Addressing the challenges of **CBD bioavailability** with CBtru® – an innovative drug product intermediate

Why CBD?

Cannabinoid molecules—like cannabidiol (CBD)—demonstrate significant potential in pharmaceutical research and development and have proven themselves to be a promising avenue for improving patients' quality of life, especially in cases of drug resistant central nervous system (CNS) disorders like epilepsy.

Following the discovery of the human endocannabinoid system in the late eighties, the science behind CBD continues to grow. The molecule is showing promising potential in several therapeutic areas, including CNS diseases, pain, cancer, sleep, mood disorders and more.

Understanding the opportunity

While there is remarkable opportunity for the development of CBD-based pharmaceutical products, formulating a highly lipophilic and poorly soluble crystalline active pharmaceutical ingredient (API) can be a complex task. In addition to physical and chemical stability challenges, the **oral bioavailability of CBD** has been shown to be **very low in humans (6%)**, as a result of incomplete absorption in the gut and significant pre-systemic elimination in the liver.[1] Innovation and formulation capabilities of the dsm-firmenich labs can help address concerns around bioavailability and open new opportunities for drug manufacturers.

Developing patient-centric solutions: How CBtru® can shape the future of modern medicine

Aiming to inspire more patient-centric solutions than those currently on the market, dsm-firmenich has developed CBtru®. This innovative formulated CBD drug product intermediate and patent-pending proprietary solution presents several opportunities for patients, healthcare professionals, and manufacturers of pharmaceutical products, including:

- The possibility to offer patients oral solid dosage forms, which have wide applicability and increase patient convenience and acceptance in comparison to existing options that are limited to liquid oil-based dosage forms.
- Higher drug loading, meaning that patients can benefit from CBD with lower daily dosages than what is currently available with oil-based dosage forms.
- A possibly more reliable and consistent CBD uptake, less dependent on food intake.
- Optimized CBD bioavailability leading to potentially more effective medicines, decreased probability of drug-drug interactions, and minimized adverse effects.[2]

Solid dosage form

- Optimized patient compliance vs liquid oil-based dosage form
- Wider applicability in finished drug products
- Good chemical and physical stability

Higher drug loading

- Lower daily dosage of final drug product vs liquid oil-based dosage form
- Lower cost in use (CIU)
- 3x to 4x increase in API loading vs commercially available product

Optimized bioavailability

Demonstrated in human clinical trial:

- Bioavailability as good as liquid oil-based reference product in fed state; higher than reference product in fasted state
- May offer a more reliable and consistent uptake of CBD, less dependent on food intake
- Safe and well tolerated

1. Perucca and Bialer. Critical aspects affecting cannabidiol oral bioavailability and metabolic elimination, and related clinical implications. Cannabinoids in Neurology and Psychiatry, 2020.
2. Millar et al. Towards better delivery of cannabidiol (CBD). Pharmaceuticals (Basel), vol. 13, pg. 219, 2020.

dsm-firmenich

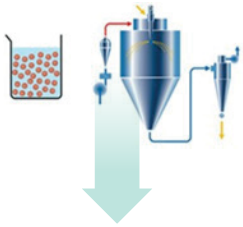
Partner with dsm-firmenich to develop your next CBD-based drug product

dsm-firmenich is investing significantly in an advanced R&D process to offer you the right solutions that help meet patient needs. We have completed a full technology screening and validation process of over 200 candidates in the lab.

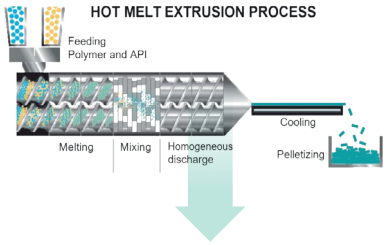
In our research we benchmarked nano-emulsification, liposomal and lipid nanoparticle (LNP) encapsulation with formation of amorphous dispersions to identify optimal solutions and build a formulation toolbox for CBD-based therapies. Through this process, CBtru® was developed—a spray-dried, nano-emulsified drug product intermediate.

In-house development

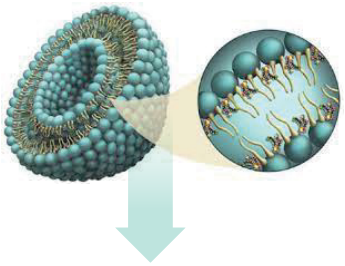
External partnerships



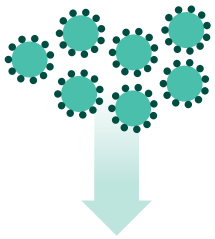
CBD spray dried powder



Amorphous solid dispersions



Liposomes & LNPs



Spray dried amorphous dispersions

In vitro bioaccessibility screening

Caco-2 assay (cell assay) was developed to determine CBD transcellular transport and measure in vitro bioaccessibility. More than 120 lab prototypes, produced using different technologies as mentioned above, were tested using Caco-2 assay. A selection of the best CBD formulations that emerged were tested for in vivo bioaccessibility.

In vivo bioaccessibility screening

- CBtru® demonstrated good physical and chemical stability
- 3x – 4x increase in API loading vs commercial products
- Similar bioavailability vs oil-based CBD formulation Epidiolex®, the first (and to this date only) commercially approved CBD drug product on the market.

Human clinical evidence

dsm-firmenich investigated the absorption and pharmacokinetic profile (bioavailability) of CBtru® vs the market-approved sesame oil-based CBD formulation, Epidiolex®, in a randomized, open-label, 4-way cross-over study (32 individuals, aged 19-55). The study findings confirmed:

- The bioavailability of CBtru® was as good as that of the liquid oil-based reference product in fed state (with a high fat meal)
- In the fasted state, CBtru® demonstrated higher bioavailability than the reference product
- CBtru® was safe and well tolerated.

The clinical study also indicated that CBtru® may offer a more reliable and consistent uptake, less dependent on food intake. By demonstrating that the bioavailability of CBtru® was as good as that of the market-reference oil-based product, Epidiolex®, we've opened new possibilities for promising research and the development of new oral solid CBD-based dosage forms.

Ready to discover the full therapeutic potential of cannabinoids, like CBD, and deliver patient-centric pharmaceuticals with purpose?

Connect with us today

dsm-firmenich