

INSOMNOLENCE: A REVIEW ON THE SLEEP DISORDER

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ABSTRACT

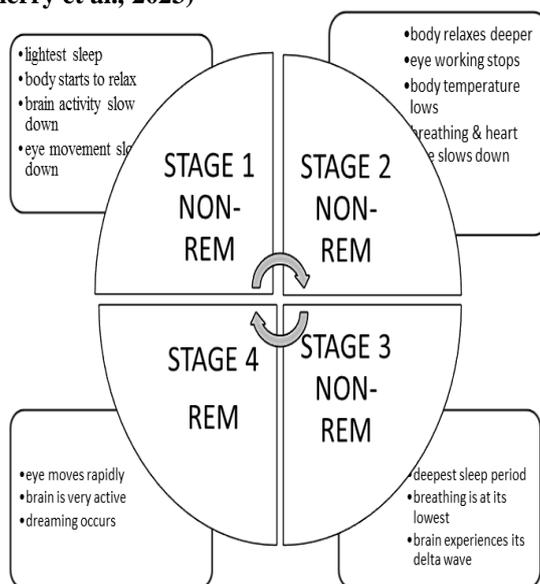
Sleep is the essential process for the biological activity of the human. The ‘GOOD’ sleep at night will make the day with full of energy and refreshment. Sleep will regulate the physiological and psychological function of the mind and body. There are many mechanisms involved to regulate the sleep. Nevertheless, many disorders are occur in the sleep and wake cycle which affect the homeostasis of the living organism. The major disorder of sleep is ‘insomnia’. Insomnia is both the disease and disorder. It literally means ‘lack of sleep at bedtime’. Types of insomnia are of primary and secondary insomnia. There are about 33% to 50% of adult population are affected by insomniac condition. The BZD receptor agonist benzodiazepine (BZD) agonist melatonin is sometimes prescribed to patients suffering from insomnia along with orexin receptor antagonists like doxepin to treat insomnia. When patients take orexin receptor antagonists instead of BZD receptor agonists, they may experience somnolence, fatigue, and drier mouths. While pharmacotherapy and psychological interventions remain important, CAM has gained popularity in the last two decades. Several gene-related studies have been conducted on sleep disorders.

**INTRODUCTION
SLEEP**

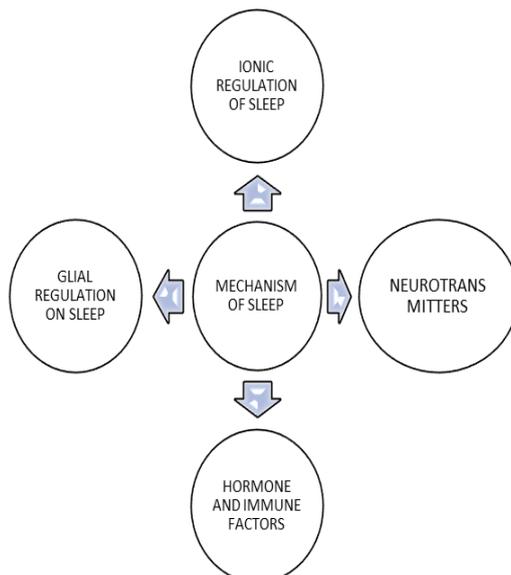
Animals that live in higher environments sleep regularly. To function optimally during the day, it is important to get a good night's sleep. (D Bhattacharya et al.,). Sleep

affects the brain, central nervous system, and physiological processes, such as metabolism, catabolism, temperature, memory, learning, and memory storage. (MH kyger et al.,).

PHASES OF SLEEP (kendra cherry et al., 2023)



MECHANISM OF SLEEP



INSOMNIA – A SLEEP DISORDER

Insomnia factually means “lack of sleep at bedtime” (latin: *insomnium*). There are several causes of insomnia, including symptoms and conditions. Diabetes, AIDS, cancer, and chronic insomnia are among the most prevalent diseases. (Jones BE *et al.*, 2005) Insomnia

disorder is characterized by the individual could experience of struggling to initiate, maintain, or obtain restorative sleep, despite having sufficient opportunity for rest which resulted in daytime dysfunction and insomniac condition recognized as a significant public health concern. (Schutte-Rodin S *et al.*, 2008).

THE MOLECULAR MECHANISM

Neurotransmitters involved in sleep/wake cycle



GENETICAL MECHANISM OF INSOMNIA

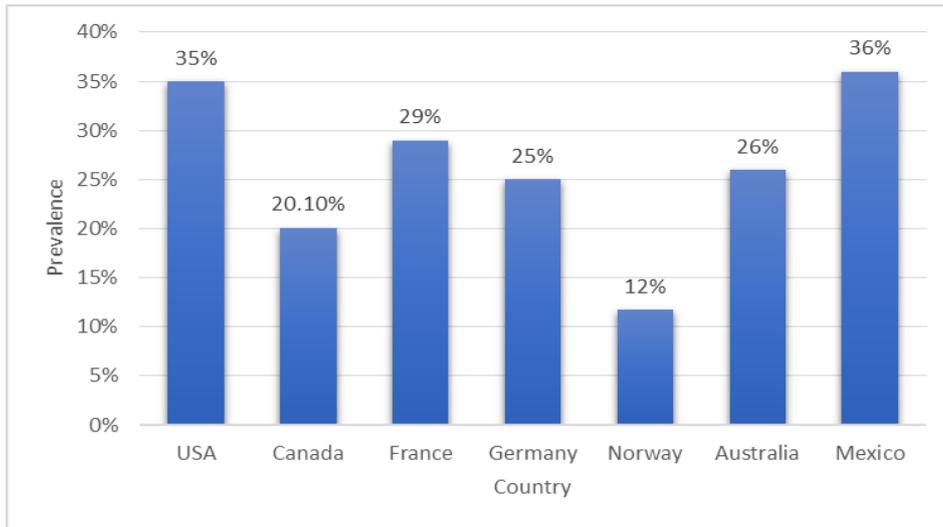
(Mikyung kim *et al.*, 2017)

The circadian rhythm is thought to be a biological process that applies to animals, plants, fungi, and cyanobacteria (Albrecht, 2012). These rhythms are affected by food, light, temperature, and genes like *Per1*, *Per2*, *Cry1*, and *Cry2*. *Per2* (*Per2*) is an extension of *Period1*, which also contains *Per3*, in addition to the suprachiasmatic nucleus (SCN). Peripheral and central nervous systems play an important role in its expression. In contrast to *Per1*, *Per2* appears to have a greater role in regulating circadian rhythms (Zheng *et al.*, 1999;

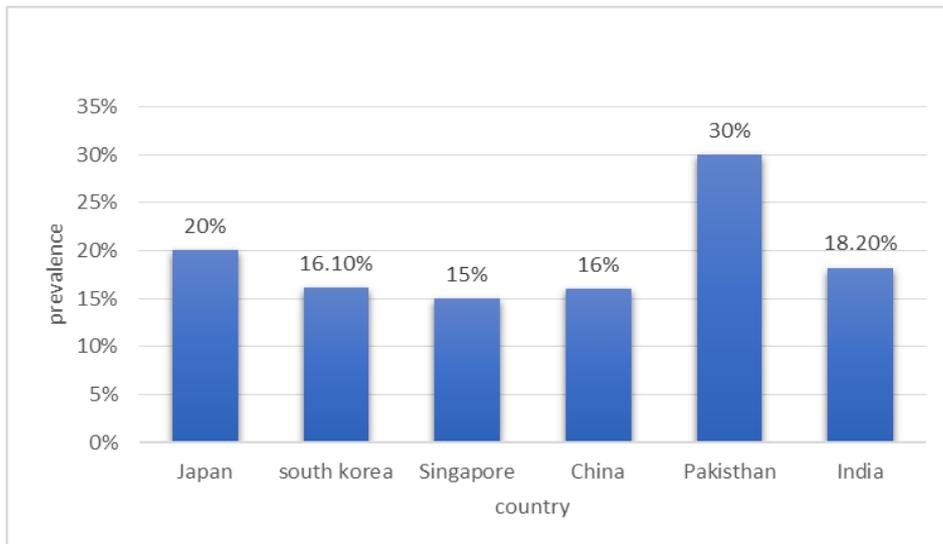
Ripperger and Albrecht, 2012). *Per2* also interacts with neurotransmitters to modulate CNS neurobiological processes. The expression levels of *Per2* and the activity of neurotransmitters can affect drug response and emotional behavior.

EPIDEMIOLOGY OF INSOMNIA- INTERNATIONAL STUDIES

Distribution of the Prevalence of Insomnia in various countries

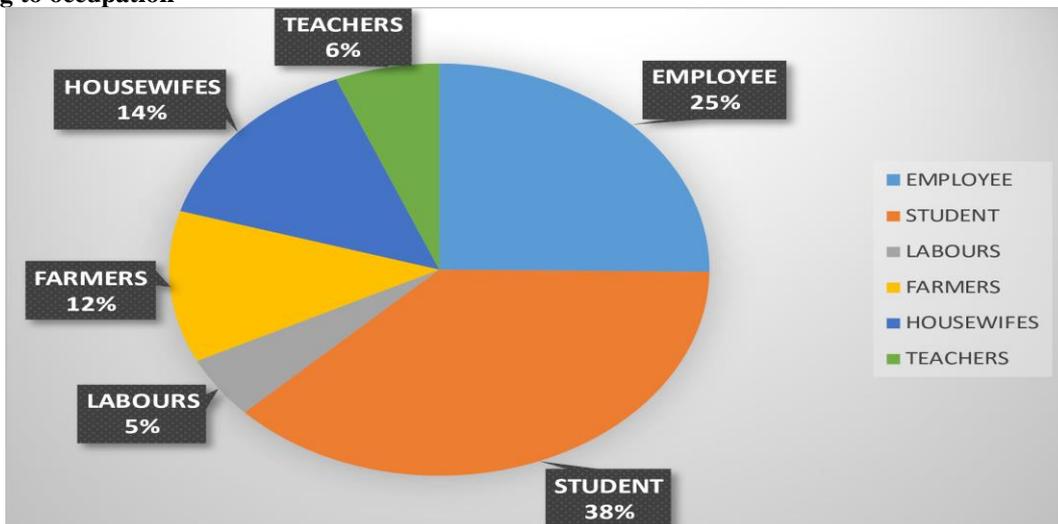


Distribution of the Prevalence of Insomnia in Asian Continent



ASSOCIATION OF VARIOUS FACTORS WITH INSOMNIA (roma gai et al.,2022)

According to occupation



According to psychartic disorder

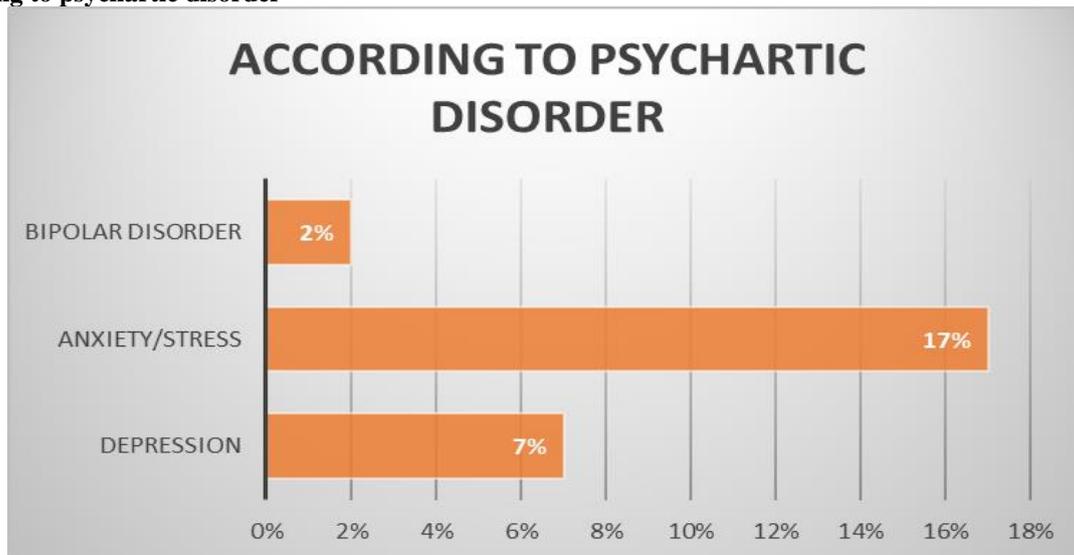


Table 1: Common Comorbid Medical Disorders, Conditions, And Symptoms For Insomnolence (Sharon Schutte-Rodin *et al.*, 2008).

System	Example of disorder, condition and symptoms
Neurological	Stroke, Dementia, Parkinson disease, seizure disorders, Headache, chronic pain disorder
Cardiovascular	Angina, Congestive Heart Failure. Dyspea, Dysrhythmias
Pulmonary	COPD, emphysema, asthma, laryngospasm Reflux
Digestive	Reflux, peptic ulcer disease, cholelithiasis, colitis, irritable bowel syndrome
Genitourinary	Incontinence, benign prostatic hypertrophy, nocturia, enuresis, interstitial cystitis
Endocrine	Hypothyroidism, hyperthyroidism, diabetes mellitus
Musculoskeletal	Rheumatoid arthritis, osteoarthritis, fibromyalgia, Sjögren syndrome, kyphosis
Reproductive	Pregnancy, menopause, menstrual cycle variations
Sleep disorder	Obstructive sleep apnea, central sleep apnea, restless legs syndrome, periodic limb movement disorder, circadian rhythm sleep disorders, parasomnias
Other	Allergies, rhinitis, sinusitis, bruxism, alcohol and other substance use/dependence/ withdrawal

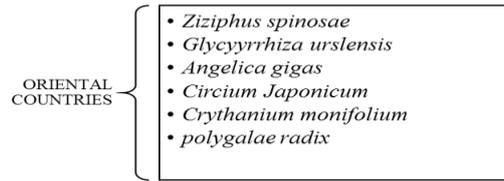
THERAPY TREATED FOR INSOMNIA IN VARIOUS COUNTRIES:

In India, the decades before many herbs are used to treat insomnia not only in India but also in oriental countries like China, Japan, Korea are also used herbs to treat

insomnia. Herbal medicine, involving the use of plants or plant-derived substances for therapeutic aims, has been employed by herbalists and indigenous groups for addressing various sleep disorders over a Extended period.

- INDIA {
- *Valerian officinalis*
 - *Marticuria reticutita*
 - *Melissa officinalis*
 - *Piper methysticum*
 - *Lavendula augustifolia*
 - *Withania somnifera*
 - *Panax ginseng*
 - *Mimosa pudica*

Ref: (Fazze Feizi *et al.*, 2019)



Ref: (hong et al., 2018)

MODERN THERAPY

The following medication are categorised according to their mechanism of action to treat sleep disorders: (Schenck C. H., 2007)

First line drugs for insomnia

- Benzodiazepine receptor agonists- - Alprazolam, triazolam, estazolam, temazepam
- Nonbenzodiazepines 'z drugs'- zolpidem, zaleplon, and eszopiclone.
- Melatonin agonist- ramelteon
- Barbiturates- phenobarbital, mephobarbital, and secobarbital

Second line drugs for insomnia

- Tricyclic antidepressant doxepin.
- Orexin receptor antagonists-suvorexant.
- Antidepressants- trazodone, mirtazapine,
- Atypical antipsychotics- quetiapine, olanzapine, and risperidone.
- Antihistamines- diphenhydramine and doxylamine.

Intricacies of Modern Pharmacotherapy

Sleep patterns can be restored by a variety of chemical medications. A benzodiazepine receptor agonist (BZD), a melatonin receptor antagonist, and a selective histamine receptor antagonist are the most commonly prescribed insomnia medications. A person who is treated with Benzodiazepine (BZD) receptor agonists may experience sleepiness, fatigue, and dry mouth due to orexin antagonists.

Even though antidepressants are potentially useful, they can cause adverse effects, such as suicidal ideation, when

taken off-label. A combination of mirtazapine and alpha-1-adrenergic antagonists, such as prazosin, is commonly prescribed for sleep disturbances, especially in posttraumatic stress disorder (PTSD). Histamine H1 and serotonin 5HT2 are antagonistic to alpha-1-adrenergic receptors. Antihypertensive properties are also provided by prazosin. Aside from insomnia, antipsychotics can be used off-label to treat grogginess, dizziness, and weight gain. Anticonvulsant drugs like gabapentin, pregabalin, and tiagabine, though less commonly used, are also employed for insomnia management. (Schweitzer PK et al., 2017) However, these interventions are associated with adverse effects, potentially leading to low patient compliance and inadequately treated insomnia.

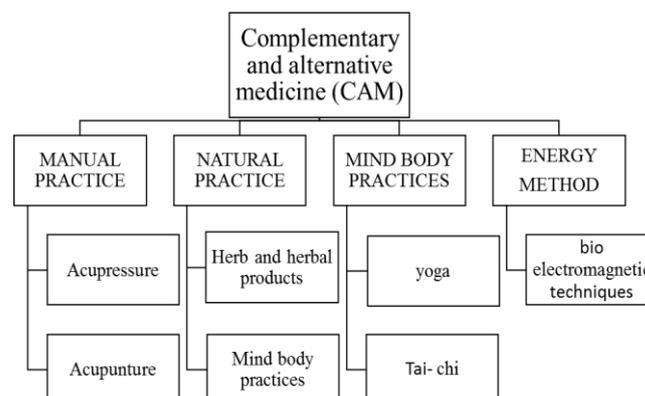
Insomnia presents a significant global prevalence, posing a burden on healthcare systems. Pharmacological treatments for insomnia often come with notable side effects. Hence, the pursuit of safe and effective alternatives derived from natural plant sources is a worthwhile endeavour.

The Influence Of Complementary And Alternative Medicine On Insomnia (kanika verma et al., 2022)

There has been an increase in the use of complementary and alternative therapies since the late 1980s, even though conventional treatments for insomnia still include pharmacotherapies and psychological interventions.

Complementary and alternative medicine Studies on complementary and alternative medicine (CAM) fall under this category "manual practices," "natural practices," and "mind-body practices."

Flow chart 4: CAM on insomnia



According to the survey, 17.4% of adults suffer from insomnia or poor sleep regularly. As for complementary or alternative medicines, 4.5% use them to treat insomnia. Among those individuals, 56% considered CAM crucial for their overall health and well-being, while 72% noted significant improvements in insomnia disorders due to CAM. Younger individuals and those with higher levels of education tend to place trust in CAM for alleviating insomnia symptoms. (Jadad *et al.*, 1996).

HERBAL REMEDY

Currently, conventional medications for insomnia often result in daytime drowsiness and disruptions in cognitive

and conscious activities. Additionally, many patients develop tolerance to specific drugs, resulting in increased reliance on sleeping pills and anxiolytic agents like alprazolam. (Sateia *MJ et al.*, 2017) Therefore, sleep disorders require additional approaches to treatment or management. A growing number of people around the world are turning to natural products, such as herbs. As international organizations such as the World Health Organization develop and enhance these natural products, the demand for them will continue to grow. (Akerele *O et al.*, 1996).

Table 2: Medicinal Plants And Its Phytoconstituent Used In Insomnia (Faezeh Feizi *et al.*, 2019).

SCIENTIFIC NAME	CONSTITUENT	BENEFITS & MECHANISM
Matricaria recutita	Flavonoid compound	Modulate GABA receptor
Melissa officinalis	Rosmaric acid, pentacyclic triterpenoids, ursolic acid, oleonic acid	Anxiety and association symptoms. Inhibition of GABA catabolism
Valeriana officinalis	Valerianic acid	Psychometric performance
Xylaria Nigaripes	5 – methyl mellein	Increasing GABA
Sinomenium acutum	Sinomenium (alkaloid)	Hypnotic effect via GABA
Angelica gigas	Decurisinol	Psychiatric & insomnia Through GABA
Euphoria longer	Gallic acid	Decrease GABA transaminase
Camelia sinensis	Epigallocatechin-o-3-galate	GABA
Circium japonicum	Flavonoid, apigenin	cl ⁻ channel complexation

CONCLUSION

We assessed sleeplessness as one of the most significant problems affecting the human species. It is linked to a wide range of disorders. Therefore, it is vital to treat the condition. Nowadays, Modern therapy has many negative effects, leading us to lose hope in allopathic treatment. We went to complementary and alternative medicine (CAM) to address sleeplessness. Natural techniques have higher efficacies in (CAM). Natural treatment includes herbs and herbal remedies. Many herbs are used to treat neurological disorders, including insomnia. To ensure the safety and effectiveness of herbal products, they must be tested. As a result, people can confidently employ plants as a cure.

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