RESEARCH PAPER

Exploring the Anticonvulsant and Neuroprotective Effects of Valeriana wallichii (Tagara) in Pediatric Epilepsy: A Narrative Review

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ABSTRACT

Background

Pediatric epilepsy is a common neurologic condition that is characterized by repeated unprovoked seizures. Antiepileptic medications are beneficial, although unpleasant effects and treatment resistance are problems with long-term therapy. In Ayurveda, Epilepsy is similar to Apasmara. Valeriana wallichii (Tagara) is used traditionally for its neuroprotective, anti-convulsant and soothing qualities.

Objective

The present study is designed to investigate phytochemical composition, neuropharmacological mechanisms, anticonvulsant activities and neuroprotective advantages of Valeriana wallichii in relation to epilepsy in children.

Methods

A narrative review was conducted using Ayurvedic traditional texts and scientific literature available in PubMed, Scopus and Google Scholar. The reviewed literature comprised neuroprotection, antioxidant, GABAergic, phytochemical and anticonvulsant studies.

Results

The main active components such as valerenic acid, valepotriates, flavonoids, alkaloids and sesquiterpenoids show anticonvulsant efficacy by modulation of GABAergic neurotransmission, oxidative effects, adenosine receptor pathways and inhibition of neuronal hyperexcitability. In PTZ and MES seizure models, experimental evidence demonstrates a decrease in seizure severity and oxidative stress.

Conclusion

Valeriana wallichii has a promising neuroprotective and anticonvulsant property but is lacking in sufficient reliable pediatric clinical research.

Keywords: Tagara, Paediatric Epilepsy, Apasmara, Valeriana wallichii, GABA, Neuroprotection, Anticonvulsant.

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INTRODUCTION

In Ayurveda, Mansika Vyadhi (mental diseases) broadly covers psychiatric and neurobehavioral disorders. Among these, Apasmara is considered a significant disease entity. Apasmara is described by Acharya Charaka as:

viLekja iqu% Le`frcqf)lÙolEIyokn~ chHkRlps"VekofLFkda re%ços'kekp{krs [1]

which means a state of temporary unconsciousness with impairment of memory (Smriti), intellect (Buddhi), mental stability (Sattva), abnormal movements and altered behavior.[2] In Ayurveda

Apasmara is understood as a medical or clinical state and not as a manifestation of supernatural forces.

The word is a combination of two words “Apa” which denotes deprivation or loss and “Smara” which means memory, awareness, intelligence and consciousness.[3] Thus Apasmara may be taken to mean a condition of disturbance or loss of memory and consciousness. Among the symptoms, loss of consciousness is considered one of the most important clinical signs of the condition. Clinical features are usually a sudden onset of seizures, loss of consciousness, falls, frothing at the mouth and subsequent recovery of consciousness following the episode. Due to the interaction of the psychological and physical.

Apasmara is termed as Mahavyadhi [4] due to its severe impact on cognition, behavior and overall functioning. The disease does not discriminate by sex, socio-economic level, or geographical region. It has a greater predilection among children. Epilepsy is one of the most common chronic neurologic illnesses in infancy and is characterized by recurrent unprovoked seizures that are the result of excessive and aberrant neuronal discharges within the brain. It is estimated that 0.5–1% of children in the world have pediatric epilepsy, leading to substantial cognitive, developmental, emotional and psychosocial deficits.

Current care is mostly based on antiepileptic medications (AEDs) including sodium valproate, phenytoin, carbamazepine and levetiracetam. Although many patients achieve adequate seizure control with these drugs, long-term exposure is often associated with side effects, treatment refractoriness, and neurobehavioral sequelae. So, there is a growing interest in studying alternative and integrative therapy options with better safety profiles.Traditional systems of medicine including Ayurveda have widely used medicinal herbs for neurological problems. Valeriana wallichii DC. (Tagara) is a significant Ayurvedic herb. It is historically prescribed for diseases when mental functions are impaired, sleeplessness, anxiety and Apasmara. Pharmacological studies are beginning to gather to support the anticonvulsant, anxiolytic, sedative, antioxidant and neuroprotective effects of Tagara. Thus, integration of classical Ayurvedic knowledge and modern neuropharmacological research may provide a promising strategy in developing therapeutic techniques in the management of pediatric epilepsy.

Aim and Objective

The present review aims to critically evaluate the traditional Ayurvedic knowledge, phytochemical profile, neuropharmacological mechanisms, and available experimental evidence regarding the anticonvulsant and neuroprotective potential of Valeriana wallichii (Tagara) in pediatric epilepsy.

Description of *Tagara* in *Samhita*

***Charak Samhita*:** *Charaka Samhita* describes *Tagara* in: *Vedanasthapana Mahakashaya Sheetaprashamana Mahakashaya*. *Acharya Charaka* explains *Tagara* as *Vedanas*, *Manasroga hara, Vatahara*. Useful in disorders affecting nervous system and mind.[5]

Tagara is also used in formulations indicated in: *Shiroroga ,Jwara ,Unmada* Neurological disorders**.***Tagara* mentioned in various ailments compound drugs as *Shirahshoolshamak lep* (headache reliever*), Sheetshamak lep (Shleyadi lep) Sheetaparshamna Mahakshaya* (pacific cold and chills), *Jwaraghna* (pacifies fever), *Vedanasthapana* (analgesic), *Rajyakshma chikitsa* (tuberculosis), *Ardit* (facial paralysis), *Unmada Pakshaghata* (hemiparalysis) (psychosomatic disorder), *Vrana, Urusthmbha, Vatarakta* (gout), *Vatavyadhi* (nerve disorders), *Yonishool* (vaginal pain), *Visha*

***Sushruta Samhita*:** *Sushruta Samhita* includes *Tagara* under: *Eladi Gana*, Aromatic *Vata-Kapha shamaka dravyas*(snake and scorpion poisoning) *Vatarakta* (gout),*Shiroroga, Vishachikitsa,Bhutavidya*, *Apasmara, Unmada*.[6]

Tagara in the compound formulation is beneficial in *Vranaropana* (wound healer), *Bhagna Chikitsa* (fracture), *Vatavyadhi, Visha* (poisoning), *Netraroga* or *Abhishandya* (conjunctivitis)

***Ashtanga Hridya*:** *Ashtanga Hridaya* describes *Tagara* as: *Nidrajanana, Medhya, Vatahara*, *Manovikara hara. Vagbhata* emphasized its use in: Mental disorders, Sleep disorders, Neurological conditions.[7]

Kashyapa Samhita: *Kashyapa Samhita* indirectly mentions aromatic *Medhya* drugs including *Tagara* in pediatric neuropsychiatric conditions and *graha* disorders affecting children.[8]

Tagara, as an ingredient of various herbal drugs used as *Vedanasthapana* (analgesic), *Vranya, Rajyakshma* (pulmonary tuberculosis), *Jwaraghna* (pacifies fever), *Sandhivata* (osteoarthritis*), Amavata* (rheumatoid arthritis), *Vatarakta* (gout), *Raktavikara* (blood disorders), *Shrotoshodhka* (purifies the channels), (conjunctivitis), (poisoning), *Netraroga* or *Abhishandya Yonishool* (vaginal pain), *Visha Rasayana* and *Vajeekarna* (immunomodulator**).**

Description of *Tagara* in *Nighantus:*

Kaiydev Nighantu and *Raj Nighantu* indicated *Tagara* for eyes, head troubles, epilepsy, psychiatric illness, intoxication, and poisoning conditions**.**[9,10] *Priya Nighantu* mentioned its medicinal properties and particular habitat in the Himalayan region commonly known as *Sugandhabala*, *Vidyatagar*, and *Granthikandak*.[11] *Shaligram Nighantu* describes *Tagara* as *Laghu* (light) and beneficial in nervous unrest, emotional troubles, epilepsy, insanity,

poisoning, eye trouble, skin diseases, and complexion dullness.[12] *Madanpal Nighantu* has made its existence in two forms- *Tagara, Varhima, Jihma, Wakrava, Nahusa* and *Nata* are the synonyms for the first variety of *Tagara,* while *Pindtagar, Cheen, Katu* and *Mahoroga* are the synonym for the second variety.[13]

MATERIAL AND METHODS

Valeriana wallichii DC., popularly known as *Tagara* or Indian Valerian. It is a perennial herb of Valerianaceae family found in Himalayan region and is a very important medicinal plant used in traditional medicine systems like *Ayurveda*, Siddha and Unani. *Tagara* is considered one of the *medhya rasayanas* which are a class of herbs with nootropic and nervine tonic qualities. *Tagara* is traditionally recommended in the management of *Anidra* (insomnia), *Manodaurbalya* (mental debility), *Apasmara* (epilepsy) and *Vatika* illnesses due to its relaxing and *Vata* pacifying effects.

Valeriana wallichii is a slightly hairy, tufted perennial herb up to 15- 45cm high, rootstock horizontal, thick with descending fibers. Leaves are radical, often crowded 2.5-7.5cm in diameter, long stalked, deeply cordate-ovate, usually toothed, or sinuate, and sharp-pointed (cauline leaves). Flowers white or tinged with pink, in terminal corymbs 2.5 7.5cm wide often unisexual; the male and female on different plants (dioecious). Fruit oblong, compressed, hairy or glabrous. Flowering and Fruiting during March-June [14]

Tagar, Nata, and *Nrip* synonyms of *Tagar* reflect its properties of destruction the poisonous effect and saving life, so preferred over other fragrances and poisonous herbs. *Vakra,* as it symbolizes the flowers is not straight. *Kutil* indicates the rhizome is twisted. *Kalanusarya, Balaka*, and *Chakra* synonyms in Ayurvedic texts are regarded via way of means of specific features and functions [15]

The roots of Valeriana wallichii are used in ayurveda for medicinal purposes. *Tagara* (Valeriana Wallichii) benefits its use in neurological, psychological, and digestive disorders. In low dosage, it calms the mind, strengthens nerves and prevents convulsions. Therefore, it is used in the treatment of disturbed sleep (insomnia), epilepsy, and paralysis[16].

It is used as a bactericide, CNS depressant, hypnotic, sedative, stomachic, nervine tonic, and tranquilizer in convulsions, hysteria, insomnia, neuralgia, and neurasthenia numbness. In Unani medicinal drug additionally, used for infections of the eyes and hair, ache in joints, sicknesses of the liver, the spleen and the kidney.Rootstock is stimulant, antispasmodic, and useful in superior ranges of fever and inflammation, epilepsy, and general debility .[17-18]

The dried roots and rhizomes are used by several indigenous cultures for their calming, anxiolytic, antispasmodic and analgesic effects. It has been used as a natural medicine for sleep difficulties, nervous agitation and gastrointestinal disturbances consistently in all cultures and has been demonstrated to have a role as a centrally acting herbal sedative.[19]

The phytochemical study showed the presence of a variety of bioactive compounds such as valerenic acids, valepotriates (iridoid esters), sesquiterpenoids, lignans, flavonoids and volatile oils, including borneol and isovaleric acid. These chemicals have been involved in modulation of gamma-aminobutyric acid (GABA) neurotransmission, providing a molecular basis for their CNS-depressant effects.

The traditional benefits of valerian in anxiety disorders, sleep problems, convulsions, and muscle spasms have been validated by both in vitro and in vivo pharmacological research. Furthermore, its interaction with benzodiazepine receptors, GABA-A regulation and antioxidant capability suggest it as a suitable candidate for integrative and complementary methods in neuropsychiatric and somatic diseases.

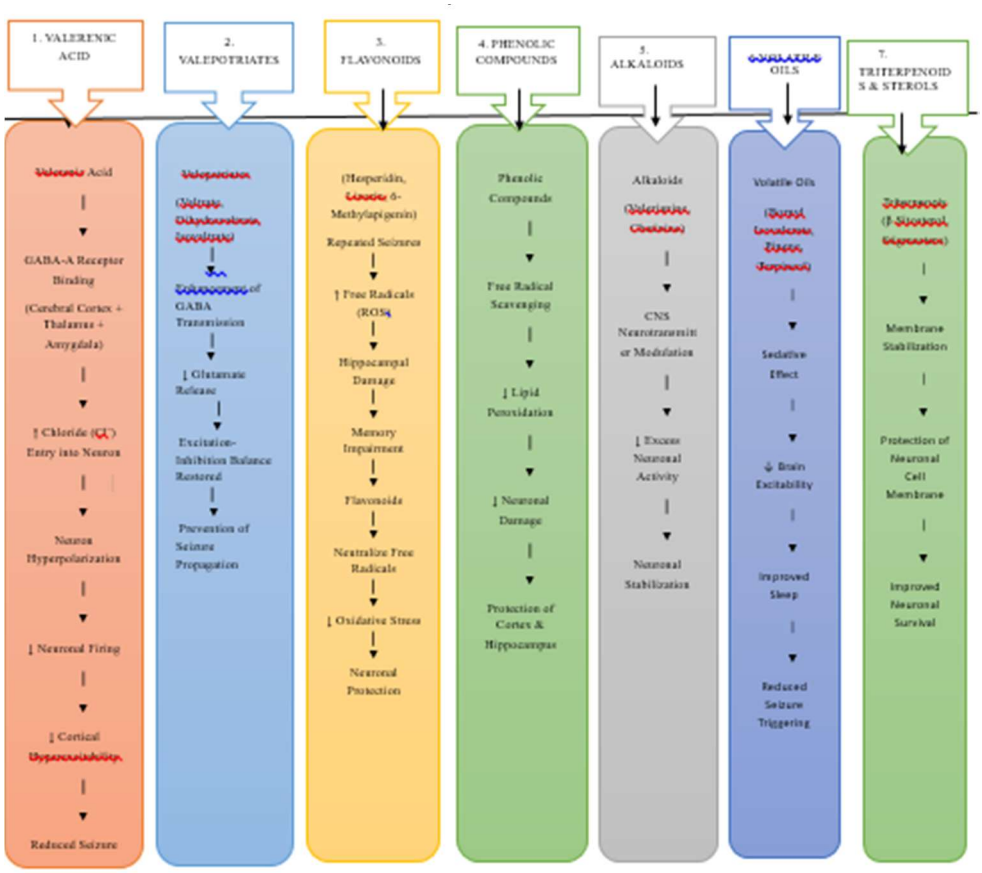
TRADITIONAL USES: -

Valeriana wallichii in classical textual indicated in *Mada* (intoxication), *Bhuta* (psychiatric disorders or microbial contamination), *Apsamara* (epilepsy) *Visha* (toxic and poisoning conditions), *Chakshuroga* (eye disorders), *Shiroroga* (headache), *Raktadosha* (blood impurity disorders), *Shula* (abdominal colic) [20] .The ancient civilizations have reportedly used the roots of V. wallichii as a diuretic, alleviating pain and spasmolytic agent [21] V. wallichii is an indigenous plant from the Indian subcontinent mentioned in all scriptures of Ayurveda. Its activity on central nervous system (CNS) is cited in *Dhanvantari Nighantu* and Bhavaprakasha, old, rare and precious books of Ayurveda [22.] It is reported to be used in the treatment of snake poisoning, obesity, insanity, epilepsy, nervous infirmity, inadequate reflexes, as hypnotic and in the diagnosis of spastic disorders, dyspeptic symptoms, habitual constipation and as cytotoxic [23.] The various actions (karma) described in ancient Ayurvedic medicine are *Medhya* (brain tonic), *Vedanasthapana* (analgesic), *Aksepahara* (anti-convulsant), *Dipana* (appetizer), *Shulprasamana, Hridaya* (cardiotonic), *Yakrduttejaka* (hepatoprotective), *Kaphaghna* (mucolytic), *Swashara* (bronchodilator), *Mutrajana* (diuretic), *Vajikarna* (aphoristic), *Arttavajanna, Vishagna* (antidote), *Balya* (tonic), *Kusta* (antileprotic), *Jwaragna* (antipyretic), *Varna Ropana* (wound healer) [24] .In ancient times, both Greece and China used Valerian, as reported by Dioscorides, Galen and available in the text of historical Chinese medication. V. wallichii is effective in dermal infections and CNS disorders [25,26]

Chemical Constituents {Phytochemistry} of Valleriana Wallichii Dc. :-

Valeriana wallichii DC. contains a diverse range of bioactive secondary metabolites concentrated mainly in the roots and rhizomes, which are responsible for its sedative, anticonvulsant, anxiolytic and neuroprotective activities.Valepotriate was first isolated from V. wallichii, and preliminary studies have confirmed the presence of a sedation ingredient. 130 iridoids from Valeriana spp. have been identified, possibly contributing to their sedative, antidepressant, and antitumor activities.[27] Rhizomes and roots contain a large proportion of volatile oil (ethereal valerianic oil), containing esters of valerianic acid (iso valerianic acid). The volatile oil contains bornyl isovalerate, formate, butyrate, and acetate, mixed with I-pinene; I camphene, and terpineol. Isovaleric acid, an oily liquid with a powerful valerianic odor and acrid burning taste is formed by ferment decomposition; two alkaloids, chatinine and valerianine, glucoside, and a resin have been recorded.[28] Rhizomes and roots also contain the principle active flavonoids 6 methylapigenin [29] Hesperdin [30] naphthalic acid, acyl linarin, linarin-O-2-methyl butyrate, valepotriates, dihydrovaltrate, linarin isovalerate.[31]The root of Valeriana wallichii contains alkaloids, tannins flavonoids, saponin, and glycosides in the methanolic extract [32] Four new iridoids, Valeriotetrates B and C (1 and 2), 8 methylvalepotriate (3), and 1,5 dihydroxy-3,8-epoxyvalechlorine A (4) were isolated from the roots of Valeriana wallichii.[33]

CHEMICAL CONSTITUENTS OF VALERIANA WALLICHII {*TAGARA*}



Details of Chemical ingredients of valeriana wallichii (tagara)[34]

1. Valepotriates (iridoid esters) - Main active principles

Valepotriates are considered as the main neuroactive ingredients of V.wallichii and display sedative, anticonvulsant and tranquilizing actions.These are unstable esters, with putative neuroactive properties. It is hypothesized that valepotriates are responsible for the anxiolytic and anticonvulsant activities. However, they are unstable and breakdown upon drying.

The major valepotriates are:

Acevaltrate , Dihydrovaltrate ,Homovaltrate , Isovaltrate , Isovaleroxyhydroxy-dihydrovaltrate ,Valtrate ,Valtrate hydrin

These compounds are unstable and degrade to baldrinals, which may also contribute to CNS effects.

Pharmacological importance: -

- GABAA modulation
- Sedative impact
- Anticonvulsant action
- Anti-anxiety (Anxiety reliever)

2. Sesquiterpenoids (sedative and anxiolytic action): These compounds are principal bioactive constituents considered to act on GABA-A receptors, which is why the plant has its depressing effects on the central nervous system. Sesquiterpenes are responsible for the aroma and neuropharmacological activity.

Important sesquiterpenes: - Valerenic acid, Hydroxyvalerenic acid, Acetoxyvalerenic acid,Isovalerenic acid, Valeranone Valerenol, Bornyl isovalerate,Valerenal, Kessyl glycol derivatives Patchouli alcohol, Viridiflorol Maalio, 8-acetoxy, patchouli alcohol

Some chemotypes of V. wallichii are rich in maaliol (≈64%) whilst other chemotypes have higher amounts of patchouli alcohol (≈40%).

Activities:

- Anxiolytic
- Spasmolytic
- Brain protection
- Inflammation-fighting

3. Essential oils (volatile oils): - Aromatic volatile oils rich in monoterpenes and sesquiterpenes are present in roots and rhizomes.

Reported constituents are: Bornyl isovalerate, Bornyl acetate, Camphene, α-Pinene, β-Pinene, Terpineol, Limonene, Caryophyllene, Myrtenyl acetate

These compounds assist:

- Aromacity
- Sedative action, light
- antimicrobial activity

4. Alkaloid

Alkaloids occur in smaller quantities but may influence CNS activity.

As an example:

• Valeriane, Chattinine, Actinidine, Valerine

Potential actions:

- Nervous system effects
- Modulation of CNS
- Sedative effects

5. Flavonoids

Flavonoids has antioxidant and neuroprotective properties.

Identified flavonoids: - Derivatives of 6-Methylapigenin ,Hesperidin, Linarin ,Quercetin, Apigenin

Biological role:

- Antioxidant activity
- Neuro-protective
- Anti-inflammatory action
- Lowered oxidative stress in neurons

6. Phenolic Compounds

Phenolics as antioxidants.

Examples are: - Phenolic acids, Tannins, Polyphenols

Biological role:

- Free radical scavenging
- Protection of the nervous system
- Anti-inflammatory effects

7. Lignans

Reported lignans in Valeriana species include compounds with:

- Antioxidant activity
- Anti-inflammatory action
- Cytoprotective

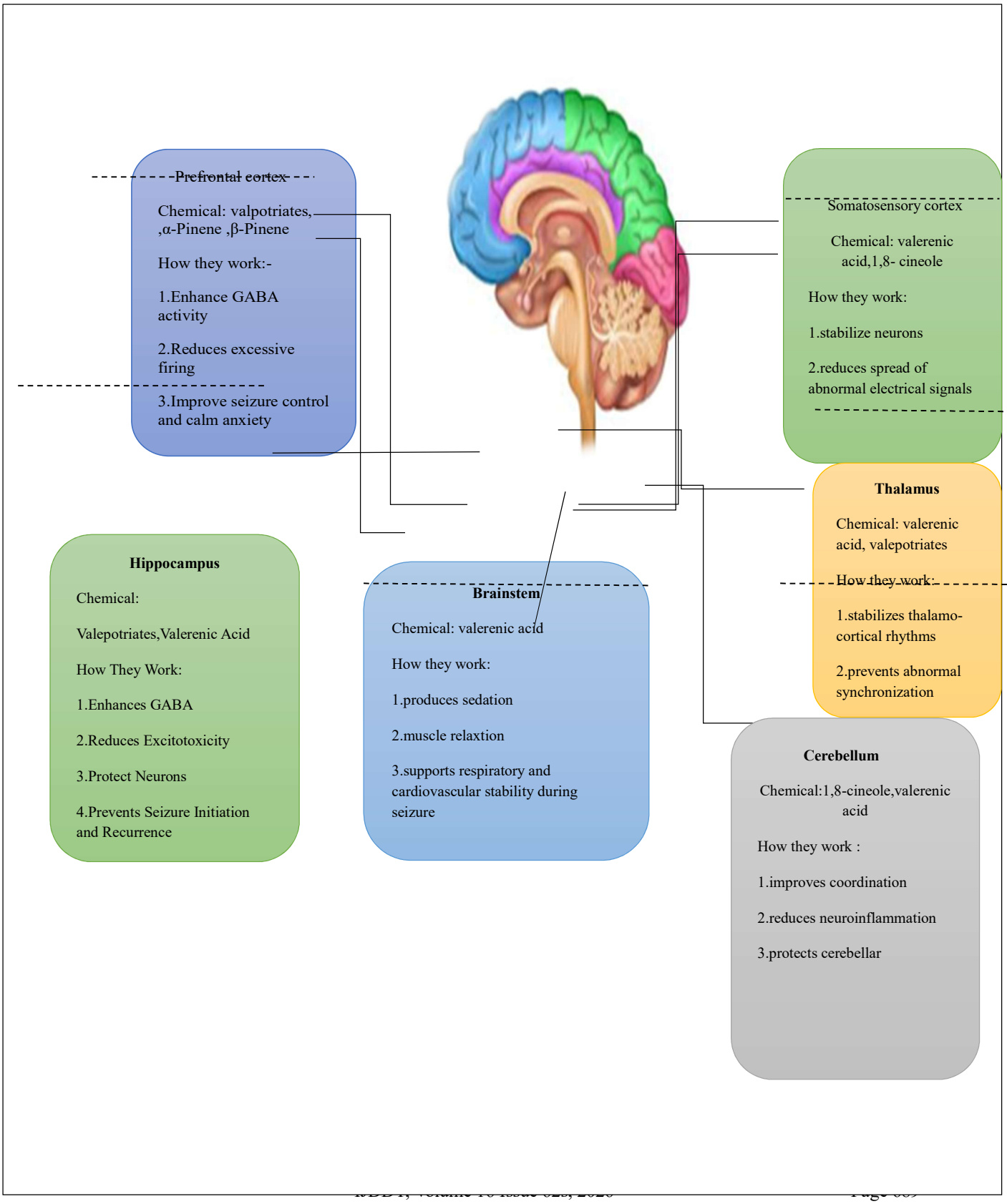
Lignans are currently being extensively investigated for their neuroprotective and anticancer properties.

8. Sterols and Triterpenes

Minor compounds are: - β-Sitosterol, Stigmasterol, Triterpenoid derivatives

Function:

- anti-inflammatory
- Stabilisation of membranes
- Immune modulation


Prefrontal cortex
Chemical: valpotriates, ,α-Pinene ,β-Pinene
How they work:-
1.Enhance GABA activity
2.Reduces excessive firing
3.Improve seizure control and calm anxiety
Somatosensory cortex
Chemical: valerenic acid,1,8- cineole
How they work:
1.stabilize neurons
2.reduces spread of abnormal electrical signals
Thalamus
Chemical: valerenic acid, valepotriates
How they work:-
1.stabilizes thalamo-cortical rhythms
2.prevents abnormal synchronization
Hippocampus
Chemical:
Valepotriates,Valerenic Acid
How They Work:
1.Enhances GABA
2.Reduces Excitotoxicity
3.Protect Neurons
4.Prevents Seizure Initiation and Recurrence
Brainstem
Chemical: valerenic acid
How they work:
1.produces sedation
2.muscle relaxtion
3.supports respiratory and cardiovascular stability during seizure
Cerebellum
Chemical:1,8-cineole,valerenic acid
How they work :
1.improves coordination
2.reduces neuroinflammation
3.protects cerebellar

2. Temporal lobe epilepsy: - Associated with: - Impaired consciousness - Memory disturbance - Emotional changes

3. Parietal and occipital epilepsy: -Associated with: Sensory symptoms Visual aura

Pathological findings: cortical Dysplasia, Neuron loss, Synaptic remodelling , Channelopathies

Tagara Potential action: - Pharmacological studies show that Valerenic acid, one of the principal ingredients of Valeriana species, has a beneficial modulation on GABA(A) receptors and potentiates inhibitory neurotransmission. Increased GABAergic activity decreases cortical excitability and inhibits epileptic discharges.

Implication:

Tagara may prevent aberrant cortical activity by the potentiation of inhibitory circuits

2. Hippocampus: An Important Structure in Temporal Lobe Epilepsy[41]

The hippocampus is one of the most sensitive structures in the process of epileptogenesis, especially in temporal lobe epilepsy. Hippocampal sclerosis is a frequent observation in refractory epilepsy and is characterized by neuronal loss and gliosis.

Histopathology findings: Growth of mossy fibers, Cell death, Increased excitatory synaptic connectivity, loss of neurons in certain areas, Gliosis, Synaptic reorganization, Oxidative damage

Repeated seizures can damage the hippocampus and affect memory and cognition.

Possible action of Tagara:

Valeriana wallichii has been shown to exhibit antioxidant and neuroprotective effects that may protect hippocampal neurons from seizure-induced oxidative stress.Repeated seizures dramatically raise oxidative stress markers. Antioxidants reduce brain damages.

implication: Neuroprotection of hippocampal neurons may delay epileptogenesis and maintain cognitive function.

3. Thalamus: Generator of Generalized Epileptic Oscillations[42,43]: -

The thalamus is reciprocally connected to the cerebral cortex through thalamocortical circuits play a crucial role in the generation and maintenance of Generalized epilepsy, especially absence seizures are linked to abnormal oscillatory activity in these circuits.

Typical observation:

Spike-wave discharges

Responsibilities: Relay of sensory, being aware, Regulating sleep, Synchrony of the cortex

Generalized epilepsy is characterized by rhythmic spike-wave discharges due to thalamocortical dysfunction.

Possible function of Tagara:

The sedative and CNS depressive characteristics of Tagara may calm thalamocortical oscillations, and minimize pathological synchronization.Valerian extracts are known to enhance sleep and lower CNS excitability, which indirectly affects control of the thalamus.

4. Amygdala and Limbic System: Emotional Aspects of Epilepsy

The amygdala is important in processing emotions and in temporal lobe seizures. Behavioral characteristics of epilepsy are hypothesized to be related to activation of the limbic circuitry.

Clinical signs: Being afraid, Worries, Emotional mood**,** Aggravation, Dysfunction of the autonomic system

Possible measures for Tagara:

Tagara may exert its anxiolytic impact by acting to diminish limbic hyperexcitability. Experimental studies show changes in GABAergic signaling associated with lower anxiety and emotional instability.

5. Basal Ganglia: Inhibitory Modulators of Seizure Propagation

The basal ganglia exert a modulatory influence on movement and inhibit cortical excitability.

There is rising evidence of participation in control of seizure termination and propagation.

Disruption means: Motor signs, Increased spread of seizure

Possible effect of Tagara:

Tagara may induce wide-spread CNS depression and modulate neurotransmitters to indirectly increase inhibitory pathways.

6. Brainstem and Reticular Activating System

The brainstem reticular formation is a network of neurons that contributes to the regulation of alertness, consciousness, and propagation of nerve signals throughout the brain. It also helps spread seizure activity from one part of the brain to another.

Potential Action of Tagara (*Valeriana wallichii*):

Tagara has chemicals like valerenic acid and valepotriates that relax the central nervous system and may boost GABA activity, helping to quiet down overactive neural firing,decrease neuronal excitability in the reticular formation, and may inhibit the spread of seizure activity to other areas of brain.It may help to better regulate seizures and to lower the intensity of seizures.

Probable Mode of Action of Valeriana Wallichii (Tagara): -

1. Epilepsy

Excess Neuronal Excitation

2. Administration Of Tagara

(Valeriana Wallichii)

3.Active Constituents

Valerenic Acid,Valepotriates,Flavonoids,Alkaloids,Other

Enhances Gaba Activity

Increases Inhibition (Increases Gaba Levels And Receptor Activity)

Reduces Glutamate Release

Decrease Excitation (Decreases Glutamate Release

5. Stabilization Of Neuronal Activity

Restores Balances Between Excitation And Inhibition

6.Antioxidant And Neuroprotective Action

Reduces Oxidative Stress And Protects Neurons From Damage

7.Ion Channel Modulation

Open K^+ Channels (Stabilizes Membrane)

Inhibits Ca^+ Influx (Prevents Hyperexcitability)

8.Sedative And Anxiolytic Effect

Reduces Anxiety,Sress And Improves Sleep Quality

Over All Effect

Reduces Seizure Frequency and Severity

Decreases Neuronal Hyperexcitability

Protects Brain and Improves Quality Of Life

1
. GABAergic Modulation (main pathway)
GABA (γ-Aminobutyric acid) is an important inhibitory neurotransmitter in the mammalian cerebral cortex and plays a key role in controlling neuronal excitability and optimal brain function.The temporal cortex is extremely susceptible to neurodegenerative processes. GABAergic neurotransmission is severely impaired. Valeric acid, the main active ingredient from rhizomes of Valeriana wallichii, increases the amount of GABA in brain. It achieves this by blocking α-ketoglutarate dehydrogenase and GABA transaminase, enzymes involved in the metabolism of GABA. Therefore, the breakdown of GABA is inhibited and its availability is raised.Valeric acid is also a functional modulator that potentiates activation of GABA-A receptors. This leads to greater entry of chloride ions into neurons, causing hyperpolarization and a decrease in neuronal activity.[44] Its impact is mediated by inhibition of GABA breakdown and potentiation of GABAergic neurotransmission and therefore creating neuroprotective effects. Furthermore, valeric acid and its class of chemicals are modulators or agonists at GABA_A receptors, resulting in enhanced chloride ion influx and neuronal inhibition.[45]
Experimental investigations have shown that Valeriana wallichii extract and pure valeric acid significantly improve cognitive function and memory in animal models of neurodegeneration. The reduction in oxidative stress, restoration of antioxidant levels and potentiation of GABAergic transmission are related to these effects . The effects were also reversed by GABAA receptor antagonists such as picrotoxin, indicating the participation of GABAA receptor-mediated pathways in the mechanism of action.[46,47]
2. Modulation of Adenosine Receptors [48]
Adenosine is a natural substance in the brain that acts on G protein-coupled receptors, mainly the A1 subtype, to dampen neuronal activity.Valeriana wallichii (Tagara) acts on adenosine system mainly through A1 adenosine receptors. The extract has increased affinity to A1 receptors and acts as a partial agonist, i.e., it activates the receptor but with moderate intensity.
Tagara acts by stimulating A1 receptors resulting in:

- Inhibition of adenylate cyclase
- Reduced intracellular cAMP levels
- Neuronal firing is reduced

So, Tagara makes: • Sedative and relaxing properties • Lower brain hyperactivity • Neuroprotective and possibly anticonvulsant effects
3. Ion Channel Modulation (Mechanistic Support)
Abnormal ion channel activity is a major contributor in the genesis of seizures. Tagara stabilizes neuronal membranes through:

- K+ channel activation → hyperpolarization
- Ca^{2+} influx block → neurotransmitter release reduction

these actions diminish neuronal hyperexcitability and suppress aberrant electrical discharges in the brain

Evidence-Based Pharmacological Actions of *Valeriana wallichii: -*
1. CEREBRO PROTECTIVE ACTIVITY: -
Experimental studies suggest the neuroprotective potential of Valeriana wallichii as it decreases the cerebral infarct size and improves the memory, motor coordination and neurological function against ischemia-reperfusion induced cerebral injury .[49]
2. ANTIDEPRESSANT AND ANXIOLYTIC ACTIVITY: -
The root essential oil of V. wallichii was found to have anti-depressant like activity by changing the level of norepinephrine and serotonin in the forebrain probably through the nitric oxide route. Also, hesperidin-containing extracts have shown anxiolytic effects through the modulation of GABA-A receptor, and might boost the therapeutic effectiveness of benzodiazepines.[50,51]
3. Sleep-Enhancing Activity: -
Bioactive components such as 6-methylapigenin and hesperidin operate on benzodiazepine-binding sites of GABA-A receptors, which result in sedative, anxiolytic and sleep promoting activities. Aqueous root extracts have also been reported to increase sleep quality by modulation of brain monoamine levels.[52,53]
4. Antioxidant and Anti-Inflammatory Activity: -
Valeriana wallichii rhizome extract possesses significant antioxidant and anti-inflammatory activities that reduces oxidative stress and neuroinflammation in experimental models of Parkinson's disease hence promoting neuroprotection.[54]
DISCUSSION
The present review reveals that Valeriana wallichii (Tagara) offers enormous therapeutic promise in pediatric epilepsy on the basis of its multi-target neuropharmacological effects. Classical ayurveda texts support the traditional use of tagara in treatment of seizures. Tagara is mentioned as a useful therapy in apasmara and other neurological illnesses.
Experimental studies have proven anticonvulsant effects of Tagara possibly through regulation of GABAergic neurotransmission and rebalancing of the excitatory - inhibitory balance disrupted during epileptogenesis. Its effects on adenosinergic pathways and ion-channel modulation may possibly contribute to seizure suppression. It also exhibits strong antioxidant and neuroprotective properties that may

potentially minimize seizure-induced oxidative stress, neuronal damage and hippocampus dysfunction.

Besides seizure control, Tagara has demonstrated anxiolytic, sedative and cognition boosting properties that may be beneficial in the therapy of common comorbidities associated with pediatric epilepsy such as sleep difficulties, anxiety and cognitive impairment. The pharmacologic profile of Tagara suggests that it may have broader neurotherapeutic benefits beyond its anticonvulsant effect.

However, present findings are mostly based on preclinical investigations and there are limited well-designed clinical studies in young populations. Variability in phytochemical content, extraction methods and dosage regimens further support the need for standardization. Future investigations should include mechanistic studies, standardized formulations and randomized controlled trials in clinical practice to determine the efficacy and safety of Tagara in pediatric epilepsy.

In conclusion, the present results support the possible use of Valeriana wallichii as a suitable supplementary therapy in pediatric epilepsy. However, it needs extensive clinical validation before it can be used widely for evidence-based care of epilepsy.

Conclusion

Valeriana wallichii (Tagara) is a well-known medicinal herb in Ayurveda and modern medicine for its neuroprotective, anxiolytic and sedative qualities. Ayurveda recommends it for balancing Vata and Kapha doshas. Traditionally, it is utilized in insomnia, anxiety, mental stress and neurological disorders. Recent studies of the traditional usage of the medication have shown benefit in epilepsy, sleep problems and neurodegenerative diseases.

The pharmacological properties of Tagara are mainly attributable to bioactive components including valerenic acid and sesquiterpenoids having GABAergic, antioxidant, anti-inflammatory and anticonvulsant activity. These therapeutic effects are associated with seizure management, cognitive support and protection against oxidative stress produced brain damage. In conclusion, the evidence appears to show that Tagara is a promising natural therapeutic agent for neurological illnesses, but more clinical trials are needed to verify its efficacy and safety for routine use.

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