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A double-blind, randomised, placebo-controlled clinical study on the Efficacy and Safety of Jatamansi, Vacha, Tagar, Khurasani Ajwain, Dhatura Beej extract in the form of Mediwin's Sleep eeze Capsules by MEDIWIN Research & Healthcare in Insomnia.

***Dr. Ravi Raj, **Dr. Harish Kumar, ***Dr. Nitin Kumar, ****Dr Ajay Mittal**

* Associate Professor, Department of Ras Shastra & Bhaishajya Kalpana, SKG Ayurvedic College & Hospital, Kurukshetra, Haryana

** PG Scholar, Department of Panchkarma.

*** PG Scholar, Department of Panchkarma.

**** Professor, Department of Medicine, Adesh Medical College & Hospital, Mohri Shahbad (M)

Abstract:

A common sleep problem called insomnia can have a serious negative effect on both a person's physical and mental health. The majority of insomnia medications now on the market have negative side effects. As a result, herbal medicines may be useful in the treatment of insomnia.

This was a randomized, double-blind, placebo-controlled study conducted at Shri Krishna Govt. Ayurvedic College & Hospital, Kurukshetra, Haryana, India on Efficacy and safety of *Jatamansi*, *Vacha*, *Tagar*, *Khurasani Ajwain*, *Dhatura Beej* extract in the form of Mediwin's Sleep eeze Capsules by MEDIWIN Research & Healthcare in Insomnia

The effectiveness of Mediwin's Sleep eeze capsule in insomnia is assessed in the current study. In our OPD, we have administered Mediwin's Sleep eeze capsules.

Keywords: *Dhatura Beeja* (*Datura metal*), Insomnia, Jatamansi (*Nordostachys jatamansi*), Khurasani Ajwain (*Hyoscyamus niger*), Mediwin's Sleep eeze capsules, Tagar (*Valeriana wallichii*), Vacha (*Acorus calamus*).

INTRODUCTION:

The essential need of human health is replenishing the normal health decays, which is met by sleep cycles. Sleep is a necessary component of life that renews us on a physiological, biochemical, cellular, and molecular level as well. The average person sleeps for more than 30% of their life [1]. In addition to rejuvenation, sleep is closely linked to the proper operation of the central nervous system, blood pressure regulation, metabolism, catabolism, temperature regulation, memory consolidation, and several other vital physiological processes [2]. Insomnia, often known as sleeplessness, has recently become a widespread illness that affects a big portion of the world's population and negatively impacts their overall health and mental well-being. Clinical signs of insomnia include

difficulties falling asleep, staying asleep, or a mix of both, as well as impairment of everyday functions. Average sleep latency of more than 30 minutes, alertness after sleep onset of more than 30 minutes, and sleep efficiency of less than 85% of total sleep time of fewer than 6.5 hours are the clinical indicators of insomnia [3].

Although *Jatamansi* (*Nordostachys jatamansi*) has not been mentioned in the management of *Anidra* (insomnia) in historical Ayurvedic literature, Jatamansone (Valeranone), the active component of Jatamansi rhizome, has been described by Arora et al. in 1963 to have tranquillizing properties [4]. Its administration produces a behavioural impact that is comparable to benzodiazepines. The neurotransmitter gamma-aminobutyric acid (GABA) may have a stronger action at the GABA receptor when combined with jitamansone [5]. *Jatamansi* also has alkaloids, including Spirojatamol, Valerenic Acid, and Virolin, which have Tranquilizing, hypotensive, anti-inflammatory, anti-stress, CNS depressive, anti-anxiety, and analgesic properties [6,7]. Based on these actions, Jatamansi had a considerable impact on the primary insomnia symptoms.

Rhizome of *Vacha* (*Acorus calamus*) has been utilised in Ayurveda for its advantageous function as a brain tonic (*Medhya*) [8]. The Tranquilizer, antibacterial, antidiarrheal, neuroprotective, antioxidant, antihelminthic, anti-convulsant, anti-inflammatory, and analgesic properties of *Vacha* have also been found in recent investigations. Aromatic oil, which has been utilised for therapeutic purposes since ancient times and is commercially harvested, is found in the rhizomes of *Vacha* [9,10].

There are references to *Tagar* as a nootropic herb (*Medhya*) with sleep-inducing properties (*Nidrajanak*) [11]. Tranquilizing, hypnosis, antibacterial, antiviral, and anti-tumour action are among Tagar's claimed pharmacological effects [12]. As a result, Tagar confirmed the tranquillizing activity in patients with insomnia.

The herb known as Khurasani Ajwain has calming and painkilling properties. It revitalises body cells and offers the body energy. These herbs function similarly to the belladonna drug, but they don't excite the nervous system or make you feel lightheaded like belladonna does.

Datura is well-known around the world as a medicinal herb as well as a plant hallucinogen. Datura was used in ceremonial and therapeutic rites in prehistoric times by the indigenous people of the Indian subcontinent [13]. The majority of plants have one or more of these substances, including alkaloids, tannins, saponins, and cardiac glycosides, which are responsible for their medicinal properties. The phytochemical screening identified the presence of glycosides, alkaloids, flavonoids, phenols, steroids, saponins, and tannins. As competitive antagonists of muscarinic cholinergic receptors, atropine and scopolamine depress the central nervous system [14].

AIMS AND OBJECTIVES

- To determine the efficacy and safety of Mediwin’s Sleep eeze Capsules in patients with insomnia.
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MATERIAL AND METHODS

Mediwin’s Sleep eeze capsules were taken as a pre-clinical trial drug which is prepared with *Jatamansi*, *Vacha*, *Tagar*, *Khurasani Ajwain*, and *Dhatura Beej* as herbal extracts. Mediwin’s Sleep eeze capsules are composed of dry extracts of *Jatamansi* – 125mg, *Vacha – 125mg*, *Tagar – 125mg*, *Khurasani Ajwain – 125mg*, *Dhatura Beej* – 5mg, manufactured at Mediwin Research & Healthcare, 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	*Valeriana wallichii*	125 mg	Root (Dry Extract)	Bhav Prakash Nigahntu
Khurasani Ajwain	*Hyoscyamus niger*	125 mg	Seed (Dry Extract)	Bhav Prakash Nigahntu
Dhatura Beej	*Datura metal*	5 mg	Seed (Dry Extract)	Bhav Prakash Nigahntu

After taking Mediwin's Sleep eeze capsules to standardize the drug capsules of 505 mg were taken from a said batch number which was having a batch size of 50,000 capsules through analytical test reports were done in a well-intact and sealed packing. A proper dossier of the drug with special reference to Ayurvedic Pharmacopoeia of India was obtained from the manufacturer.

Patients were selected from OPD of Rasa Shastra Evum Bhaishajya Kalpana Department of Shri. Krishna Govt. Ayurvedic College Kurukshetra, 136118 Haryana India. Had selected the fulfilling criteria irrespective of age, sex, religion etc. Patients were selected between the age group of 20 to 60 years. A routine blood examination was carried out to rule out any other pathology & monitor the normal values of blood.

INCLUSION CRITERIA:

- All the patients suffering from insomnia were selected.
- All patients in the age group of 20-60 were selected.

EXCLUSION CRITERIA:

- Patients which were not willing to the trial.
- Patients below age 20 and above age 60.
- worked on the night or rotating shifts in the previous seven days before study initiation.
- Patients with complications of the disease.
- Alcohol and drug abuse.

DURATION OF THE TRIAL:

- The total duration of the trial was 30 days.

METHOD OF STUDY:

Received the patients' signed agreement to include them in the trial. The clinical trial included 75 registered participants. Randomization was done among the 75 enrolled participants in a 2:1 ratio. Thus, 25 patients were randomly assigned to the control group (placebo group), while 50 patients were taken into account for the experimental group (testing the Mediwin's Sleep eeze capsules). The materials for the experimental and control studies were packaged so that they looked the same for both the test and control products. Participants were not aware of their group assignments in this trial. Researchers and clinicians were blinded as well.

Trial Group I - (50 Patients with Insomnia)

To examine the impact of the form of Mediwin's Sleep eeze capsules as a tranquillizer on a few chosen signs and symptoms present in the disorder collectively, all 50 patients were included in this group. There was one dropout from the trial out of 50, and 49 patients completed the trial.

Trial Group II - (25 Patients with Insomnia)

To examine the combined effects of a few selected signs and symptoms present in disorders, all 25 patients were added to this group to observe how a Placebo as a tranquillizer affected them. This group had 1 dropout out of the 25, and 24 patients finished the trial.

Drug and Dose:
One capsule of Mediwin's Sleep eeze capsule is given at bedtime after dinner.

OBJECTIVE CRITERIA:
The assessment was done with Insomnia Severity Index and reviewed for statistical analysis, recording all the signs and symptoms according to the index based on improvements reported by the patients. The insomnia Severity Index has 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 impairing the quality of your life?	0	1	2	3	4
	Not at all Worried	A Little	Somewhat	Much	Very Much Worried
6. How worried/distressed are you about your 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:

Following randomization, the 75 participants were divided into two groups - an experimental and a control group in a 2:1 ratio. One from each group and two volunteers dropped out of the study. Utilizing the data from the remaining 73 subjects, per-protocol (PP) analysis was used to carry out the analysis. The Insomnia Severity Index was used to evaluate the quality of sleep. The table below presents the statistical results of the non-parametric hypothesis testing on the patients who adhered to the regimen. In contrast to the placebo group, those who use Mediwin's Sleep eeze capsules see a progressive increase in their sleep quality. As the p-value decreased throughout the study (before treatment, $p = 0.697$, and after 30 days, $p = 0.002$), it can be concluded that the test treatment performed better than the placebo.

	Mediwin's Sleep eeze 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%		
Very Poor	21	42.9%	9	37.6%		
AT						

Excellent	9	18%	0	0%	9.481	0.002
Very Good	12	24%	0	0%		
Good	18	36%	3	12.5%		
Fair	5	10%	7	29.2%		
Poor	4	8%	9	37.5%		
Very Poor	2	4%	5	20.8%		

DISCUSSION:

Due to the modern urban lifestyle and other socio-economic changes, insomnia has become a worldwide concern. According to a recent global survey, complaints of stress-related sleeplessness, sleep apnea, and hormone imbalance are the main causes of this condition. Chronic insomnia frequently results in chronic fatigue, endocrinological problems, energy depletion, lack of attention, and other symptoms before illness related to mild to severe disease conditions, such as high blood pressure, depression, renal disease, cognitive impairment, diabetes, cardiovascular diseases, and others, develop. The primary causes of insomnia are a decrease in the amount of sleep each night and an increase in daily stress. An examination of the clinical history can help in determining the causes contributing to the disease condition. Buysse also suggested behavioural treatment because insomnia is frequently clinically difficult to recognise and characterise [1].

The current 30-day study documents the influence of the sleep quality's appreciable improvement as measured by the Insomnia Severity Index. The results against the placebo group were determined to be statistically significant, pointing to a considerable impact of Mediwin's Sleep eeze capsules on patients' sleep quality.

Mediwin's Sleep eeze capsules contain 5mg extract of *Datura metal* L. seeds as the main ingredient which is about 0.99 % of the complete composition. The seeds of *Datura metal* L. are considered naturally toxic. Pre-clinical toxicity evaluation is an important step to determine the safety of drugs; helps in the determination of safe doses to use in humans and animals for therapeutic purposes. Oral administration of a single dose of Mediwin's Sleep eeze capsules at a dose of one capsule at bedtime did not produce any toxicologically significant changes concerning behavioural signs of toxicity, body weight gain, feed intake, haematology parameters, biochemistry profile, and gross necropsy. No untoward effect was noted and Mediwin's Sleep eeze capsules were found to be safe in a dose of 5mg as done in a toxicological study where it was found to be safe in the acute toxicity study tested at 2000 mg/kg. So, the LD50 of Mediwin's Sleep eeze capsule as per OECD guidelines-425 is greater than 2000 mg/kg. [16]

Second, the same pre-clinical studies have been done in the case of *Khurasani Ajwain* (*Hyoscyamus niger*) seed Dry extract, that is in a dose of 125 mg. As per Unani classical literature, seeds and leaves are used for various therapeutic purposes in which tranquillizing property is one of the important therapeutic effects. In Unani classical text, the dose of *Khurasani Ajwain* (*Hyoscyamus Niger*) is mentioned as 500 –750 mg but we have used only 125 mg of dry extract of seed. Constituting the formulation with 125mg of extract of seed of *Khurasani Ajwain* (*Hyoscyamus Niger*)[17].

CONCLUSION:

We have looked at how well Mediwin's Sleep eeze capsules work as a Tranquilizing for insomnia-like conditions. The antistress effect of Mediwin's Sleep eeze capsule is also beneficial in stress-induced Insomnia. To correct the pathogenesis of Nidra Nasha, the medications are chosen, which are vatahara and nidrajanya in nature and encourage mental serenity, assisted by minimising indications and symptoms.

At doses of 5mg of *Datura metal* L. and 125mg of extract of seed of *Khurasani Ajwain* (*Hyoscyamus niger)*, together with other ingredients like *Jatamansi*, *Vacha* and *Tagar*, an acute toxicity study with Mediwin's Sleep eeze capsules revealed no toxic signs and symptoms or mortality in any of the patient, concerning behavioural signs of toxicity, body weight gain, feed intake, haematology parameters, biochemistry profile, and gross necropsy. It is an effective and safe medicine for insomnia for both males and females aged 20 to 60 years.

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