Natural plant with antiepileptic properties: A review on epilepsy and it's control through naturopathy

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ABSTRACT – Epilepsy is a chronic condition characterised by transient brain dysfunction due to abrupt aberrant discharges of neuronal activity. The seizure mechanism of epilepsy is intricately linked to neurotransmitter imbalance, synaptic reorganisation, and glial cell growth. Furthermore, epileptic convulsions may result in mitochondrial impairment, oxidative stress, and disruption of glucose metabolism. Despite advancements in epilepsy research at the genetic level, current treatment and recovery outcomes for epilepsy seem unpromising. Recently, natural medicines have garnered more study attention due to their minimal toxicity and side effects, along with their remarkable effectiveness, particularly in chronic conditions. This research investigated the antiepileptic mechanisms of bioactive components in natural pharmaceuticals to inform the development of potential antiepileptic medications. This evaluation enables the clinical selection of medications based on their distinct therapeutic mechanisms among natural substances. Enhancing the precision of medicine and the cure rate is anticipated to offset the deficiency of traditional epilepsy therapy pharmaceuticals. This review manuscript is designated as a small but effective work to focus toward naturopathy for epilepsy in holistic approach and associative therapy with advance pharmacological consideration.

INTRODUCTION

Epilepsy is a neurodegenerative idiopathic hyper impulsive reoccurrence disorder. Inflammation is a physiological observative diagnostical part of this disease. Physicians tried to understand the mechanism of inflammation since they tried to know about this disease. Inflammation serves as a defensive reaction to eradicate harmful substances or damaged tissues, therefore preserving homeostasis, preventing further tissue damage, and restoring normal function. Microglia, the intrinsic immune cells of the central nervous system, become activated during inflammatory responses, resulting in harmful neurotoxic effects through the production of excessive pro-inflammatory mediators, including prostaglandin E2 (PGE2), nitric oxide (NO), cytokines, and reactive oxygen species (ROS). Activated microglia, when subjected to continuous inflammation from several stimuli, may cause neuronal damage to adjacent neurones, contributing to different neurodegenerative disorders such as multiple sclerosis, Alzheimer's disease, and Parkinson's disease. Consequently, the inhibition of inflammatory mediators by activated microglia may serve as a therapeutic target for neuroinflammatory disorders. The activation of microglial cells facilitates the abnormal production of inflammatory mediators, including nitric oxide (NO) and prostaglandin E2 (PGE2). This is considered a hallmark of neuroinflammation that leads to neuronal damage, ultimately resulting in neurodegenerative diseases. Increasing data further substantiates the involvement of reactive oxygen species (ROS) in modulating the synthesis of nitric oxide (NO) and prostaglandin E2 (PGE2), leading to inflammatory responses in microglia.
The current investigation shown that ESEAF reduces the generation of NO and PGE2 in LPS-induced BV-2 cells. The neurotoxic nitric oxide is produced from L-arginine via the catalysis of the inducible isoform of nitric oxide synthase. An

abnormal increase in iNOS levels accelerates the rise in NO production, which is regarded as a strong neurotoxin that damages lipids, DNA, and proteins.

GAMMA-AMINOBUTYRIC ACID ROLE IN EPILEPSY

Synapses and Receptors of GABA are the principal inhibitory neurotransmitter receptor combo as transducer in the cerebral cortex that regulates inhibitory tension to equilibrate neuronal excitement. Disruption of this equilibrium results in seizures. The enzyme glutamic acid decarboxylase (GAD) facilitates the production of neuronal GABA from glutamic acid, which is encoded by two distinct genes, GAD2 and GAD1. GAD1 is primarily responsible for GABA synthesis in the embryonic brain, whereas GAD2's contribution starts to rise postnatally. GAT-1 and GAT-3 are GABA transporters (GATs), and elevated levels of GAT content have been linked to seizures. GABA receptors are classified into three categories according to their distinct pharmacological properties: GABA-A, GABA-B, and GABA-C receptors. The GABA-type A receptor (GABA-A R) is identified as the primary genetic target for heritable human epilepsy. GABA-A promotes epilepsy primarily via regulating chloride ion flow or by disrupting GABAergic inhibitory input, resulting in synchronous excitatory activity throughout the neuronal population and, eventually, seizures. GABAB, via raising potassium conductance, diminishes Ca2+ influx and suppresses the release of further presynaptic transmitters. Currently, diminished or atypical GABA activity has been seen in both hereditary and acquired animal models of epilepsy, as well as in human epileptic brain tissues.

OXIDATIVE STRESS AS A PART OF EPILEPSY AND OTHER NEURODEGENERATIVE DISORDER

Oxidative stress arises when excessive reactive oxygen species (ROS) are produced together with the impairment of the endogenous antioxidant system. The increase of reactive oxygen species (ROS) activates microglia, hence intensifying neuroinflammatory responses and contributing to the advancement of neurodegenerative diseases. The abnormal generation of reactive oxygen species (ROS) triggers inflammatory responses that inappropriately release several pro-inflammatory chemicals, including as nitric oxide (NO) and prostaglandin E2 (PGE2), in microglia via the activation of many downstream signalling mediators, including NF-kB and MAPK. Consequently, the reduction of reactive oxygen species production in microglial cells emerges as a prevalent treatment objective for neuroinflammation-associated disorders. In accordance with this concept, our findings demonstrated that ESEAF effectively mitigated the generation of ROS in LPS-induced BV-2 cells, in contrast to LPS alone, which resulted in a substantial buildup of ROS. The findings show that ESEAF restores redox equilibrium and protects microglia by scavenging intracellular ROS.

Increasing scientific data indicates that therapy with anti-inflammatory drugs exhibiting antioxidant properties may reduce microglial activation and hence enhance neuronal cell survival in many neurodegenerative diseases.

NATUROPATHIC HOLISTIC APPROACH TOWARD EPILEPSY AND OTHER NURODEGENERATIVE DISORDER: *ELEPHANTOPUS SCABER*

Elephantopus scaber L. (family: Asteraceae) has been conventionally used as a traditional remedy and has been scientifically shown to possess anti-

inflammatory properties in many in vivo inflammatory models. Consequently, the antioxidant properties of *E. scaber* were examined in this work. Antioxidants are responsible for eliminating free radicals, scavenging reactive oxygen species (ROS), or limiting their excessive production, hence mitigating inflammatory and carcinogenic reactions. Various varieties of medicinal plants are designated as gojihva in India. One often referred to as gojihva is *Elephantopus scaber Linn* (E. scaber), which is part of the Asteraceae family. The herb gojihva is used to address several ailments, including respiratory disorders, cardiac troubles, coagulation problems, fever, and wound healing. Gojihva exhibits kashaya-tikta rasa, laghu guna, sheeta virya, and madhura vipaka, possessing characteristics that soothe kapha and vata doshas. Extensive research has been undertaken on Gojihva to assess its effectiveness in treating several ailments; moreover, it has notable pharmacological attributes, including anti-cancer, anti-microbial, anti-inflammatory, hepatoprotective, and antioxidant characteristics. E. scaber plants are uncommon and challenging to get due to inadequate culture and multiplication methods. Consequently, we have tried to consolidate all therapeutic benefits of E. scaber from various sources. *Entomobrya scaber* Linn is a terrestrial plant of to the Asteraceae family, widely found across India, particularly in Bengal and eastern India. The rootstock is a short, upright, rigid, perennial plant, reaching a height of around 60 cm. Leaves mostly radical in the basal rosette, with a few cauline, slightly dentate, and obovate-oblong in shape. Numerous homogeneous capitula grouped in terminal dichotomous cymose clusters. Small, actinomorphic, epigynous flowers, ranging from purple to dull pink, are each clustered and supported by a stiff, ovate leaf-like bract. The inner bracts are leafy, distinct, and light green, with a cuneate base; the pappus is bristly and hairy. The flowering and fruiting period occurs from August to December.

CHEMICAL CONSTITUENTS IN *E. SCABER*

The major chemical constitutes present in *Elephantopus scaber* are

a) **Sesquiterpene:**

Deoxyelephantopin	Isodeoxyelephantopin	Scabertopin
Isoscabertopin	Scabertopinol	Iso17,19-dihydrodeoxyelephantopin
Molephantinin	Elescaberin	Dihydrodeoxyelephantopin
Glucozaluzanin-C	Deacylcyanopicrin	Deacylcyanopicrin 3B-glucopyranoside

b) Phenolic compounds:

3,4-dihydroxybenzaldehyde, p-coumaric acid, vanillic acid, syringic acid, isovanillic acid, p-hydroxybenzoic acid, ferulic acid. 3-methoxy-4-hydroxycinnamaldehyde, tricin, Oglucuronide 6"-methyl ester and luteolin-4-O-B-D syringic acid. E-3-(3-ethoxy-4-hydroxyphenyl) acrylic glucoside was found with three polyphenolic acids, including 2-hydroxybenzoic acid, which were isolated from the trans-p-coumaric acid, methyl trans-caffeate, and trans-caffeic ethanol fractions of the plant, as well as flavonoid glycosides.

c) Triterpenoids and steroids:

Friedelin Epifriedelinol Lupeol, Betulinic Acid 30 Hydroxylupeol Lupeol Acetate, Ursolic Acid Acid ursa-12-ene-3B-heptadecanoate Stigmasterol, Stigmasterol-3-O-β-D-glucoside B-sitosterol, Daucosterol, 2,6,23-trienolide.

COMBINED UTILISATION OF NATURAL MEDICINES AND CONVENTIONAL ANTI-EPILEPTIC PHARMACEUTICALS

Pharmacotherapy remains the predominant method for managing epilepsy. The effectiveness of Western medication in managing epilepsy is evident,

accompanied by several recognised side effects, including anorexia, impaired liver function, dizziness, headaches, leukopenia, cognitive impairment, and worse quality of life. Particularly for paediatric patients, the physical harm caused by Western treatment is much larger. Conversely, natural medications exhibit little toxicity and side effects, resulting in reduced pain for patients compared to Western pharmaceuticals. Recent research have shown that the integration of traditional Chinese and Western medicine offers hope to epilepsy patients unresponsive to Western treatments. Furthermore, traditional Chinese medicine and its prescriptions may significantly enhance the effectiveness of Western treatment while efficiently mitigating unpleasant responses.

NOBILETIN WITH CLONAZEPAM

Nobiletin and clonazepam significantly reduce seizure severity. The treatment of clonazepam and nobiletin may attenuate seizure-induced elevations in apoptotic protein expression and apoptotic cell count, restore the Glu/GABA equilibrium, and control the expression of GABAA and GAD 65. Furthermore, the treatment of nobiletin and clonazepam may markedly enhance the phosphoinositide 3-kinase/protein kinase B (PI3K/Akt) signalling pathway.

NARINGIN AND PHENYTOIN

Naringin, when combined with phenytoin, has shown a protective effect against seizures and enhanced the conditioned avoidance response in a PTZ-induced kindling paradigm. This combination may enhance neurochemical equilibrium by augmenting GABA and dopamine levels, reducing Glu and MDA levels, and increasing antioxidant levels of GSH, SOD, CAT, and total thiol. Consequently, the co-administration of naringin with phenytoin is a prospective therapeutic approach for epilepsy.

Table – 1 Natural occurring plant supplements and their principal constituents used in epilepsy

Natural Drugs	**Compounds**
Salvia miltiorrhiza Bunge (Lamiaceae)	Tanshinone IIA
Curcuma longaL. (“turmeric,”Zingiberaceae)	Curcumin
MatricariachamomillaL. (Chamomile)	Apigenin
Greentea(Camellia sinensis(L.) Kuntze)	EGCG
Withaniasomnifera(L.) Dunal (Solanaceae)	WithanolideA
Curcuma longaL. (Zingiberaceae)	Curzerene
GinkgobilobaL. (Ginkgoaceae)	Bilobalide
Saffron(CrocussativusL.)	Safranal
PipernigrumL. (Piperaceae)	Piperine
AcorustatarinowiiSchott (AcorusL.Araceae)	β-asarone

CONCLUSION

Approximately 70 percent of individuals with epilepsy can effectively control seizures by medication and certain surgical interventions; nonetheless, it is crucial to acknowledge that epilepsy remains incurable and there is a persistent risk of experiencing more seizures. Epilepsy often manifests in youth, commonly between the ages of 5 and 20, however it may impact individuals of any age. Often, individuals with epilepsy have a familial history of epilepsy or seizures. Occasionally, seizures may be provoked by factors beyond your control. A high temperature may induce a seizure, even when epilepsy drugs are used. Elevated or decreased blood glucose or salt levels, as well as the use of certain drugs, may potentially precipitate a seizure. Apart from conventional drugs, naturopathy may be emerging milestone if it in accompanied with modern therapy.

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