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A study on the safety and effects of the drug DMT in healthy smoking individuals

Submission date
10/05/2022

Recruitment status
No longer recruiting

Registration date
24/05/2022

Overall study status
Completed

Last Edited
19/05/2022

Condition category
Other

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
DMT is a drug that has been used for a very long time by different cultures to cause a so-called 'trip'. DMT is used in these cultures as a component of a drink, called Ayahuasca, made from plants. During such a trip, people often experience hallucinations (not limited to seeing and hearing things that are not there) and a change of thinking about themselves and the environment and therefore behaving differently than usual, a feeling of heaviness in the body , transient anxiety, and/or feeling intoxicated. Because of these effects, DMT is also called a hallucinogenic substance. DMT causes a trip by stimulating the place in the brains (receptor) where normally the messenger substance serotonin exerts itis function. Serotonin is present in many different brain areas and has several functions. It plays an important role in regulation of mood, sleep, perception, emotions, and memory.
The increase in serotonin may cause people with psychiatric disorders to experience less complaints. Previous research has shown that hallucinogenic substances that increasing serotonin, can be used in the treatment of anxiety, depression and nicotine addiction. Entheon Biomedical wants to investigate the medicinal product DMT, developed as part of a new nicotine addiction treatment.

In this study, we aim to investigate how safe DMT is and how well it works. We are testing DMT in different strengths in healthy subjects and we will compare the effect of DMT with the effect of a placebo.

Who can participate?
This study will consist of 5 cohorts of 10 healthy smoking male and female subjects.

What does the study involve?
The treatment phase will consist of 1 treatment period. The subjects will receive DMT over 90 minutes or placebo.
During the study safety measures such as measurement of blood pressure, heart rate, respiratory rate and ECG will be done. Additionally, one computerized test battery will be performed several times to test, for example, memory and coordination. Lastly, several questionnaires to t

What are the possible benefits and risks of participating?
DMT is a substance with a hallucinogen or psychedelic effect. Therefore, during the administration of the study drug the followings effects can occur:
- Seeing or hearing things that are not there (hallucinations)
- Changes in the way of thinking and experiencing the surroundings and acting differently because of this
- Having a heavy feeling in the body
- Transient anxiety
- The feeling of being intoxicated or in a rush
- Feeling an intense rush, after which thoughts, feelings and experience of the body are completely different compared to normal
- Feeling confused, suspicious or anxious and changing your behaviour accordingly
- The feeling of being separated from the body (this is called dissociation).

Additionally, the following physical side effects can occur:
- Temporary increase in blood pressure
- Nausea
- Headache
- Dizziness when standing up
- Fatigue
- Decreased tension in the muscles

These side effects occur during the administration of the DMT and are not permanent. The complaints quickly diminish and completely disappear 30 to 60 minutes after stopping the infusion. All effects will be closely monitored up to 24h following DMT hemifumarate administration.
There will be no benefit from participating in this study. However, participation will provide valuable information for future research into nicotine addiction.

Where is the study run from?
Centre for Human Drug Research (Netherlands)

When is the study starting and how long is it expected to run for?
August 2021 to January 2023

Who is funding the study?
Entheon Biomedical (Canada)

Who is the main contact?
G. Jacobs (Principal investigator), clintrials@chdr.nl

Contact information

Type(s)
Scientific

Contact name
Dr Gabriel Jacobs

Contact details

Zernikedreef 8
Leiden
Netherlands
2333 CL
+31 71 5246 400
clintrials@chdr.nl

Type(s)
Principal investigator

Contact name
Dr Gabriel Jacobs

Contact details
Zernikedreef 8
Leiden
Netherlands
2333 CL
+31 71 5246 400
clintrials@chdr.nl

Additional identifiers

Clinical Trials Information System (CTIS)
2021-005207-12

Protocol serial number
CHDR2031

Study information

Scientific Title
An adaptive, randomized, double-blind, placebo-controlled, single ascending dose (SAD) study to evaluate the pharmacodynamics, pharmacokinetics and safety of a target controlled intravenous infusion of N,N-dimethyltryptamine (DMT) in healthy smokers

Study objectives
DMT could potentially be effective in reducing nicotine addiction in humans

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 28/01/2022, Stichting BEBO (Doctor Nassaulaan 10, 9401 HK Assen, The Netherlands; +31 592-405871; info@stbebo.nl), ref: NL79463.056.22

Primary study design
Interventional

Study design

Single centre single-dose double-blind randomized placebo-controlled

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Reducing nicotine addiction in humans

Interventions
The study will consist of 5 treatment groups of 10 subjects. Each subject will receive 1 dose of DMT hemifumarate(0.12 mg/kg with a maximum anticipated dose of 2.1 mg/kg) dissolved in 0.9% saline or placebo (0.9% saline). The study drug will be administered as a 90-minute continuous IV infusion given on Day 1 of the treatment period.
Subjects will enter the clinical unit on Day -1 and be discharged on Day 2. They will have an in person follow up visit after 7 to 9 days and a phone call follow up after 4-6 weeks.
Subjects will be randomized using a 4 digit subject number. They will be randomized in a consecutive order, starting with the lowest number. The randomization code will be generated using SAS version 9.4 (or a more recent version) by a study-independent, CHDR statistician. The randomization code will be unblinded/broken and made available for data analysis only after study closure, i.e., when the study has been completed, the protocol deviations determined, and the clinical database declared complete, accurate and locked. The randomization code will be kept strictly confidential. Sealed individual randomization codes, per subject and per treatment, will be placed in a sealed envelope with the label 'emergency decoding envelopes' in a safe cabinet at CHDR.

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
N,N-dimethyltryptamine (DMT)

Primary outcome(s)
Measuring safety of DMT using:
1. Treatment-emergent (serious) adverse events ((S)AEs) and concomitant medication throughout the study at every study visit.
2. Vital signs, respiratory rate and ECG at baseline, 1.5h, 3h, 6h and 24h.
3. Clinical laboratory tests (Hematology, blood chemistry and urinalysis) at baseline and 24h
4. Occurrence of psychotic symptoms as measured with the BPRS at baseline, 4h and 24h.
5. Occurrence of central serotonergic toxicity as measured with the Hunter criteria.
6. Occurrence of suicidal thoughts and ideations as measured with the CSSRS at baseline, 4h and 24h.

Key secondary outcome(s)
1. Measuring drug effects, sedation, memory and coordination using the Neurocart test battery at baseline, 15 minutes, 1h, 2h, 6h and 24h.
2. Establishing the minimum DMT dose required to produce moderate subjective psychedelic effects using plasma PK results, changes in intensity scores from baseline to the end of infusion and changes in subjective psychedelic experience rating scales that include the HRS, MEQ and

5D-ASC administered on baseline and 6h.
3. Characterize the pharmacokinetic profile of DMT in plasma at baseline, 5 minutes, 15 minutes, 30 minutes, 50 minutes, 75 minutes, 1.5h, 100 minutes, 110 minutes, 2h, 130 minutes and 4h.
4. Characterize the effect of DMT on neurological activity using continuous electroencephalography (EEG) at baseline, 15 minutes, 1h, 2h, 6h and 24h.
5. Optimize the infusion rate of DMT required to maintain steady-state PD effects by using a non compartmental pharmacokinetic analysis and changes in subjective psychedelic experience rating scales that include the HRS, MEQ and 5D-ASC administered retrospectively following each cohort.
6. Changes in subjectively reported nicotine use measured in changes from baseline to EOS in nicotine use as measured by the FTND and the QSU administered on baseline, Day 7 and the last follow up visit.
7. Assess the relationship between personality characteristics, general psychopathology and individual response to DMT using the DPQ/ NPV, the TCI, the STAI and the BPRS at baseline and the last visit.

Completion date
01/01/2023

Eligibility

Key inclusion criteria
1. Healthy male and female volunteers.
2. Aged 21 - 60 years inclusive.
3. Regular use of nicotine (at least 1 cigarette daily 5 to 10 cigarettes daily).
4. Self-report of at least one prior hallucinogen drug experience that included a meaningful altered state of consciousness (a state in which the subject experienced phenomena that altered his psychological functioning, such as loss of ego boundaries, impaired control of actions and cognition, disembodiment, changed meaning of percepts, visual alterations and audio-visual synesthesia) the past 5 years. Hallucinogenic substances can include psilocybin, LSD, DMT, ayahuasca, mescaline, ibogaine, 2C-drugs (such as 2CB, 2CI and 2CE) and/or ketamine.
5. Participant has a body mass index (BMI) between 18.0 and 30.0 kg/m^2 inclusive
6. Subject must be healthy based on physical examination, medical history, vital signs, and 12-lead ECG. Minor abnormalities in ECG, which are not considered to be of clinical significance by the investigator, are acceptable.
7. Subjects must be healthy based on clinical laboratory tests performed at screening. If the results of the serum chemistry panel, hematology, or urinalysis are outside the normal reference ranges, the subject may be included only if the investigator judges the abnormalities to be not clinically significant. This determination must be recorded in the subject's source documents and initialed by the sub investigator.
8. Agree to refrain from using any psychoactive drugs, including alcoholic beverages within 24 hours of each drug administration.
9. Each subject must sign an informed consent form (ICF) indicating that he or she understands the purpose and procedures required for the study and are willing to participate in the study.
10. A woman of childbearing potential must agree to practice an effective means of birth control during their participation in the clinical trial, up to and including the 90-day follow-up after their last DMT dose. Birth control method and written agreement to practice this method throughout the duration of the study will be documented on the Medical History Case Report Form. Effective contraception is defined as the regular use of one of the following: Established use of oral, injected, or implanted hormonal methods of contraception; Placement of an intrauterine device (IUD) or intrauterine system (IUS); Barrier methods: Condom or Occlusive cap used with a

spermicide; female sterilization/hysterectomy (with documentation of surgery); post-menopausal (>12 months since last menses at the time of screening); Male sterilization (with post-vasectomy documentation); True abstinence.
11. Agree to refrain from using any psychoactive drugs from 30 days before dosing and until the last follow up visit and to refrain from using alcoholic beverages within 24 hours of each drug administration

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
All

Key exclusion criteria
1. Subject has a history of or current liver or renal insufficiency; significant cardiac, vascular, pulmonary, gastrointestinal, endocrine, neurologic, hematologic, rheumatologic, psychiatric, or metabolic disturbances, any inflammatory illness or any other illness, which are considered to be of clinical significance by the investigator.
2. Clinically relevant abnormal history, physical finding, 12-lead safety ECG12-Iead safety ECG (e. g. PQ/PR interval >21 Oms, presence of Left Bundle Branch Block (LBBB), AV Block (second degree or higher), or a permanent pacemaker or implantable cardioverter defibrillator [lCD]), or laboratory value at screening that could interfere with the objectives of the trial or the safety of the volunteer.
3. Subject has a history of or current hypertension (systolic blood pressure >140 mmHg or diastolic blood pressure >90 mmHg).
4. Presence or history of cardiovascular disease, including acute coronary syndrome or angina, ischemic disease, ventricular arrhythmias or cardiac transplantation as determined by self-report during review of medical history.
5. Subject has a history of chronic or frequent migraines.
6. Subject has a history of hepatitis B surface antigen (HBsAg) or hepatitis C antibody (anti-HCV) positive, or other clinically active liver disease, or tests positive for HBsAg or anti-HCV at screening.
7. Subject has a history of human immunodeficiency virus (HIV) antibody positive, or tests positive for HIV at screening.
8. History or current significant ophthalmologic or neurologic condition that would adversely affect the eye movement assessments.
9. A history of any kind of hypersensitivity (e.g.,drugs/excipients) or allergic reactions to any of the inactive ingredients contained in the active or placebo drug products, including compounds related to DMT.
10. Females of childbearing potential with positive urine pregnancy at screening or the day of the first treatment.
11.Subject drinks, on average, more than 8 cups of tea/coffee/cocoa/cola/caffeinated beverages

(e.g., energy drink) per day.
12. Subject received an investigational intervention (including investigational vaccines) or used an invasive investigational medical device within 90 days (or 5 half-lives whichever is longest) before the planned first dose of study intervention or is currently enrolled in an investigational study.
13. Subject has a history of drug or alcohol use disorder according to DSM-IV or DSM 5 within the past five years.
14. Subject has a positive test result(s) for alcohol and/or drugs of abuse (including: opiates (including methadone), cocaine, amphetamines, methamphetamines, cannabinoids, barbiturates, and benzodiazepines) at screening or admission to the clinical unit.
15. Current or history of any clinically relevant psychiatric disorder as classified according to DSM-IV or DSM 5 (e.g. psychotic disorder e.g. schizophrenia/schizo-affective disorder, bipolar disorder Type I or Type II, personality disorder, major depressive disorder/persistent depressive disorder, obsessive-compulsive disorder, panic disorder, anorexia nervosa, bulimia nervosa, generalized anxiety disorder (GAD), post-traumatic stress disorder (PTSD) or autism spectrum disorder (ASD).
16. Family history of a relevant psychiatric disorder in first-degree relatives. Psychiatric history in second degree relatives will be discussed on a case to case basis.
17. Persistent psychological effects following the previous use of psilocybin, LSD, DMT, ayahuasca, mescaline, ibogaine, 2C-drugs (such as 2CB, 2CI and 2CE) and/or ketamine. Such effects might include but are not limited to anxiety, depressed mood, paranoid ideation and/or hallucinations (including hallucinogen persisting perception disorder- HPPD) or recurrent flash-backs related to use.
18. Risk of suicide, as judged by an Investigator, based upon available source information - including the C-SSRS or family history of suicide -indicating current suicidal ideation or a history of active suicidal ideation or suicide attempts
19. Donated and/or received any blood or blood products or blood loss of more than 500 mL (e. g. through surgery) within 3 months before screening.
20. Vulnerable subjects (e.g., a person kept in detention or a person under guardianship).
21. Subject is an employee of the investigator or study site, with direct involvement in the proposed study or other studies under the direction of that investigator or study site, as well as family members of the employees or the investigator.
22. Subject is unable to read and understand the consent forms, complete study-related procedures, and/or communicate with the study staff.
23. Positive SARS-CoV-2 rapid antigen test analysis prior to first dosing.

Date of first enrolment
22/02/2022

Date of final enrolment
13/11/2022

Locations

Countries of recruitment
Netherlands

Study participating centre

Centre for Human Drug Research
Zernikedreef 8
Leiden
Netherlands
2333 CL

Sponsor information

Organisation
Entheon Biomedical Corp

Funder(s)

Funder type
Industry

Funder Name
Entheon Biomedical Corp

Results and Publications

Individual participant data (IPD) sharing plan
The current data sharing plans for this study are unknown and will be available at a later date.

IPD sharing plan summary
Data sharing statement to be made available at a later date