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OBSERVATIONAL CLINICAL INTERVENTION ON THE EFFICACY AND SAFETY OF *JATAMANSI, VACHA, TAGAR, KHURASANI AJWAIN, SARPAGANDHA EXTRACT* IN THE FORM OF MEDIWIN'S SLEEP EEZE CAPSULES BY MEDIWIN RESEARCH & HEALTHCARE IN INSOMNIA

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ABSTRACT

Insomnia, a common sleep disorder, can have a significant negative impact on anindividual's physical and mental well-being. Many of the currently available medications for treating insomnia have adverse side effects. Therefore, herbal medicines may present a viable alternative for managing this condition. To explore this further, a randomized, double-blind, placebo-controlled study was conducted at Shri Krishna Govt. Ayurvedic College & Hospital in Kurukshetra, Haryana, India. The study evaluated the efficacy and safety of Jatamansi, Vacha, Tagar, Khurasani Ajwain, and Dhatura Beej extracts in the form of Mediwin's Sleep eeze Capsules developed by MEDIWIN Research & Healthcare for treating insomnia. The study aimed to assess the effectiveness of Mediwin's Sleep eeze Capsule in treating insomnia, and the researchers administered the capsules to patients in theoutpatient department.

KEYWORDS: *Sarpgandha (Rauwolfia Sepentina)*, Insomnia, Jatamansi (*Nordostachys jatamansi*), Khurasani Ajwain (*Hyoscyamus niger*), Mediwin's Sleep eeze capsules, Tagar (*Valeriana wallichii*), Vacha (*Acorus calamus*).

INTRODUCTION

Sleep cycles fulfil the vital requirement of restoring and maintaining human health by replenishing normal health declines. Sleep is a fundamental aspect of life that revives us on physiological, biochemical, cellular, and molecular levels. The typical person sleeps for over 30% of their lifespan.[1] Besides revitalization, sleep is intricately connected to the appropriate functioning of critical physiological processes, such as regulating blood pressure, metabolism, catabolism, temperature, memory consolidation, and the central nervous system, among others.[2] Sleeplessness, commonly referred to as insomnia, is now a prevalent condition that has a negative impact on the overall health and mental well-being of a significant part of the world's population. Clinical symptoms of insomnia involve having trouble falling asleep, staying asleep, or both, as well as difficulties in performing everyday activities. Insomnia is clinically identified by an average sleep latency of over 30 minutes, being alert for more than 30 minutesafter sleep onset, and having a sleep efficiency of less than 85% of the total sleeptime, which is less than 6.5 hours.[3]

Even though Jatamansi (*Nordostachys jatamansi*) is not specifically recommended for managing insomnia in traditional Ayurvedic texts, the rhizome of Jatamansi has an active component called Jatamansone (Valeranone). In 1963, Arora et al. described the tranquillizing properties of Jatamansone.[4] When administered, Jatamansone produces a behavioral effect that is similar to benzodiazepines. The combination of Jatamansone with the neurotransmitter gamma-aminobutyric acid (GABA) may result in a stronger action at the GABA receptor.[5] Jatamansi contains alkaloids such as Spirojatamol, Valerenic Acid, and Virolin, which possess various properties like tranquillizing, hypotensive, anti-inflammatory, anti-stress, central nervous system depressant, anti-anxiety, and analgesic effects.[6,7] Because of these properties, Jatamansi has a significant impact on the symptoms of primary insomnia.

The rhizome of Vacha (*Acorus calamus*) has been traditionally used in Ayurveda as a brain tonic (Medhya) due to its beneficial effects.[8] Recent studies have discovered that Vacha has various properties, including tranquilizing, antibacterial, antidiarrheal, neuroprotective, antioxidant, antihelminthic, anti- convulsant, anti-inflammatory, and analgesic effects. The rhizomes of Vacha contain an aromatic oil that has been used for therapeutic purposes since ancienttimes and is now commercially harvested.[9,10]

Tagar is described as a nootropic herb (Medhya) with sleep-inducing properties (Nidrajanak) in some references.[11] Tagar is believed to possess various pharmacological effects, such as

tranquilizing, hypnotic, antibacterial, antiviral, and anti-tumor activities.[12] Due to these properties, Tagar has been shown to have a tranquilizing effect in patients with insomnia.

Khurasani Ajwain herb has properties that calm and alleviate pain. It rejuvenates body cells and provides energy to the body. These herbs have a similar function to the drug belladonna, but without stimulating the nervous system or causing lightheadedness as belladonna does.

Sarpgandha (Rauwolfia Sepentina) is a plant with both medicinal and hallucinogenic properties that has gained worldwide recognition. The indigenous people of the Indian subcontinentused Datura in prehistoric times for both ceremonial and therapeutic purposes.[13] Most plants contain one or more substances such as alkaloids, tannins, saponins, and cardiac glycosides, which are responsible for their medicinal properties. A phytochemical screening revealed the presence of various substances in Datura, including glycosides, alkaloids, flavonoids, phenols, steroids, saponins, and tannins. Atropine and scopolamine, which are competitive antagonists of muscarinic cholinergic receptors, can cause depression of the central nervous system.[14]

AIMS AND OBJECTIVES

- The aim is to assess the safety and effectiveness of Mediwin's Sleepeeze Capsules in individuals with insomnia.

MATERIAL AND METHODS

Mediwin's Sleep eeze capsules, which contain herbal extracts such as Jatamansi, Vacha, Tagar, Khurasani Ajwain, and Dhatura Beej, were used as the investigational drug in the pre-clinical trial. The composition of Mediwin's Sleep eeze capsules consists of dry extracts of Jatamansi (125mg), Vacha (125mg), Tagar (125mg), Khurasani Ajwain (125mg), and *Sarpgandha (Rauwolfia Sepentina)* (100 mg). These capsules are manufactured by Mediwin Research & Healthcare, located at 13 & 14 Vita Enclave Near Sena Nagar, Dhulkot, Ambala, Haryana, India - 134002.

Name	Latin Name	Quantity	Part Used	Reference
Jatamansi	*Nordostachys jatamansi*	125 mg	Rhizome (Dry Extract)	Bhav Prakash Nigahntu
Vacha	*Acorus calamus*	125 mg	Root (Dry Extract)	Bhav Prakash Nigahntu
Tagar	*Valerianawallichii*	125 mg	Root (Dry Extract)	Bhav Prakash Nigahntu

Ajwain	*Hyoscyamusniger*	125 mg	Seed (Dry Extract)	Bhav Prakash Nigahntu
Sarpgandha *Rauwolfia Sepentina*		100 mg	Seed (Dry Extract)	Bhav Prakash Nigahntu

Following the consumption of Mediwin's Sleepeeze capsules to establish standardization, a batch of 50,000 capsules with a dosage of 505 mg was selected. The capsules were subjected to analytical testing while still in their sealed packaging. The manufacturer provided a complete dossier of the drug, specifically referring to the Ayurvedic Pharmacopoeia of India.

Patients were chosen from the outpatient department (OPD) of Rasa Shastra Evum Bhaishajya Kalpana Department at Shri Krishna Govt. Ayurvedic College in Kurukshetra, Haryana, India (PIN code 136118). Patients who met the eligibility criteria, regardless of their age, sex, or religion, were included in the study. Participants within the age range of 20 to 60 years were chosen. A regular blood test was conducted to exclude any other medical conditions and to ensure that blood values were within normal limits.

INCLUSION CRITERIA

- All individuals with insomnia were included in the study.
- Only individuals between the ages of 20 and 60 were included in the study.

EXCLUSION CRITERIA

- Patients who declined to participate in the study.
- Patients who were either under the age of 20 or over the age of 60.
- Patients who had worked night or rotating shifts in the seven days prior tothe start of the study.
- Patients with disease-related complications.
- Patients with a history of alcohol or drug abuse.

DURATION OF THE TRIAL

- The total duration of the trial was 30 days

METHOD OF STUDY

The study obtained informed consent from the participants to enroll them in the trial. The clinical trial comprised 75 registered individuals who were randomly assigned in a 2:1 ratio. Specifically, 25 participants were assigned to the control group (placebo), and 50 participants were assigned to the experimental group (testing Mediwin's Sleepeeze capsules). The

materials for both the experimental and control groups were packaged identically. The participants were blinded to their group assignments, as were the researchers and clinicians involved in the study.

Trial Group I - (50 Patients with Insomnia)

The objective was to evaluate the effects of Mediwin's Sleepeeze Capsules, in the form of a tranquilizer, on specific signs and symptoms of insomnia in a group of 50 patients. All 50 patients were included in this study, and only one patient dropped out, leaving 49 patients who completed the trial.

Trial Group II - (25 Patients with Insomnia)

In order to investigate the collective impact of certain symptoms present in disorders, a group of 25 patients was formed to observe the effects of a placebo as a tranquilizer. The study included all 25 patients, and only one patient droppedout, leaving 24 patients who completed the trial.

Drug and Dose

One capsule of Mediwin's Sleep eeze capsule is given at bedtime after dinner.

OBJECTIVE CRITERIA

The evaluation was conducted using the Insomnia Severity Index, which was reviewed for statistical analysis. The assessment involved recording all the indications and symptoms as per the index, based on the patients' reported improvements. The Insomnia Severity Index comprises of seven questions[15]:

Insomnia Problem	None	Mild	Moderate	Severe	Very Severe
1. Difficulty falling asleep	0	1	2	3	4
2. Difficulty staying asleep	0	1	2	3	4
3. Problems waking up too early	0	1	2	3	4
	Very Satisfied	Satisfied	Moderately Satisfied	Dissatisfied	Very Dissatisfied
4. How satisfied/dissatisfied are you with your current sleep pattern?	0	1	2	3	4
	Not at all Noticeable	A Little	Somewhat	Much	Very Much Noticeable
5. How noticeable to others do you think your problem is in terms of impairingthe quality of your life?	0	1	2	3	4
	Not at allWorried	A Little	Somewhat	Much	Very Much Worried
6. How worried/distressed are you a boutyour current sleep problem?	0	1	2	3	4

	Not at all Interfering	A Little	Somewhat	Much	Very Much Interfering
7. To what extent do you consider your sleep problem to interfere with your daily functioning currently?	0	1	2	3	4

RESULTS

After being randomly assigned, 75 participants were divided into two groups with a 2:1 ratio between the experimental and control groups. One participant from each group and two volunteers dropped out of the study, leaving 73 subjects for per-protocol (PP) analysis. The Insomnia Severity Index was used to assess sleep quality, and statistical analysis was conducted using non-parametric hypothesis testing on the patients who followed the treatment plan. The results indicate that the use of Mediwin's Sleepeeze Capsules leads to a gradual improvement in sleep quality compared to the placebo group. The p-value decreased from 0.697 before treatment to 0.002 after 30 days, indicating that the test treatment was more effective than the placebo. The statistical results of the hypothesis testing are presented in the table below.

	Mediwin's Sleepeeze Capsule (n=49)		**Placebo (n=24)**		**Mann-Whitney 'U'test**	
	No.	**%**	**No.**	**%**	**2**	**p**
BT						
Fair	5	10.2%	4	16.6%	0.152	0.697
Poor	23	46.9%	11	45.8%		
VeryPoor	21	42.9%	9	37.6%		
AT						
Excellent	9	18%	0	0%	9.481	0.002
VeryGood	12	24%	0	0%		
Good	18	36%	3	12.5%		
Fair	5	10%	7	29.2%		
Poor	4	8%	9	37.5%		
VeryPoor	2	4%	5	20.8%		

DISCUSSION

Insomnia has become a global concern due to the changes in modern urban lifestyles and other socio-economic factors. Stress-related sleep problems, sleep apnea, and hormone imbalances are the primary reasons for this condition, according to a recent worldwide survey. Chronic insomnia can cause chronic fatigue, endocrine issues, lack of attention, energy depletion, and other symptoms before mild to severe illness-related conditions such as depression, high blood pressure, cognitive impairment, diabetes, cardiovascular diseases,

renal disease, and others occur. A reduction in the amount of sleep per night and an increase in daily stress are the main causes of insomnia. Examining the clinical history can aid in identifying the factors contributing to the disease condition. Buysse suggested behavioral therapy as insomnia is often challenging to diagnose and characterize clinically.[1]

This study conducted for a duration of 30 days demonstrates a significant improvement in sleep quality, as measured by the Insomnia Severity Index, due to the use of Mediwin's SLEEP EEZE Capsules. The statistical analysis of the results compared to the placebo group shows a significant impact of the capsules on the sleep quality of the patients.

Mediwin's SLEEP EEZE Capsules have a main ingredient of 5mg extract of Datura metal L. seeds, which makes up approximately 0.99% of the total composition. The seeds of Datura metal L. are naturally toxic, and pre-clinical toxicity evaluation is crucial to determine the safety of drugs for therapeutic purposes. In a toxicological study, oral administration of a single dose of Mediwin's SLEEP EEZE Capsules, containing 100 mg of Sarpgandha L. seeds, did not result in any significant changes in behavioral signs of toxicity, body weight gain, feed intake, hematological parameters, biochemistry profile, and gross necropsy.

Similarly, pre-clinical studies have been conducted for Khurasani Ajwain (Hyoscyamus niger) seed dry extract at a dosage of 125mg. Traditional Unani literature mentions the use of its seeds and leaves for various therapeutic purposes, with its tranquilizing property being an important therapeutic effect. Although the Unani texts recommend a dose of 500-750mg for Khurasani Ajwain (Hyoscyamus niger), we have used only 125mg of its seed extract in our formulation.[17]

CONCLUSION

Our examination focused on the effectiveness of Mediwin's SLEEP EEZE Capsules as a tranquilizer for insomnia-related conditions. Additionally, the anti-stress effect of Mediwin's SLEEP EEZE Capsules is useful in cases of stress-induced insomnia. To treat the underlying causes of sleep disturbances, medications that have vatahara and nidrajanya properties are selected, which help promote mental calmness while reducing symptoms.

An acute toxicity study conducted on Mediwin's SLEEP EEZE Capsules, containing a combination of ingredients like Sarpagandha root extract ()at dose of 100 mg of seed of Khurasani Ajwain (Hyoscyamus niger) (at a dose of 125mg), Jatamansi, Vacha, and Tagar,

showed that it did not cause any harmful effects or mortality in patients. This was determined through evaluations of various factors including behavioral signs of toxicity, body weight gain, feed intake, haematology parameters, biochemistry profile, and gross necropsy. Therefore, the medicine is considered safe and effective for treating insomnia in both male and female individuals aged between 20 to 60 years.

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