



**nanoHEMP**

VALIDATED SCIENCE | CONSISTENT MANUFACTURING

Absorption-Bioavailability of nanoHEMPs'  
nano-Enhanced CBD is Greatly Increased.

**Introduction:** Cannabidiol (CBD) from industrial hemp is a multi-functional molecule. Scientific studies indicated that it may be a more powerful antioxidant than either Vitamin C or E, and CBD offers the prospect of successfully fighting chronic inflammation and protecting brain cells from reactive oxygen species. (1-2)

CBD's beneficial potential is discussed in numerous published papers. It has promise in stabilizing and even reducing blood sugar levels; as a painkiller; for reducing the risk of artery blockage; in suppressing muscle spasms, seizures, and convulsions; for fighting varied cancers; and more. (3-8)

Such promise is accompanied by a major limitation to its usefulness — low bioavailability.

This means that any beneficial effects from CBD become patchy or erratic due to problems in getting CBD into the body in adequate amounts. (9-14) For a supplement taken by mouth, bioavailability means the proportion of a dose that enters the bloodstream from the small intestine. 15-17 Once in the blood, the supplement can find its way to the target organ or body system, where it then goes to work in supporting health and wellness.

On average, only 5-6% of almost any CBD preparation gets into the bloodstream. The rest is wasted. Such poor oral bioavailability guarantees variable or unpredictable effects, along with increased costs from having to take larger doses to compensate. Appropriate formulation strategies that assist in getting into the bloodstream are thus mandatory for CBD to attain its health-giving potential, let alone in a cost-efficient or economical fashion.

nanoHEMP's development has yielded a patented CBD technology using GRAS ingredients that resolve CBD's bioavailability problem. This patented technology is the first of its kind. "**GRAS**" means that a substance is **Generally Recognized As Safe** by the US Food and Drug Administration and that it can consequently be used in foods and beverages. (18)



Ingredient & Material Components in Decreasing Order of Weight or %	What is the Ingredient's US regulatory Status?					List Applicable Reference(s)
	GRAS	Self-Affirmed GRAS	GRAS Notification Dietary Supplement	Food of Flavor Additive Regulation	Not Applicable	CFR Regulation
Industrial Hemp					X	
Polyoxyethylene Sorbitan Monooleate	X					21 CFR 172.840
Propylene Glycol	X					21 CFR 184.6666
Medium Chain Triglycerides	X					21CFR 170.36; GRAS Notice 000449: Medium Chain Triglycerides
Polyoxyl 35 Castor Oil	X					21CFR 176.210
Phosphatidyl Choline	X					21 CFR 184.1400

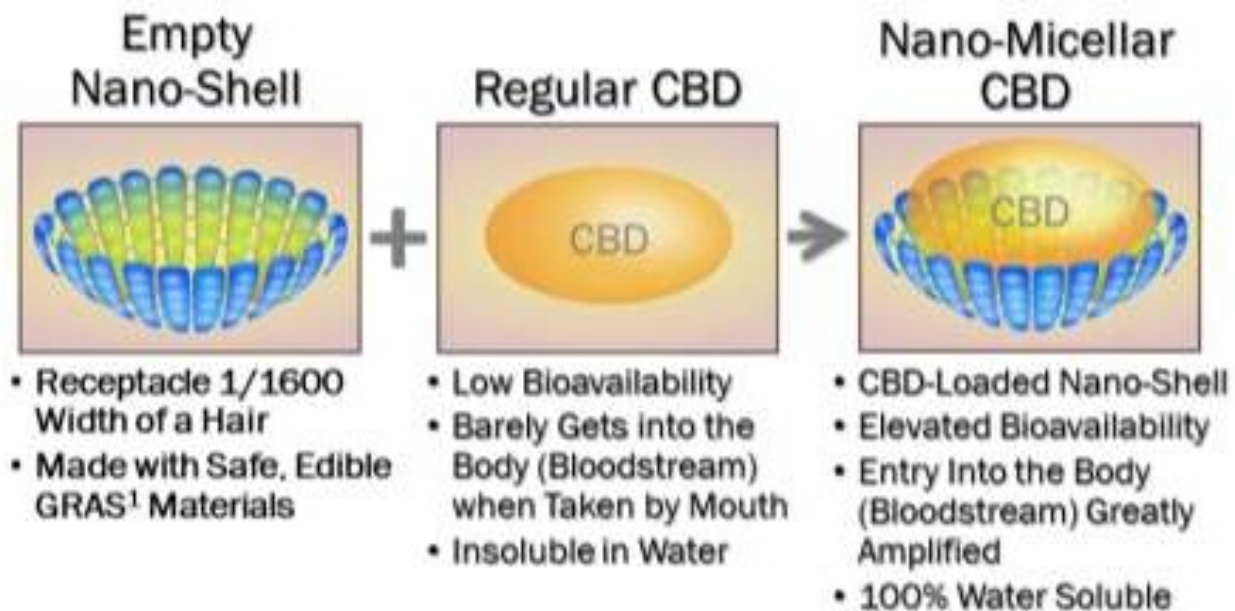


Figure 1. Patented, proprietary technology (nānoHEMP) involves highly-ordered constructs made from GRAS compounds into which CBD is affixed. This technology makes nānoHEMP 100% absorbed when taken by mouth.

**Purpose.** This study compares the bioavailabilities of regular CBD and Full absorption of nānoHEMP's enhanced CBD in laboratory rats. The bioavailability and absorption of substances taken by mouth are comparable between rats and humans. (19-28)

**Methods.** This demonstration looks at the plasma contents of cannabidiol (CBD) after a single oral dose administered by gavage (through a tube leading down the throat to the stomach; 29 ) of regular CBD and nānoHEMP's enhanced CBD over a 24-hour period.

Female Sprague-Dawley rats (240-265 gm body weight) were used. The study design and animal usage were reviewed and approved by an Institutional Animal Care and Use Committee (IACUC) for compliance with regulations prior to study initiation. Animal welfare for this study with the U.S. Department of Agriculture's (USDA) Animal Welfare Act (9 CFR Parts 1, 2, and 3) and the Guide for the Care and Use of Laboratory Animals (30).

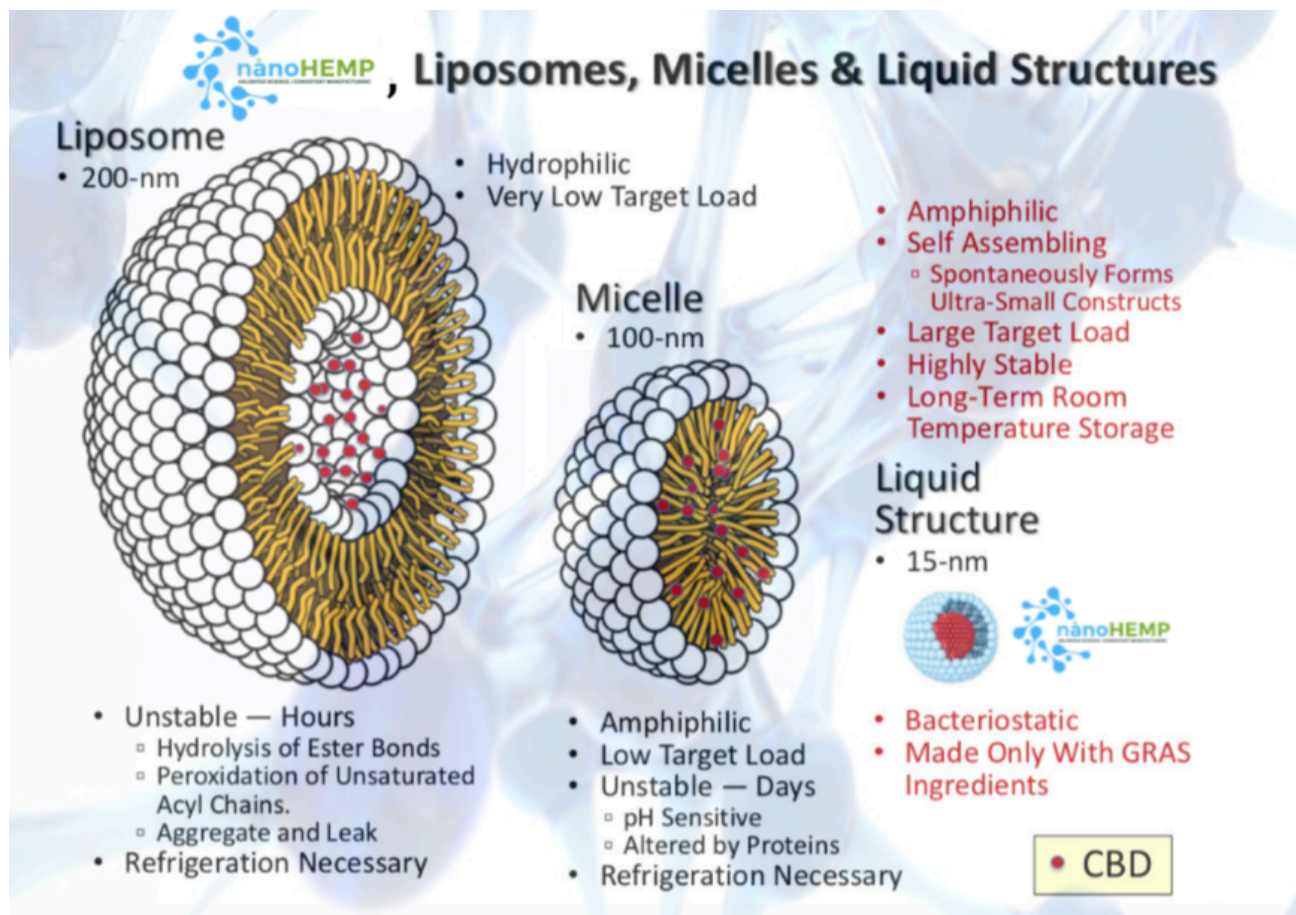
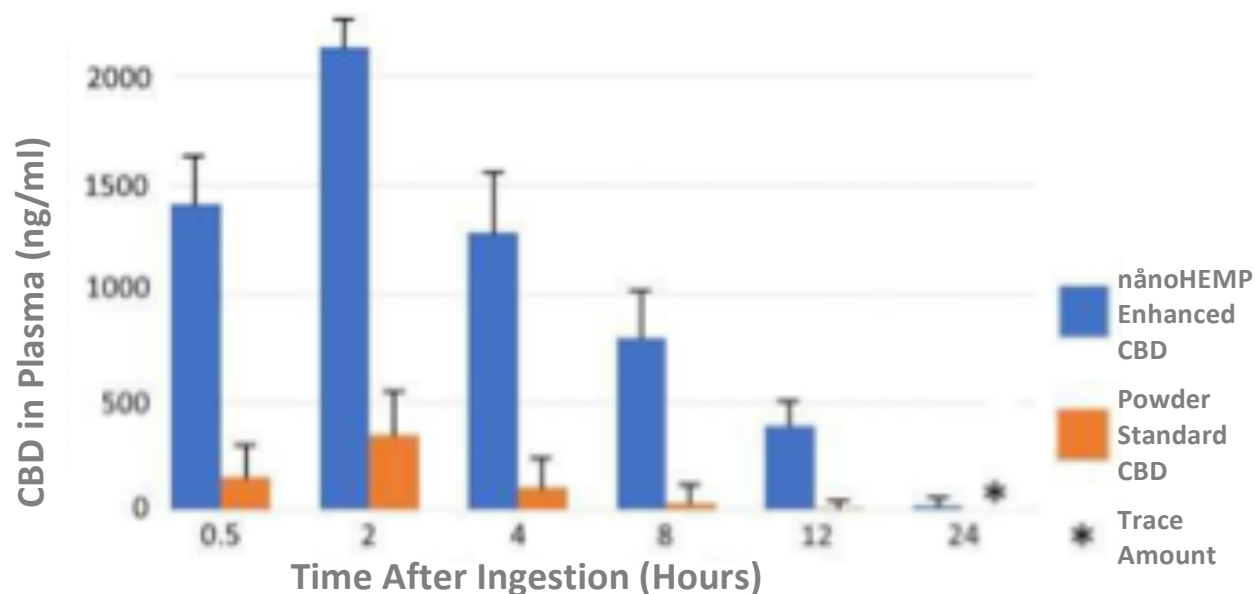
A 50-mg CBD/kg body weight model was examined in animals given nānoHEMP's nano-enhanced CBD and a control group for which powdered pure CBD in the same amount was fed. Ten animals were in each group.

Blood samples were taken immediately prior to gavage as well as 0.5, 1.0, 2.0, 4.0, 8.0, 12.0 and 24.0 hours after dosing. Venous blood was collected in an EDTA blood collection tube.

Plasma was separated from red blood cells by centrifugation at 400 g for 15 min., transferred to a fresh microcentrifuge tube, and stored at -80°C. CBD was quantified using validated high-performance liquid chromatography with tandem mass

spectroscopy (LC-MS-MS) in multiple reaction monitoring (MRM) mode.

**Findings.** The results verify that nanoHEMP's enhanced CBD greatly improves absorption/bioavailability. It was tremendously more bioavailable than regular CBD at 0.5 and 2 hours. The results suggest far lower dosing is needed for enhanced CBD versus standard CBD (Isolate, distillate, HEMP oil). In other words, a little will go a long way. The results also intimate that products containing the regular, non-enhanced CBD found in most products may suffer from low bioavailability and a consequent ineffectiveness.



## References

1. Burstein, S. 2015. Cannabidiol (CBD) and its analogs: a review of their effects on inflammation. *Bioorganic & Medicinal Chemistry* 23(7):1377-1385.
2. Couch, D.G., H. Maudslay, B. Doleman, J.N. Lund, and S.E. O'Sullivan. 2018. The use of cannabinoids in colitis: a systematic review and meta-analysis. *Inflammatory Bowel Disease* 24(4):680-697.
3. Campos, A.C., M.V. Fogaça, A.B. Sonego, and F.S. Guimarães. 2016. Cannabidiol, neuroprotection and neuropsychiatric disorders. *Pharmacological Research* 112:119- 127.
4. Mannucci, C., M. Navarra, F. Calapai, E.V. Spagnolo, F.P. Busardò, R.D. Cas, F.M. Ippolito, G. Calapai. 2008. Neurological aspects of medical use of cannabidiol. *CNS & Neurological Disorders Drug Targets* 16(5):541-553.
5. McAllister, S.D., L. Soroceanu, and P.Y. Desprez. 2015. The antitumor activity of plant-derived non-psychoactive cannabinoids. *Journal of Neuroimmune Pharmacology* 10(2):255-267.
6. Pisanti, S., A.M. Malfitan, E. Ciaglia, A. Lamberti, R. Ranieri, G. Cuomo, M. Abate, G. Faggiana, M.C. Proto, D. Fiore, C. Laezza, and M. Bifulco. 2017. Cannabidiol: state of the art and new challenges for therapeutic applications. *Pharmacology & Therapeutics* 175:133-150.
7. Robson, P.J. 2014. Therapeutic potential of cannabinoid medicines. *Drug Testing and Analysis* 6(1-2):24-30.
8. Russo, E.B. 2008. Cannabinoids in the management of difficult to treat pain. *Therapeutics and Clinical Risk Management* 4(1):245-259.
9. Agurell, S., S. Carlsson, J.E. Lindgren, A. Ohlsson, H. Gillspie, L. Hollister. 1981. Interaction of THC with cannabinal and cannabidiol following oral administration in man. Assay of cannabinal and cannabidiol by mass fragmentography. *Experientia* 37:1090–1092.
10. Gaston, T.E., and D. Friedman. Pharmacology of cannabinoids in the treatment of epilepsy. *Epilepsy & Behavior* 70(Pt. B):313-318.
11. , F. 2003. Pharmacokinetics and pharmacodynamics of cannabinoids. *Clinical Pharmacokinetics* 42(4):327-360.
12. McGilveray, I.J. 2005. Pharmacokinetics of cannabinoids. *Pain Research and Management* 10(Suppl. A):15A-22A.
13. Ohisson, A., J.E. Lindgren, S. Andersson, S. Agurell, H. Gillespie, L.E. Hollister. 1986. Single-dose kinetics of deuterium-labeled cannabidiol in man after smoking and intravenous administration. *Biomed Environ Mass Spectrometry* 13:77–83.
14. Samara, E., M. Bialer, R. Mechoulam. 1988. Pharmacokinetics of cannabidiol in dogs. *Drug Metabolism and Disposition* 16:469–472.
15. El-Kattan, A.F. 2017. Oral Bioavailability Assessment: Basics and Strategies for Drug Discovery and Development (Wiley Series on Pharmaceutical Science and Biotechnology: Practices, Applications and Methods). First Edition. Wiley, New York, 448 p.
16. GRAS Substances (SCOGS) Database. U.S. Food and Drug Administration. <https://www.fda.gov/Food/IngredientsPackagingLabeling/GRAS/SCOGS>
17. Akonur, A.I., C.J. Holmes, and J.k. Leypoldt. 2014. Predicting the peritoneal absorption of icodextrin in rats and humans including the effect of  $\beta$ -amylase activity in dialysate.

Peritoneal Dialysis International 35(3):288-296.

18. Fagerholm, U., M. Johansson, and H. Lennernäs. 1996. Comparison Between Permeability Coefficients in Rat and Human Jejunum. *Pharmaceutical Research* 13(9):1336-1342.
19. Lawless E., B.T. Griffin B, A. O'Mahony A, and C.M. O'Driscoll. 2015. Exploring the impact of drug properties on the extent of intestinal lymphatic transport - in vitro and in vivo studies. *Pharmaceutical Research* 32(50):1817-1829.
20. Nagahara, N., Y. Akiyama, K. Higaki, and T. Kimura. 2006. Animal models for predicting potency of oral sustained-release adhesive microspheres in humans. *International Journal of Pharmacy* 331(1):46-53.
21. Pang, K.S. 2003. Modeling of intestinal drug absorption: roles of transporters and metabolic enzymes. *Drug Metabolism and Disposition* 31(12):1509-1517.
22. Salphati, L., K. Childers, L. Pan, K. Tsutsui, and L. Takahashi. 2001. Evaluation of a single-pass intestinal-perfusion method in rat for the prediction of absorption in man. *Journal of Pharmacy and Pharmacology* 53(7):1007-1013.
23. Stewart, B.H., O.H. Chan, R.H. Lu, E.L. Reyner, H.L. Schmid, H.W. Hamilton, B.A. Steinbaugh, and M.D. Taylor. 1995. Comparison of intestinal permeabilities determined in multiple in vitro and in situ models: relationship to absorption in humans. *Pharmaceutical Research* 12(5):693-699.
24. Zenghui Teng , Z., C. Yuan , F. Zhang, M. Huan, W. Cao, K. Li, J. Yang, D. Cao, S. Zhou, and Q. Mei. 2012. Intestinal absorption and first-pass metabolism of polyphenol compounds in rat and their transport dynamics in Caco-2 cells. *PLoS One* 7(1):e29647.
25. Zakeri-Milania,P., H. Valizadeha, H. Tajerzadehc, Y. Azarmia, Z. Islambolchilara, S. Barzegara, and M. Barzegar-Jalalia. 2007. Predicting human intestinal permeability using single-pass intestinal perfusion in rats. *International Journal of Pharmacy and Pharmaceutical Sciences* 10(3):368-379.