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The beneficial effect on sleep function of a food supplement based on melatonin, Withania somnifera (L.) Dunal, L-ornithine, magnesium and Crocus sativus L.

Submission date
26/01/2024

Recruitment status
No longer recruiting

Registration date
04/03/2024

Overall study status
Completed

Last Edited
04/03/2024

Condition category
Mental and Behavioural Disorders

[ ] 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 represents the sleep disorder with the highest incidence globally. People with this condition have difficulty starting or maintaining sleep, which can lead to an alteration in the sensation of well-being, leading, in some cases, to psychological, cognitive, and somatic alterations. It is estimated that one-third of adults suffer from insomnia, 10%-15% complain of daytime symptoms associated with insomnia, and 6%-10% are affected by insomnia disorder. Furthermore, compared to men, women represent the most affected category, with a gender ratio of about 1.44:1. The prevalence of insomnia disorders in the general Italian population has been studied in a representative sample composed of 3970 individuals aged 15 years or older. Participants were interviewed about their sleep habits and sleep disorders and classified according to DSM-IV criteria. Symptoms of insomnia were found in 27.6% of cases, sleep dissatisfaction (associated with daytime sleepiness) in 10.1%, and insomnia disorders in 7% of the population sample. Compared to previous years, the number of people suffering from insomnia disorders has tripled during the COVID-19 pandemic.
Insomnia is a significant risk factor for cardiovascular (heart) disease. Specifically, insomnia represents a risk factor for arterial hypertension (high blood pressure), myocardial infarction (heart attack), and chronic heart failure. In addition to insomnia itself, there is evidence to suggest that short sleep duration (sleeping less than 6 hours on average at night) is a risk factor for obesity, type 2 diabetes, hypertension, and cardiovascular disease. Insomnia appears to be a risk factor with an actual correlation for major depression, as it has been shown that insomnia often occurs in the absence of major depression, but precedes and is a risk factor for the first onset of major depression.
Numerous clinical studies have explored the effects of food supplement ingredients, either in single or mixed forms, on sleep health. The aim of this study is to evaluate the effect of supplementing the diet with the ANTUR SLEEP food supplement on the sleep function of people with primary insomnia.

Who can participate?
Patients aged 18-65 years with impaired sleep function (primary insomnia)

What does the study involve?
Participants are randomly allocated to consume the ANTUR SLEEP food supplement for 56 days and a placebo (dummy) for 56 days in different orders.

What are the possible benefits and risks of participating?
No risks are foreseen. An improvement in sleep function is expected with ANTUR SLEEP. However, no benefit may be achieved.

Where is the study run from?
General practitioner's medical center (Italy)

When is the study starting and how long is it expected to run for?
March 2022 to June 2023

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

Who is the main contact?
1. Dr Maria Luisa Conza (scientific), marialuisa.conza@antur.it
2. Dr Fabiana Antoniali (public), laboratorio@antur.it

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Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
ANTURSLEEP_01

Study information

Scientific Title
Efficacy study on a food supplement based on melatonin, Withania somnifera (L.) Dunal, L-ornithine, magnesium and Crocus sativus L. for sleep management: single-centre, placebo-controlled, randomized, double-blind cross-over, clinical study with a period of run-in

Acronym
ANTURSLEEP01

Study objectives
The aim of this efficacy study is to demonstrate that the ANTUR SLEEP food supplement, based on
melatonin, Withania somnifera (L.) Dunal, L-ornithine, magnesium and Crocus sativus L., is useful in improving sleep-wake balance in subjects with primary insomnia disorder, without clinically relevant manifestations linked to the sleep disorder.

Ethics approval required
Ethics approval required

Ethics approval(s)

approved 30/11/2022, Ethics Committee of Campania Nord (Contrada Amoretta – Città Ospedaliera, Avellino, 83100, Italy; +39 (0)825/203025; comitatoeticoav@gmail.com), ref: 1972

Study design
Interventional monocentric randomized cross-over double-blind placebo-controlled clinical trial

Primary study design
Interventional

Study type(s)
Quality of life, Efficacy

Health condition(s) or problem(s) studied
Primary insomnia

Interventions
The subjects recruited in the present clinical study consumed a food supplement based on based on melatonin, Withania somnifera (L.) Dunal, L-ornithine, magnesium and Crocus sativus L. (commercial name: ANTUR SLEEP) and a placebo for 56 days, in different administration orders based on crossover design and on the randomization group.

In particular, to maintain the double-blind design, both participants and physicians are unaware of the study treatment administration sequence orders.
The randomization sequence has been 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 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 were enrolled and divided into two groups (33 for each group):

Group 1: participants who received first the food supplement based on melatonin, Withania somnifera (L.) Dunal, magnesium, L-ornithine, Crocus sativus L (treatment A), and, following the washout period of 2 weeks, the placebo (treatment B). ORDER OF TREATMENTS: AB

Group 2: participants who received first the placebo (treatment B), and, following the washout period of 2 weeks, the food supplement based on melatonin, Withania somnifera (L.) Dunal, magnesium, L-ornithine, Crocus sativus L (treatment A). ORDER OF TREATMENTS: BA

The applied daily dose was one tablet of 1.2 g, which provides: 300 mg/day L-ornithine, 250 mg /day W. somnifera extract, 200 mg/day magnesium, 15 mg/day C. sativus extract, 1 mg/day melatonin.

Participants undergo nine visits (screening visit, start of run-in, end of run-in, start of first treatment period, end of first treatment period, start of second treatment period, end of second treatment period) in an outpatient setting. After each clinical visit, all data are filled in the case report form by physicians.

Intervention Type
Supplement

Primary outcome(s)
Sleep-wake balance assessed using the Pittsburgh Sleep Quality Index (PSQI) questionnaire at the start and the end of each study period

Key secondary outcome(s))
1. Insomnia severity assessed using the Insomnia Severity Index questionnaire at the start and the end of each study period.
2. Parameters derived from the sleep diary (self-registered every day):
2.1. Total time in bed (TTB) = time interval in minutes between the time the patient lays down in bed and the time he gets out of bed
2.2. Sleep latency (SOL – sleep onset latency) = time interval (in minutes) between the time the patient gets ready to sleep (turns off the light or the TV) and the time he falls asleep
2.3. Number of awakenings (NR) = number of nocturnal awakenings
2.4. Duration of nocturnal awakenings (WASO – wakefulness after sleep onset) = intra-nocturnal wakefulness given by the overall sum of the wakefulness (in minutes) of nocturnal awakenings
2.5. Total sleep time (TTS) = time interval (in minutes) between the time the patient falls asleep and the time he finally wakes up in the morning minus the overnight wakefulness
2.6. Sleep Efficiency Index (SEI) = TTS/TTB*100
3. Pain assessed using the Visual Analog Scale (VAS) at the start and the end of each study period

Completion date
30/06/2023

Eligibility

Key inclusion criteria
1. Subjects aged 18-65 years of both sexes
2. Subjects able to understand and sign the informed consent
3. Subjects who have a score between 5 and 7 in the Patient Health Questionnaire-9 (PHQ-9), corresponding to subjects with slightly altered mood, not frankly pathological, whose score in the Patient Health Questionnaire-9 is lower than the maximum limits of subthreshold depression (which has a score of 9 in the PHQ-9)
4. Subjects who present a mild mood alteration (subthreshold depression) (Patient Health Questionnaire-9 between 5 and 7) and who are not eligible to take antidepressant drugs
5. Subjects who do not present anxiety and who have a GAD-7 score ≤7

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Upper age limit
65 years

Sex
All

Total final enrolment
66

Key exclusion criteria
1. Aged <18 and >75 years
2. A medical history or condition that could affect the subject's safety or negatively impact the validity of the study results
3. Pregnant or breastfeeding women
4. A history of allergy to ingredients contained in the study treatments (dietary supplement and placebo)
5. Exposed to a high risk of cardiovascular events based on eight risk factors (sex, age, diabetes, smoking habits, systolic blood pressure, total cholesterolemia, HDL-cholesterolemia, and antihypertensive treatment)
6. Following drug therapy for diabetes even at low dosages
7. Taking supplements to control cholesterol, blood sugar, and metabolic syndrome, in the 2 weeks prior to recruitment
8. Women who are suspected to be pregnant or are planning pregnancy
9. Non-self-sufficient individuals
10. Do not show a propensity to collaborate
11. Have difficulty getting to the reference facility within the scheduled time
12. Are not considered suitable by the investigators due to the presence of other pathologies considered incompatible with enrollment

Date of first enrolment
05/12/2022

Date of final enrolment
10/01/2023

Locations

Countries of recruitment
Italy

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General practitioner's medical center
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Sponsor information

Organisation
ANTUR S.r.l

Funder(s)

Funder type
Industry

Funder Name
ANTUR S.r.l.

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated and/or analyzed 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