Article preview
Abstract
Introduction
Section snippets
References (60)
Cited by (67)

Journal of Ethnopharmacology
Volume 264, 10 January 2021, 113276

Clinical evaluation of the pharmacological impact of ashwagandha root extract on sleep in healthy volunteers and insomnia patients: A double-blind, randomized, parallel-group, placebo-controlled study

Deepak Langade MBBS, MD, PGDASS (Applied statistics) (Professor & Head, Pharmacology) [a], Vaishali Thakare MBBS, MD (Asso. Prof. of Pharmacology) [a], Subodh Kanchi (Professor & Head, Pharmacology) [b], Sunil Kelgane BAMS, PDCR, Fellowship in preventive cardiology (Emergency Medical Service Officer) [c]

https://doi.org/10.1016/j.jep.2020.113276

Highlights

- Ashwagandha is having sleep promoting quality.
- First study with Ashwagandha for insomnia patient.
- Sleep parameters and anxiety were improved in insomnia patients.
- Ashwagandha could be an alternative sleep promoting supplement.

Abstract

Ethnopharmacological relevance

Ashwagandha (*Withania somnifera* (L.) Dunal.) is long known for its sleep-inducing effects. Ashwagandha can be proposed as an alternative to the recommended present treatments for insomnia. This study aimed to evaluate the pharmacological effect of Ashwagandha root extract on sleep in healthy subjects and also in the subjects having insomnia.

Material and methods

We performed a randomized, parallel-group, stratified design, placebo-controlled study. A total of 80 eligible participants, 40 in Arm-A (healthy) and 40 in Arm-B (insomnia) were assigned to two groups, either Ashwagandha or placebo and studied for 8-weeks. The assessment was done based on the sleep parameters (Sleep Onset Latency, Total Sleep Time, Wake After Sleep Onset, Total time in bed, and Sleep Efficiency), Pittsburgh Sleep Quality Index and Hamilton Anxiety scale-A questionnaire, mental alertness on rising assessment, and sleep quality questionnaire. Safety and adverse events along with the concomitant medication were also assessed.

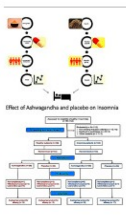
Results

In both healthy and insomnia subjects, there was a significant improvement in the sleep parameters in the Ashwagandha root extract supplemented group. The improvement was found more significant in insomnia subjects than healthy subjects. Repeat measure Analysis of variance (ANOVA) confirmed the significant improvement in SOL (p 0.013), HAM-A outcomes ($p<0.05$), mental alertness (p 0.01), and sleep quality ($p<0.05$) of the insomnia patients. A two-way ANOVA was used to confirm the outcomes that denoted sleep onset latency ($p<0.0001$) and sleep efficiency ($p<0.0001$) as the most improved parameters, followed by TST ($p<0.002$) and WASO($p<0.040$). All these parameters (SOL, TST, WASO, TIB, SE, PSQI, HAM-A, Mental Alertness, and Sleep quality) were also statistically assessed for the significant improvement within the group both for the treatment, and the placebo groups in the healthy and the insomnia datasets. Obtained results suggest statistically significant ($p<0.0001$) changes between the baseline values and the end of the study results except for the HAM-A and the mental alertness scoresn the healthy subject group.

Conclusion

The present study confirms that Ashwagandha root extract can improve sleep quality and can help in managing insomnia. Ashwagandha root extract was well tolerated by all the participants irrespective of their health condition and age. Additional clinical trials are required to generalize the outcome.

Graphical abstract



Introduction

Sleep is one of the most important physiological aspects of human health that helps in recycling energy, vitality, and rejuvenation. Insomnia has become the most common sleep disorder with a high prevalence rate (Morin et al., 2006). The condition is characterized by troubled sleep quality or insufficient sleep duration, physical or mental difficulty falling asleep, intermittent or incomplete sleep, and non-restorative or poor sleep quality (Morin and Benca, 2012). Due to the impaired quality of life and cognitive functions, insomnia is regarded as a clinical condition (Ranjbar et al., 2018). The clinical condition can be situational, recurrent or can turn into a persistent problem over time (Morin and Benca, 2012). Therefore, persistent insomnia can get associated with depression and anxiety disorders (Baglioni et al., 2011; Fernandez-Mendoza and Vgontzas, 2013). Such health conditions inevitably increase healthcare costs along with a gradual deterioration of the quality of life (Leger and Bayon, 2010).

Chronic primary insomnia occurs due to the sleep-initiation or sleep-maintenance problem for at least a month, while secondary insomnia induces due to medical, psychological issues, and drug reaction (Vgontzas et al., 1998, 2011). As insomnia is both a symptom and a disorder in itself, detailed self-evaluation of the problem is imperative before the clinical diagnosis (Sahoo, 2010). Even though polysomnography (PSG) is the accepted gold standard for sleep assessment, there is considerable variability in the sleep pattern of the insomniacs. Moreover, a minute evaluation may produce valuable results that may not be obtained from an individual's usual sleep pattern. Often, clinical and psychological conditions evaluation is mandatory for precise diagnosis. The application of Actigraphy enabled us to evaluate and monitor sleep patterns with a detailed data recording. Actigraphy helps in recording and integrating precise movements of the limbs of a person over time.

The use of device-based monitoring, such as actigraphy, is accurate, continuous, and effortless. Actigraphic devices are put on the wrist or ankle for sleep monitoring (Smith et al., 2018; Ancoli-Israel et al., 2003).

Pharmacotherapy and psychotherapy are the conventional treatments for insomnia (Morgenthaler et al., 2006; Schutte-Rodin et al., 2008). Effective pharmacological treatments include short and long-acting benzodiazepines. However, many such drugs cause adverse effects and daytime sedation, and patients become dependent on continued use (Gillin and Byerley, 1990). Cognitive-behavioral therapy for Insomnia (CBT-I) is another common treatment option for insomnia. However, the lack of trained practitioners prevents the proper therapeutic outcomes for insomnia patients (Edinger and Sampson, 2003). Insomnia is associated with anxiety disorders, depression, suicide, substance abuse, decreased immune functioning, and cardiovascular diseases (Taylor et al., 2003).

Alternative medicinal approaches can provide a solution to these issues. Herbal medicinal practices including Ayurveda are being explored as a complementary and alternative treatment approach (Gyllenhaal et al., 2000). A United States national survey reported that 4.5% of adults prefer complementary and alternative medicine as a treatment measure for insomnia (Pearson et al., 2006).

Ashwagandha (*Withania somnifera* (L.) Dunal.) is being used in Ayurveda for long. This shrub belongs to the *Solanaceae* family and is popularly known as winter cherry and Indian ginseng (Dafni and Yaniv, 1994; Andallu and Radhika, 2000). Ashwagandha is categorized as "*Rasayana*" (rejuvenator) and is believed to maintain health, rejuvenate the body, and may enhance longevity (Sivarajan and Balachandran, 1994). Significant phytochemical constituents such as alkaloids, steroidal lactones (withanolides, withaferins), saponins, glycol-withanolides are present in Ashwagandha (Shah et al., 2006). This plant material has a wide range of pharmacological beneficial effects including anxiolytic, hypotensive, sedative, immunomodulatory, analgesic, anti-inflammatory, anti-tumor, anabolic, antifungal, hematopoietic, and cardiorespiratory enhancing (Choudhary et al., 2015; Shenoy et al., 2012). The plant parts, especially the root, is also used as an adaptogen and antioxidant (Mishra et al., 2005; Sandhu et al., 2010; Kulkarni and Dhir, 2008; Verma and Kumar, 2011). Ashwagandha root extract can increase memory and cognitive abilities in people with mild cognitive impairment (Choudhary et al., 2017a, Choudhary et al., 2017b), can improve the sexual function in both males and females (Dongre et al., 2015; Ambiye et al., 2013; Gupta et al., 2013), aids in body weight management in adults and improves an individual's resistance towards stress and anxiety (Choudhary et al., 2017a, Choudhary et al., 2017b; Chandrasekhar et al., 2012).

The species name *Somnifera* refers to sleep induction in Latin. Hence, for years the herb is having literal evidence for sedation or sleep induction. Animal studies demonstrated that oral administration of Ashwagandha root extract induced sleep in rats (Kumar and Kalonia, 2007, 2008). However, human studies on the effect of Ashwagandha related to insomnia are limited. Therefore, the objective of the present study was to assess the efficacy and safety of Ashwagandha root extract compared to the placebo for insomnia and anxiety. Stratified randomization was used to parallelly understand the impact of the herbal extract on healthy volunteers, and insomnia patients. Sleep onset latency was the primary outcome of the study. Total sleep time, sleep efficiency, total time in bed, and wake after sleep onset were the secondary outcomes of the study. Monitoring and assessment of the outcomes were done using actigraphy, Hamilton anxiety scale (HAM-A), mental alertness on rising, and sleep quality. In this study, safe and efficacious outcomes for the participants used Ashwagandha root extract was expected compared to the placebo.

Section snippets

Study design

The study was designed as a randomized, double-blind, placebo-controlled, parallel-group stratified comparative clinical study, and it was conducted for 8 weeks. Outcome measurements were conducted at baseline, week 1, week 4, and week 8, respectively. Associated International ethical norms and national ethical guidelines were followed throughout this study. Declaration of Helsinki was strictly obeyed and the ethical clearance for the trial was obtained from the ethics committee of DY Patil …

Participants distribution

A total of 116 subjects (64 healthy subjects and 52 patients with insomnia) were assessed for eligibility. Out of these, 36 subjects were excluded from the study (18 did not meet the inclusion criteria, 8 declined to participate and 10 had other reasons to refuse participation). As a consequence, a total of 80 participants were recruited for the study (Arm-A consisting of 40 healthy subjects and Arm-B consisting of 40 insomnia patients). All the participants were randomly assigned to two …

Discussion

The effect of Ashwagandha was evaluated on the quality of sleep in healthy subjects and insomnia patients in the present study. The analysis outcomes were compared over 8 weeks to the placebo groups. Stratified randomization was opted due to the presence of defined subject groups before the allocation.

Insomnia is affecting the global population of different age groups, specifically the elderly populations. Recent studies and surveys suggested that insomnia is on the rise in the younger and …

Limitations

The present study provided valuable information for considering Ashwagandha root extract as an alternative therapeutic component for insomnia. However, a large multi-centric study with a diverse population can generalize the impact of the present findings. The present study lacks the scope of herb-drug and herb-herb interaction as the included insomnia patients were not using any other medication. The study protocol was developed to evaluate the effect of placebo and the Ashwagandha only, no …

Conclusions

Insomnia is one of the leading global health problems due to our present stressful lifestyle. The presently available medications are not sufficient to counter the situation and have several restrictions of use such as demographic issues like age, clinical issues such as the existence of specific conditions like diabetes, and hypertension. Hence, a solution in the form of an alternative supplement may become helpful. Ashwagandha is having a tremendous reputation as a somatogenic herb in the …

Declaration of competing interest

The authors declare no conflict of interest. …

Acknowledgment

The authors thank Ixoreal Biomed Inc, Los Angeles, California, USA for supplying the KSM-66 Ashwagandha root extract used in the study treatment. …

References (60)

C. Baglioni *et al.*
Insomnia as a predictor of depression: a meta-analytic evaluation of longitudinal epidemiological studies
J. Affect. Disord. (2011)

D.J. Buysse *et al.*
The Pittsburgh sleep quality index: a new instrument for psychiatric practice and research
Psychiatr. Res. (1989)

A. Dafni *et al.*
Solanaceae as medicinal plants in Israel
J. Ethnopharmacol. (1994)

A. Gupta *et al.*
Efficacy of Withania somnifera on seminal plasma metabolites of infertile males: a proton NMR study at 800 MHz
J. Ethnopharmacol. (2013)

C. Gyllenhaal *et al.*
Efficacy and safety of herbal stimulants and sedatives in sleep disorders
Sleep Med. Rev. (2000)

S.K. Kulkarni *et al.*
Withania somnifera: an Indian ginseng
Prog. Neuro-Psychopharmacol. Biol. Psychiatry (2008)

D. Leger *et al.*
Societal costs of insomnia
Sleep Med. Rev. (2010)

P.H. Luppi *et al.*
Sleep-wake physiology

C.M. Morin *et al.*
Chronic insomnia
Lancet (2012)

C.M. Morin *et al.*
Epidemiology of insomnia: prevalence, self-help treatments, consultations, and determinants of help-seeking behaviours
Sleep Med. (2006)

Cited by (67)

The evolving role of quantitative actigraphy in clinical sleep medicine
2023, Sleep Medicine Reviews

Citation Excerpt :
…Concerning alternative therapies, of ten studies, five used actigraphy as a secondary outcome [62–67]. With respect to actigraphy measures, regardless of the type of therapy, almost all of the studies (27/32) used actigraphy to measure TST [43–45,47–61,63–70], followed by SE (25/32) [43,46–59,61,63–68,70,71], WASO (20/32) [43,45,47–56,58,61–65,67,68,70] and SOL (18/32) [43,45,47,49–54,56–58,61,63,64,67,68,70,71]. In contrast, only five studies focused on actigraphy measures on NAWK [48,53,62,64], while total wake time (TWT) (consisting of SOL + WASO) was reported in three studies [43,44,59].…

Show abstract

Cancer Metabolism as a Therapeutic Target and Review of Interventions
2023, Nutrients

Does Ashwagandha supplementation have a beneficial effect on the management of anxiety and stress? A systematic review and meta-analysis of randomized controlled trials
2022, Phytotherapy Research

Effect of Ashwagandha (Withania somnifera) extract on sleep: A systematic review and meta-analysis
2021, Plos One

Medicinal Plants for Insomnia Related to Anxiety: An Updated Review #
2021, Planta Medica

Effects of withania somnifera (Ashwagandha) on stress and the stressrelated neuropsychiatric disorders anxiety, depression, and insomnia
2021, Current Neuropharmacology