A Phase I Trial of the Safety, Tolerability, and Pharmacokinetics of Cannabidiol Administered as Single-dose Oil Solution and Single and Multiple doses of a Sublingual Wafer in Healthy Volunteers

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Abstract

Aims: This study investigated the safety, tolerability, and PK after administration of a specific Cannabis sativa cultivar extract, standardised to CBD content as sublingual wafer or oil formulation compared to nabiximols oromucosal spray. Methods: For the single-dose study, the design was an open-label, four-way crossover in 12 healthy volunteers randomised to receive a sequence of four different single doses of CBD as a sublingual wafer (25 or 50 mg CBD), oil solution (50 mg CBD), or nabiximols oromucosal spray (20 mg CBD, 21.6 mg THC). For the multiple-dose study, sublingual wafer (50 mg CBD) was administered twice a day for five days. Results: The extract was generally well tolerated by participants when administered in either wafer or oil form, with some adverse events, including mild or moderate somnolence, sedation and altered mood. The relative bioavailability of CBD after administration as a sublingual wafer was comparable with that of oil solution with 90% confidence interval of 83–131%. The median maximum concentrations of CBD after administration of oil solution and wafer was 9.4 and 11.9 ng mL-1, respectively. Maximum concentrations of CBD occurred 4 hours after administration, with an estimated terminal elimination half-life of 6 hours. There was no statistically significant difference between the AUC0-t of CBD after administration of oil solution or wafer compared with nabiximols oromucosal spray. Conclusion: Oil solution and sublingual wafer formulations of the extract standardised with CBD were well tolerated and demonstrated safe and achieved equivalent concentrations of CBD when compared to an available commercial formulation.

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