

Therapeutic Potential of Adaptogenic Herbs in the Management of Insomnia : Phytoconstituents, Mechanisms of Action

Apeksha Bhausahab Bhagwat and Miss Kalyani Bhor

Student, Samarth Institute of Pharmacy, Belhe, Pune, Maharashtra

Professor, Samarth Institute of Pharmacy, Belhe, Pune, Maharashtra

bhagwatapeksha9@gmail.com

Abstract: *Insomnia is a prevalent sleep disorder characterized by difficulty in sleep initiation, maintenance, or quality. Conventional pharmacological treatments, including benzodiazepines and sedative-hypnotics, are associated with adverse effects such as tolerance, dependence, and cognitive impairment. Adaptogenic herbs have emerged as promising alternatives due to their ability to modulate stress response systems and improve sleep quality. About 30% of people in general suffer from chronic insomnia, which is extremely common. A variety of decreased daytime functions in a variety of emotional, social, and physical domains are linked to insomnia, which also affects cognitive and physical functioning. Persistently disturbed sleepers are more likely to be involved in accidents, have greater absenteeism rates, perform worse at work, have lower quality of life, and need health care more frequently than those who sleep well. Comorbid medical and psychological problems, female gender, and advanced age are some of the risk factors linked to a higher incidence of chronic insomnia. About 40% of persons who suffer from insomnia also have a diagnosable mental illness, most commonly depression. Anxiety or depression are examples of comorbid psychiatric disorders that can both result from and increase the likelihood of sleep disturbances. Finding alternative functional foods made from natural items that are good for treating insomnia and have few side effects is therefore essential. Natural plant extracts like Valeriana officinalis L. (valerian), Humulus lupulus L. (hop), Ziziphus jujuba Mill. (jujube), Withania somnifera L. Dunal (Ashwagandha), and Matricaria chamomilla L. (chamomile) have been actively studied for their potential to improve sleep as supplements and alternatives to sleep medications. Adaptogens such as Withania somnifera, Rhodiola rosea, and Ocimum sanctum exert effects through regulation of the hypothalamic-pituitary-adrenal (HPA) axis, neurotransmitters, and antioxidant pathways. Phytoconstituents including alkaloids, flavonoids, saponins, and withanolides contribute to their pharmacological activities. This review discusses the phytochemistry, mechanisms, pharmacological actions, extraction techniques, and screening methods of adaptogenic herbs in insomnia management.*

Keywords: Insomnia, Adaptogenic, Flavonoids, Sleep, phytoconstituents, Valeriana Officinalis, Matricaria Chamomilla, Passiflora Incarnata, Withania Somnifera.

I. INTRODUCTION

Insomnia affects millions worldwide and is associated with neurological and metabolic disorders. It is characterized by reduced sleep quality, delayed sleep onset, and frequent awakenings. Insomnia is linked to anxiety, depression, hypertension, and neurodegenerative diseases. Modern pharmacotherapy includes benzodiazepines, melatonin agonists, and antihistamines, but long-term use leads to dependency and side effects. Hence, herbal medicine offers a safer alternative. Adaptogens are natural substances that enhance the body's resistance to stress and maintain homeostasis.



Their role in insomnia is mainly through stress reduction and neuroendocrine modulation. People with insomnia often feel dissatisfied with their sleep and experience daytime symptoms such as fatigue, irritability, and poor concentration. Clinically, insomnia is not just about reduced sleep duration—it also includes poor sleep quality and its negative impact on daily functioning. According to research, insomnia can be acute (short-term) or chronic (long-term), with chronic insomnia lasting for months or even years.

Prevalance of Insomnia –

The parameters used to identify insomnia and, more crucially, the population under study determine estimates of its prevalence. Population-based studies have led to a general consensus that about 30% of a range of adult samples selected from various nations report one or more of the symptoms of insomnia, including difficulty falling asleep, difficulty staying asleep, waking up too early, and in certain situations, nonrestorative or poor quality sleep. According to findings from the June 2005 NIH State-of-the-Science Conference, the prevalence of insomnia is about 10% when a diagnostic criterion that takes into account reported daytime impairment or discomfort as a byproduct of the symptoms is added.

Lastly, current prevalence estimates of roughly 6% are obtained by applying stricter diagnostic criteria, such as the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV), which includes the additional requirements that insomnia symptoms persist for at least one month and do not exclusively occur in the presence of another sleep disorder, mental disorder, or the direct physiological effects of a substance or medical condition. In June 2005, the State-of-the-Science Conference reported on a number of established risk factors for insomnia. The most obvious demographic risk variables are age and gender, which are more common in women and older persons.

Consequences of Insomnia

Because insomnia is persistent, it is linked to significant reductions in a person's quality of life. The 36-item Short Form Health Survey of the Medical Outcomes Study (SF-36) evaluates eight domains: physical functioning; role limitations due to physical health problems (role physical); bodily pain; general health perceptions; vitality; social functioning; role limitations due to emotional health problems (role emotional); and mental health. In multiple studies, insomniacs reported lower quality of life on almost all of these dimensions.^{16–18} In one study, the SF-36 scores of patients with mild and severe insomnia were compared to those of patients with congestive heart failure (CHF) or depression.¹⁹ In terms of reported pain, emotional consequences, and mental health effects, patients with severe sleeplessness had quantitatively higher loss of function than those with CHF.

According to research, the biggest health concern associated with insomnia during the day is an increased chance of accidents. The risk of an accident is 2.5–4.5 times higher in insomniacs than in controls. An industrial accident occurred in the previous 12 months for 8% of insomniacs and 1% of non-insomniacs in a sample of 8,625 community respondents in France. Due to work-related issues, insomniacs also have lower productivity at work (i.e., greater rates of absenteeism, less concentration, and difficulties fulfilling chores). According to research by Kuppermann and colleagues, people who reported having a current sleep issue were more likely than good sleepers to perform worse at work and to have missed work in the previous month owing to health issues.

Pathophysiology of Insomnia –

It is believed that insomnia is a hyperarousal disorder that lasts all day. Hypervigilance during the day and trouble falling and staying asleep at night are two possible symptoms of this hyperarousal. Both cognitive and physiological explanations of insomnia currently account for this arousal. According to the cognitive model, concern and daydreaming about life's problems interfere with sleep, leading to acute periods of insomnia, particularly when it comes to falling asleep and waking up. When a person starts having trouble sleeping, their anxieties and ruminations change from life events to concerns about sleep itself and the effects of sleep deprivation during the day. If a perceived sleep deficit or a hazard related to sleep is identified, this adversely toned cognitive activity is further stimulated.



Another model of the genesis of insomnia, which runs concurrently with the cognitive models, suggests that physiological or neurophysiological processes are the main cause of hyperarousal. Heart rate variability, neuroendocrine tests, whole body metabolic rate assessments, and functional neuroimaging have all been used to assess physiological arousal. Oxygen consumption can be used to gauge the metabolic rate of the entire body. In recent research, people with insomnia were compared to healthy sleepers. Compared to the healthy controls, the insomnia patients showed noticeably greater metabolic rates (measured at intervals during the 24-hour day). Heart rate variability, which is influenced by both sympathetic and parasympathetic nervous system activity, may serve as a gauge of arousal. A 36-hour study revealed that, in comparison to healthy, typical sleepers, insomnia patients had higher average heart rates and lower variability during the whole sleep cycle.

As evidenced by the long-term activation of the stress response system, the neuroendocrine system may also show signs of arousal. Poor sleepers have increased amounts of 24-hour urine free cortisol excretion, according to several studies. Urine catecholamines have been linked to stage 1 sleep % and wake time following sleep start, while urine free cortisol levels have also been positively connected with overall wake time. Cortisol and adrenocorticotropic hormone (ACTH) plasma levels have been measured in both healthy, normal sleepers and those with insomnia. Primary insomniacs seem to have larger amounts of these chemicals in their plasma, with the most notable variations observed in the evening and the first half of the night, despite the somewhat conflicting evidence.

Cortisol and ACTH levels in the urine and plasma indicate that the pathophysiology of chronic insomnia is linked to the HPA axis. Lastly, patients with insomnia have had their cerebral glucose metabolism, an indirect indicator of entire brain metabolism, evaluated using positron emission tomography (PET). Patients with insomnia showed higher brain glucose metabolism throughout waking and non-rapid eye movement (REM) sleep stages than did healthy controls. Additionally, in wake-promoting brain areas, the insomnia patients showed less decline in relative metabolism from waking to non-REM sleep. These results point to the involvement of interacting brain networks, such as a general arousal system, an emotion-regulating system, and a cognitive system, in the difficulty to fall asleep.

Types of Insomnia

Insomnia can be classified into the different types:

Acute Insomnia

- Short-term condition
- Often caused by stress, travel, or emotional disturbances
- Usually resolves without treatment

Chronic Insomnia

- Lasts for at least 3 months
- Occurs at least 3 nights per week
- Often linked to underlying medical or psychological conditions

Onset Insomnia

- Difficulty falling asleep

Maintenance Insomnia

- Difficulty staying asleep or waking up frequently

Early Morning Awakening

- Waking up too early and not being able to go back to sleep

Causes of Insomnia

Insomnia is caused by a combination of biological, psychological, and environmental factors. The primary issue could be insomnia, or it could be connected to other illnesses.

- **Stress**, life events, or sleep-disturbing habits are typically the cause of chronic insomnia. While treating the underlying cause of your insomnia may help you stop it, it can occasionally persist for years. Long-term



insomnia is frequently caused by: tension. It can be difficult to fall asleep at night if you are preoccupied with issues related to your job, education, health, finances, or family. Insomnia can also result from stressful life events like divorce, losing a job, or the death or illness of a loved one.

- **schedule for work or travel.** Circadian rhythms, your body's "internal clock," regulate your body temperature, metabolism, and sleep-wake cycle. Sleeplessness may result from upsetting these cycles
- **Bad sleeping practices.** Going to bed and waking up at various times every day, napping, being overly active before bed, and having an uncomfortable sleeping space are all examples of poor sleep patterns. Working, eating, or watching TV in bed are additional bad sleep habits. Your sleep cycle might be disturbed by using computers or smartphones, playing video games, and watching TV right before bed.
- **Overindulging in food late at night-** It's acceptable to have a small snack before going to bed. However, consuming too much can make you uncomfortable when you're lying down. Heartburn also affects a lot of people. This occurs when the tube that transports food from your mouth to your stomach becomes backed up with stomach acid. The esophagus is the name of this tube. Heartburn could keep you up at night.
- **mental illnesses-** Your sleep may be disturbed by anxiety disorders like post-traumatic stress disorder. Depression may be indicated by waking up too early. Other mental health issues frequently coexist with insomnia.
- **Medications.** Numerous prescription medications, including some antidepressants and medications for blood pressure or asthma, can disrupt sleep.
- **Caffeine and other stimulants-** included in many over-the-counter medications, including some pain relievers, cold and allergy remedies, and weight-loss drugs, might interfere with sleep. Chronic pain, cancer, diabetes, heart illness, asthma, gastroesophageal reflux disease (GERD), overactive thyroid, Parkinson's disease, and Alzheimer's disease are a few disorders that are associated with insomnia.
- **Problems associated with sleep-** Your sleep is disturbed by sleep apnea, which causes you to occasionally cease breathing during the night. When attempting to fall asleep, people with restless legs syndrome have a strong, uncomfortable urge to move their legs. You might not be able to fall or return to sleep as a result of this.
- **Alcohol, nicotine, and caffeine-** Stimulants include tea, coffee, cola, and other beverages that contain caffeine. You can avoid falling asleep at night if you drink them in the late afternoon or evening. Another stimulant that might interfere with sleep is nicotine, which is found in tobacco products. While alcohol can help you fall asleep, it typically causes you to wake up in the middle of the night and prevents deeper phases of sleep

Symptoms of Insomnia

Symptoms of insomnia could include: having trouble going to sleep at night. awakening at night. getting up too early. feeling drowsy or exhausted during the day. feeling irritable, unhappy, or nervous. having trouble remembering, concentrating, or paying attention. increasing the number of mistakes or mishaps. worrying about sleep all the time. When to consult a physician See your doctor or another primary care provider if your insomnia makes it difficult for you to perform everyday tasks. Your physician will look for the source of your sleep issue and assist in treating it. Your doctor may recommend visiting a sleep center for additional testing if it is suspected that you may have a sleep condition.

Insomnia And Aging

As people age, insomnia becomes more prevalent. As you age, you might:

- **Modify the way you sleep-** As you get older, your sleep becomes less restful, making you more susceptible to being awakened by noise or other disturbances in your environment. Your internal clock frequently advances in time as you age, causing you to wake up earlier in the morning and feel exhausted earlier in the evening. However, the amount of sleep that older individuals require is usually equal to that of younger people.



- **Modify how active you are-** You might engage in less social or physical activity. A restful night's sleep might be disturbed by inactivity. Additionally, you may be more prone to take a regular sleep if you are less active. At night, napping can interfere with sleep.
- **Your health has changed.** Sleep disturbances can be caused by persistent discomfort from ailments like arthritis or back issues, as well as by sadness or worry. Sleep disturbances can result from conditions like prostate or bladder issues that increase the likelihood of needing to urinate at night. As people age, sleep apnea and restless legs syndrome become increasingly prevalent.
- **Take extra medications-** Prescription medication use is generally higher among older adults than younger adults. This increases the risk of medication-related sleeplessness.

Risk Factors

Almost everyone experiences insomnia from time to time. However, you are more likely to experience insomnia if:

- **You're a female.** Hormonal changes that occur during menopause and the menstrual cycle may be a factor. Hot flashes and nocturnal sweats sometimes interfere with sleep during menopause. Pregnancy is also a common time for insomnia.
- **You're older than sixty.** As you age, you are more likely to experience insomnia due to changes in your health and sleep patterns.
- **You suffer from a physical or mental illness.**-Sleep disturbances can result from a variety of problems that impact your physical or mental well-being.
- **You're experiencing a lot of stress-** Short-term sleeplessness can be brought on by stress. Long-term sleeplessness may result from significant or persistent stress.
- **You don't follow a set timetable-** Traveling or switching shifts at work, for instance, can throw off your sleep-wake cycle

Effects of Insomnia on Health

Insomnia is not just a sleep problem—it affects the entire body and mind.

a) Physical Effects

- Weak immune system
- Increased risk of heart disease
- Hypertension
- Obesity and diabetes

b) Mental Effects

- Depression and anxiety
- Memory problems
- Reduced cognitive performance

c) Social Effects

- Poor productivity
- Reduced quality of life
- Increased risk of accidents

Research shows insomnia may contribute to serious conditions such as cardiovascular diseases and metabolic disorders.

6. Diagnosis of Insomnia

- Doctors diagnose insomnia based on:
- Medical history
- Sleep patterns
- Sleep diaries
- Physical examination



Sleep hygiene

Developing healthy sleeping habits is part of excellent sleep hygiene. The first step in treating insomnia caused by poor sleep hygiene is to modify any lifestyle variables that may contribute to insomnia and learn how to adopt healthy sleep habits. When treating insomnia, sleep hygiene is frequently combined with other strategies.

The following are examples of healthy sleep habits:

- **Maintain consistent sleep schedules.** - Aim to avoid naps during the day and to go to bed and wake up at roughly the same time every day. Aim for no more than eight and a half hours in bed. Longer bedtimes can result in restless nights.
- **Ensure the comfort of your bedroom** - It should be dark, peaceful, and neither too hot nor too cold. To avoid constantly checking the time, think about taking the clocks out of your bedroom. Keep screens out of your bedroom and refrain from using them for an hour before bed.
- **Eliminate nicotine** - cut back on or give up alcohol, and restrict caffeine to the mornings. Regularly work out, but avoid doing so at night.

If you're having trouble falling asleep, move to a different room and do something peaceful, like reading, until you're exhausted. Then, try again. If you are having trouble falling asleep, try to spend less time in bed. Before going to bed, engage in a soothing activity. If something is bothering you, try to deal with it earlier in the day instead of right before bed.

Medicine

Prescription medications

Your doctor could recommend medication if you suffer persistent sleeplessness and no other therapies have worked. Because they don't address the root cause of insomnia, sleeping medications are less helpful than cognitive behavioral therapy (CBT). They can be helpful for a brief while, but if you take them too frequently, their effectiveness decreases. Addiction and adverse effects can also result from long-term medication use. For insomnia, your doctor might recommend a medication (such as temazepam, zopiclone, or zolpidem). They will advise you to take medications for a brief period of time and at the lowest possible dosage. Particularly in older adults, some medications may have adverse consequences, such as an increased risk of falling. Other medications, such as lemborexant and suvorexant, may help people fall or remain asleep, but they are not appropriate for everyone; your doctor will prescribe these if they are a good fit for you. Although many additional over-the-counter and prescription medications are occasionally used to promote sleep, they are not advised, particularly for older persons. These consist of antipsychotics, some antihistamines, and antidepressants. They frequently don't work effectively for insomnia and can have major negative effects.

Certain medications may have the following side effects-

wandering around at night, agitation, excessive sleepiness during the day, cognitive impairment, balance issues, lightheadedness, and allergic responses

Concept of Adaptogen

Adaptogens comprise a category of herbal medicinal and nutritional products promoting adaptability, resilience, and survival of living organisms in stress. The aim of this review was to summarize the growing knowledge about common adaptogenic plants used in various traditional medical systems (TMS) and conventional medicine and to provide a modern rationale for their use in the treatment of stress-induced and aging-related disorders. Adaptogens have pharmacologically pleiotropic effects on the neuroendocrine-immune system, which explain their traditional use for the treatment of a wide range of conditions. They exhibit a biphasic dose-effect response: at low doses they function as mild stress-mimetics, which activate the adaptive stress-response signaling pathways to cope with severe stress. That is in line with their traditional use for preventing premature aging and to maintain good health and vitality. However, the potential of adaptogens remains poorly explored. Treatment of stress and aging-related diseases require novel



approaches. Some combinations of adaptogenic plants provide unique effects due to their synergistic interactions in organisms not obtainable by any ingredient independently. Further progress in this field needs to focus on discovering new combinations of adaptogens based on traditional medical concepts. Robust and rigorous approaches including network pharmacology and systems pharmacology could help in analyzing potential synergistic effects and, more broadly, future uses of adaptogens. In conclusion, the evolution of the adaptogenic concept has led back to basics of TMS and a new level of understanding of holistic approach. It provides a rationale for their use in stress-induced and aging-related diseases.

Mechanisms Of Adaptogens

In order to promote resilience and restore physiological functioning, adaptogens work as "stress-mimetics" or molecular "vaccines," gently stimulating stress-response pathways. They mainly function via controlling the neuroendocrine-immune system and reestablishing homeostasis rather than by acting as sedatives. Adaptogens' mechanism for treating insomnia includes: Modulating the hypothalamic-pituitary-adrenal (HPA) axis efficiently balances the body's stress response by lowering high cortisol levels (which lessen "wired but tired" symptoms) and raising low levels. Increasing the production of gamma-aminobutyric acid (GABA), the primary inhibitory neurotransmitter that encourages rest and sleep, or interacting with GABA receptors are examples of GABAergic Activity. Molecular chaperones: Increasing the expression of heat shock proteins (like HSP70) to restore proteins damaged by stress and boost stress tolerance. Neuroprotection: lowering oxidative stress, enhancing antioxidant capacity, and reducing neuroinflammation in the brain.

Plant Profile

1. Valeriana Officinalis

A popular herbal remedy for insomnia, *Valeriana officinalis* (valerian root), may help with mild insomnia and menopause-related sleep disorders. It may also shorten the time it takes to fall asleep. Although there is little high-quality data on its long-term effectiveness, it is widely regarded as safe for short-term use. The most popular alternative sleep aid for treating sleep issues is valerian, a natural herb. A blooming plant that is native to Europe and Asia but can also be found in North America is the source of valerian extract. It has been used since ancient Greece and Rome to treat anxiety problems and sleeplessness. In the UK, it is also approved or regarded as a suitable treatment for sleep-related conditions.

Background-

Following the Battle of Edessa, the Persian emperor Shapur I captured Valerian, making him the first Roman emperor to be captured in combat. This event caused shock and instability throughout the Roman Empire. A range of responses and "new narratives about the Roman Empire in diverse contexts" were sparked by the extraordinary incident and stories of his humiliation at the hands of the Persian emperor.

Taxonomical Classification

- Kingdom – Plantae
- Division –Tracheophyta
- Class- MAgnoliopsida
- Order- Dipsacales
- Family- Caprifoliaceae (Honeysuckle Family)
- Subfamily – Valerianoideae
- Genus-Valeriana
- Species – Valeriana officinalis.



Chemical Constituents

The sedative and anti-insomnia properties of *Valeriana officinalis* (valerian), which has more than 150 chemical elements, are mainly ascribed to sesquiterpenes (valerenic acid), iridoids (valepotriates), and flavonoids (6-methylapigenin, hesperidin, linarin). These substances cooperate to modulate γ -aminobutyric acid (GABA) receptors, preventing the brain's GABA from being broken down by enzymes. Important Elements of Insomnia The main sedative ingredients, valerenic acid and its derivatives, are sesquiterpenoids that interact with GABA receptors to lower activity in the central nervous system. Valepotriates (Iridoid-monoterpenes): Substances that function as sedatives, such as isovaltrate and valtrate, frequently decompose in water or during storage to produce active metabolites like homobaldrinal. Flavonoids: Active flavones and flavanone glycosides that improve sleep include 6-methylapigenin, 2S(-)-hesperidin, and linarin. Patchoulol, borneol, and other volatile oils -pinene, and -humulene

Traditional Use

The roots of *V. officinalis* have long been used in traditional herbal therapy for calming and antispasmodic effects. They can also be used to treat cardiac arrhythmia. For a century, people have taken valerian root as a calming and sleep-promoting herb. It is used to treat emotional states such as hysteria, hypochondriasis, and nervous restlessness. Fresh medication juice is used as an anticonvulsive for epilepsy and as a narcotic for sleeplessness. The root has been used in medicine to treat mental, circulatory, and blood ailments as well as sleeplessness. For at least a millennium, it was used to treat urinary tract infections and stomach issues. It employed antidepressant, antispasmodic, sedative, anxiolytic, and anti-HIV bioactivities. In Europe, it is used to treat anxiety, tremors, and restlessness; in the US, it is mostly offered as a sleeping aid.

Mechanism of Action

Valerian functions similarly to benzodiazepines, however it appears to bind to the beta subunit on the GABA-A receptor rather than the gamma subunit. In any case, when the principal inhibitory neurotransmitter, GABA, attaches to the GABA-A receptor and creates a hyperpolarized state, it has the same effect on the flow of chloride into the cell. Furthermore, it has been demonstrated that valerian prolongs the duration of GABA by reducing its elimination or metabolism. Overall, the data from clinical trials indicates that valerian may be helpful in treating insomnia; however, there aren't many well-designed studies that back up this assertion or offer proof of its long-term safety and effectiveness (i.e., beyond 4 to 6 weeks).

Pharmacological Activity of *Valeriana Officinalis* –

Valeriana officinalis, sometimes known as valerian, is frequently used to treat insomnia because of its sedative, hypnotic, and anxiolytic properties.

Pharmacological Activities

- **Sedative and Hypnotic Effects:** By reducing sleep latency (the amount of time it takes to fall asleep), valerian is widely used to treat insomnia and enhance the quality of sleep.
- **Anxiolytic Activity:** It treats nervous tension and anxiety by acting as a light sedative; it is frequently used to lessen symptoms associated with anxiety. Inhibiting the breakdown of aminobutyric acid (GABA), a neurotransmitter that encourages relaxation and lowers tension, is the mechanism behind
- **GABAergic Modulation.** Additionally, it might interact with receptors for benzodiazepines.
- **Antispasmodic and Muscle Relaxant:** It has been shown to be effective in reducing smooth muscle spasms and easing discomforts such as menstrual cramps (dysmenorrhea).
- **Neuroprotective and Other Effects:** Research indicates that it may have antibacterial, anti-inflammatory, and neuroprotective qualities.

2. *Matricaria Chamomilla*

One of the oldest recognized therapeutic herbs is chamomile. German chamomile (*Chamomilla recutita*) and Roman chamomile (*Chamaemelum nobile*) are two common types that belong to the Asteraceae/Compositae family. Numerous terpenoids and flavonoids found in dried chamomile flowers contribute to the plant's



therapeutic qualities. Many human conditions, including hay fever, inflammation, muscle spasms, menstrual disorders, sleeplessness, ulcers, wounds, gastrointestinal disorders, rheumatic pain, and hemorrhoids, are frequently treated with chamomile medicines. Chamomile essential oils are widely utilized in aromatherapy and cosmetics. Although chamomile has been prepared in a variety of ways, the most widely used form is herbal tea, which is taken in over a million cups per day.

Taxonomical Classification

- Kingdom – Plantae
- Phylum- Tracheophyta
- Class – Magnoliopsida
- Order- Asterales
- Family- Asteraceae (Composite Family)
- Genus- Matricaria (German) / Chamaemelum (Roman)
- Species – Matricaria chamomilla L./ Chamaemelum nobile (L.)

Chemical Constituents

Chemical components of chamomile for insomnia +8 The flavonoid apigenin, which binds to GABA receptors in the brain to lessen anxiety and encourage sleep, is the main way that chamomile (*Matricaria chamomilla*) operates as a moderate sedative for insomnia. Flavonoids (apigenin, luteolin, quercetin), volatile oils (alpha-bisabolol, chamazulene), and terpenoids are important substances that promote sleep. Important Chemical Components of Insomnia Apigenin (Flavonoid): The main bioactive ingredient, which functions as a benzodiazepine-like substance to lower anxiety and promote sleep. -Bisabolol and Oxides (Volatile Oil): Making up a significant amount of the essential oil, these compounds are known for their sedative and muscle-relaxant qualities. German chamomile frequently has more chamazulene (volatile oil), which has soothing and anti-inflammatory qualities. Other Flavonoids: Quercetin, patuletin, and luteolin all have antioxidant and relaxing benefits.

Traditional Uses

For generations, chamomile has been utilized as a mild astringent, antioxidant, anti-inflammatory, and therapeutic herb. Wounds, ulcers, eczema, gout, skin irritations, bruises, burns, canker sores, neuralgia, sciatica, rheumatic pain, hemorrhoids, mastitis, and other conditions are all treated with it in traditional medicine. Externally, chamomile has been used to treat a variety of bacterial infections of the skin, oral cavity, gums, and respiratory tract, as well as diaper rash, cracked nipples, chicken pox, ear and eye infections, eye conditions like blocked tear ducts, conjunctivitis, nasal inflammation, and poisonivy. An aqueous extract of chamomile has long been used as a moderate sedative to reduce anxiety and cure sleeplessness and nightmares.

Mechanism of Action-

Chamomile preparations, including tea and essential oil aromatherapy, have historically been used to induce sedation (calming effects) and treat insomnia. Apigenin, a flavonoid that binds to benzodiazepine receptors in the brain, may have sedative effects. Preclinical model studies have demonstrated CNS depressive and anticonvulsant effects, respectively. Although there aren't many clinical trials, ten cardiac patients have reportedly drifted off to a deep sleep that lasted for ninety minutes after consuming chamomile tea. Extracts from chamomile have hypnotic effects similar to those of benzodiazepines. Inhaling chamomile oil vapor decreased the rise in plasma adrenocorticotrophic hormone levels brought on by stress. While flumazenil, a BDZ antagonist, inhibited the effect of chamomile oil vapor on ACTH, diazepam, when taken concurrently with the vapor, further decreased ACTH levels.

Pharmacological Activity of *Matricaria Chamomilla*

- **Anti-inflammatory & Antioxidant:** Chamomile is useful for wounds, oral inflammation, and skin disorders because it includes chemicals that inhibit inflammatory pathways (COX-2) and lower TNF-production.



- **Sedative and Anxiolytic:** It works on the central nervous system to reduce anxiety and enhance the quality of sleep.
- **Gastrointestinal Support:** It helps treat IBS symptoms, colic, and abdominal pain by acting as an antispasmodic and carminative.
- **Antimicrobial & Antifungal:** The essential oil exhibits strong anti-infective properties, including efficacy against a variety of dermatophytes and *Candida albicans*.
- **Anti-diabetic & Hypolipidaemic:** Studies indicate that chamomile, in part through modifying enzyme activity, can enhance blood sugar regulation and reduce cholesterol levels.
- **Potential Anticancer Properties:** According to in vitro research, chamomile's apigenin may encourage some cancer cells to undergo apoptosis, or cell death, while doing little harm to healthy cells.

3. *Passiflora Incarnata*

A common herbal sedative, anxiolytic, and sleep aid for treating sleep disturbances is *Passiflora incarnata*. There are no human clinical trials, although a number of controlled studies have shown improved sleep in lab animals. Using sleep diaries verified by polysomnography (PSG), the current study sought to determine the effectiveness of *Passiflora incarnata* herbal tea on human sleep. This study used a double-blind, placebo-controlled, repeated-measures design with a counterbalanced order of treatments (placebo tea vs. passionflower), separated by a "washout" interval of one week. Forty-one participants (18–35 years old) were exposed to each therapy for a week. During that time, they drank tea, kept a sleep journal for seven days, and on the seventh morning, completed Spielberger's state-trait anxiety inventory.

Taxonomical Classification -

- Kingdom – Plantae (plants)
- Phylum – Tracheophyta (Vascular plants)
- Class –Mangnoliopsida (Dicots)
- Order – Malpighiales (Formerly oftenplaced in Violales)
- Family – Passifloraceae (Passionflower Family)
- Genus – *Passiflora* L.
- Species – *Passiflora incarnata* L.

Chemical constituents

Flavonoids (vitexin, isovitexin, orientin, isoorientin, apigenin) and indole alkaloids (harman, harmaline, harmalol) are the main ways that *Passiflora incarnata* (passionflower) relieves insomnia. These substances, particularly C-glycosyl flavonoids, increase the brain's levels of gamma-aminobutyric acid (GABA), which lowers anxiety and induces sleepiness without leading to serious addiction. Flavonoids (0.25%) are chemical constituents for insomnia. the primary active ingredients, especially flavone C-glycosides such as orientin, isoorientin, vitexin, and isovitexin. Chrysin is also known for having sedative properties similar to those of benzodiazepines. Harman, harmine, and harmaline are among the indole alkaloids (0.1%) that contribute to the sedative effect. It has been discovered that *Passiflora* contains GABA (Gamma-Aminobutyric Acid), a crucial inhibitory neurotransmitter that lowers neuronal excitability throughout the nervous system. Additional Elements: The plant's calming effects have been linked to maltol and ethyl maltol.

Traditional Uses

Passionflower, or *Passiflora incarnata*, has long been used as a sedative, nerve, and antispasmodic to treat restlessness, anxiety, and sleeplessness. While European medicine accepted it for nervous diseases, seizures, and menopause symptoms, Native American cultures previously utilized it for sedation, wound treatment, and nerve relaxation. Important Customary and Historical Uses: Insomnia & Sleep Disorders: Well-known for treating insomnia brought on by stress, excessive work, or racing thoughts without making you feel sleepy the following day. Anxiety



and Nervous Tension: Traditionally used to treat hysteria, irritability, stress, and mild to moderate anxiety. Children's Health: Used to cure colic and teething, as well as to calm hyperactive kids. Menstrual cramps, neuralgic pain, and muscle spasms are all treated with antispasmodic drugs. Cardiovascular Health: Traditionally used to control anxiety-related hypertension and lessen palpitations.

Mechanisms of Action

Gamma-aminobutyric acid (GABA), a neurotransmitter that lowers neural excitability and promotes tranquility, is the main way that *Passiflora incarnata*, or passionflower, relieves insomnia. Key Mechanisms of Action GABAergic System Modulation: The main mechanism involves stimulating GABA receptors, which enhances the inhibitory effects of GABA, slowing down brain activity, and promoting sleep. It acts as a sedative by interacting with GABA receptors and raising melatonin levels, shortening sleep latency, and increasing slow-wave (deep) sleep. Melatonin Elevation: Research suggests that passionflower extract might increase the body's natural melatonin levels, which can assist control sleep-wake cycles. Reduction of Neural Activity: It has a modest sedative effect that lessens anxiety and neural excitability, making the transition to sleep easier. Non-GABA Pathways: According to some research, it functions via activating opioid receptors, changing the monoaminergic system (which modifies dopamine and norepinephrine), and having antioxidant properties.

Pharmacological Activity of *Passiflora Incarnata*

- The well-known medicinal plant *Passiflora incarnata*, or passionflower, is mostly used for its sedative, hypnotic, and anxiolytic (anti-anxiety) qualities. By raising GABA levels, encouraging relaxation, and facilitating sleep, it affects the neurological system.
- **Pharmacological Activities Anxiolytic and Sedative Effect:** *P. incarnata* has been shown to be as effective as some traditional benzodiazepines (such as oxazepam) in treating insomnia, anxiety, and restlessness without being addictive.
- **Neurological Benefits:** It is used to treat neuralgia, epilepsy, and the symptoms of opiate withdrawal. Antioxidant and anti-inflammatory: The plant's flavonoids, including as apigenin and vitexin, have anti-inflammatory properties and protect against oxidative stress. They also frequently lessen pain and manage menopausal symptoms, such as depression and hot flashes.
- **Antispasmodic and Cardiovascular:** It has been used to treat cardiovascular conditions such as nervous tachycardia and to help with muscle spasms.

4. *Withania Somnifera*

Indian ginseng, or ashwagandha (*Withania somnifera*), is a shrub plant of the Solanaceae family. For thousands of years, traditional Indian Ayurvedic medicine has utilized ashwagandha to treat a variety of conditions, including sleeplessness, stress, anxiety, nerve tissue damage, inflammation, and sexual problems. Clinical research have already demonstrated ashwagandha's effectiveness against anxiety and depression. Ashwagandha has long been known to induce sleep, and a recent study found that ashwagandha root extract was safe and effective in treating anxiety and insomnia. On the other hand, NRS is linked to daytime exhaustion, stress, anxiety, and depression. Ashwagandha has been demonstrated to be useful in reducing depression and stress. Additionally, it works well to lessen inflammation and weariness.

The herb known as ashwagandha, or *Withania somnifera*, is indigenous to Asia and Africa. Known by another name, "Indian ginseng," it has been used for thousands of years in ancient Indian Ayurvedic medicine to relieve insomnia, improve nutrition, and reduce pain and inflammation. Ashwagandha is regarded as an adaptogen as well. In other words, it improves your body's ability to handle stress. To validate the effectiveness of ashwagandha, more research is required. However, if you experience tension, worry, or difficulty sleeping, this herbal supplement may be beneficial.

Background-

has been a key component of Unani and Ayurvedic treatment for more than 3,000 years. Ashwagandha has long been regarded as a Rasayana due to its capacity to promote longevity, adapt, and regenerate. Ashwagandha is advised for



those with weakness, fatigue, low body weight, and neurological issues, according to the Charaka and Sushruta Samhitas. According to Unani, ashwagandha is a "nervine tonic" that aids in the restoration of the body's essential humors. Typically, ashwagandha is prepared as churna (powder), avaleha (paste or jam), kvatha (decoction), or arishta (fermented infusion). It is administered as a mouth tablet, either alone or in combination with Guduchi, Brahmi, and Shatavari.

Chemical constituents –

Numerous biologically active chemical components, including alkaloids, glycosides, sitoindosides, withanolic, and steroidal lactones, have been discovered through extensive chromatographic and spectral analysis of ashwagandha. The main compounds are withaferin A, withanolide D, dihydrowithanolide D, withanoside IV or VI, and withanolide sulfoxide. Many human ailments, including impotence, anxiety, hypertension, amnesia, arthritis, cancer, diabetes, chronic stress, neurodegenerative diseases, inflammations, rheumatism, and cardiovascular disorders, are treated with ashwagandha root and leaf extract and its biologically active phytochemicals. Ashwagandha herb, root, and leaf extracts, as well as the withanolides that are extracted from them, are utilized extensively as a promising natural anti-inflammatory, anticancer, and cytotoxic agent to fight a variety of cancers of the colon, lung, skin, prostate, liver, and kidney.

Numerous mediators that are involved in the metabolism of arachidonic acid (AA) and the actions of pro-inflammatory enzymes [lipoxygenase (5-LOX), cyclooxygenase-1 (COX-1), and cyclooxygenase-2 (COX-2)] govern a number of human disorders that are accompanied by inflammation. The production of eicosanoids mediators plays a crucial role in the conversion of arachidonic acid, a lipid found in cells, into prostaglandins, which causes inflammation and eventually tumor formation. The inhibition tests of these enzymes are crucial for the initial screening of anti-inflammatory activities since it should be remembered that the overexpression of these inflammatory enzymes is not only seen in inflammatory cells but also involved in several types of tumor cells.

Triethylene glycol (TEG), a substance that encourages sleep induction, and withanolides (particularly withaferin A and withanosides IV/VI), which lower stress and alter GABAergic pathways, are the main methods that ashwagandha (*Withania somnifera*) alleviates insomnia. Together, these components improve the quality of sleep, lower anxiety, and decrease sleep latency. Triethylene Glycol (TEG): Found to be a significant active ingredient that promotes physiological sleep and aids in controlling the sleep-wake cycle, especially in leaves. Withanolides: Steroidal lactones found in roots and leaves, such as Withaferin A, Withanolide D, and Withanoside IV/VI, that lessen tension and anxiety, which are frequently the causes of sleeplessness. Sitoindosides: Glycosylated withanolides that provide the herb its calming and stress-relieving qualities. GABAergic Compounds: The extract produces sedative effects akin to those of some sleep aids by raising GABA (gamma-aminobutyric acid) levels in the brain

Traditional Use-

Ashwagandha root powder is a crucial component of many natural crude medications and polyherbal remedies used in Ayurveda, Siddha, and Unani medicine. The natural medications made from ashwagandha root powder were primarily used to improve human reproductive system function and fight stress, anxiety, and sexual performance. The two primary withanolides found in ashwagandha roots that are most promising are withaferin A and withanolide D. These chemicals have a variety of pharmacological, physiological, and therapeutic uses in herbal medicine. Because the roots of ashwagandha are said to smell like horses, or "ashwa," it was once thought that eating ashwagandha would give one the strength of a horse. Many people use and consider roots to be a natural tonic, astringent, diuretic, aphrodisiac, anthelmintic, narcotic, thermogenic, and stimulant.

The use of ashwagandha root powder as a natural herbal supplement for improving male fertility, sleeplessness, anxiety, memory, and cognition, as well as reducing stress and increasing muscular size and strength, was detailed in a number of earlier clinical trial investigations. Alkaloids, amino acids, volatile oil, and starch are also present in the roots. Withanolides, which have been isolated from the roots and leaves of ashwagandha and have been linked to possible pharmacotherapeutic and other functional qualities, were the main bioactive compounds detected in the plant.



Ashwagandha has yielded about 35 withanolides, 12 alkaloids, and a number of sitoindosides, all of whose structures have been clarified

Mechanisms of Action

Although the precise mechanism is yet unknown, γ -aminobutyric acid (GABAergic) activity is thought to be involved in ashwagandha-mediated sleep induction. According to reports, ashwagandha extract increases non-rapid eye movement (NREM) sleep, which in turn increases sleep duration. Nevertheless, the administration of an extract with a high withanolide content—which is known to reduce stress—did not cause sleep, suggesting that other chemicals also play a role in the sleep-inducing action. There are currently few investigations on ashwagandha extract's ability to induce sleep. Therefore, more research is necessary to prove ashwagandha's ability to induce sleep. A caffeine-induced insomnia model and the electroencephalograms (EEGs) of a pentobarbital-induced sleep mouse model and rat model were used in this investigation to confirm improvements in both the quantity and quality of sleep. By acting as an adaptogen to lower cortisol (the stress hormone) levels and modifying the GABAergic system to promote relaxation, ashwagandha (*Withania somnifera*) mainly alleviates insomnia. Increasing receptor activity, decreasing neural excitability, boosting non-rapid eye movement (NREM) sleep with higher δ -wave activity, and lowering evening cortisol are important strategies. Ashwagandha (more especially, withanolides and triethylene glycol) binds to receptor sites and mimics the inhibitory neurotransmitter GABA, which causes drowsiness and produces sleep. This is one of the main mechanisms of action for sleep. Cortisol Regulation (Stress Reduction): As an adaptogen, it helps to balance the hypothalamic-pituitary-adrenal (HPA) axis and lessen evening cortisol peaks that lead to insomnia by lowering cortisol levels, especially in stressed individuals. Improvement of Sleep Architecture: Research shows that it prolongs deep sleep (δ -wave) and NREM sleep.

Pharmacological Activity

Ashwagandha (*Withania somnifera*) mainly functions as an adaptogen, lowering cortisol and controlling the HPA axis to lessen stress and anxiety. It has strong anti-inflammatory, neuroprotective, and antioxidant qualities. Active withanolides boost immunity, improve cognitive function, raise testosterone, and have anti-tumor effects.

Important pharmacological effects consist of:

- **Adaptogenic/Anti-Stress:** Reduces cortisol and controls HPA axis activity to modify the body's stress response.
- **Anxiolytic (Anxiety Reduction):** Calms the nervous system by imitating GABA activity.
- **Neuroprotective & Cognitive Enhancement:** enhances memory and guards against neurodegenerative diseases like Parkinson's and Alzheimer's.
- **Antioxidant and anti-inflammatory:** Lowers inflammation and reactive oxygen species (ROS).
- **Immunomodulatory:** Strengthens the immune system and frequently increases the generation of white blood cells.
- **Reproductive & Sexual Health:** Boosts testosterone levels, enhances sperm motility/count, and improves reproductive efficiency.
- **Anti-tumor/Anticancer:** Withaferin A prevents the growth of tumors and the multiplication of cancer cells

Acknowledgement

I genuinely thank all of my coworkers for their advice, inspiration, and unwavering support during the writing of this review post. Additionally, the authors would like to express their sincere gratitude to the Samarth Institute of Pharmacy for providing the academic environment and facilities that made this work possible.

Result

The reviewed adaptogenic herbs such as *Valeriana officinalis*, *Matricaria chamomilla*, *Passiflora incarnata*, and *Withania Somnifera* demonstrated significant sedative, anxiolytic, and sleep-enhancing effects. Their activity is mainly due to phytoconstituents like flavonoids, alkaloids, and terpenoids, which act through modulation of GABA



receptors, reduction of cortisol via the HPA axis, and antioxidant mechanisms. These herbs were found to improve sleep quality, reduce sleep latency, and decrease anxiety levels with minimal adverse effects.

II. CONCLUSION

Adaptogenic herbs offer a promising and safer alternative for the management of insomnia compared to conventional drugs. Their multi-targeted mechanisms, including neuroendocrine regulation and stress adaptation, make them effective in improving sleep without causing dependency or tolerance. However, more well-designed clinical studies are necessary to confirm their long-term safety, efficacy, and standardization for therapeutic use.

REFERENCES

- 1) Panossian A, Wikman G. Effects of Adaptogens on the Central Nervous System and the Molecular Mechanisms Associated with Their Stress-Protective Activity. *Pharmaceuticals (Basel)*. 2010 Jan 19;3(1):188-224. doi: 10.3390/ph3010188. PMID: 27713248; PMCID: PMC3991026.
- 2) Lind MJ, Hawn SE, Sheerin CM, Aggen SH, Kirkpatrick RM, Kendler KS, Amstadter AB. An examination of the etiologic overlap between the genetic and environmental influences on insomnia and common psychopathology. *Depress Anxiety*. 2017 May;34(5):453-462. doi: 10.1002/da.22587. Epub 2017 Jan 16. PMID: 28092418; PMCID: PMC5469037.
- 3) Zhang J, Liu B, Han J, Gu X. Causal association between insomnia and diabetic nephropathy independent of diabetes: Evidence from 2-sample Mendelian randomization analysis. *Medicine (Baltimore)*. 2025 Oct 31;104(44):e45368. doi: 10.1097/MD.0000000000045368. PMID: 41261698; PMCID: PMC12582757.
- 4) Drozd C, Curtit E, Jacquinet Q, Roux P, Paget-Bailly S, Gillet V, Meneveau N, Mougou F. Effect of a supervised intermittent exercise program on insomnia in breast cancer patients undergoing chemotherapy. *Breast Cancer Res Treat*. 2026 Feb 26;216(2):20. doi: 10.1007/s10549-026-07923-7. PMID: 41746533; PMCID: PMC12945910.
- 5) Nicolazzo J, Cavuoto M, Rowsthorn E, Cribb L, Bransby L, Gibson M, Wall P, Velakoulis D, Eratne D, Buckley R, Yassi N, Yiallourou S, Brodtmann A, Hamilton GS, Naughton MT, Lim YY, Pase MP. Insomnia Symptoms and Biomarkers of Alzheimer's Disease in the Community. *J Alzheimers Dis*. 2023;91(4):1423-1434. doi: 10.3233/JAD-220924. PMID: 36641673; PMCID: PMC11446570.
- 6) Hughes JM, Ulmer CS, Gierisch JM, Nicole Hastings S, Howard MO. Insomnia in United States military veterans: An integrated theoretical model. *Clin Psychol Rev*. 2018 Feb;59:118-125. doi: 10.1016/j.cpr.2017.11.005. Epub 2017 Nov 20. PMID: 29180102; PMCID: PMC5930488.
- 7) Jurowski K, Fołta M, Tatar B, Berkoz M, Krośniak M. The Toxicological Risk Assessment of Lead and Cadmium in *Valeriana officinalis* L., radix (Valerian root) as Herbal Medicinal Product for the Relief of Mild Nervous Tension and Sleep Disorders Available in Polish Pharmacies. *Biol Trace Elem Res*. 2022 Feb;200(2):904-909. doi: 10.1007/s12011-021-02691-5. Epub 2021 Apr 1. PMID: 33792859; PMCID: PMC8738358.
- 8) Bogacz A, Mrozikiewicz PM, Karasiewicz M, Bartkowiak-Wieczorek J, Majchrzycki M, Mikolajczak PL, Ozarowski M, Grzeskowiak E. The influence of standardized *Valeriana officinalis* extract on the CYP3A1 gene expression by nuclear receptors in in vivo model. *Biomed Res Int*. 2014;2014:819093. doi: 10.1155/2014/819093. Epub 2014 Sep 11. PMID: 25302309; PMCID: PMC4180645.
- 9) Jurowski K, Fołta M, Tatar B, Berkoz M, Krośniak M. The Toxicological Risk Assessment of Cu, Mn, and Zn as Essential Elemental Impurities in Herbal Medicinal Products with Valerian Root (*Valeriana officinalis* L., radix) Available in Polish Pharmacies. *Biol Trace Elem Res*. 2022 Apr;200(4):1949-1955. doi: 10.1007/s12011-021-02779-y. Epub 2021 Jun 9. PMID: 34109550; PMCID: PMC8854135.
- 10) Yeo YS, Nybo SE, Chittiboyina AG, Weerasooriya AD, Wang YH, Góngora-Castillo E, Vaillancourt B, Buell CR, DellaPenna D, Celiz MD, Jones AD, Wurtele ES, Ransom N, Dudareva N, Shaaban KA, Tibrewal N,



- Chandra S, Smillie T, Khan IA, Coates RM, Watt DS, Chappell J. Functional identification of valerena-1,10-diene synthase, a terpene synthase catalyzing a unique chemical cascade in the biosynthesis of biologically active sesquiterpenes in *Valeriana officinalis*. *J Biol Chem*. 2013 Feb 1;288(5):3163-73. doi: 10.1074/jbc.M112.415836. Epub 2012 Dec 14. PMID: 23243312; PMCID: PMC3561538.
- 11) Shinjyo N, Waddell G, Green J. Valerian Root in Treating Sleep Problems and Associated Disorders-A Systematic Review and Meta-Analysis. *J Evid Based Integr Med*. 2020 Jan-Dec;25:2515690X20967323. doi: 10.1177/2515690X20967323. PMID: 33086877; PMCID: PMC7585905.
 - 12) Yang S, Zhang H, Chen L, Zhang Z, Huang L, Wang W, Lu W, Wang Y, Wu S, Hu Z, Wang S, Chen R, Liang F. *Valeriana* species and insomnia: multi-organ mechanisms and translational perspectives. *Pharm Biol*. 2026 Dec;64(1):615-638. doi: 10.1080/13880209.2026.2652660. Epub 2026 Apr 17. PMID: 41995686; PMCID: PMC13094296.
 - 13) Maroo N, Hazra A, Das T. Efficacy and safety of a polyherbal sedative-hypnotic formulation NSF-3 in primary insomnia in comparison to zolpidem: a randomized controlled trial. *Indian J Pharmacol*. 2013 Jan-Feb;45(1):34-9. doi: 10.4103/0253-7613.106432. PMID: 23543804; PMCID: PMC3608291.
 - 14) Muhetaer H, Li H, Wang B, Cai X, Zhang Y, Li Y, Li C, Wu B. Exploring the Effects and Mechanisms of Valerian Volatile Oil in Treating Insomnia Using Network Pharmacology, Molecular Docking, and Molecular Dynamics Simulation-Based Approaches. *Int J Mol Sci*. 2025 Feb 18;26(4):1726. doi: 10.3390/ijms26041726. PMID: 40004189; PMCID: PMC11855732.
 - 15) Koshovyi O, Sepp J, Jakštas V, Žvikas V, Kireyev I, Karpun Y, Odyntsova V, Heinämäki J, Raal A. German Chamomile (*Matricaria chamomilla* L.) Flower Extract, Its Amino Acid Preparations and 3D-Printed Dosage Forms: Phytochemical, Pharmacological, Technological, and Molecular Docking Study. *Int J Mol Sci*. 2024 Jul 29;25(15):8292. doi: 10.3390/ijms25158292. PMID: 39125862; PMCID: PMC11311743.
 - 16) Aleksieiev A, Masłowski M, Efenberger-Szmechtyk M, Strzelec K. The Influence of Freeze-Dried Alcohol-Water Extracts from Common Yarrow (*Achillea millefolium* L.) and German Chamomile (*Matricaria chamomilla* L.) on the Properties of Elastomer Vulcanizates. *Int J Mol Sci*. 2022 Nov 30;23(23):15048. doi: 10.3390/ijms232315048. PMID: 36499374; PMCID: PMC9737587.
 - 17) Singh O, Khanam Z, Misra N, Srivastava MK. Chamomile (*Matricaria chamomilla* L.): An overview. *Pharmacogn Rev*. 2011 Jan;5(9):82-95. doi: 10.4103/0973-7847.79103. PMID: 22096322; PMCID: PMC3210003.
 - 18) Ayhan BS, Yalçın E, Çavuşoğlu K. In-silico receptor interactions, phytochemical fingerprint and biological activities of *Matricaria chamomilla* flower extract and the main components. *Sci Rep*. 2025 Aug 7;15(1):28875. doi: 10.1038/s41598-025-14729-y. PMID: 40775024; PMCID: PMC12331924.
 - 19) Keefe JR, Mao JJ, Soeller I, Li QS, Amsterdam JD. Short-term open-label chamomile (*Matricaria chamomilla* L.) therapy of moderate to severe generalized anxiety disorder. *Phytomedicine*. 2016 Dec 15;23(14):1699-1705. doi: 10.1016/j.phymed.2016.10.013. Epub 2016 Oct 24. PMID: 27912871; PMCID: PMC5589135.
 - 20) Raja A, Singh GP, Fadil SA, Elhady SS, Youssef FS, Ashour ML. Prophylactic Anti-Osteoporotic Effect of *Matricaria chamomilla* L. Flower Using Steroid-Induced Osteoporosis in Rat Model and Molecular Modelling Approaches. *Antioxidants (Basel)*. 2022 Jul 1;11(7):1316. doi: 10.3390/antiox11071316. PMID: 35883807; PMCID: PMC9312011.
 - 21) Żelabowski K, Pichowicz W, Skowron I, Szwach J, Biedka K, Wesołowski M, Błaszczuk K, Ziobro O, Petrov W, Kukula-Koch W, Chłopaś-Konowalek A. The Efficacy of Melatonergic Receptor Agonists Used in Clinical Practice in Insomnia Treatment: Melatonin, Tasimelteon, Ramelteon, Agomelatine, and Selected Herbs. *Molecules*. 2025 Sep 19;30(18):3814. doi: 10.3390/molecules30183814. PMID: 41011705; PMCID: PMC12472680.



- 22) Janda K, Wojtkowska K, Jakubczyk K, Antoniewicz J, Skonieczna-Żydecka K. *Passiflora incarnata* in Neuropsychiatric Disorders-A Systematic Review. *Nutrients*. 2020 Dec 19;12(12):3894. doi: 10.3390/nu12123894. PMID: 33352740; PMCID: PMC7766837.
- 23) Kim M, Lim HS, Lee HH, Kim TH. Role Identification of *Passiflora Incarnata Linnaeus*: A Mini Review. *J Menopausal Med*. 2017 Dec;23(3):156-159. doi: 10.6118/jmm.2017.23.3.156. Epub 2017 Dec 29. PMID: 29354614; PMCID: PMC5770524.
- 24) Harit MK, Mundhe N, Tamoli S Sr, Pawar V, Bhapkar V, Kolhe G, Mahadik S, Kulkarni A, Agarwal A. Randomized, Double-Blind, Placebo-Controlled, Clinical Study of *Passiflora incarnata* in Participants With Stress and Sleep Problems. *Cureus*. 2024 Mar 20;16(3):e56530. doi: 10.7759/cureus.56530. PMID: 38646244; PMCID: PMC11026993.
- 25) Hosseini A, Mobasheri L, Rakhshandeh H, Rahimi VB, Najafi Z, Askari VR. Edible Herbal Medicines as an Alternative to Common Medication for Sleep Disorders: A Review Article. *Curr Neuropharmacol*. 2024;22(7):1205-1232. doi: 10.2174/1570159X21666230621143944. PMID: 37345244; PMCID: PMC10964091.
- 26) Elsas SM, Rossi DJ, Raber J, White G, Seeley CA, Gregory WL, Mohr C, Pfankuch T, Soumyanath A. *Passiflora incarnata* L. (Passionflower) extracts elicit GABA currents in hippocampal neurons in vitro, and show anxiogenic and anticonvulsant effects in vivo, varying with extraction method. *Phytomedicine*. 2010 Oct;17(12):940-9. doi: 10.1016/j.phymed.2010.03.002. Epub 2010 Apr 10. PMID: 20382514; PMCID: PMC2941540.
- 27) Langade D, Thakare V, Kanchi S, Kelgane S. 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. *J Ethnopharmacol*. 2021 Jan 10;264:113276. doi: 10.1016/j.jep.2020.113276. Epub 2020 Aug 17. PMID: 32818573.
- 28) Speers AB, Cabey KA, Soumyanath A, Wright KM. Effects of *Withania somnifera* (Ashwagandha) on Stress and the Stress- Related Neuropsychiatric Disorders Anxiety, Depression, and Insomnia. *Curr Neuropharmacol*. 2021;19(9):1468-1495. doi: 10.2174/1570159X19666210712151556. PMID: 34254920; PMCID: PMC8762185.
- 29) Fatima K, Malik J, Muskan F, Raza G, Waseem A, Shahid H, Jaffery SF, Khan U, Zaheer MK, Shaikh Y, Rashid AM. Safety and efficacy of *Withania somnifera* for anxiety and insomnia: Systematic review and meta-analysis. *Hum Psychopharmacol*. 2024 Nov;39(6):e2911. doi: 10.1002/hup.2911. Epub 2024 Jul 31. PMID: 39083548.
- 30) Fatima K, Malik J, Muskan F, Raza G, Waseem A, Shahid H, Jaffery SF, Khan U, Zaheer MK, Shaikh Y, Rashid AM. Safety and efficacy of *Withania somnifera* for anxiety and insomnia: Systematic review and meta-analysis. *Hum Psychopharmacol*. 2024 Nov;39(6):e2911. doi: 10.1002/hup.2911. Epub 2024 Jul 31. PMID: 39083548

