**Enhancing the Solubility of Cannabinol with Cyclodextrins and Human Serum Albumin**

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**Background and aims.** Cannabinol (CBN) is a minor phytocannabinoid from cannabis that has pro-sleep effects that may be useful for treating insomnia (1). While formulating CBN as solid dosage forms would best ensure physicochemical stability, its low aqueous solubility poses a significant delivery challenge. Few studies have been reported on improving the solubility of CBN. Cyclodextrins and serum albumin have been used to increase the solubility and bioavailability of hydrophobic drugs (2-4), including cannabidiol (5-7), but their solubilising effects on CBN have not yet been studied. This study aimed to develop a CBN powder with enhanced solubility using cyclodextrins and human serum albumin (HSA) as excipients.

**Methods.** Solubility tests were conducted using α-cyclodextrin, β-cyclodextrin, γ-cyclodextrin, methyl-β-cyclodextrin, 2-hydroxypropyl-β-cyclodextrin, and HSA. HSA showed the strongest solubilising power, so it was co-dissolved with CBN in 50:50 v/v water:tert-butanol and spray freeze-dried to obtain a powder. The CBN-to-HSA mass ratio in the formulation was 20:80. The resultant particles were imaged by scanning electron microscopy and sized by laser diffraction. Their residual solvent content, crystallinity, thermal behaviour, and response to moisture were measured by thermogravimetric analysis, X-ray diffraction, differential scanning calorimetry, and dynamic vapour sorption, respectively. Dose uniformity was assayed by high performance liquid chromatography.

**Results.** The aqueous solubility of CBN in the presence of the excipients followed the order of: HSA > methyl-β-cyclodextrin = 2-hydroxypropyl-β-cyclodextrin > β-cyclodextrin > α-cyclodextrin = γ-cyclodextrin (Figure 1). The co-spray freeze dried CBN-HSA particles were amorphous, with a median volumetric diameter of 27.3 ± 1.6 μm and residual solvent content of 6.9%. The CBN assayed dose was uniform, at 101.7 ± 3.5%. No crystallisation was observed upon exposing the powder up to 90% relative humidity.



**Figure 1.** Solubility of CBN in the presence of (a) cyclodextrins and (b) HSA.

**Conclusion.** The solubility of CBN was increased the most by HSA. The spray freeze dried CBN-HAS powder was amorphous, uniform in content, and stable at high humidity. It could be further developed into solid dosage forms for enhanced CBN delivery.

**References.**

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