky] nature of the pure material at room temperature. Early experiments demonstrated excellent solubility of Δ^9-THC in conventional ethanol–difluorodichloromethane [propellant 12]–tetrafluorodichloroethane [propellant 114] solvent systems. Attempts at evaluation of these dosage forms in animals, however, indicated excessive tack of the spray and hence poor transport to the lungs.

The current preparation includes sorbitan trioleate [Arlacel 85] as a detacifier, and a higher pressure solvent system to generate smaller aerosolized particles. The Arlacel 85 is a surface-active agent currently used in at least two medicinal inhalation aerosol products.

For a single aerosol container of 15 ml capacity fitted with 67 microliter metered dose valve (Emson Research Inc. Bridgeport Conn 06605) the formula giving 1 mg per actuation is: Δ^9-THC 2% in alcohol U.S.P., 6·0 ml; alcohol U.S.P., 3·0 ml; Arlacel 85, 0·068 g; propellant 114, 2·5 g; propellant 12, 5·0 g.

The Δ^9-THC alcohol solution is measured into a clean aerosol container and the alcohol evaporated with filtered N_2. The Arlacel 85 is added as a suspension in the alcohol called for in the formula. Propellant 114 is cold filled, followed by the propellant 12. The cooled valve is fitted and crimped.

The resulting aerosol is a true solution with apparent good stability if protected from light. Weight loss measurements indicate an average 78 mg delivery per actuation of which 1 mg is the drug. This concentration can easily be adjusted if desired.

Preliminary results in man show a marked increase in specific airway conductance without a marked increase in heart rate following administration of aerosolized Δ^9-THC. Ten mg of aerosolized Δ^9-THC increased specific airway conductance 89 $\pm$16% and increased pulse 17 $\pm$ 4% in four subjects. No placebo controls were used, however more comprehensive studies are currently underway. The values we found compare favourably to an increase in specific airway conductance of 53 $\pm$ 10% and an increase of 56 $\pm$ 11% in pulse rate following marijuana smoking of approximately 10 mg of Δ^9-THC. Furthermore, the delivery of aerosolized Δ^9-THC is potentially easier to quantify than delivery by pyrolysis since pyrolysis may convert Δ^9-THC into other compounds.

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