Safety profile and effects of Mitragynine (MG)

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The current study will evaluate the safety, pharmacokinetcs and the effects of MG, especially on subjective outcomes, pain perception, cognitive perfomances and impulsivity.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON52572

Source
ToetsingOnline

Brief title
Mitragynine (MG)

Condition

- Other condition

Synonym
not applicable

Health condition

Veiligheid, effecten, farmacokinetiek

Research involving
Human

Sponsors and support

Primary sponsor: Universiteit Maastricht
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Effects, Mitragynine, Novel psychoactive substance, Safety

Outcome measures

Primary outcome

vital signs: body temperature, blood pressure, heart rate, respiration rate,

peripheral capillary Oxygen saturation, hematology, biochemistry and

urinalysis, subjective drug experience, pain perception

Secondary outcome

pharmacokinetics, cognitive performance and impulsivity

Study description

Background summary

Kratom has recently become popular as NPS in Western countries. Mitragynine (MG) is the most abundant alkaloid present in Kratom. It is used also for the treatment of opioid withdrawal symptoms and of pre-existing mental health symptoms in non medical settings. MG is a dose dependent agonist of opioid receptors in the central nervous system (CNS) as well as non-opioid receptors. Its non-selectivity likely results in the beneficial multimodal effects of kratom. The adverse effects or the toxicities have been studied mainly in vitro and in animal models. In humans they have been documented only in case reports or online surveys, and there are just two controlled studies. Despite the fact that Kratom became popular and is easily available, the potential risks and real benefits in humans are insufficiently known. That's why, with the current study, we intend to elucidate safety, pharmacokinetics and effects of MG, particularly its abuse liability and its impact on pain perception, neurocognitive measures and impulsivity in a well-controlled manner.

Study objective

The current study will evaluate the safety, pharmacokinetcs and the effects of MG, especially on subjective outcomes, pain perception, cognitive perfomances and impulsivity.

Study design

This intervention (placebo-controlled, single blind, within subjects) study will be performed in 16 healthy participants. In the first part, an escalating dosing scheme will be used in 8 participants, with each participant receiving placebo and 3 single doses of 5, 10 and 20 mg of MG. Participants will be closely monitored for 7 hours after drug administration. Only when the administration in the previous participant did not cause serious adverse effects, administration of the same dose will be repeated in a next participant. Only in case the lower dose did not cause serious adverse effects in any of the 16 participants, administration of the subsequent dose will be started for the participant. Participants will stay under an observation period of 7 hours after the administration. Then, the experimenter will check whether it is safe for the participant to be discharged. In case the participant still shows signs of intoxication, he/she will be kept under observation until these signs will have disappeared. A wash-out period at least of 5 days between each dose will be used and subjects will be tested once per week for 4 consecutive weeks.
In the second part of this study, a new group of healthy volunteers (N=8) will receive placebo and 40 mg MG on separate test days. The design of this part is otherwise identical to the first part. An interim evaluation will be performed after half of the participants have completed the study, in order to evaluate safety and appropriateness of the dose.

Intervention

0, 5, 10, 20, 40 mg MG

Study burden and risks

During the test day subjects remain 7.5 hours in the department, where their vital signs will be monitored at regular intervals. Blood and urine samples are taken at the baseline and at the end of the test day. A small blood sample for pharmacokinetics will be taken twice after drug intake and at the end of the test day. A few times the subject must perform pain tolerance test and cognitive tasks. He also must fill out scales and questionnaires regarding drug experience, safety and impulsivity.
The subject may experience side effects that are similar or less strong than those with low dose of Kratom. A medical doctor will be present and can intervene in time in case of serious side effects.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

*Age between 18 and 45 years
*Healthy (the participant is, in the opinion of the investigator, generally healthy based on assessment of medical history, physical examination, vital signs, electrocardiogram (ECG), and the results of the haematology, clinical chemistry, urinalysis, and other laboratory tests (thyroid function test, TSH)
* a resting pulse and heart rate (as measured by the medical doctor) *51 bpm and *100 bpm. For participants in good physical condition, the lower limit is *45 bpm.
* a resting systolic blood pressure *91 mmHg and *140 mmHg and a resting diastolic blood pressure *51 mmHg and *90 mmHg.
*clinical laboratory test values within the reference ranges. Borderline values may be accepted if they are, in the opinion of the investigator, clinically insignificant.
*Absence of any major medical, endocrine and neurological condition, as determined by the medical history, medical examination, electrocardiogram and laboratory analyses (haematology, clinical chemistry, urinalysis)
*Weight range between normal and overweight:body mass index (BMI:

weight/height2) between 19,5 and 28 kg/m2
*To be proficient in Dutch or English
*Written Informed Consent

Exclusion criteria

*Current or history of medical or psychiatric disorder (determined by the medical questionnaire and medical examination)
*Any use of medications (except paracetamol if it is necessary)
*History of drug abuse or addiction (determined by the medical questionnaire, drug questionnaire and medical examination)
*Excessive drinking (> 20 alcoholic consumptions a week)
*Pregnancy or lactation or failure to use contraceptives
*Serious side effects to previous Mitragynine administration
*Simultaneous participation in another clinical trial
*For women: not using reliable contraceptive

Study design

Design

Study type: Interventional

Masking:	Single blinded (masking used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	16-04-2021
Enrollment:	22
Type:	Actual

Ethics review

Approved WMO

Date:	26-02-2021

Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	28-07-2021
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	20-12-2021
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

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
CCMO	NL73317.068.20
Other	Not yet available