A PHASE 1, OPEN-LABEL, PHARMACOKINETIC TRIAL TO INVESTIGATE POSSIBLE DRUG-DRUG INTERACTIONS BETWEEN CLOBAZAM, STIRIPENTOL OR VALPROATE AND CANNABIDIOL (GWP42003-P) IN HEALTHY SUBJECTS

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Seizures (incl subtypes)
Study type	Interventional

Summary

ID

NL-OMON43875

Source
ToetsingOnline

Brief title
Cannabidiol drug-drug interaction trial with common anti-epileptic drugs

Condition

- Seizures (incl subtypes)

Synonym
epilepsy

Research involving
Human

Sponsors and support

Primary sponsor: GW Pharma
Source(s) of monetary or material Support: Farmaceutische industrie

Intervention

Keyword: cannabidiol, drug-drug interaction, PK, safety

Outcome measures

Primary outcome

The effect of multiple dose administration of GWP42003-P on steady state plasma concentrations of clobazam, stiripentol or valproate will be assessed. In addition, the effec tof multiple dose administration of clobazam, stiripentol or valproate on steady state plasma concentrations of GWP42003-P will be assessed.

Secondary outcome

The safety and tolerability of GWP42003-P with clobazam, stiripentol or valproate will be assessed with respect to:

- adverse events
- vital signs
- ECG
- Clinical laboratory parameters
- physical examination
- C-SSRS

Study description

Background summary

Cannabidiol (CBD) is a new investigational compound that may eventually be used for the treatment of epilepsy. It is extracted from cannabis plants under highly controlled conditions to ensure the product is always the same. Within the human body there is a biological system named the endogenous cannabinoid system (ECS). CBD is absorbed and distributed very rapidly to tissues and a number of the therapeutic actions of CBD are thought to be produced via the body*s own ECS. In GW studies CBD is not known to have the hallucinating effect that is known of cannabis.
CBD is not yet registered as a drug but has been given to humans in both clinical studies and as part of an approved product in combination with another drug in a number of countries.

The other compounds that will be given in this study are clobazam, stiripentol and valproate which are approved drugs and already available in the market under several dosages and formulations. They are prescribed for the treatment of epilepsy.

It is possible that cannabidiol and clobazam, stiripentol or valproate will be co-administered in the future.

Study objective

During this study it will be investigated what the effect is of multiple doses of CBD on the absorption and elimination from the body (this is called pharmacokinetics) of clobazam, stiripentol or valproate. It will also be investigated what the effect is of multiple doses of clobazam, stiripentol or valproate on the pharmacokinetics of CBD. The study will also look at how safe and well tolerated the combined administration of CBD and clobazam, stiripentol or valproate is.

The study will be performed in 77 healthy male and/or female participants, divided over 6 groups.

This study is not intended to improve your health, but is necessary for the further development of CBD.

Study design

In this study 2 study compounds will be administered: CBD and clobazam, CBD and stiripentol or CBD and valproate. Day 1 is the first day of administration of study compound. Should, in the opinion of the investigators, unacceptable

adverse effects appear, the study will be discontinued.
During the study, the volunteer will stay in the clinical research center in Groningen for 3 periods.

Intervention

In this study 2 study compounds will be administered: CBD and clobazam, CBD and stiripentol or CBD and valproate.

Study burden and risks

CBD
All potential drugs cause side effects; the extent to which this occurs differs.
The following side effects were experienced among a portion of the 213 patients who have taken CBD oral solution; however this was not within a formal clinical study (there was no placebo treatment). All were considered to be caused by the study compound. They have been categorized by the likelihood of them occurring, and listed in the order they have most commonly been reported.

Very common side effects which may affect more than one person in every 10 are: Feeling drunk, sleepy or abnormal, feeling tired, diarrhea and eating less than usual.

Common side effects which may affect more than one person in every 100 are (excluding the very common side effects above): Eating more than usual, weight gain, weight loss, convulsions, difficulty in walking and amounts of medicines in the body were higher than usual (increases of levels of other medicines), increased appetite, decreased appetite, feeling drugged.

Previously in this study an unusually high number of non-serious and temporary rash events was seen. Despite the changes that have now been introduced in the study, skin rash may still occur after CBD intake.

The following side effects have been seen in 107 patients who have previously taken other CBD medicines (either CBD botanical drug substance or purified CBD) within clinical studies. It should be noted that 87 of these patients took a formulation containing small amounts of other cannabinoids including tetrahydrocannabinol (THC) and so may have resulted in a higher incidence of side effects than with the study compound you will be using. They have been categorized by the likelihood of them occurring, and listed in the order they have most commonly been reported. The side effects in bold have been seen in 20 patients who have previously taken study medication of purified CBD, all being classed as common, with the exceptions of headache and diarrhea which were very common.

Very common side effects which may affect more than one person in every 10 are: Diarrhea, headache, feeling sick.

Common side effects which may affect more than one person in every 100 are (excluding the very common side effects above): Mouth problems (including, pain, discomfort, change in sense of taste or loss of sense of taste, dry mouth, reduction in or loss of sensation), feeling tired, indigestion, sickness, eating less than usual, feeling drunk or abnormal, feeling dizzy, neck pain, belching, urgency to pass motions, increased frequency in passing water, rashes, change in liver function blood tests or hematology blood tests, cold symptoms, abdominal pain, constipation, feeling depressed or confused, abnormal dreams, nose bleed, feeling weak or unwell, flushing, muscle spasms.

As CBD may affect some blood tests, if you need a blood test please tell the doctor or nurse you are taking this study compound.

Clobazam
Clobazam is a drug that is already available in the market under several dosages and formulations. It is prescribed for the treatment of epilepsy. The most frequently observed side effects are: sleepiness and drowsiness. Please also carefully read the patient information leaflet of clobazam.

Stiripentol
Stiripentol is a drug that is already available in the market under several dosages and formulations. It is prescribed for the treatment of epilepsy. The most frequently observed side effects are: anorexia, weight loss, insomnia, drowsiness, ataxia (lack of voluntary coordination of muscle movements), hypotonia (low muscle tone) and dystonia (twisting and repetitive movements or abnormal postures). Please also carefully read the patient information leaflet of stiripentol.

Valproate
Valproate is a drug that is already available in the market under several dosages and formulations. It is prescribed for the treatment of epilepsy. The most frequently observed side effects are: thrombocytopenia (decrease of platelets), nausea, vomiting, diarrhea, gastrointestinal disorders, increased ammonemia (too much ammoniac or ammonium), temporary hair loss, irregular menstruations and weight gain. Please also carefully read the patient information leaflet of valproate.

Contacts

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Scientific
GW Pharma

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- healthy male/ female subjects
- 18-55 yrs, inclusive
- BMI: 18.0-32.0 kg/m2, inclusive

Exclusion criteria

Suffering from hepatitis B, hepatitis C, cancer or HIV/AIDS. In case of participation in another drug study within 90 days before the start of this study or being a blood donor within 60 days from the start of the study. In case of donating more than 1.5 liters of blood (for men) / 1.0 liters of blood (for women) in the 10 months prior the start of this study.

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	04-11-2015
Enrollment:	72
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Cannabidiol
Generic name:	n/a
Product type:	Medicine
Brand name:	Clobazam
Generic name:	n/a
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Stiripentol
Generic name:	Diacomit
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Valproate sodium
Generic name:	Depakine EC

Ethics review

Approved WMO

Date:	01-10-2015
Application type:	First submission

Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	22-10-2015
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	28-12-2015
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	01-03-2016
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	12-07-2016
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	02-08-2016
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	27-10-2016
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2015-002656-80-NL
CCMO	NL55010.056.15