Liposomal Cannabidiol Delivery: A Pilot Study

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Abstract

OBJECTIVE: The aim of this study was to measure the bioavailability of equivalent amounts of cannabidiol (CBD, 10 mg) as a stand-alone active ingredient compared with a liposomal preparation (CELLg8 Hemp).

METHODS: This pharmacokinetic pilot study included 15 healthy patients who were not taking a CBD product at baseline. A crossover study design was used to analyze peak blood CBD levels at baseline and 1 hour after ingesting the liposomal and nonliposomal preparations, with a 2-week washout period between each preparation.

RESULTS: CBD was detected in the blood of all 15 patients who ingested the liposomal preparation at 1 hour, whereas the stand-alone ingredient was only found in 40% of the individuals at the same time point. Serum levels of CBD were significantly higher ($P<0.0001$) in patients after use of the liposomal preparation compared with the stand-alone CBD.

CONCLUSION: The findings suggest that the bioavailability of oral CBD is higher in the liposomal preparation than the nonliposomal CBD preparation.

Introduction

Although oral cannabidiol (CBD) formulations are increasingly popular, studies show that oral CBD has a much lower bioavailability than inhaled CBD.[1] This study was designed to compare the bioavailability of 2 different preparations of oral CBD, with and without a liposomal delivery system.

Puffin Hemp (http://www.puffinhemp.com) has a patent-pending liposome manufacturing technology that is used to prepare CBD products with high bioavailability, using a proprietary CELLg8 delivery system. This natural liposomal preparation is designed to increase the amount of active ingredient that is absorbed into the bloodstream. We have previously published on a similar liposomal delivery system for vitamin C, where increased absorption was observed compared with a nonliposomal product.[2]

Methods

Study participants were recruited from the general population in Colorado using the following inclusion criteria:

- Men and women 25 to 70 years of age
- Able to read and sign the informed consent and complete the protocol
- Ability to comply with study requirements and study schedule
- Not taking a CBD product at baseline
- In good general health

Exclusion criteria included the inability to complete the protocol and the presence of a terminal illness.

Fifteen individuals met the inclusion criteria and were recruited for the pharmacokinetic pilot study. A crossover study design was used to analyze peak blood CBD levels at baseline and 1 hour after ingesting the liposomal and nonliposomal preparations, with a 2-week washout period between each preparation.

At the first study visit, participants completed the informed consent process and were randomized to either stand-alone CBD or liposomal CBD. Liposomal CELLg8 CBD, derived from industrial hemp, was provided by Puffin Hemp. Participants were instructed to wait at least 4 hours after eating before undergoing a blood draw to measure baseline CBD blood levels. Then, they ingested 10 mg of CBD either with or without the liposomal delivery system. At 1-hour post-ingestion, blood was collected to compare the concentration of CBD before and after ingestion.

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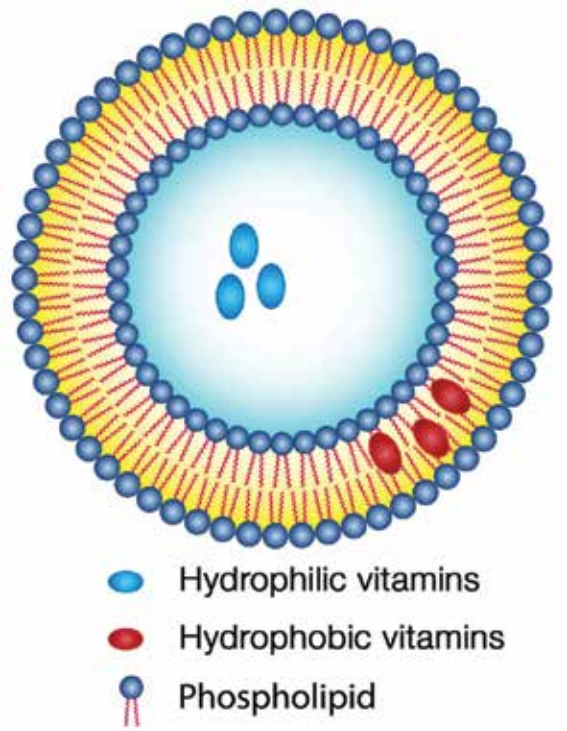

Figure. Liposomes are injected with vitamins, minerals or other active compounds to facilitate absorption through the digestive tract.

Image courtesy of Puffin Hemp.

Liposomal CBD
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At the second study visit (2 weeks later), the same procedure was repeated in all study participants with the alternate preparation. This 2-week dosing schedule was designed to allow for a washout period. The blood draws were completed at Any Lab Test Now where a clinical chemist was chaperoning study participants. Compensation for participation in the study included a bottle of liposomal CBD for each blood draw.

Results

All participants showed absorption of CBD in the bloodstream via liposomal delivery at 1 hour. In contrast, no CBD was detected in 9 of the 15 participants at 1 hour after ingestion of nonliposomal CBD. Table 1 shows CBD blood levels measured at baseline and 1-hour post-ingestion for both CBD preparations. Two participants demonstrated baseline CBD levels >0 (0.1 and 0.19 ng/mL) before ingesting the liposomal preparation but because they were already randomized, they were still included per intention to treat analysis (ITT).

Statistical analysis was performed to calculate the area under the curve (AUC) using the trapezoid method. The mean CBD level at 1-hour post-ingestion was significantly higher when participants received the liposomal preparation compared to the nonliposomal preparation (1.77 and 0.24, respectively; $P<0.0001$; Table 2). Results were not markedly altered by the 2 participants with baseline CBD levels.

> "The results of this study demonstrate that liposomal [CBD] has significantly greater bioavailability than stand-alone CBD."
>
> *—Emek Blair, PhD*

The highest concentration of CBD detected at 1 hour was 5.9 ng/mL in the liposomal CBD preparation compared with 1.3 ng/mL in the nonliposomal preparation. The mean area under the curve (AUC) for CBD concentration was significantly higher (0.89±0.75 ng/mL) in the liposomal preparation compared with the nonliposomal preparation (0.12±0.20 ng/mL; $P<0.0001$).

Participants were monitored for adverse events and were asked to report any form of discomfort or unusual effects including stomach upset, nausea, or headache. No issues were reported.

Discussion

The present study suggests that the bioavailability of oral CBD is higher in the liposomal preparation than in the nonliposomal preparation. To my knowledge, this is the first study to compare the bioavailability of 2 preparations of oral CBD in humans.

A review by Millar et al. states that "literature in humans is not sufficient" in regard to understanding CBD bioavailability.[1] A recent study by Tayor et al. investigated the metabolism of CBD in 8 individuals with varying degrees of renal impairment, finding that renal impairment had no effect on the metabolism of CBD.[3] Another pharmacokinetic study evaluated the safety and tolerability of oral CBD in 32 healthy individuals, finding support for twice-daily administration of CBD.[4] These recently published studies are

Table 1. CBD Levels Before and After Ingestion of 10 mg CBD as a Liposomal and Nonliposomal Preparation

	Nonliposomal CBD		Liposomal CBD	
Participant	Baseline (ng/mL)	1-hour post-ingestion (ng/mL)	Baseline (ng/mL)	1-hour post-ingestion (ng/mL)
1	0	0.87	0	5.9
2	0	0	0	0.87
3	0	0.14	0.1	2
4	0	0	0.19	2.4
5	0	0.45	0	1.6
6	0	0	0	0.35
7	0	1.3	0	2.7
8	0	0	0	0.43
9	0	0	0	0.13
10	0	0.17	0	1.7
11	0	0	0	0.65
12	0	0	0	3.4
13	0	0	0	2.5
14	0	0	0	0.86
15	0	0.65	0	1

CBD, cannabidiol.

Table 2. CBD Concentration 1 Hour After Ingestion of 10 mg CBD as a Liposomal and Nonliposomal Preparation

	Nonliposomal		Liposomal		
	Mean (SD)	95% CI	Mean (SD)	95% CI	*P* value
Post-ingestion, ng/mL	0.24 (0.40)	0.02-0.46	1.77 (1.50)	0.93-2.60	<0.0001
Change from baseline to 1 hour, ng/mL	0.24 (0.40)	0.02-0.46	1.75 (1.50)	0.92-2.58	<0.0001
AUC, ng/mL*h	0.12 (0.20)	0.01-0.23	0.89 (0.75)	0.47-1.31	<0.0001

AUC, area under the curve; **CBD,** cannabidiol.

critical contributions to this emerging area of research, but to my knowledge, none has investigated a liposomal delivery system.

With the rapidly expanding use of hemp extract and CBD products, a thorough understanding of the rate of absorption of CBD is critical to the development of CBD as a health food and supplement. In fact, Vandrey et al. reported on the mislabeling of CBD content in medical marijuana products. The authors found only 13 of 44 products containing CBD that accounted for the ingredient on the label.[5] Furthermore, 4 of the products were underlabeled and 9 were overlabeled for CBD content. These findings support the need for a more thorough understanding of CBD dosage in humans and improved quality control within the industry.

Results of this study show greater absorption of liposomal CBD than the stand-alone active ingredient and higher ratio per peak concentration. This demonstrates that the liposomal preparation may provide a more efficient delivery of CBD to the bloodstream than oral ingestion of the stand-alone ingredient.

Study limitations include the potential carryover effect that may occur with a crossover study design. Future studies with larger populations are needed to fully understand the crossover effect between the standard and liposomal preparations. The 2 participants who demonstrated baseline CBD levels before ingesting the liposomal preparation may be a confounding factor in the ITT. Finally, further studies with additional time points should be conducted in the future to measure duration and more closely compare the rate at which liposomal CBD and stand-alone CBD enter the bloodstream.

Liposomal delivery systems may help bypass the digestive system, where active ingredients are broken down or rejected via first-pass rejection.[6] Theoretically, liposomal preparations may allow for lower doses of CBD to be given to achieve the same effect as a nonliposomal product. For these reasons, a liposomal CBD preparation may be preferred.

A recent safety study on the same liposomal CBD preparation showed that 7 of 10 of blood measures (comprehensive metabolic panel or complete blood cell count measure) that were out of range at baseline normalized in all individuals after taking liposomal CBD daily for 30 days.[7] Additionally, all 5 individuals who were in the high range for baseline glucose level exhibited normalized values after taking liposomal CBD. Liposomal CBD appears to be safe and effective in healthy patients, although further research in larger studies is needed.

> **"Larger studies with more time points are needed to replicate results and validate that liposomal [CBD] is a more efficient and universal delivery system than nonliposomal preparations of [CBD]."**
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> ***—Emek Blair, PhD***

Conclusion

The results of this study demonstrate that liposomal CBD has significantly greater bioavailability than stand-alone CBD. Larger studies with more time points are needed to replicate results and validate that liposomal CBD is a more efficient and universal delivery system than nonliposomal preparations of CBD.

References

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