A Crossover Study Evaluating the PK Parameters of a Novel Cannabis Delivery Method as Compared to an Oil-Based Oral Tincture

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Background

In the context of drug development, there are a multitude of factors that one must consider but perhaps no one single factor is more important than the method of administration. Common modalities include oral consumption (swallowing), sublingual administration, inhalation, transdermal absorption, or injection, each of which has its own distinct advantages and disadvantages. Selection of the appropriate delivery modality is paramount in drug development as not all administration methods are suitable for the drug in question and/or the desired outcome. Some drugs; however, are available in several modalities, one such example being cannabinoid-based therapies which can be found in inhaled, sublingual, orally consumed, transdermal, injectable, and rectally administered formats. The wide range of drug delivery options for cannabinoid-based therapies is largely driven by consumer preferences, medical conditions, and desired effects.

This large variation in administration modality; however, also results in a large variation in pharmacokinetic profiles in addition to efficacy. To address this variation we subjected an oil-based cannabis preparation to a unique drug delivery system called self-nanoemulsifying drug delivery systems (SNEDDS) and compared the pharmacokinetic outcomes to the same cannabis dose administered via oral tincture. This technology is designed to enhance the bioavailability and solubility of poorly water-soluble drugs such as cannabis preparations. SNEDDS are anhydrous homogenous liquid mixtures consisting of oil, surfactant, drug and coemulsifier or solubilizer, which spontaneously form oil-in-water nanoemulsion. Thus, may significantly improve therapeutic outcomes by facilitating better and faster absorption as well as improved systemic availability.

Objective & Study Design

Objective

To evaluate the pharmacokinetic properties of an orally administered Self-NanoEmulsifying Drug Delivery System (SNEDDS) cannabis product as compared to oral tincture of the same dose both of which are designed to be immediately swallowed.

Study Design

This was open-label cross-over study. After review on the inclusion/exclusion criteria eligible patients were consented. Subjects received one of two products, a powdered oral cannabis preparation which employed the Capsoil ® SNEDDSs technology or an oral tincture both of which contained the same dose (8mg THC and 8mg CBD). Subjects would then provide eight (8) blood samples over ten (10) hours. Upon completion the subjects were dismissed from the clinic to begin their 30 day washout. After completion of a 30-day wash-out period subjects returned to the clinic and were assigned the alternate treatment (whichever they had not previously been assigned) sampling procedures were then repeated.

Inclusion

- No use of cannabis products within past 30 days
- Willing to report to study site for all visits
- 21- 65 years of age
- In overall good health as evidenced by physical exam, ECG, vital signs, comprehensive metabolic panel

Exclusion

- Female that yield a positive urine screen for pregnancy
- Those with known allergies to cannabinoids
- Severe underlying medical conditions
- Chronic medication use
- History of substance abuse disorder

Study Population

- 9 patients were included in the study and received both treatments
- Female N=7 (77.78%)
- Male N=2 (22.22%)
- Age mean (std) 41.67 (±11.1)
- BMI mean (std) 26.75 (±3.78)

Results

Table 1. Pharmacokinetics characteristics of delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD) and their primary active metabolites 11-OH-THC and 7-OH-CBD in the plasma following two delivery systems; oil-based Tincture versus powder-based SNEDDS delivery technology

	SNEDDS Delivery N=9	Oral Tincture N=9	
	Mean ± std or %	Mean ± std or %	p-value
THC			
Cmax (ng/mL)	47.05±50.53	12.66±13.59	**0.046**
Tmax (Hr.)	3.72±4.26	4.89±3.3	0.631
11-OH-THC			
Cmax (ng/mL)	15.06±4.13	4.87±2.4	**<0.001**
Tmax (Hr.)	0.78±0.36	5.56±3.68	**0.004**
CBD			
Cmax (ng/mL)	10.62±9.08	4.02±4.15	0.089
Tmax (Hr.)	1.83±1.89	5.56±3.68	**0.049**
7-OH-CBD			
Cmax (ng/mL)	3.23±1.41	0.83±0.52	**<0.001**
Tmax (Hr.)	0.89±0.55	5.5±3.76	**0.006**

Figure 3. Area under the curve analysis

AUC Analysis, N=9		THC	11-OH-THC	CBD	7-OH-CBD
SNEDDS delivery	**Mean**	100.83	52.27	28.86	12.39
	Std.	117.14	13.82	20.53	4.36
Oil tincture	**Mean**	30.74	15.61	10.36	2.50
	Std.	37.60	7.95	10.41	1.71
	Z (W)	-2.3102	-2.6656	-2.6656.	-2.6656
	Pv (W)	**0.020888**	**0.007699**	**0.007699**	**0.007699**
	Relative Bioavailability F(Oil/SE)	**30%**	**30%**	**36%**	**20%**

Figure 1. THC mean plasma concentration per hour post cannabis administration

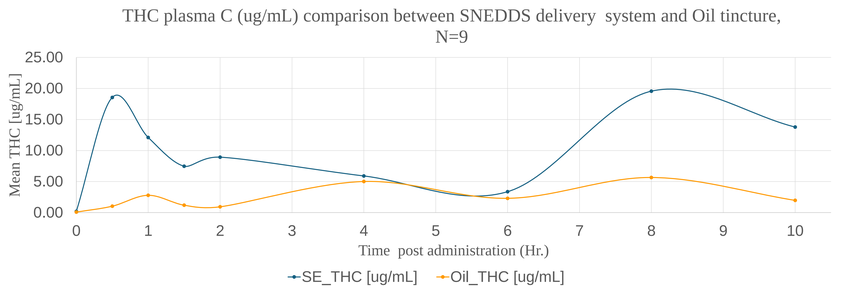


Figure 2. 11-OH-THC mean plasma concentration per hour post cannabis administration

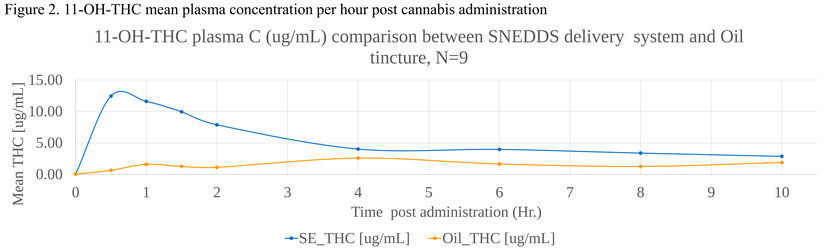


Figure 3. CBD mean plasma concentration per hour post cannabis administration

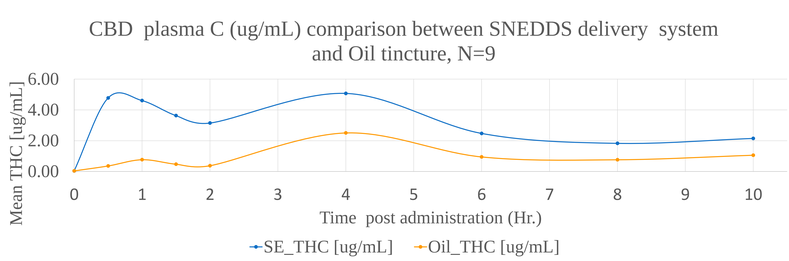


Figure 4. CBD mean plasma concentration per hour post cannabis administration

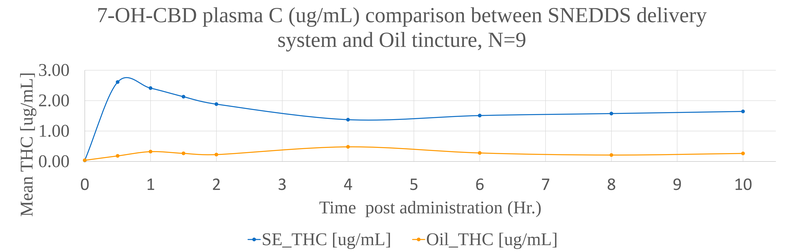
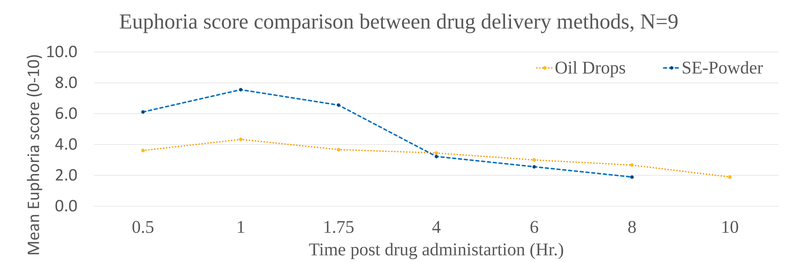


Figure 5. Euphoria score post cannabis administration per study group



Conclusion

Results of this study suggest that utilization of the Capsoil ® Self NanoEmulsifying Drug Delivery System for oral cannabis products results in a higher Cmax, shorter Tmax, and greater bioavailability as compared to oil-based tinctures of the same starting dose. Bioavailabilities of THC, 11-0H-THC, CBD, and 7-OH-CBD were 3.28x, 3.34x, 2.79x, and 4.96x times higher when cannabis was administered via Capsoil® SNEDDS as compared to the oral tincture, respectively. The favorable clinical outcomes that were displayed offer hope to patients who wish to utilize an orally administered product with attractive pharmacokinetics. While larger trials are needed preliminary data suggests that utilization of Capsoil ® SNEDDs technology for cannabis preparations facilitates the rapid onset typically seen in inhaled modalities with the benefit of a prolonged half-life associated with orally consumed cannabis products.

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