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Title: Dermal absorption of cannabis

Background: Although recent legislation has brought marijuana into the spotlight recently, cannabinoids have long generated a complex body of literature aimed at clarifying its possible role in therapeutic roles, with some promising effects in multiple sclerosis, glaucoma, neuropathic pain, and pain in cancer patients. As therapeutic targets of cannabinoid preparations become better defined, research has therefore turned to other methods of delivery to better exploit possible therapeutic benefits, including sublingual and transdermal preparations.

As might be expected with the creativity often present in unregulated recreational drug use, novel delivery systems including "edibles" and vapes have also been employed in recreational use. Dermal delivery has also made a reappearance, with skin preparations of THC currently on sale from local marijuana dispensaries.

Dermal preparations of cannabinoids have been of interest even as early as the 1970s, and have shown promise as a delivery system in both in vitro and in vivo models. In particular, the benefit of avoiding first-pass metabolism is expected to increase delivery of active cannabinoid, while decreasing the negative side effects seen in inhalation. However, it has never been shown that dermal cannabinoid preparations result in detectable urine levels of THC's primary metabolite, 11- nor-9-carboxy- Δ 9 tetrahydrocannabinol (THC-COOH), which is also the molecule that current urine drug screens detect. It is therefore unknown if screening urine tests, such as might be undertaken by employment or regulatory bodies, would be expected to turn positive.

Aims: We hope to better characterize the dermal absorption and kinetics of THC and cannabidiol in humans, with a specific view toward legal ramifications. Blood levels will help to characterize the kinetics of dermally-delivered THC, and our lab will also run our institution's qualitative urine screen (Roche Cannabinoids II) to determine if dermal delivery results in a positive screen at current cutoff concentrations of 100 ng/mL.

We hypothesize that dermal preparations of THC may not reach levels that would trigger a positive urine screen at current cutoff concentrations. Furthermore, we hypothesize that cannabidiol will not trigger positive urine screens due to its metabolites, which are poorly characterized and not known to contain THC-COOH.

Methods: This is a single-center study in healthy volunteers that will examine the dermal absorption of a topical application of cannabinoids. An Institutional Review Board application has been submitted to UCSD Medical Center as the sole investigating site. The study aims to acquire data for 12 healthy volunteers. Participants will qualify for the study by having an initial negative screen for THC-COOH, and will subsequently be randomized into 3 categories according to which type of preparation they will receive: low-concentration THC, high-concentration THC, and high-concentration CBD. The samples used in these groups will be provided by a local dispensary, who employ a chemist to verify concentration and composition of these samples.

The samples will be applied in the form of an adhesive bandage impregnated with a coconut-oil-based product. All bandages will be applied to the same location in all eligible participants - the right deltoid. At 1 hour, 6 hours and 10 hours after application of the THC product, volunteers will provide simultaneous blood and urine samples, which will then undergo analysis at our institution's advanced clinical laboratory.

Major Limitations/Questions: The kinetics of transdermal THC delivery have not been clarified, and so our sample collection times can be structured only around a best estimate of peak concentrations. Furthermore, as we plan to use samples given to us by a local dispensary, we cannot easily generalize our results to other dermal preparations available across the country, as the process of making these is completely unregulated. However, the company does have an internal chemist who will verify the concentrations of THC in the samples, and we plan to verify this at a separate clinical laboratory.