Safety, Tolerability, and Pharmacokinetics of "Pharmaceutical-Grade Full Spectrum Cannabidiol" Administered as Single Sublingual Wafer and Oil Solution in Healthy Volunteers

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Background

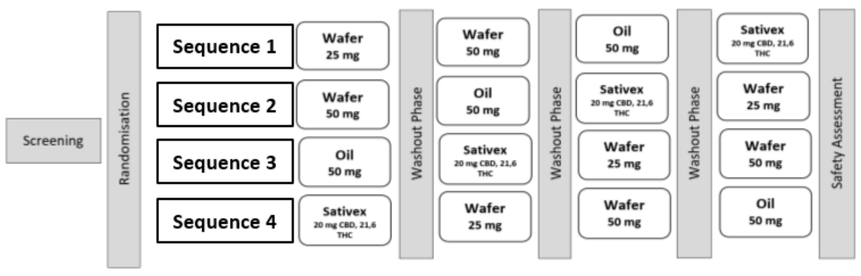
Cannabidiol (CBD) is the non-psychoactive component of the cannabis plant that has shown therapeutic effect for multiple conditions. There is limited information on CBD's pharmacokinetics (PK) in human.

Objectives

To determine the safety, tolerability, and PK of Bod Proprietary CBD Extract after oral administration of single sublingual wafer and oil in healthy volunteers and to compare the PK profiles of CBD with Sativex oromucosal spray.

Methods

- Open Label, Four-way Crossover in 12 healthy volunteers.
- Randomised to receive one of four treatment sequences with a washout period of 24 hrs between dosing.



- For each treatment sequence, the following assessments were performed:
  - **Safety Assessments**: Vital signs, 12-Lead ECG, Laboratory evaluation.
  - **Pharmacokinetics Blood Samples:** at pre-dose, then 15 & 30 min post-dose & 1, 1.5, 2, 2.5, 3, 4, 6, 8, 12, 12 and 24 hrs post-dose.
  - **Pharmacokinetics Urine Samples:** pre-dose, 0-12 and 12-24 hrs post-dose.

Results

Table 1. Baseline Characteristics

Characteristics	Subjects n=12 (Range)
Age (Yr)	33 (32-49)
Height (cm)	179 (162-200)
BMI (kg/m^2)	25 (20-29)
Weight (Kg)	81 (66- 108)
Gender	1 Female, 11 Male

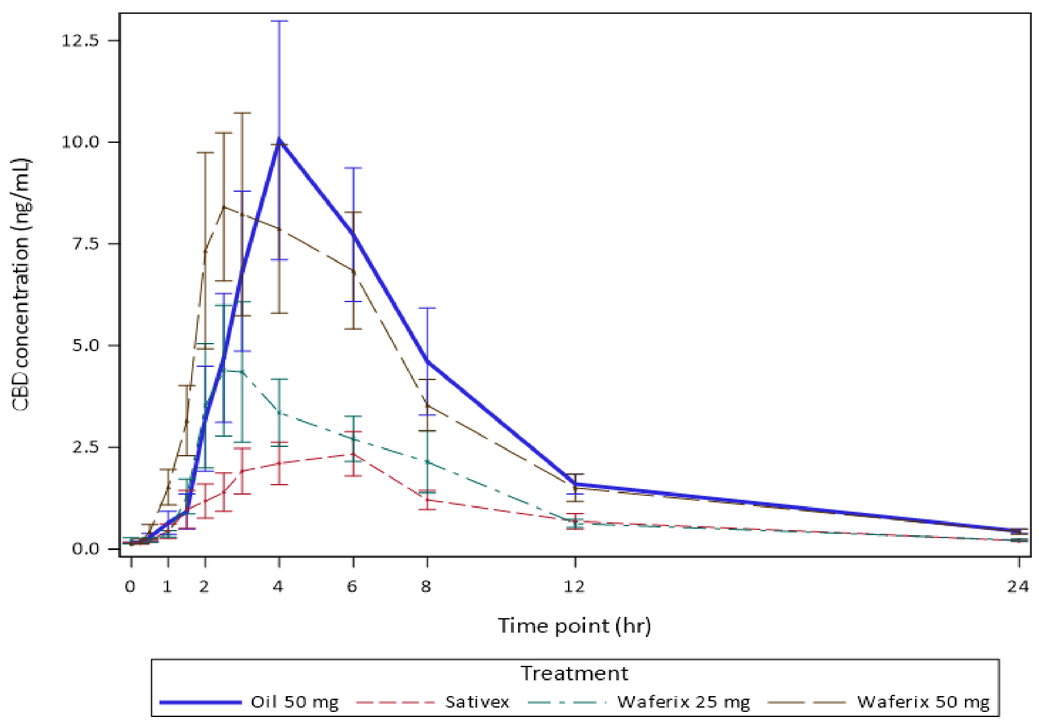
Pharmacokinetics Results:

- The plasma exposure of CBD increased in a dose-proportional manner.
- The Waferix 25 mg CBD had 25% greater exposure (AUC) than the equivalent dose of Sativex.
- Waferix 50 mg CBD had almost 30% greater peak plasma CBD concentration than the same dose of the CBD Oil.

Table 2. CBD Pharmacokinetic Parameters by Treatment Group

Parameter	WaferiX 25 mg CBD	WaferiX 50 mg CBD	Oil 50 mg CBD	Sativex20 mg CBD*
	mean ± SD			
C_{max} (ng/mL)	9.2 ± 6.7	15.0 ± 8.9	14.0 ± 9.3	4.6 ± 2.4
T_{max} (hr)	4.5 ± 2.2	4.1 ± 2.0	5.2 ± 1.8	4.5 ± 2.0
AUC_{0-t} (ng*hr/mL)	31.1 ± 12.9	67.3 ± 29.5	69.8 ± 34.1	26.6 ± 11.2
$AUC_{0-\infty}$ (ng*hr/mL)	33.5 ± 13.9	71.0 ± 1.8	73.8 ± 35.2	29.3 ± 12.3
Half-life (hr)	7.1 ± 4.2	5.7 ± 1.8	5.8 ± 2.3	6.7 ± 2.3
Clearance (L/hr)	872 ± 356	740 ± 397	826 ± 366	810 ± 317

Figure 1. Mean Plasma CBD Concentration Time Profile



Safety Results:

- The most common related AEs were somnolence, sedation and mood altered. All AEs were mild or moderate in severity.
- There were no Serious Adverse Events reported .
- No clinically significant abnormalities were reported in vital signs, ECG, physical findings or safety laboratory tests.

Table3. Treatment Emergent Adverse Events by Treatment Group

System Organ Class	Preferred Term	WaferiX 25 mg CBD	WaferiX 50 mg CBD	Sativex 20 mg CBD	CBD Oil 50 mg CBD	Overall
		n=12 n (%)				
Any subject reporting an AE		2 (17)	5 (42)	10 (83)	4 (33)	10 (83)
Eye disorders		**0**	**0**	**2 (17)**	**0**	**2 (17)**
	Eye irritation	0	0	2 (17)	0	2 (17)
Gastrointestinal disorders		**0**	**1 (8)**	**1 (8)**	**1 (8)**	**3 (25)**
	Abdominal pain	0	1 (8)	0	0	1 (8)
	Nausea	0	0	1 (8)	1 (8)	2 (17)
General disorders and administration site conditions		**0**	**0**	**2 (17)**	**0**	**2 (17)**
	Fatigue	0	0	1 (8)	0	1 (8)
	Feeling drunk	0	0	1 (8)	0	1 (8)
Infections and infestations		**0**	**1 (8)**	**1 (8)**	**0**	**2 (17)**
	Upper respiratory tract infection	0	1 (8)	1 (8)	0	2 (17)
Injury, poisoning and procedural complications		**0**	**0**	**0**	**1 (8)**	**1 (8)**
	Contusion	0	0	0	1 (8)	1 (8)
Nervous system disorders		**2 (17)**	**3 (25)**	**5 (42)**	**3 (25)**	**9 (75)**
	Dizziness	0	0	1 (8)	0	1 (8)
	Presyncope	0	0	0	1 (8)	1 (8)
	Sedation	0	1 (8)	2 (17)	1 (8)	4 (33)
	Sensory disturbance	0	0	1 (8)	1 (8)	2 (17)
	Somnolence	2 (17)	2 (17)	2 (17)	1 (8)	6 (50)
Psychiatric disorders		**0**	**1 (8)**	**5 (42)**	**0**	**5 (42)**
	Agitation	0	0	1 (8)	0	1 (8)
	Anxiety	0	0	1 (8)	0	1 (8)
	Disorientation	0	0	1 (8)	0	1 (8)
	Dysphoria	0	0	1 (8)	0	1 (8)
	Euphoric mood	0	0	2 (17)	0	2 (17)
	Mood altered	0	1 (8)	0	0	1 (8)

* Values for Sativex 20 mg CBD were normalised to 25 mg CBD

Summary:

- The Bod proprietary CBD extract demonstrated a considerably sound safety profile in the form of wafer and oil.
- The CBD extract resulted in a lower rate of related Adverse Events (AEs) compared to Sativex.
- The pharmacokinetic profile of CBD was fully characterised following single and multiple dose administration of the Bod proprietary CBD extract as wafer and oil.