ISRCTN12126820 https://doi.org/10.1186/ISRCTN12126820

The beneficial effect on sleep of a food supplement based on Scutellaria lateriflora L. (aerial parts of the plant)

Submission date
22/05/2024

Recruitment status
No longer recruiting

Registration date
03/06/2024

Overall study status
Completed

Last Edited
14/06/2024

Condition category
Mental and Behavioural Disorders

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

Plain English summary of protocol

Background and study aims
Insomnia is the most common sleep disorder worldwide, where people have trouble falling or staying asleep. This affects their overall well-being, and can lead to mental, cognitive, and physical health issues.

About one-third of adults experience insomnia, with 10%-15% reporting daytime problems, and 6%-10% being diagnosed with insomnia disorder. Women are 1.44 times more likely to suffer from insomnia than men.

Insomnia significantly increases the risk of heart diseases like high blood pressure, heart attacks, and chronic heart failure. Research also links insomnia to a higher risk of type 2 diabetes. Additionally, sleeping less than 6 hours a night is linked to obesity, type 2 diabetes, high blood pressure, and heart diseases. Insomnia is also connected to major depression, often preceding and predicting its onset.

A U.S. survey found that 4.5% of adults prefer natural remedies over medications for mild insomnia. This study aims to show that a dietary supplement can improve sleep in people with primary insomnia who don't have severe symptoms.

The plant genus Scutellaria, which includes over 350 species, has been traditionally used for treating various disorders like nerve issues, chronic diseases, liver problems, and anxiety. Scutellaria lateriflora, or skullcap, is the focus of this study. Traditionally used by Native Americans to improve blood flow, reduce anxiety, and treat mental health issues, skullcap is now used in North America to treat epilepsy, nerve damage from infections, insomnia, anxiety, nerve pain, and withdrawal from tranquilizers.

Scutellaria lateriflora contains many active compounds, including flavones like baicalein, baicalin, chrysin, and wogonin, which are believed to improve mood. Baicalein weakly binds to benzodiazepine receptors, explaining its mild calming effects through interaction with GABA receptors in the nervous system. Baicalein also partially blocks the GABAA receptor, while

wogonin shows anxiety-reducing effects through benzodiazepine receptors. Other compounds interact with serotonin receptors.
In vitro studies (conducted outside of a living organism) have shown that an extract of Scutellaria lateriflora inhibits enzymes that break down GABA, a neurotransmitter that calms the nervous system, contributing to its anxiety-reducing effects.
Another study tested a 100 mg dose of Scutellaria lateriflora extract on rats and found it significantly reduced anxiety and depression behaviors.

The goal of this study is to evaluate how effective a dietary supplement made from Scutellaria lateriflora is at improving sleep in people with primary insomnia.

Who can participate?
Sixty-six subjects aged 18-70 years of either sex, who present mild to moderate primary insomnia and who can understand and sign the informed consent.

What does the study involve?
A single-center, placebo-controlled, randomized, cross-over clinical study will be conducted with a two-week run-in period, in double-blind fashion.

During the two-week run-in period, during which all enrolled subjects will take the placebo, potential compliance with the study will be observed to minimize subject drop-out and thus increase the internal validity of the clinical study. Additionally, at the end of the run-in period, any physiological responses to the placebo, as well as false adverse effects (although very unlikely - see ADVERSE EVENTS section), will be identified, the eligibility of the subjects and therefore the sample population will be confirmed, and initial data regarding the quality and severity of insomnia in the recruited subjects can be obtained.

What are the possible benefits and risks of participating?
No risks are foreseen. An improvement in the sleep function of the subjects treated with the food supplement is hypothesized. However, no benefit may be achieved.

Where is the study run from?
Epo S.r.l. (Italy)

When is the study starting and how long is it expected to run for?
July 2023 to November 2024

Who is funding the study?
Epo S.r.l. (Italy)

Who is the main contact?
1. Prof. Maria Daglia (scientific) maria.daglia@unina.it
2. Dr. Alessandra Baldi (public) alessandra.baldi.alimenti@gmail.com

Contact information

Type(s)
Scientific

Contact name
Prof Maria Daglia

ORCID ID
https://orcid.org/0000-0002-4870-7713

Contact details
Via Domenico Montesano, 49
Naples
Italy
800016
+ 39 3398177623
maria.daglia@unina.it

Type(s)
Public

Contact name
Ms Alessandra Baldi

ORCID ID
https://orcid.org/0000-0002-2877-9445

Contact details
Viale delle Medaglie d'Oro, 305
Rome
Italy
00136
+39 3483854114
alessandra.baldi.alimenti@gmail.com

Type(s)
Principal investigator

Contact name
Dr Matteo Laringe

Contact details
Viale Maria Bakunin, 41
Naples
Italy
80126
+ 39 3939406629
matteo.laringe@gmail.com

Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
SCUTESLEEP23_01

Study information

Scientific Title
Efficacy study of a food supplement based on Scutellaria lateriflora L. (aerial parts of the plant) for sleep management: single-center, controlled, randomized, cross-over, double-bind clinical study with a run-in period.

Acronym
SCUTESLEEP23

Study objectives
This study aimed to evaluate the efficacy of the supplementation of the diet with a food supplement based on Scutellaria lateriflora L. (aerial parts of the plant), in the maintenance of the sleep-wake balance, through the improvement of sleep onset and maintenance phase, in subjects where insomnia is independent of other comorbid conditions. Insomnia is considered a significant risk factor for cardiometabolic diseases.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 30/01/2024, Ethics Committee of CAMPANIA 1 (Via Mariano Semmola, 53, Naples, 80131, Italy; +39 081/17770131; comitatoetico@istitutotumori.na.it), ref: 2/23

Study design
Interventional monocentric randomized crossover two-arm double-blind placebo-controlled clinical trial

Primary study design
Interventional

Study type(s)
Prevention

Health condition(s) or problem(s) studied
Subjects with mild to moderate primary insomnia

Interventions
The subjects recruited in the present clinical study will consume, a food supplement based on Scutellaria lateriflora L. (aerial parts of the plant) in capsules at 400 mg/day dose, and a placebo, in a different order, based on the randomization group, for two treatment periods of 56 days, interspersed with a wash-out period of 28 days.
The treatment consists of the BlueCALM® dietary supplement, notified to the Ministry of Health (notification number: 164522).
To maintain the double-blind design, both treatments will be made unrecognizable as the packaging will be identical, and the dosage forms will be the same in color, shape, weight, and taste.

The randomization sequence will be generated by a statistician using STATA 16 software (Stata Statistical Software: Release 16. College Station, TX: StataCorp LLC) and the randomization list will be kept hidden. The participants will be assigned to each of the two treatment groups (food supplement or placebo) casually and by simple randomization (1:1: allocation ratio). The randomization code will consist of a three-digit number as indicated in the respective Case Report Form (CRF).

In the clinical study, 66 participants will be enrolled and divided into two groups (33 for each group):

GROUP 1 subjects who will first take treatment A and, following the wash-out period, treatment B. TREATMENT ORDER: AB
GROUP 2 subjects who will first take treatment B and, following the wash-out period, treatment A. TREATMENT ORDER: BA

Participants will undergo seven visits (start of run-in = tr, at the start of the first treatment period = t0, after 28 days from the start of the first treatment period = t1, at the end of the first treatment period = t2, at the start of the first treatment period = t3, after 28 days from the start of the first treatment period = t4, at the end of the first treatment period = t5) in an outpatient setting. After each clinical visit, all data are filled in the CRF by physicians.

Intervention Type
Supplement

Primary outcome(s)
Sleep quality: Pittsburgh Sleep Quality Index (PSQI) [Time frame: tr (run-in start), t0 (baseline), t1 (after 28 days of the first treatment period), t2 (after 56 days of the first treatment period), t3 (baseline of the second treatment period), t4 (after 28 days of the second treatment period), t4 (after 56 days of the second treatment period)]

Key secondary outcome(s))
Evaluation of the following parameters of the sleep-wake cycle using The Integrated Sleep Diary completed daily for the entire duration of the study, starting from the beginning of the run-in period until the last day of the second treatment period:
1. Total Time in Bed (TTL) = the time interval in minutes between when the patient goes to bed and when they get up from bed;
2. Sleep Onset Latency (SOL) = the time interval (in minutes) between when the patient goes to bed (turns off the lights or TV) and when they fall asleep;
3. Number of Awakenings (NR) = the number of nighttime awakenings;
4. Duration of nocturnal awakenings (WASO - wakefulness after sleep onset) = intranight wakefulness given by the total sum of wakefulness (in minutes) during nighttime awakenings;
5. Total Sleep Time (TTS) = the time interval (in minutes) between when the patient falls asleep and when they wake up definitively in the morning minus intranight wakefulness;
6. Sleep Efficiency Index (IES) = TTS/TTL*100.

7. Evaluation of the possible presence of pain or discomfort that could affect sleep quality using the Visual Analogue Scale (VAS). [Time frame: tr (run-in start), t0 (baseline), t1 (after 28 days of the first treatment period), t2 (after 56 days of the first treatment period), t3 (baseline of the second treatment period), t4 (after 28 days of the second treatment period), t4 (after 56 days of the second treatment period)].

Completion date
30/11/2024

Eligibility

Key inclusion criteria
1. Subjects aged 18 - 70 years of both sexes
2. Subjects able to understand and sign the informed consent
3. With primary insomnia, present for at least one month
4. With ISI questionnaire scores <22
5. With GAD-7 questionnaire scores <5
6. With PHQ-9 questionnaire scores <5

Participant type(s)
Healthy volunteer, Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Upper age limit
70 years

Sex
All

Total final enrolment
66

Key exclusion criteria
1. Aged < 18 and > 70 years
2. Pregnant or breastfeeding individuals
3. Subjects with secondary insomnia or other sleep disorders, such as obstructive sleep apnea, narcolepsy, nocturnal myoclonus, restless legs syndrome, advanced sleep phase disorder, delayed sleep phase disorder, paradoxical insomnia, parasomnias
4. Subjects with ISI questionnaire scores >22
5. Subjects with GAD-7 questionnaire scores >5
6. Subjects with PHQ-9 questionnaire scores >5
7. Subjects suffering from psychiatric disorders: major depression, generalized anxiety disorder, post-traumatic stress disorder, panic attacks, bipolar disorder, dementia, schizophrenia
8. Subjects with chronic and acute pain conditions (e.g., arthritis, fibromyalgia, back pain, headaches, respiratory diseases, asthma, diabetes, heart diseases, injuries, hyperthyroidism, gastroesophageal reflux, epilepsy, Parkinson's disease, Alzheimer's disease, kidney diseases)
9. Subjects who abuse alcohol, amphetamines, caffeine, theine
10. Subjects taking antidepressants, diuretics

11. Subjects with hypothyroidism
12. Subjects who have taken monoamine oxidase inhibitors in the 14 days prior to recruitment
13. Subjects taking antibiotics or who have taken antibiotics in the last four weeks, or in the last 6 months, based on the intensity and duration of antibiotic treatment
14. Subjects with cognitive disorders that may hinder the response to questionnaires
15. Subjects with known allergy to the ingredients of the experimental products (active - placebo)
16. Subjects with acquired immunodeficiency syndrome from HIV

Date of first enrolment
10/06/2024

Date of final enrolment
17/06/2024

Locations

Countries of recruitment
Italy

Study participating centre
COMEGEN Soc. Coop. Sociale
Viale Maria Bakunin, 41
Naples
Italy
80126

Sponsor information

Organisation
Epo S.r.l.

Funder(s)

Funder type
Industry

Funder Name
Epo S.r.l.

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated and/or analysed during the current study will be published as a supplement to the subsequent results publication.

IPD sharing plan summary
Published as a supplement to the results publication