WESTERN SYDNEY
UNIVERSITY

Participant Information Sheet – Medical (Extended)

Project Title: Crossover design pharmacokinetics investigation of ANTG's CBD MCT oil with and without fasting in healthy volunteers

Project Summary:

You are invited to participate in a research study being conducted by researchers from Western Sydney University, who are interested in investigating the absorption, distribution, metabolism, and elimination processes of a single dose of the Australian Natural Therapeutics Group's (ANTG) Medium-chain triglyceride (MCT, coconut oil) 100mg Cannabidiol (CBD) oil in the human body. As part of this study, we are recruiting healthy adult participants who have obtained an agreement from their medical doctor to take part in both study conditions, fasting and feeding.

CBD is a widely used treatment for various medical conditions, such as epilepsy, carcinoma, substance use disorders, psychotic disorders, anxiety disorders and neurocognitive disorders. This research aims to assess the concentration of the drug across time for the ANTG's MCT 100mg/mL CBD oil product in healthy adults via testing the blood samples. The results of this study will help in determining whether this product can achieve a Schedule 3 listing. Schedule 3 listing makes the product accessible to the public without the need for a medical prescription.

The researchers involved with this project are Dr Mitchell Low, Dr. Guoyan Yang, Dr. Carolyn Ee and Professor Dennis Chang, all from the NICM Health Research Institute of Western Sydney University, Australia.

This research project has been approved by the Western Sydney University Ethics Committee (H15050).

How is the study being paid for?

This study is being sponsored by the Australian Natural Therapeutic Group (ANTG). The study is co-funded by the NSW government tech voucher program.

What will I be asked to do?

This crossover study is open to people from Australia who must meet the following criteria.

Inclusion:

- Aged 18 to 45 years old at the time of consent.
- Able and willing to comply with all study procedures.
- Willing and able to give informed written consent.
- Fluent English speaking.

Exclusion:

- Tobacco smoker, current or former.
- Binge drinker, current or former (defined as more than 4 standard drinks in a single session OR more than 10 standard drinks in a week).
- Takes ANY prescription medication, especially blood thinners/anti-thrombotic agents, anti-inflammatory drugs, hypoglycemics, H2 blockers, proton pump inhibitors, and immunosuppressants.
- Frequent use (more than twice weekly) of any non-prescription NSAIDs (including ibuprofen and diclofenac).
- Diagnosis of metastatic cancer and in active treatment (including chemo/radio/hormonal/immunotherapy) or with recurrence on last follow-up with oncologist.
- Pregnant, breastfeeding, plan to conceive within 6 months (both women and men) or unwillingness to use oral contraceptives.
- History of psychiatric disorders (including suicide attempt, schizophrenia, severe depression or anxiety, personality disorder, or history of psychosis).
- History of cognitive impairment, seizures, or epilepsy.
- History of gastric, small bowel or colonic surgery.
- History of liver or renal disease, hyperacidity, gastric/duodenal ulcers, gallbladder problems, or hyperglycaemic, haemophiliac diseases.
- History of Type 1 or 2 diabetes, impaired glucose tolerance or with fasting blood sugar level <5.5 mmol/L.
- History of substance use disorder (ICD-10 criteria (abuse, dependence)) to alcohol, opioids, benzodiazepines or simulants (excluding caffeine, tobacco).
- Had taken cannabinoids for a cannabinoid-based medicine within 6 months prior to the study or provides a blood sample at the initial timepoint (before the dose) that tests positive for cannabinoids.
- Severe unstable heart disease (unstable angina or ischaemic heart disease, heart failure >NYHA Grade 2; uncontrolled hypertension/hypotension);
- Allergies to MCT oil (as derived from coconut oil) or cannabidiol.
- Vegan, vegetarian, or religiously required to abstain from meat and/or dairy products included in the standardised fat-rich fast-food breakfast meal.
- Participation in a clinical trial of another chemical entity.
- Conditions causing irreversible or blood transfusion dependent anaemia where the volume of blood sampling required for this study is contraindicated in the opinion of the clinician PI.
- Currently on a weight loss program, or ketogenic diet unless it had been stable for 4 weeks before the initial assessment visit and throughout the entire trial period
- Participants will be excluded if according to the judgment of their physician they might be vulnerable to drug addiction or mental instability.
- Not willing to abstain from recreational drug use (excluding: caffeine, and alcohol that is not recognised as binge drinking) during the study.
- Under academic supervision or employed by a member of the research team

You will be asked to spend one day and return the next day on two occasions to the NICM Health Research Institute, Westmead campus of Western Sydney University.

On the first occasion, you will be asked to fast overnight (for a minimum of 10 hours) before coming to NICM Health Research Institute in the morning. In the morning you will be given 1ml (equivalent to

100 mg) of ANTG's CBD MCT oil. Your blood samples will be collected at various times via a cannula. These times are at 0.5, 1, 1.5, 2, 2.5, 3, 3.5, 4, 4.5, 5, 6, 7, 8, 10, 12, and 30 hours following ingestion. The blood samples will be 5 mL drawn from a cephalic (arm) vein. You will be asked to stay for 12 hours on the first day with the cannula inserted (removed if discomfort occurs) and return to NICM Health Research Institute on the following day for a sample collection at 30-hour timepoint.

After 6-week washout period, you will be asked to return to the NICM Health Research Institute, where you will receive the same dose 30min after a high-fat fast-food breakfast (provided). The same sampling technique and timepoints will be used to collect blood samples, which will once again require participants to leave the institute at the 12-hour timepoint and return the following day for the 30-hour timepoint.

During both test days, a light lunch and dinner will be provided. You will have unrestricted access to water and are free to use the public facilities at the NICM Health Research Institute.

How much of my time will I need to give?

The total time commitment is approximately 30h for this study. On each of the two occasions, you need to stay at NICM Health Research Institute for 12 hours on the first day and return the following day at a 30-hour time point. There will be a 6-week gap between the two occasions. An eligibility pre-screening phone call, a visit to the NICM Health Research Institute to meet the Chief investigator and clinician to finalise eligibility and collect consent, and a follow-up call 7 days after receiving each dose will also require a small portion of your time.

What benefits will I, and/or the broader community, receive for participating?

Our aim is to contribute towards the Schedule 3 'Pharmacist only' listing of the low-dose CBD drug in the MCT oil base, by enhancing our understanding of the absorption, distribution, metabolism and elimination of the drug across time for this specific formulation and under fed and fast conditions. This may contribute towards increasing the accessibility of low-dose CBD for patients without the need for prescription, for ailments that can be identified by patients (and verified by a pharmacist) in circumstances where it is substantially safe. This means that some patients will not have to wait for a medical prescription (or for the renewal of such a prescription) to access this low-dose CBD product in Australia. As healthy participants, this might not directly benefit you.

Participants will be reimbursed $600 ($300 for each session, via Visa gift voucher) for their time at the end of the sample collection (30-hour timepoint) on the second (final) visit.

Will the study involve any risk or discomfort for me? If so, what will be done to rectify it?

You may feel some discomfort on the test days associated with insertion of the cannula and blood sampling, which may lead to irritation and bruising at the site of cannulation. This method of blood sampling was designed in the interest of your comfort, as it should lead to less discomfort than repeated venepuncture. In each visit, a volume of 80 mL shall be drawn, so there shall be negligible risk of fainting or iron deficiency anaemia when compared to typical blood donations of 500 mL.

You may feel some discomfort associated with fasting before the first visit (for a minimum of 10 hours) and for a further 4 hours into the visit. Fasting for this duration is widely recognised as safe and tolerable, and we will provide a light lunch to break your fast at no expense to you.

You may feel inconvenienced by participating, as you would be asked to stay at the NICM Health Research Institute for 12 hours and return the next day for the final sample collection. To minimise inconvenience, you are welcome to bring reading material, a tablet or portable device, and light handicrafts to minimise boredom.

In response to the administration of CBD, low doses are generally recognised as safe. However, you might experience mild to moderate sedation, dizziness, drowsiness, headache, lethargy, fatigue, fever, decreased appetite, convulsion, nausea, vomiting, diarrhea and/or abdominal pain. Our medical staff are experienced and will ensure to keep you safe during the trial. You will be medically cared for at the institute and will be transferred to the Westmead Hospital in case of an emergency.

How do you intend to publish or disseminate the results?

It is anticipated that the results of this research project will be published and/or presented in a variety of forums. In any publication and/or presentation, information will be provided in such a way that the participant cannot be identified, except with your permission. Participants may request a de-identified summary of the pooled data and/or their individual results. The expected academic outputs include at least one peer-reviewed journal article and one or more conference presentations, once the sponsor Australian Natural Therapeutics Group (ANTG) secures IP or met commercial interests.

Will the data and information that I have provided be disposed of?

Please be assured that only the researchers will have access to the raw data you provide. However, your data may be used in other related projects for up to 15 years, which may include comparative analyses of the absorption of the CBD in different population demographics.

Can I withdraw from the study?

Participation is entirely voluntary, and you are not obliged to be involved. If you do participate you can withdraw at any time without giving a reason. Whatever your decision, it will not affect your medical treatment or your relationship with the medical or academic staff.

Can I tell other people about the study?

Yes, you are welcome to discuss this study with others, as peer-to-peer referrals are accepted as a recruitment method. If you discuss this study, please direct others to this participant information sheet.

How do I get to the study site?

Initial screening, the dosing and blood collection will occur at the NICM building 158 Hawksbury road Westmead. The building is across the road from Westmead train station. There is limited parking on site and it is a long 12h+ day, so it is recommended that you take public transport or arrange a lift if you are able.

What if I require further information?

Please contact the chief investigator Dr. Mitchell Low should you wish to discuss the research further before deciding whether to participate. Ph: +61 0431 067 086. E: Mitchell.Low@westernsydney.edu.au.

What if I have a complaint?

If you have any complaints or reservations about the ethical conduct of this research, you may contact the Ethics Committee through Research Engagement, Development and Innovation (REDI) on Tel +61 2 4736 0229 or email humanethics@westernsydney.edu.au.

Any issues you raise will be treated in confidence and investigated fully, and you will be informed of the outcome.

If you agree to participate in this study, you may be asked to sign the Participant Consent Form. The information sheet is for you to keep and the consent form is retained by the researcher/s.

This study has been approved by the Western Sydney University Human Research Ethics Committee. The Approval number is H15050.