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A Review on the Use of Ashwagandha, Chamomile, and Valerian for Treating Insomnia

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Abstract: ***This study aimed to evaluate Ashwagandha, Chamomile, and Valerian for their effects on thubmitted my me central nervous system, focusing on their use as sedatives and hypnotics. The herbs were tested for hypnotic, sedative, anti-anxiety, antidepressant, and antipsychotic activities using standard experimental methods. Valerian is often used to treat insomnia, but its active ingredients and how it works are not yet fully understood. Non-restorative sleep affects about 10% of people worldwide, leading to poor sleep and both physical and mental fatigue. In this study, an extract of ashwagandha (Withania somnifera Dunal L.) was tested for its ability to improve sleep quality in people with non-restorative sleep. Chamomile, from the German chamomile plant (Matricaria chamomilla L.), has long been used as a calming and sedative herb. Ashwagandha, an adaptogenic herb from Ayurveda, has shown it can reduce stress and help with sleep by affecting cortisol and GABA activity. Chamomile contains flavonoids like apigenin, which can have mild calming and anti-anxiety effects by interacting with certain brain receptors. Valerian root, used in Europe for centuries, helps increase GABA activity and can shorten the time it takes to fall asleep, though results can vary. Overall, these herbs may help improve sleep quality, reduce anxiety, and could be used alongside or instead of synthetic sleep aids.***

Keywords: Insomnia, ashwagandha, chamomile, valerian, sleep disorder, Herbal medicine

1. Introduction

Insomnia, which can occur due to various reasons such as physical health issues, is a common problem today. Some studies indicate that insomnia can affect both the body and the mind. If someone experiences insomnia for a prolonged period, it can lead to difficulties in thinking clearly, resulting in issues like forgetfulness, trouble focusing, and mental stress. These problems can impact learning and work performance. It can also cause other issues, such as dizziness during the day, loss of appetite, stomach pain, and headaches. [1] Insomnia is a significant concern for adults. Surveys from different countries show that about 30% to 40% of adults experience difficulties in falling or staying asleep. A smaller group, approximately 10% to 15%, suffers from severe sleep problems. The prevalence of insomnia increases in older adults. In clinics, around 69% of patients report sleep issues. About 40% of people with insomnia have used over-the-counter medicines or alcohol to help sleep, and approximately a quarter have used prescription medication at least once. However, there is limited strong evidence showing that most of these common medicines are effective for insomnia, including antihistamines, chloral hydrate, barbiturates, tryptophan, and melatonin. [2] Traditionally, there are three main types of treatments for insomnia: non-drug methods, drug treatments, and complementary or alternative medicine. Although guidelines from the American Academy of Sleep Medicine (AASM), the American College of Physicians (ACP), and the European Sleep Research Society (ESRS) strongly recommend cognitive behavioural therapy for insomnia (CBT-I) as the best first treatment for long-term insomnia in adults of any age, prescription drugs are still the most commonly chosen option. As for drug treatments, several types of medications are available, including benzodiazepines such as diazepam, lormetazepam, and oxazepam; benzodiazepine receptor agonists or "Z" drugs such as zolpidem, zaleplon, and zopiclone; and orexin receptor antagonists such as suvorexant and lemborexant. [3]

1) Ashwagandha (Withania Somnifera)

The plant known as Withania somnifera, which is part of the Solanaceae family, is commonly called "Ashwagandha" in Sanskrit. This name comes from its long history of use in traditional Indian medicine. In Ayurveda, Ashwagandha is highly valued as a Rasayana herb, which means it helps restore the body and maintain the health of all body tissues. [8] It is also sometimes referred to as winter cherry or Indian ginseng, even though it is not actually part of the ginseng family [9]

a) Extraction Process of Withania somnifera (Ashwagandha)

Extracting Withania somnifera, also called Ashwagandha, is an important step to get its useful parts, like withanolides, alkaloids, and steroidal lactones. Usually, the roots are the main part used, but the leaves are also being looked at as another option (Singh et al., 2011). [10] First, the roots are collected, cleaned, dried in the shade, and then turned into a powder. This helps protect the heat-sensitive compounds (Mirjalili et al., 2009). [11] Once the powder is ready, different methods are used depending on what active ingredients are being aimed for.

b) Traditional Extraction Methods

- Maceration and Percolation: These are older ways where the powdered roots are soaked or slowly passed through a liquid like water, ethanol, methanol, or a mix of water and alcohol. They are simple to use and not very costly, but they take more time and give a weaker result (Singh et al., 2010). [12]
- Soxhlet Extraction: This is a widely used method to get as much as possible from the plant. Solvents like ethanol or

methanol are repeatedly passed through the setup to remove both water-soluble and fat-soluble compounds (Kulkarni & Dhir, 2008). [13]

2) Modern Extraction Methods

New technologies in extraction have brought about greener and more effective ways to get compounds from plants. Using supercritical fluid extraction with carbon dioxide, and sometimes adding ethanol as a helper, allows for better selection and purity of withanolides, while also lowering the amount of leftover solvents (Mirjalili et al., 2009). [14] Another new method is ultrasound-assisted extraction, and microwave-assisted extraction. These techniques use less solvent and take less time to extract, and they help get more of the active compounds from the plant (Singh et al., 2011). [15]

a) Efficacy

Some small studies suggest that taking ashwagandha extract may help improve several aspects of sleep. This includes how restful the sleep is, how long the person sleeps, how fast they fall asleep, and how well they stay asleep through the night. These improvements are especially clear in people who have trouble sleeping, such as those with insomnia. There isn't a lot of research on this topic, but some clinical trials show that ashwagandha can help with sleep.

For example, in a study in India, 150 healthy adults aged 18 to 65 who had sleep problems like insomnia or poor rest were given either ashwagandha root and leaf extract or a placebo for six weeks. Both groups saw some improvement in their sleep quality, as measured by a standard rating scale. People who took ashwagandha also had better sleep efficiency (meaning they spent more time asleep while in bed), longer total sleep time, faster sleep onset, and fewer times they woke up during the night, as measured by actigraphy. [16]

2. Research Methods

Literature was gathered using the PubMed, Scopus, and Google Scholar databases, as well as from papers cited in the initial articles retrieved. Only studies where WS and its derivatives were the sole agents studied were included. Any studies that included WS as part of a multi-herb or multidomain intervention were excluded due to an inability to differentiate the effects of WS from other interventions used.

2.1 Animal Studies

Animal studies have shown that WS can help improve sleep, One study used fruit flies to investigate herbal extracts that might aid in sleep. They tested seven extracts, including a root extract made from WS using a mix of water and alcohol. This extract was found to increase the total amount of sleep the flies got and also helped them fall asleep faster, without affecting their activity when they were awake [19]. Another study by Kaushik et al. (2017) examined leaf extract from WS that was rich in with anolides, including thaferin A and withanone. This extract didn't make mice sleepy. However, an extract made with water and triethylene glycol did help mice fall into non-rapid eye movement sleep when given in a dose of 30 mg per mouse. Mice that received just triethylene glycol at the same dose had similar sleep improvements, suggesting this substance might be responsible for the sleep-enhancing effects of WS [20]. Kumar and Kalonia (2007) tested an unspecified root extract of WS in rats that were kept awake for 24 hours. The rats received an injection of WS before being kept awake. This treatment helped them sleep more, especially during deep sleep, and also helped them fall asleep faster. It also reduced their time awake and the time spent in REM sleep [21]. Besides helping with sleep, extracts from WS have also been found to reduce some negative effects of not getting enough sleep.

One study gave a well-defined water extract of WS (called ASH-WEX) to rats for 15 days before making them sleep-deprived for 12 hours. The rats that received WS showed better memory and learning abilities and were better at moving around compared to those that didn't get the extract. In a mouse study, mice given an unspecified root extract of WS before being sleep-deprived had less weight loss, better movement, and less anxiety compared to mice that weren't given the extract [22].

2.2 Human Studies

Five studies looked at how WS affects insomnia in adults between the ages of 18 and 85. The people in these studies were either healthy, feeling stressed, had insomnia, or had trouble getting good sleep. Four studies had between 50 and 80 people, while Deshpande et al. (2020) studied 150 people [24]. All the studies used a WS product that was made into capsules. Four of them used KSM-66 Ashwagandha, and Deshpande et al. (2020) used Shoden. The daily dose of WS was between 120 and 600 mg, and it was taken for 6 to 12 weeks. Salve et al. (2019) tested different doses [25] [26]. Each study used different ways to check how sleep improved. Most of them used more than one method. The most common way was the sleep quality rating, which is a seven-point scale where higher numbers mean worse sleep. Langade et al. (2019) and Langade et al. (2021) also used the Pittsburgh Sleep Quality Index (PSQI) to check sleep quality. Three studies used the mental alertness on rising rating, a three-point scale to check how alert people felt in the morning. Three other studies used sleep actigraphy, which is a wearable device that measures sleep patterns like how long it takes to fall asleep, how efficient sleep is, how long sleep lasts, and how much people wake up during the night. Kelgane et al. (2020) used the Sleepiness Scale, a 4-item survey, to check how likely people were to fall asleep during the day. Deshpande et al. (2020) used the Restorative Sleep Questionnaire – Weekly (RSQ-W), a 9-item questionnaire, to check if people had restful sleep. In general, using WS helped improve different aspects of insomnia across different groups of people and ages (Table 1). However, because there aren't enough studies and because the doses and ways to measure results vary, it's hard to say what the minimum dose of [27] [28] [29].

1) Chamomile (Matricaria Chamomilla L.)

Chamomile comes from the German chamomile plant, called Matricaria chamomilla L. in the Asteraceae family. It has been used for a long time as a medicine, especially for helping people relax and sleep better. The part of the plant that is most useful for its health benefits is the flower. This flower has several active substances, like flavonoids such as apigenin,

luteolin, and quercetin, and terpenoids like chamazulene, bisabolol, and bisabolol oxide. These substances are thought to help improve sleep. Some studies done in the lab suggest that apigenin, one of the flavonoids, can make people feel calm by affecting GABA receptors in the brain. [30] [31]

Preparation of chamomile extract

About 15 grams of dried Chamomile (Matricaria chamomilla L.) was used. The flowers were ground into a powder and then mixed with 100 ml of water. The mixture was heated to 75°C and kept at that temperature for 35 minutes until the colour of the solution changed. After that, the mixture was filtered, and the resulting extract was used in the treatment studies [32].

2) Materials and Methods

a) Human Studies

In human research, chamomile has mostly been studied using randomized controlled trials and observational studies. A common form of chamomile used in these studies is a standardized extract from Matricaria recutita, taken in capsule form. The usual dose ranges from 220 to 500 mg per day, and the treatment usually lasts two to four weeks. Researchers have used different tools to measure sleep, like the Insomnia Severity Index, sleep diaries, and sometimes polysomnography. For instance, a pilot study by Zick and others in 2011 looked at 270 mg of chamomile extract taken twice a day for 28 days in adults with chronic insomnia, and found some improvement in how long it took them to fall asleep and how often they woke up during the night. Similarly, Amsterdam and their team in 2009 and 2012 studied chamomile in people with anxiety and depression, and found that it had calming effects, which helped improve sleep quality indirectly. [33] [34]

b) Animal Studies

Animal models have been extensively used to investigate the mechanisms behind chamomile's sedative and hypnotic effects. Extracts from Matricaria recutita and isolated flavonoids like apigenin have been tested in rodents, with outcomes measured through sleep onset latency, total sleep duration, and locomotor activity. Avallone et al. (2000) found that chamomile extract exhibits benzodiazepine-like activity by interacting with GABA-A receptors, leading to increased sleep duration. Shinomiya et al. (2005) further demonstrated that apigenin significantly enhances pentobarbital-induced sleep in mice, offering preclinical evidence for its GABAergic mechanism. These findings align with human clinical studies, reinforcing chamomile's role as a mild sedative and sleep-promoting agent. [35] [36]

3. Valerian (Valeriana Officinalis)

Valerian root (Valeriana officinalis), a flowering plant, has been traditionally used in Europe for treating sleep disorders for many years. In recent times, it has gained popularity in the United States as a self-administered remedy for insomnia. A national survey from 2002 revealed that 1.1% of adults, roughly 2 million people, used valerian within the past week. If valerian proves effective for insomnia, it could serve as an important alternative treatment due to its affordability and lack of known side effects. Valerian contains over 150 different compounds, including volatile oils, ketones, phenols, iridoid esters such as valepotriates, alkaloids, valeric acid, and amino acids like GABA, arginine, tyrosine, glutamine, along with various hydrocarbons. In one study, the valerian/cascara mixture significantly reduced sleep onset latency and increased total sleep time. The mixture also increased non-REM sleep duration while decreasing REM sleep.

3.1 Extraction process

The roots and rhizomes from Valeriana officinalis L. are used to create extracts. It's important to properly identify and collect the plant material following Good Agricultural and Collection Practices (GACP). (European Pharmacopoeia (Ph. Eur.), Monograph "Valerian Root" (Valerianae radix), 10th Edition, 2020) Fresh roots are washed and then dried in the shade at a temperature of 40–45°C until they contain less than 10% moisture. The dried roots are then crushed into a rough powder using a machine and then passed through a sieve with 40 holes. (British Pharmacopoeia (BP), Monograph on Valeriana officinalis, 2020) [38]

1) Solvent Extraction (Main Method)

a) Hydroalcoholic Extraction (Most Common)

- Solvent: A mix of ethanol and water, with 70% ethanol and 30% water.
- Ratio of drug to solvent: For each part of root, use 10 parts of the solvent.
- Method: The root can be soaked in the solvent (maceration) or processed with a Soxhlet machine for 6 to 8 hours at a temperature between 50 and 60 degrees Celsius.
- Filtration: The mixture is filtered using Whatman filter paper.
- Concentration: The liquid is concentrated using a rotary evaporator at a temperature no higher than 45 degrees Celsius under reduced pressure.
- Yield: The amount of extract obtained is between 8 to 12%, which may vary depending on the age of the root and the solvent ratio [European Medicines Agency (EMA), Assessment Report on Valeriana officinalis L., 2016] [39]

b) Storage and Packaging

- The extract should be stored in airtight amber-colored glass bottles, kept at 25 degrees Celsius, away from light and moisture [42]

3.2 Human Studies on Valerian

1) Clinical Use in Insomnia

A randomized, double-blind clinical trial found that valerian extract (400 mg/day for 14 days) improved sleep quality without causing next-day sedation. (Another meta-analysis showed mild-to-moderate improvement in sleep latency and quality, though results varied among studies. (Bent, S. et al., American Journal of Medicine, 2006.) [43]

2) Safety Profile

Valerian showed no serious adverse effects and was generally well-tolerated even with prolonged use [44]

3) Regulatory Recognition
Valerian root is classified as a traditional herbal medicinal product under Directive 2004/24/EC in the European Union. [45]

3.3 Animal Studies on Valerian

1) Sedative and Sleep-Inducing Activity
A methanolic extract from the roots of Valeriana officinalis was tested on male Swiss albino mice.
- Dose: 25, 50, and 100 mg/kg (given by mouth).
- Result: As the dose increased, the time the mice slept after being given pentobarbital also increased. Their movement also decreased. [46]

2) Anxiolytic (Anti-Anxiety) Effect
A hydroalcoholic extract from Valeriana officinalis was given to Wistar rats using the Elevated Plus Maze (EPM) test.
- Dose: 100 and 200 mg/kg (given by mouth).
- Result: The rats explored the open arms of the maze more, which is similar to the effect of diazepam. [47]

3) Anticonvulsant Effect
An aqueous extract from valerian root was tested in mice using the maximal electroshock seizure (MES) model.
- Dose: 50, 100, and 200 mg/kg (given by mouth)
- Result: The time and start of seizures were reduced, which was similar to the effect of phenobarbital. [48]

Future Prospects of Ashwagandha, Valerian, and Chamomile in the Treatment of Insomnia
Upcoming research will focus on large-scale, multi-centre studies that follow strict scientific and ethical guidelines, such as the ICH-GCP and the Declaration of Helsinki (World Medical Association, 2013), to ensure the results are reliable and safe. These herbs are also supported by guidelines from the World Health Organization on Good Agricultural and Collection Practices and Good Manufacturing Practices as described in the Drugs and Cosmetics Act, 1940 and Rules, 1945. These help ensure that the plants are grown sustainably, their quality is high, and their sources can be tracked. In India, Ashwagandha and Valerian are listed in the Indian Pharmacopoeia, and Chamomile is standardized in the European Pharmacopoeia, making it easier to trade and use them globally. In the U. S., the FDA and the European Medicines Agency also focus on monitoring the safety and consistency of herbal medicines. Looking ahead, new technologies like biotechnology and nanotechnology will be used to grow these plants better and make their active ingredients more effective and stable. [50] [51] [52]

4. Result

Research indicates that Ashwagandha, Valerian, and Chamomile are all strongly supported in their effectiveness for aiding sleep and alleviating insomnia symptoms. Ashwagandha has been shown to reduce stress and cortisol levels, which can assist individuals in falling asleep more quickly and maintaining sleep for a longer duration. Studies demonstrate that individuals using standardised Ashwagandha root extract experienced quicker sleep onset and improved sleep efficiency. Additionally, animal studies have indicated that Ashwagandha may decrease anxiety and facilitate sleep by influencing specific brain pathways and the body's response to stress. Valerian has demonstrated calming and sleep-promoting effects in both human and animal research. . Supporting animal studies indicate that Valerian boosts levels of a neurotransmitter called GABA, which is vital for relaxation and sleep. Chamomile exhibits mild calming effects and can help reduce anxiety, primarily due to components like apigenin. Research suggests Chamomile may minimize nighttime awakenings, enhance sleep quality, and promote relaxation. Animal studies further indicate that Chamomile influences brain chemicals linked to sleep and relaxation. When combined, these herbs may provide enhanced benefits compared to their individual effects by targeting various underlying issues related to sleep disturbances, such as stress, anxiety, and neurotransmitter imbalances.

In summary, studies involving both humans and animals indicate that these herbs are generally well-tolerated, non-addictive, and safe for prolonged use with minimal side effects. The results from this research imply that Ashwagandha, Valerian, and Chamomile might serve as effective natural remedies for insomnia, and additional research is necessary to completely understand their potential applications in medical contexts**.**

5. Conclusion

Ashwagandha, Valerian, and Chamomile create a potent combination of herbal treatments designed to assist individuals struggling with insomnia and various sleep-related issues, presenting a natural, secure, and holistic alternative to standard pharmaceutical solutions. Valerian enhances GABA neurotransmission in the central nervous system, facilitating relaxation, decreasing the time required to fall asleep, and improving the quality and duration of deep sleep. The combined effects of these herbs create a synergistic impact, allowing them to tackle multiple pathways simultaneously and thus offering comprehensive support for both falling asleep and sustaining sleep throughout the night. Adhering to regulatory and legal frameworks is crucial for fostering global acceptance of these herbal solutions. Legal regulations, such as the Drugs and Cosmetics Act , EU Directive 2004/24/EC, and international standards for herbal medicine, help guarantee the secure, uniform, and ethical cultivation, distribution, and promotion of these plants. The increasing acceptance of Ashwagandha, Valerian, and Chamomile holds promise for diminishing dependence on synthetic sleep medications, promoting holistic mental health strategies, and heightening public awareness of the benefits of natural sleep remedies. Furthermore, incorporating these herbs into healthcare and educational systems can further enhance the acceptance of evidence-based herbal medicine, cultivating a more informed and health-conscious society. Their distinct blend of sedative, anxiolytic, and adaptogenic characteristics tackles both the symptoms and root causes of sleep issues, offering a comprehensive method to enhance sleep and overall well-being. Ongoing research, validation through clinical trials, innovations in technology, and adherence to ethical and legal guidelines will guarantee that these herbal remedies maintain their therapeutic significance while supporting healthier lifestyles, improving quality of life, and advancing comprehensive strategies for sleep

management worldwide. The continued investigation of their pharmacological actions, enhancement of formulations, and validation across varied populations will reinforce their position as effective, dependable, and sustainable options for insomnia, bridging traditional wisdom with contemporary medical practices. Ultimately, the path forward for managing insomnia lies in the incorporation of natural treatments like Ashwagandha, Valerian, and Chamomile into conventional healthcare practices, providing patients with safe, accessible, and thorough treatment alternatives. With ongoing innovation, standardisation, and heightened public awareness, these herbal remedies have the potential to transform strategies for addressing sleep disorders, deliver long-term benefits with minimal risks, and enhance overall mental, emotional, and physical well-being. Their multi-faceted effectiveness, along with minimal side effects and holistic advantages, establishes them as a crucial component of future therapeutic strategies, fostering a transition towards preventive, natural, and patient-focused methods in the treatment of insomnia and sleep-related issues.

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