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Research Article

NATURAL SEDATIVES AND HYPNOTICS: AN OVERVIEW ON VALERIAN, HOPS, AND PASSION FLOWER

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Abstract :-

This review highlights the sedative and hypnotic properties of Valeriana officinalis (Valerian), Humulus lupulus (Hops), and Passiflora incarnata (Passion flower), widely used in herbal medicine for insomnia and anxiety. These plants primarily act through modulation of the gamma-amino butyric acid (GABA) pathway, resulting in central nervous system depression and improved sleep induction. Valerian root, rich in valerenic acid and valepotriates, enhances GABA activity, producing mild sedation and reducing sleep latency. Hops, containing humulone and lupulone, exhibit synergistic effects with valerian, reinforcing relaxation and promoting deeper sleep. Passion flower, characterized by flavonoids such as vitexin and chrysin, enhances GABA binding affinity, contributing to its tranquilizing and sleep-promoting actions. Recent studies support the combined use of these botanicals as effective natural alternatives to synthetic hypnotics, with minimal side effects or dependency risks. Collectively, these herbs demonstrate strong potential in the formulation of phytotherapeutic agents for safe management of mild to moderate insomnia.

Keywords :- Valeriana officinalis, Humulus lupulus, Passiflora incarnata, sleep disorders, herbal sedative, hypnotics, GABAergic pathway

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INTRODUCTION:

Sleep is an essential physiological mechanism for maintaining physical and emotional health. Healthy sleep is critical for peak cognitive performance, which includes attention, emotional reactivity, learning, and memory. Sleep also benefits a variety of other physiological functions, including metabolic and endocrine health, as well as immune system strength.(1)

According to a study, 18.5% to 23.8% of teenagers have sleep issues, such as insomnia. (2) Insomnia is described as the subjective sense of trouble with sleep initiation, duration, consolidation, or quality, despite sufficient sleep opportunity, and resulting in some kind of regular impairment. (3)

A sedative drug reduces activity, moderates excitement, and calms the recipient, whereas a hypnotic drug induces drowsiness and facilitates the onset and maintenance of a state of sleep with electroencephalographic characteristics similar to natural sleep and from which the recipient can be easily awakened.

The latter is sometimes called hypnosis, but the sleep induced by hypnotic medications does not resemble the experimentally induced passive state of suggestibility, also called hypnosis. (4)

A wide range of drugs have the ability to depress CNS function, resulting in calming or drowsiness. Although synthetic medications can alleviate insomnia, their use has certain drawbacks as clinical research advances. Along with the negative consequences of these sedatives, such as daytime weariness and cognitive impairment, physical dependency may also develop. However, herbal medicines can be used to cure insomnia. Medicinal plants are popular among insomniacs because of their low risk of adverse effects. (5)

Herbal medications cure insomnia by affecting the synthesis of GABA and GABA-metabolizing enzymes, both of which impact sleep quality. Herbal medicines, on the other hand, have less side effects and nearly double the benefits of benzos. (6)

❖ **Valerian :-**

Figure No 1:- Valerian (*V. officinalis*)

- Valerian is a flowering plant genus belonging to the *Caprifoliaceae* family,

commonly known as valerians. The name Valerian is derived from the Latin term "valere," which means "health" or "well-being."(7,8)

- *V. officinalis* var. *latifolia* is a perennial herb obtained from the Valeriana genus of the *Valerianaceae* family found in North America, Europe, and Asia (9)
- It is a glabrous or pubescent herb that grows up to 1.5 meters tall. Rootstocks are small, suberect, barely thicker than the stem, and stoloniferous; stems are solitary, erect, and furrowed. (10)

- **Toxonomical classification :- (11)**

Kingdom: Plantae

Unranked: Angiosperms

Unranked: Eudicots

Unranked: Asterids

Order: Dipsacales

Family: *Caprifoliaceae/Valerianaceae*

Genus: Valeriana

Species: *Officinalis*

- **History :-**

- Dioscorides, the Greek physician, reportedly suggested valerian root as a treatment for a variety of ailments, such as urinary tract infections, epilepsy, digestive issues, and heart palpitations. In the second century, Galen suggested Valerian as a remedy for sleeplessness. By the 18th century, valerian was widely used as a sedative and to treat neurological diseases related with a "restless" digestive tract and "vapors" in women.
- Valerian was included as a sleep aid and anxiolytic on the national formulary of the United States until the 1940s. Valerian re-emerged in the 1980s as a popular non-prescription hypnotic and daytime sedative, particularly in France, Belgium, Switzerland, the United Kingdom, Russia, and Germany. (12,13)

- **Chemical constituents :-**

- The primary component is thought to be valerenic acid.
- Two primary groups of constituents are found in the roots and rhizomes of *V. officinalis*: valepotriates (valtrate, didrovaltrate, acevaltrate, and isovaleroxyhydroxyvaltrate), which are an extension of flavonoids, triterpenes, lignans, and alkaloids, and sesquiterpenes of the volatile oil (valerenic acid and its derivatives, valeranone, valeranal, and kessyl esters).

- Volvalerenals A–F are among the several sesquiterpenoids that have been identified from *V. officinalis*. (14)

▪ Pharmacological Activity :-

- The mechanism of action of valerian in general, and especially as a moderate sedative, remains unknown.
- Valerian extracts and some of its constituents, particularly valerenic acid, appear to have strong affinity for the GABAA receptor, but the specific mechanism of action is unknown. Benke et colleagues discovered a unique binding site on GABAA receptors with nM affinity for two valerian components, valerenic acid and valerenol. Valerenol and valerenic acid both boosted GABA responses at various types of recombinant GABAA receptors.
- Thus, neurons expressing beta3 containing GABAA receptors are the primary cellular substrates for valerian extract's anxiolytic activity.
- Valerenic acid, as well as its derivatives acetoxvalerenic acid and hydroxyvalerenic acid, must cross the blood-brain barrier to interact with this receptor in the brain. (15)

▪ Dosage :-

- A single recommended dose ranges from 300 mg to 900 mg, taken about 30 minutes before bedtime. (21)
- 2 to 3 g of dried herbal valerian root can be soaked in one cup of boiling water for 10 to 15 minutes. 25 extract the product 30 minutes to two hours before bedtime. (22)

▪ Uses :-

- For decades, extracts of the valerian root have to promote sleep in the US and Europe. (16)
- Valerian extracts contains high valerenic acid which is used for its anti anxiolytic activity. (17)
- *Valeriana officinalis* (valerian) is used to relieve headaches and reduce their frequency and intensity. (18)
- Current valerian indications include restlessness, nervousness and tension. (19)
- Valerian contains flavonoids, sesquiterpenes, and other chemicals that are antioxidants and anti-inflammatory.
- Valerian has been examined for potential cardiovascular effects.
- Valerian has long been used to relieve gastrointestinal problems such as cramps, bloating, and indigestion. (20)

Hops :-

Figure No 2 :- Hops (*Humulus lupulus*)



- Hop (*Humulus lupulus* Linnaeus) is a dioecious, perennial plant belonging to the *Cannabaceae* family (23)
- The plant climbs in a clockwise fashion around any accessible support, using its downward facing strong trichomes (hairs), and can reach a height of 10 to 18 meters. The leaves are opposite or alternating, with 3 to 5 lobes and serrated margins. (24)
- Originating in Eurasia, hops have been grown for over a millennium. There are also distinct lineages that are indigenous to North America's temperate regions. Furthermore, the plant has been brought to cooler regions of Australia, South Africa, and South America as a cultivar. (25)

▪ Taxonomical classification :- (26)

Kingdom: Viridiplantae
Phylum: Streptophyta
Subphylum: Streptophytina
Superdivision: Embryophyta
Division: Tracheophyta
Subdivision: Euphyllophyta
Class: Magnoliopsida
Order: Rosales
Family: *Cannabaceae*
Genus: *Humulus*
Species: *Humulus lupulus* L.

▪ History :-

- Only the hop (*Humulus lupulus* L.) is today acknowledged as a key raw ingredient in global brewing, out of all the herbs that have been utilized to flavour and preserve beer throughout history. Although hops were cultivated in Babylon as early as 200 A.D., there is no record of their use in beer until around 1079. (27)

- Hops have been scientifically researched since the 19th and early 20th centuries, proving their traditional benefits. Hops' sedative and sleep-inducing properties are well-documented.(28) Nowadays there are approximately 250 hop cultivars cultivated, domesticated, and distributed worldwide, each varying in bitter acid concentrations, essential oil composition, vigour/growth, and disease resistance. (29)
- **Chemical constituents :-**
 - Hop resins make up 10--30% of the cone's dry content. They are classified as soft (9.0-27.5% of cone dry mass) or hard (1.5-2.5% of cone dry bulk).
 - Hops' bitter acids contain the prenylated phloroglucinol derivatives humulons (α -acids) and lupulons (β -acids). (30)
 - Hops also include flavonol glycosides (kaempferol, quercetin, quercitrin, rutin) and catechins (catechin gallate, epicatechin gallate). (31)
 - Xanthohumol (XN) is the most common chemical among hop polyphenols, accounting for 80-90% of all hop prenylflavonoids. (32)
 - The Comet variety, with an essential oil level ranging from 0.8 to 3.3%, is considered a variety for both scent and bitterness.
 - Hops include the majority of hydrocarbons, including monoterpenes like β -myrcene, limonene, and α -pinene. They can be acyclic, monocyclic, or bicyclic.
 - These chemicals were responsible for an average of 19.52% of the essential oil content. (33)
- **Pharmacological Activity :-**
 - Hops (*Humulus lupulus* L.) promotes sleep primarily via modulating the GABA sub-A / sub receptor, a major inhibitory receptor in the central nervous system. Humulone, a kind of α -bitter acid, activates GABA sub-A/sub receptors, resulting in drowsiness and enhanced sleep.
 - Furthermore, xanthohumol, a flavonoid found in hops, interacts with GABA sub A/sub receptors and promotes sleep, as well as providing antioxidant and anti-inflammatory qualities that may assist nervous system stability. These substances serve to offset stress-induced changes to the autonomic nervous system, which frequently result in sleep problems.
 - The sedative efficacy varies by hop variety due to differences in flavonoid content. (34)
- **Dosage :-**
 - Hops has been used as a mild sedative or sleep aid, with the dried strobile given in doses of 1.5 to 2 g. An extract combination with valerian, Ze 91019 (ReDormin, Ivel) has been studied at a hops dose of 60 mg for insomnia.
 - 1-2 doses should be taken half to one hour before bedtime.
 - Children: The preparation is not recommended for children under 12 years of age. (37)
- **Uses :-**
 - Hops is mainly used in management of insomnia, exerting sleep promoting and sedative action. (34)
 - *Humulus lupulus*, the most both culturally and economically significant species in the genus, has been used in beer production for centuries. (35)
 - Essential oils and flavonoids found in *Humulus* species have strong antioxidant properties, which help to reduce oxidative stress.
 - The antimicrobial activities against resistant organisms point to the possibility of alternative natural antibiotics and preservatives.
 - Molecular mechanisms for β -caryophyllene and xanthohumol involve anti-inflammatory and pro-apoptotic pathways.
 - Xanthohumol derived from *H. lupulus* exhibits antiviral properties against bovine viral diarrhoea virus, cytomegalovirus, Herpes simplex virus type 1 and 2, and human immunodeficiency virus (36)
- ❖ **Passion flower :-**



Figure No 3 :- Passion Flower
(*Passiflora incarnate*)

- Passion flower, a tropical plant from the *Passiflora* genus, has over 450 species with high genetic variety. (38)
- *P. alata* has been used to treat anxiety and as a sedative. Secondary metabolites including saponins and C-glycosidic

flavonoids are considered to be responsible for these effects. (39)

- *Passiflora incarnata* (maypop) is native to the United States, Central and South America, and Native Americans used it to cure insomnia, hysteria, epilepsy, and as a mild painkiller. (40)
- *Passiflora* plants are shrubs and herbs, typically climbing with axillary tendrils. The stem can be herbaceous or woody, typically ascending but rarely arborescent.
- Alternate leaves can be simple, whole, lobed, palmate, complex, or imparipinnate. Stipules germinate at the base of petioles and are rarely absent. (41)
- **Toxonomical classification:- (41)**
 - Kingdom:** Plantae
 - Division (Phylum):** Magnoliophyta
 - Class:** Magnoliopsida
 - Order:** Malpighiales
 - Family:** *Passifloraceae*
 - Genus:** *Passiflora* L.
 - Species:** *Passiflora incarnata* L.
- **History :-**
 - *Passiflora incarnata* was used in prehistoric times in North America during the Late Archaic period, which lasted from 8000 to 2000 B.C. Passionflower was first discovered by Spanish conquerors from pre-Columbian peoples who utilized it as a sedative for insomnia and uneasiness.
 - In 1569, Spanish explorers in Peru discovered the passion flower, which they interpreted as a symbol of Christ's passion and approval for their efforts. This is the origin of both the scientific and commonly used name. (42) Until the 17th century, decorative cultivation of the passion flower was limited to wild species such as *P. caerulea* L. and *P. incarnata* L., which are still utilized today only in 1819 were *Passiflora* hybrids reported. (43)
- **Chemical constituents: -**
 - *P. incarnata* plant contains 0.04% of β -carboline alkaloids, including harmine, harmine, and harmalol.
 - *P. incarnata* herb contains a variety of biologically active substances (BAS) such as chlorophyll and pectin, saponins, vitamins, and oxycoumarin.
 - A sedative flavonoid complex (vitexin, quercetin, luteolin, apigenin); coumarins, quinones.
 - *P. incarnata* plant contains many flavonoid glycosides that includes apigenin, kaempferol, and quercetin glycosides. (44)
- **Pharmacological Activity :-**

- Preclinical studies gave insight on the various processes through which *Passiflora incarnata* exerts its medicinal properties.
- According to studies, flavonoids, notably chrysin and apigenin, bind to GABA receptors and have anxiolytic and sedative effects. Amanet et al. (2016) discovered that *Passiflora incarnata* effectively altered GABAergic transmission in animal models, implying a mechanism of action similar to benzodiazepines but without the concerns of dependency or tolerance.
- Some studies also found increases in serotonin and dopamine levels, which are involved in mood regulation. (45)
- Anxiety and depressive disorders are associated with GABA system dysfunction. *P. incarnata*'s pharmacological actions are assumed to be mediated by GABA system regulation, which includes affinity for GABA(A) and GABA(B) receptors as well as GABA absorption. (46)
- **Dose: -**
 - A daily dose of 600 mg *Passiflorine incarnata* extract was taken along with water by the subjects in the SIVI (*Passiflora incarnata* extract) group at bedtime for 30 days. (48)
- **Uses :-**
 - Many of the chemical components of passion flower (passicol) in *Passiflora* species have antimicrobial activity.
 - The *P. nitida* and *P. palmeri* extracts were distinguished by their significant antioxidant capacity, which was associated with high catechin and o-diphenol content, as well as shoe and microbiological activity.
 - *P. edulis* leaf and steam have cytotoxic anticarcinogenic properties.
 - Passion flower is used to treat nervous restlessness, sleep disorders, restlessness, nervous symptoms, and anxiety.
 - *P. edulis* and *P. nepalensis* are commonly used to treat hypertension. (47)

CONCLUSION:

- Valerian, hops, and passion flower demonstrate significant pharmacological potential in treating insomnia and anxiety through synergistic modulation of neurotransmitter systems. Their natural origin, safety, and efficacy make them valuable candidates for developing standardized herbal formulations and phytotherapeutic products. Continued research and clinical validation are essential to establish optimal dosages and enhance their integration into evidence-based sleep management therapies.

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