Determination of the sleep improving effects of phenolics from an orange peel extract

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The present study aims to determine whether hesperidin or a hesperidin/apigenin combined preparation can improve objective sleep duration and/or sleep quality, and/or improve perceived sleep quality and feelings of rest.

Ethical review	Approved WMO
Status	Completed
Health condition type	Sleep disturbances (incl subtypes)
Study type	Interventional

Summary

ID

NL-OMON57211

Source
ToetsingOnline

Brief title
The sleep improving effects of orange phenolics

Condition

- Sleep disturbances (incl subtypes)

Synonym
insomnia, Poor quality of sleep

Research involving
Human

Sponsors and support

Primary sponsor: Medisch Universitair Ziekenhuis Maastricht
Source(s) of monetary or material Support: BioActor BV

Intervention

Keyword: fatigue, orange, polyphenols, sleep

Outcome measures

Primary outcome

The primary endpoint for the study is the determination of the sleep quality,

as assessed objectively with an unobtrusive portable sleep monitoring system,

based on EEG/EMG coupled with an automatic sleep phase classifier.

Secondary outcome

Secondary endpoints consist of subjective sleep quality ratings and

fitness/tiredness/cognitive ratings, obtained through questionnaires.

Study description

Background summary

Against the background of numerous detrimental effects of reduced sleep and sleep quality in the developed world, substances that are capable of improving sleep have been of growing interest. Especially natural products, e.g. for functional foods and nutritional supplements, such as valerian extracts have been of interest. Valerian roots contain several polyphenolic compounds, some of which are identical to polyphenols found in citrus fruits, specifically hesperidin, linarin and apigenin. Published studies have indicated that hesperidin, when administered intraperitoneally acutely prolonged sleep in rodents, while it exhibited anxiolytic effects when administered chronically over a four week time period orally. The positive effects of hesperidin on sleep are exerted by the intact molecule, while the main metabolite, hesperitin does not seem to exhibit potent effects. Recent in-vivo studies have shown that orally administered Hesperidin does not impart sleep-promoting activity. Hence, the need to develop and test a dosage form that make Hesperidin bioavailable by avoiding premature metabolization in the gut and liver, and to subsequently asses their efficacy in sleep improvement.

Study objective

The present study aims to determine whether hesperidin or a hesperidin/apigenin

combined preparation can improve objective sleep duration and/or sleep quality, and/or improve perceived sleep quality and feelings of rest.

Study design

The study is designed as a randomized cross over study in 76 healthy subjects. During test nights, subjects will consume in randomized order a single dose of (1) the orange peel extract standardized for 90-95% hesperidin, (2) the orange peel extract standardized for 90-95% hesperidin with apigenin, or (3) a placebo, after which a portable sleep monitor is worn throughout the night. Test nights are separated by at least one day in between. Questionnaires are completed on the morning and evening before and after the test night.

Intervention

The study will take approximately 3-6 weeks per subject, during which the selected dosage forms and a placebo is tested in triplicate, which adds up to 9 test nights. Test nights are separated by at least one day in between.

Study burden and risks

During the screening, one venepuncture is performed to obtain 10 mL blood for clinical testing. Furthermore, subjects are interviewed during the screening, to assess their suitability regarding potential sleep disorders and other inclusion/exclusion criteria. Before the actual study nights, subjects are asked to wear the sleep monitor for five nights of their own choosing to get acquainted with the device and the feeling of wearing it. During this part of the study, subjects have to fill in four questionnaires, i.e. in the morning and evening of the day before and in the morning and evening of the day after each test night. Furthermore, one serving of a finished dosage form has to be consumed according to instructions and a sleep monitor has to be worn during the night. The sleep monitor is an unobtrusive system, consisting of a wireless headband that contains three small sensors on the forehead. The discomfort associated with wearing this system was experienced as significantly less than the discomfort associated with wearing an eye cover in a multi night try out by one of the researchers. 76 subjects are asked to come to the university once for screening. At home, subjects are asked to fill in 36 questionnaires, wear the sleep monitor for 5 unmonitored nights and 9 monitored nights. The overall burden is relatively small. The risks associated with the intake of hesperidin are negligible.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

(1) Age 18 - 75, (2) Non-smoking, (3) Healthy, (4) Light disturbed sleep for at least six months, on a regular basis

Exclusion criteria

1) Severe sleep disorders (sleep apnoea, restless legs syndrome), (2) no apparent cause for the sleep disorders (3) Clinically significant abnormal liver functioning, (4) Clinically significant abnormal serum creatinin, (5) BMI lower than 18 or higher than 30, (6) Use of concomitant medications or supplements, (7) Blood donation during the last 4 weeks prior to the first dosing. It is advised not to donate blood till 4 weeks after the last dosing.

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	01-01-2014
Enrollment:	77
Type:	Actual

Ethics review

Approved WMO Date:	12-12-2013
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	14-03-2014
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	NL43845.068.13
Other	Volgt nog. Registratie bij NTR