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(52) KH-001 BUT NOT OTHER TESTED ALKALOIDS DERIVED FROM *SCELETIUM TORTUOSUM* DELAYS EJACULATION IN THE RAT PARA-CHLOROAMPHETAMINE (PCA) MODEL

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Objectives: To determine the efficacy and potency of purified alkaloids (KH-001, KH-002, KH-003, KH-004) derived from *Sceletium tortuosum* in the PCA-induced ejaculation rat model.
Methods: Male Wistar rats received the following compounds intraperitoneally, shortly before anaesthesia and 1h before the induction of ejaculation with PCA (5 mg/kg): KH-001 (20 μg/kg - 20 mg/kg; n=12), KH-002 (20 mg/kg; n=12), KH-003 and KH-004 (10, 20 mg/kg; n=6) or aqueous vehicle (0.5% (w/v) methylcellulose; n=12). The proportion of ejaculating rats within a dose group, the latency to first ejaculation and physiological determinants of emission (seminal vesicle pressure (SVP)) and expulsion (bulbospongiosus (BS) muscle burst) were determined. Data describing latency to first ejaculation were described by Kaplan-Meier analysis, and statistical significance relative to vehicle-treatment was determined by Cox regression. SVP and BS muscle burst were analysed using Student's t-test or one-way ANOVA.
Results: While KH-001 increased latency to first ejaculation in a dose-dependent fashion, with a minimum effective dose of 200μg/kg, no such effect was observed with the other tested kanna alkaloids up to 20mg/kg. SV contractions were significantly reduced by all alkaloids, with no effect on BS muscle burst.
Conclusions: These novel findings indicate the potential utility of KH-001 in the symptomatic treatment of premature ejaculation in humans. Interestingly, of the four alkaloids examined, delayed ejaculation was observed with only KH-001, indicating that the various kanna alkaloids tested have a differentiated pharmacological profile. Studies are underway to determine mechanism(s) of action, and the relationship between the pharmacodynamics and pharmacokinetics of kanna-derived alkaloids.
Conflicts of Interest: RG and MK are employees and shareholders of Kanna Health Ltd. LMNS, FRB, RP, NG, and TP are shareholders of Kanna Health Ltd. RP is an employee of Kanna Health US LLC.