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"Herbal Neurocosmatic Remedies to Prevent and Treat Epilepsy"

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ABSTRACTS

Epilepsy affects people of all ages and is one of the most common non-communicable brain disorders. About 50 million people worldwide suffer from epilepsy and 80 percent of cases happen in less developed countries because they cannot afford or acquire the treatments they need. Another way to use the phrase is to describe the proportion of people with active epilepsy who do not receive the proper medical attention. Medication for some epilepsy are expensive, takes a long time to start working, is prone to drug combinations, and can have dangerous adverse effects. Several synthetic drugs such as phenytoin (PHT), diazepam, and valproate are used to treat epilepsy. In addition to having a greater range of efficacy some drugs have more recent adverse effects. Both developed and developing countries now use herbal medicines and cutting-edge techniques to treat patients in order to control seizures, avoid synthetic antiepileptic drugs side effects or preserve general health. Gene therapies, stem cell therapy, deep brain stimulation, Vagus nerve stimulation, ketogenic diet therapy, biodegradable nanoparticles, nasal spray and other novel medicines for epilepsy are among the ones that are now on the market. Herbal and neuro-cosmatic remedies are being used by patients in both developed and developing nations to manage their seizures, lessen the side effects of antiepileptic medications or maintain overall health. Herbal medicines are increasingly being used as an adjuvant to treat epilepsy since they seem to be more effective and have fewer side effects. In order to enhance the interactions between the skin and the neural system, the "modern" cosmetology business is concentrating on research aimed at finding new neurocosmetic functional components. Neurocosmetic products are being developed by several cosmetic firms that operate through various processes to influence the neuro-mediators through the skin hence displaying their activity on the cutaneous nervous system. In addition to describing the characteristics of several functional molecules and products that are now available in the market this study attempts to correlates neurocosmetics entities more precisely considering the regulatory requirements. Neurocosmetic components for reducing stress are discussed along with the possible stress pathways that are linked to skin aging. Neurocosmetic techniques and "neuro-relaxing" anti-aging substances made from plant extracts are offered to fight inflammatory reactions brought on by skin stress. The molecular causes of sensitive skin and the best neurocosmetic components to address this issue are also covered. Skin aging and its theory are also discussed in order to highlight the primary use of substances that resemble Botox as the first neurocosmetics available on the market. The idea of cosmetic claims is examined in order to verify the effectiveness of the cosmetics available on the market.

Keywords: Epilepsy, seizures, antiepileptic drugs, gene therapies, Biodegradable nanotechnology, herbal medication, neurocosmetics. ingredients; skin care cosmetics; skin aging; skin stress; anti-wrinkle; cosmetics; sensitive skin; Botox-like ingredients

Key Words:-"Herbal remedes Neurocosmatic. Epileptic Therapies"

I.INTRODUCTION

The main characteristic of epilepsy, a chronic disorder affecting the central nervous system (CNS), is abnormal electrical activity in the cortical and hippocampus neurons. According to the World Health Organization (WHO), more than 5 million new instances of epilepsy are identified annually, and more than 50 million people worldwide have the disorder . In developed nations, there are about 50 instances of epilepsy for every 100,000 individuals, while in low-income nations, there are 139 cases for every 100,000 persons (Scheuer M Let.al,1990).Among the several prevalent and debilitating neurological conditions, epilepsy is now considered to be one of the most deadly .This definition defines epilepsy as a chronic alteration of the central nervous system characterized by a disturbance in neuronal electrical activity Numerous recurrent, unpredictable seizures

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are brought on by this imbalance, and depending on how severe they are, they may induce the death of neurons in particular parts of the brain (Adams M,2012) . Epilepsy can also be brought on by head trauma, brain tumors, strokes, illnesses including encephalitis or meningitis, birth defects, and sometimes even variations in blood sugar or sodium levels (FraserD.A.1996).The frequency and severity of seizures can be affected by individual variability, the area of the brain where epileptic seizures begin, and other factors(Sucher N Jand Carles M C, 2015). A large percentage of deaths from epilepsy are caused by falls, drowning, burns, and untreated prolonged seizures (Shashi K P.et.al,2014). The International League Against Epilepsy (ILAE) has defined epilepsy as a neurological disorder characterized by any of the following traits in its most recent definition: • • At least two unprovoked reflexive seizures that occur more than twenty-four hours apart. Having at least one unprovoked seizure, also known as a reflex seizure, with a high likelihood of more seizures in the ensuing decade (Jangra M K,et.al,2014). • seizures consistent with a known form of epilepsy. An epileptic seizure is a brief episode of symptoms caused by abnormally high or coordinated brain neuronal activity (Macdonald R L and Kolly K M.1995).

Types of seizures-

1. Partial focal seizures:

Origin: Begin in a single brain region. +

Depending on whether the person maintains or loses awareness during the seizure, awareness can be further categorized as follows:

i.) Simple Partial Focal Awareness: The individual is nonetheless attentive and cognizant of their environment.

ii.) Complex Partial Focal Impaired Awareness: The individual loses consciousness or has altered awareness.

Examples:

- **Focal Aware:** alterations in perception, odd tastes or scents, and jerky or twitching motions in a single body area.
- **Focal Impaired Awareness:** Disorientation, repetitive motions (such as biting or lip-smacking), or diminished awareness.

Different type of Seizures

2. Generalized Seizures:

Origin: From the beginning, influence both sides of the brain.

Types are:

Absence seizures are common in children and are characterized by brief bouts of gazing, occasionally accompanied by mild bodily movements.

Muscles become rigid during **tonic seizures**, which frequently affect the arms, legs, and back. Drop seizures, also known as **atonic seizures**, are characterized by an abrupt loss of muscular control that causes collapse or falling.

Clonic seizures are typified by jerky, rhythmic muscular movements.

Arm and leg twitches or sudden, short jerks are known as **myoclonic seizures**.

The symptoms of **tonic-clonic seizures** (grand mal) include shaking, stiffness, and loss of consciousness.

Epilepsy pathophysiology:-

The chronic neurological condition known as epilepsy is typified by frequent, unprovoked seizures that are brought on by aberrant, excessive, and synchronized brain neuronal activity. The basic pathophysiology of epilepsy centres on an imbalance between excitatory and inhibitory neurotransmission, namely involving the gamma-amino butyric acid (GABA) and glutamate systems**(Treiman, D. M. (2001)**.

1. An imbalance of neurotransmitters:-

- Seizures cause glutamate, the primary excitatory neurotransmitter in the central nervous system, to become hyperactive, which increases neuronal activity.
- On the other hand, the brain's capacity to calm hyperactive circuits may be diminished if GABA, the primary inhibitory neurotransmitter, is absent or functionally compromised.

The characteristics of seizure genesis, hyperexcitability and hypersynchrony, are

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exacerbated by this mismatch**(Treiman, D. M. (2001).**

2. Dysfunction of Ion Channels:-
The regulation of neuronal excitability is mostly dependent on ion channels, particularly sodium, potassium, calcium, and chloride channels. These channels' mutations or dysregulation may result in**(Noebels, J. L. (2003):**

- Sustained depolarization
- mpaired repolarization
- Lower seizure thresholds

3. Plasticity and Reorganization of Synapses:-
Seizures in chronic epilepsy occur because of anatomical alterations including mossy fiber sprouting and hippocampal neurogenesis, which create abnormal excitatory pathways**(Sutula, T., He, X. X., Cavazos, J., Scott, G. (1988).**

4. Neuroinflammation:-
Epileptogenesis has been linked to persistent inflammation in the brain. The activation of microglia and the production of pro-inflammatory cytokines, such as TNF-α and IL-1β, may change the integrity of the blood-brain barrier and increase hyperexcitability.

5. Oxidative Stress and Mitochondrial Dysfunction:-
Increased reactive oxygen species (ROS) and mitochondrial damage can cause apoptosis and disrupt neuronal metabolism, which can lead to brain injury and the spread of seizures.

Neurochemical Processes in Epilepsy:

Epilepsy is fundamentally a disorder of neural excitability, in which imbalances in neurochemical signaling pathways lead to recurrent, unprovoked seizures. Three major components of this imbalance include the **GABAergic inhibitory system**, the **glutamatergic excitatory system**, and **ion channel dynamics**.
a. GABAergic Inhibition:- The primary inhibitory neurotransmitter in the brain is gamma-aminobutyric acid (GABA). It is essential for maintaining neuronal activity stability since it**(Treiman, D. M. (2001))**:-

- Hyperpolarizing neuronal membranes via **GABA_A receptor-mediated Cl^- influx**.
- Modulating synaptic and extrasynaptic inhibition to suppress abnormal electrical discharges.

A decrease in GABAergic transmission causes hyperexcitability in several forms of epilepsy, either by**(Treiman, D. M. (2001)):**

i. Reduced production or release of GABA

ii. Modified expression or function of GABA receptors

iii. Increased breakdown of GABA

b. Glutamatergic Excitation:- The primary excitatory neurotransmitter in the central nervous system, glutamate is essential for memory, learning, and synaptic plasticity. But in cases with epilepsy**(Meldrum, B. S. (2002)):**

- Neurons can be harmed or killed by excitotoxicity, which is caused by excessive glutamate release or poor absorption.
- The beginning of seizures and synchronized firing of neurons are caused by the overactivation of ionotropic glutamate receptors, particularly NMDA and AMPA.

c. Ion Channel Dysfunction:- A number of channelopathies contribute to seizure activity in epilepsy. Ion channels control the movement of ions across neuronal membranes, which is necessary for the production of action potentials and neuronal excitability**(Noebels, J. L. (2003))**.

- Long-term depolarization and recurrent firing of neurons can result from mutations or dysfunctions in voltage-gated sodium channels (Na^+).
- Inhibition or delayed activation of potassium channels (K^+) results in poor repolarization, which raises excitability.

- Increased Ca^{2+} influx may induce excitotoxicity and increase neurotransmitter release through calcium channels (Ca^{2+}).
- When chloride channels (Cl^-) malfunction, GABAergic inhibition may be affected.

Mutations in sodium channel genes (e.g., SCN1A) are frequently connected to inherited epilepsies, including Dravet syndrome, but acquired epilepsy may include secondary alterations in channel expression or function.

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What is neurocosmatic ?

Neurocosmetics are cosmetic or medicinal items that influence the neurological system to improve mental health, lower stress levels, or preserve the health of neurons. This can happen directly on neural pathways or through the skin-brain axis. They frequently include bioactive substances that affect neurotransmitters, brain signaling, or sensory perception, so promoting cognitive or emotional advantages.

"**Neurocosmetics** are topical products that interact with cutaneous nerve endings and influence brain function through the skin-brain axis, promoting well-being, reducing stress, or enhancing mood."**(Misery, L. (2016)).**

Beyond Skincare: Neurocosmetics for Mood and CNS Delivery

The term neurocosmetics has historically been used to describe cosmetic products that influence the "brain-skin axis"—a two-way communication system that connects the brain and the skin's immunological, endocrine, and neurological systems. On the other hand, neurocosmetics is quickly broadening its reach to include formulations that use transdermal and olfactory delivery methods to affect mood, stress response, cognitive performance, and even neurological diseases.

1. The Brain–Skin Connection:- A two-way communication mechanism, the brain-skin link involves the cutaneous, immunological, endocrine, and neurological systems. In addition to serving as a barrier of defense, this integrated network allows the skin to function as a neuroimmunoendocrine organ that may react to physiological, emotional, and environmental inputs. Neurocosmetics, particularly those that seek to affect mood, stress reaction, or neurological function through the skin, has a scientific basis thanks to an understanding of this link.

i. Neuroendocrine Functions of the Skin: The broad network of the skin includes**(Slominski, A., Zmijewski, M. A., & Paus, R. (2013))**:

- Nerve endings that sense things (connected to the peripheral nervous system)
- receptors for neuropeptides (calcitonin gene-related peptide, for example, for substance P)
- Hormone receptors (for example, serotonin, melatonin, and cortisol)
- Keratinocytes and melanocytes that can imitate certain aspects of the HPA axis by synthesizing neurohormones such CRH (corticotropin-releasing hormone) and ACTH (adrenocorticotropic hormone).

ii. The Skin as a Sensory and Emotional Organ:- he skin has abundant C-fiber and mechanoreceptor innervation, which enables it to react to**(Arck, P. C., Slominski, A., Theoharides, T. C., Peters, E. M., & Paus, R. (2006))**:

- Feeling and temperature
- Emotional states, like tension or anxiety
- Transdermal and olfactory cues from neurocosmetic applications

This reaction is mediated by the brain-skin axis, in which cutaneous stimulation can alter brain activity, mood, and perception, while emotional impulses from the brain influence skin condition (e.g., eczema under stress).

iii. Therapeutic Implications: Herbal Neurocosmetics:- Neuroactive chemicals included in many herbal treatments can be delivered transdermally or olfactorily thanks to the brain-skin link. As an example**(Denda, M. (2014))**:

- When ingested or used topically, essential oils like lavender, bergamot, and chamomile can lower anxiety and alter brain waves.
- In topical preparations, extracts of ashwagandha and bacopa monnieri may have adaptogenic and neuroprotective effects through the skin.

Based on these discoveries, active compounds derived from plants affect brain chemistry via the skin-brain axis in herbal neurocosmetic treatments.

Herbal products as neurocosmetics:-

Products that affect the peripheral nervous system or the tiny nerve endings in the skin when applied topically are referred to as neurocosmetics. Both products intended to reduce wrinkles and facial lines and those that relieve itching are included in this category. It has long been recognized that the brain and skin are connected. However, the scientific study of skincare products that interact with the neural networks of the skin to affect both skin health and mental well-being is known as neurocosmetics. The cosmetics business is experiencing excitement as a result of the increased understanding of the connection between the skin and the brain. The way that some skin care products

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may affect mental health is a clear example of this reciprocal interaction. The application of peptides, such as neuropeptides, in neuro cosmetic formulations is one such instance. Neurotransmitters like beta-endorphins and occasionally even oxytocin are released when these peptides attach to receptors on skin cells. Our moods may be affected by the exciting or relaxing effects of this connection. These peptides also encourage the synthesis of collagen, which aids in skin renewal and healing.

Table – 1 (Herbal products as neurocosmetics)

S.no	Plant name	Uses	Reference
1	Passiflora Incarnata (passionflower)	Sedative anticonvulsant	SoulimaniR et al., 1997
2	Valerianaofficinalis (Valerian)	Sedative antispasmodic	Cropley M et al., 2017.
3	Withania Somnifera (Ashwagandha)	Anticonvulsant Adaptogen	Ulkarni S K et al., 2008.
4	Centella Asiatica (Gotu Kola)	Neuroprotective Anticonvulsant	Brinkhaus B et al., 2000
5	Glycyrrhiza Glabra (Licorice)	Anti-inflammatory Neuroprotective	Beshbishy A M et al., 2020.
6	Curcumalonga (Turmeric)	Anti-inflammatory Anticonvulsant	Vaibhav K et al., 2013
7	Piper nigrum (BlackPapper)	Enhances bioavailability of othertreatments Antic onvulsant	Sudjarwo S A et al., 2017.
8	Zingiberofficinale	Anti-inflammatory Anticonvulsant	Ali B H et al., 2003.
9	Rauwolfia Serpentina	Anticonvulsant	Akhondian J et al., 2011.
10	Scutellaria Lateriflora	Anticonvulsant Neuroprotective	Awad R et al., 2003
11	Melissaofficinalis	Sedative, reduces frequency	Cases J et al., 2011
12	Pipermethysticum (kava)	Sedative anticonvulsant	Grunze H et al. 2001.
13	Cannabissativa (Cannabis)	Anticonvulsant seizuresfrequency	Devinsky O et al., 2014.
14	Psidium guyanesis	Anticonvulsant	Komali E,2021.
15	Bacopa monnieri(Bramhi)	Anticonvulsant	Komali E,2021.
16	Taxus wallichiana(Himalayan	asthma, inflammatory	Kumar S. 2015.

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	yew)		
17	Argemone mexicana (Mexican poppy)	skin disorders, jaundice, and microbial infections	Sharma A, 2019.
18	Magnolia grandiflora(Evergreen magnolia)	epilepsy, depression, and anxiety	Kim J H.2017
19	CestrumNocturnum(Night-blooming jasmine)	Anticonvulsant	Alam M A2021
20	Ziziphus jujube (Chinese date)	Anticonvulsant	Zhao Z,2013
21	Scutellaria Baicalensis (Baikal skullcaps)	neuroprotective, antioxidant, and anti-inflammatory	Li H B, 2008.
22	Ficus platyphylla	Anticonvulsant, anti-inflammatory	Elufioye T O,2004.
23	Passiflora incarnata (Passionflower)	Anticonvulsant	Dhawan K, 2004.
24	Zingiber officinale(Ginger)	anti-inflammatory, antioxidant, and neuroprotective	Sharma M,2019
25	The Rhodiola	anti-inflammatory, antioxidant, and neuroprotective	
26	Salvia miltiorrhiza Bunge (Lamiaceae)	Antioxidant , Anti-inflammatory , Neuroprotective	Buenafe et al. (2013); Tan et al. (2014)
27	Nandina domestica Thunb (Berberidaceae)	anti-inflammatory, antioxidant, and neuroprotective	Yuan (2016)
28	Acorus tatarinowii Schott (Acorus L. Araceae)	Anti-inflammatory Anticonvulsant	Yuan et al. (2019)
29	Cortex fraxini (Fraxinus rhynchophylla Hance)	Anti-inflammatory, Antioxidant, Dermatosis	Xiang et al. (2014)
30	Erythrina mulungu Mart ex Benth (Leguminosae-Papilionaceae)	Anti-inflammatory, Antioxidant	Xiang et al. (2014)
31	Coptis chinensis Franch., C.(Ranunculaceae)	Antifungal, Anti-inflammatory, Anticancer	Yang et al. (2018)

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32	Aconitum carmichaeli Debx. (Ranunculaceae)	Analgesic, Antirheumatic, and Antiarrhythmic, Anti-inflammatory and Antitumor, Antioxidant and Anti-aging	Xiang et al. (2014)
33	Saffron (Crocus sativus L.)	Anti-inflammatory, Antioxidant	Xiang et al. (2014)
34	Capsicum annuum L. (Solanaceae)	Cosmetics and Pharmaceuticals, Anti-inflammatory, Antioxidant	Xiang et al. (2014)
35	Ginkgo biloba L. (Ginkgoaceae)	Antioxidant, Anxiety and Depression	Xiang et al. (2014)
36	Dennettia tripetala Baker f (Pepperfruit)	Anticonvulsant	Oyemitan et al. (2013)
37	Matricaria chamomilla L. (Lauraceae)	Anti-inflammatory Anticonvulsant	Garlet et al. (2017)
38	Rhododendron tomentosum (Ledum palustre)	Anti-inflammatory Anticonvulsant	Abbasi et al. (2017)
39	Radix bupleuri *(*Bupleurum L.*)*	Anti-inflammatory Anticonvulsant	Xiang et al. (2014); Xie et al. (2013)
40	Smoke tree *(*Cotinus coggygria*)*	Wound Healing, Anti-inflammatory	Diniz et al. (2015)
42	Maclura tinctoria (Moraceae)	Anti-inflammatory Anticonvulsant	Lee et al. (2018)
43	Withania somnifera (L.) Dunal *(*Solanaceae*)*	high blood pressure, arthritis, diabetes, Alzheimer's disease, and depression	Xiang et al. (2014)
44	Plantago asiatica L (Plantaginaceae	Antipyretic, anti-inflammatory	Diniz et al. (2015)
45	Glabridin	cosmetics and skin care for its potential anti-inflammatory, anti-melanogenesis, and skin-brightening properties	Hanrahan et al. (2015)
46	Uncaria rhynchophylla	Neuroprotective,	

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		Anticonvulsant, Anti-inflammatory	
47	Gastrodia elata	Anticonvulsion Anti-inflammation Antioxidation Neuroprotection	
48	Bupleurum chinense	Anticonvulsion Neuroprotection	
49	Cistanche deserticola	Anticonvulsion Antiapoptosis	
50	Bombyx mori	Anticonvulsion Antiapoptosis Antioxidation Neuroprotection	
51	Acori tatarinowii	Anticonvulsion Antiapoptosis Neuroprotection	

ADVANCED METHODS FOR COPING WITH EPILEPSY

Even with common therapies like antiepileptic medications and, in severe cases, surgery, epilepsy—a neurological condition characterized by recurrent seizures brought on by abnormal brain electrical activity—presents challenges(Akhondian J, Kianifar H R, KhajedalueeM, Tahri H) . However, new therapeutic choices are being developed as a consequence of advances in medical research, offering a way of relief to people who find conventional therapies ineffective or unsatisfying.The new method listed below is now being employed to increase the variety of treatment option(AwadR, Arnason J T, Trudeau V, Bergeron C, Budzinski J W,Cases J, Ibarra A, Feuillere N, Roller M).

I.) Vagus Nerve Stimulation (VNS)

The increasing use of vagus nerve stimulation therapy for the treatment of epilepsy, the field of neurostimulation has made considerable strides.All age groups and seizure types can benefit from VNS therapy, which entails implanting a device that sends electrical impulses to the vagus nerve, a nerve that runs from the brain to the belly.The purpose of this stimulation is to alter brain activity, which may lessen seizure frequency and intensity. A bipolar VNS lead, a programming wand with software that works with a portable device, a tunneling tool, handheld magnets, and a pulse generator are essential parts of the VNS therapeutic system. The software allows the programming wand to modify stimulation parameters by interacting with the generator, as is seen in figure, while the generator stimulates the vagus nerve through the lead(Grunze H et al.,French J A, White H S, Klitgaard H, Holmes G L, Privitera M D.).

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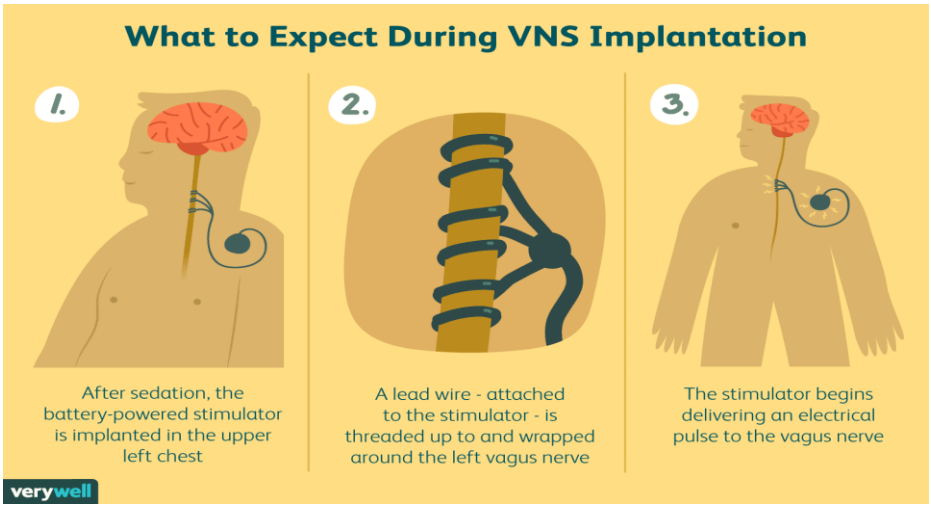

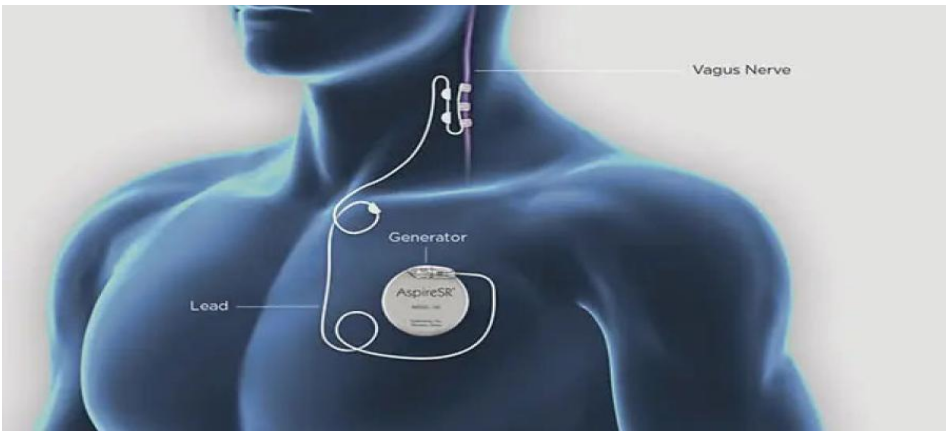

In addition to its well-established effectiveness in controlling seizures, Vagus Nerve Stimulation (VNS) therapy has been shown to improve mental health, sleep quality, hospitalization rates, and the likelihood of reducing prescription use. Modulation of VNS intensity is still essential since it enables customized modifications to minimize possible adverse effects and maximize seizure control. Additionally, the versatility of VNS treatment in conjunction with traditional anti-seizure medication is highlighted by the ability to modify stimulation levels during the day and night and to deliver increased stimulation in advance of seizures(Mesraoua B, Deleu D, Kullmann D M, Shetty A K, Boon P,Ghosh S, Sinha J K, Khan T, Devaraju K S, Singh P) .

II.) Deep brain stimulation (DBS)

As seen in figure 2, Deep Brain Stimulation (DBS) is an invasive neurosurgery procedure that uses implanted electrodes to send regulated electrical impulses to deep brain areas. Generally speaking, it is advised for those with hard-to-treat focal epilepsies who are not good candidates for traditional surgery(Fukuda M, Matsuo T, Fujimoto S, Kashii H, Kumada S, Ishiyama A.,Gonzalez H F J, Yengo-kahn A, Englot D J.).FDA-approved stimulation of particular regions, including the ictal onset zone and the anterior thalamus, has demonstrated a notable and long-lasting decrease in seizures. Clinical studies have demonstrated that DBS can dramatically lower the frequency and severity of seizures, improving the quality of life for many individuals.Research is still being done to optimize target regions and stimulation settings for DBS in order to increase its effectiveness and safety for treating epilepsy(Uthman B M, Wilder B J, Penry J K, Ramsay R E,Ben-Menachem E. ,Tobias L, Andrew P, Silvia N, Kenneth B.).

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III.) Responsive neurostimulation (RNS)

In the treatment of epilepsy, responsive neurostimulation (RNS) is a novel strategy, especially for those whose reaction to traditional therapy like medication or surgery is insufficient. With RNS technology, a neurostimulator device that continually tracks neural activity is implanted inside the brain. When the gadget recognizes aberrant electrical patterns that point to an imminent seizure, it sends out specific electrical pulses to break the patterns and stop the seizure(Laxpati N G, Kasoff W S, Gross R E).By addressing epileptogenic activity as it occurs, this responsive, real-time intervention aims to reduce seizure frequency and intensity .RNS may be a viable choice if the epileptogenic zones in individuals with focal epilepsy are challenging to treat, since studies have shown that it can considerably lower seizure frequency(Matias CM, Sharan A, Wu C.).Furthermore, RNS might provide important information for future study by shedding light on the neuronal processes of epilepsy. The system's adaptability, which permits modifications in response to the patient's changing neurological profile, gradually increases its effectiveness. RNS greatly enhances many patients' quality of life by giving them greater control over their seizures and lessening the crippling symptoms of the disorder, even if it cannot cure epilepsy(Schulze-Bonhage A.)

IV.) Gene therapy

An increasing amount of preclinical evidence suggests that gene therapy might be a useful treatment for a sizable percentage of epileptic patients for whom no other treatments are helpful.Gene therapy includes altering the function of preexisting genes and altering gene editing in addition to introducing beneficial gene variants into cells(Boon P, Vonck k, Herdt V D, Goethals M) .
Methods for treating epilepsy that involve gene therapy may be roughly divided into two categories: those that target the gene deficiency in hereditary variants of the disorder and those that concentrate on the mechanism or mechanisms producing seizures(Bergey G K, Morrell M J, Mizrahi E M.,Fisher R S et al).
To alter gene expression, target cells are exposed to exogenous nucleic acids during gene therapy. Frequently, carriers, sometimes referred to as vectors, are used to transfer these big, negatively charged macromolecules. The mechanism of gene therapy is shown in figure 4 below.Because the blood-brain barrier (BBB) prevents genetic vectors from passing through the circulation and into the brain, it presents a serious therapy obstacle for epilepsy. The selection of viral vectors, promoters, and transgenes are only a few of the variables that must be considered when using gene therapy in clinical settings(Bergey, Gregory K N,Kaur S, Kumar R, Singh A P, Singh A P, Malhotra M.,Street J S, Qui Y, Lignani G).

V.) Stem cell therapy

Stem cells may develop into a variety of cell types, are self-renewing, and are immortal.Stem cells can come from a variety of sources, such as tissues from adults, embryos, and fetuses. including other diseases, neurological problems including epilepsy, spinal cord injury, and stroke may be treated using several kinds of stem cells(Kanasty RL, Yin H, Eltoukhy AA, Vegas A J, Anderson D G,Balagura G, Guglielmo A, Riva A, Iacomino M, Amadori E.).The loss of inhibitory GABAergic neurons is connected to recurrent seizures. Therefore, damaged interneurons may be replaced with GABAergic precursors after transplantation to enhance inhibitory synaptic function and reduce the frequency of spontaneous seizures (Van Emde BW, Blume W, Elger C, Genton P, Lee P,Goodarzi P, Aghayan H R, Soleimani M, Norouzi-Javidan A). Presently, progenitors from the medial ganglionic eminence (MGE), either from fetal brains or human-induced pluripotent stem cells, have shown remarkable effectiveness in treating epilepsy, especially temporal lobe epilepsy, in a novel way.Medial ganglionic eminence cells move broadly, mature into GABAergic interneurons, and successfully integrate into the brain's hippocampal region to enhance inhibitory synaptic neurotransmission. Pluripotent cells seem to be the ideal donor cell type for MGE progenitors since they don't raise any ethical concerns and complement patient-specific cell therapy for non-genetic epilepsy(Mesraoua B, Deleu D, Kullmann DM, Shetty AK, Boon P,Shetty AK, Upadhya D,Upadhya D, Hattiangady B, Castro OW, Shuai B, Kodali M).

VI.) Biodegradable nanoparticles

Numerous therapy modalities are required for epilepsy because of its intricate etiopathogenesis. Antiseizure drugs are quite successful in controlling seizures, however their limited therapeutic index and many medication interactions make it difficult

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for them to be used widely. The blood-brain barrier (BBB) protects the brain's microenvironment and controls the flow of nutrients and xenobiotics by acting as a physical and metabolic barrier. Given this, nanoparticles (NPs) are a viable means of getting beyond the blood-brain barrier and obtaining therapeutic dosages of antiseizure drugs (ASMs).Because of their capacity to cross the blood-brain barrier, enhance brain targeting, reduce side effects, and allow for continuous medication release(Perucca P, Scheffer IE, Kiley M.,Marchi N, Granata T, Ghosh C), biodegradable nanoparticles are increasingly being used in the treatment of epilepsy. It is possible to design these nanomaterials such that they will break down into non-toxic byproducts inside the body after reaching the target site and staying stable at non-target areas. The two main categories of biodegradable nanoparticles are polymeric and lipid nanoparticles(Han H, Mann A, Ekstein D, Eyal S.,Su S, Kang PM.Jabir N, Tabrez S, Firoz CK, Zaidi S, Gan S).

VII.) Ketogenic diet therapy

The main therapy for the majority of people with epilepsy is antiseizure drugs (ASDs). Nonetheless, 30% of patients believe that ASDs are useless. In these situations, nonpharmacological treatments are taken into consideration, such as ketogenic diet therapy (KDT) and a glutamate-reduced diet.The ketogenic diet is a low-carb, high-fat strategy that simulates hunger and offers people with drug-resistant epilepsy an alternative non-pharmacological therapy(Zhu H, Zhang Y, Kong C, Du J, Wu X, Qin H.).Patients with drug-resistant epilepsy may require nutritional treatment once traditional medications are ineffective.This dietary strategy, which is advantageous for both adults and kids, calls for meals that are high in fat and low in carbohydrates(Williams T J, Henry-Barron B J, Olieman J F,Duvekot J J, Vermeulen M J, Bannink N.). The first line of treatment for diseases like pyruvate dehydrogenase insufficiency and glucose transporter 1 deficient syndrome is ketogenic diet therapy.Children who don't react well to anti-epileptic medications (AEDs) should have it. Because KDTs block vesicular glutamate transport, alter metabolism by lowering mitochondrial ATP synthesis and glycolysis, activate ATP-sensitive potassium channels to lower neuronal excitability, increase polyunsaturated fatty acids, and lower reactive oxygen species through mitochondrial dissociation, their therapeutic potential is greater than that of pharmaceuticals.Therefore, KDTs have neuroprotective benefits by resolving cellular energy deficits and guarding against brain damage caused by epilepsy, in addition to reducing neuronal hyperexcitability(Lyons L, Schoeler N E, Langan D, Cross J H,Nisa Mughal Z U, Maalik A, Rangwala B S,Perucca E.,Devinsky O, Cross H J, Wright S).

VIII.) Cannabidiol therapy (CBD)

Cannabidiol (CBD) therapy has become a viable treatment option for epilepsy, providing a fresh method of handling this intricate neurological condition. By interacting with the endocannabinoid system, CBD may have anticonvulsant effects that reduce seizure activity. It has been shown in clinical trials and observational studies to be effective in lowering the frequency and intensity of seizures, especially in individuals with refractory epilepsy syndromes including Dravet syndrome and Lennox-Gastaut syndrome(Thiele E A. Marsh E D, French J A, Mazurkiewicz-Beldzinska M, Benbadis S R, Joshi C,López-García, M.A., Feria-Romero, I.A., Segura-Uribe, J.J., Escalante-Santiago, D., Orozco-Suárez, S.). In addition, CBD has a better safety record than conventional antiepileptic medications, with less side effects. However, there are still issues in clarifying its mechanisms of action and optimizing dosage schedules. In order to ensure evidence-based practice and patient-centered care, researchers, medical professionals, and regulatory agencies must work together to further investigate the therapeutic potential of CBD in the treatment of epilepsy(Smith, Yolanda.). This synthesis provides a thorough assessment of the state of knowledge and potential future paths of CBD therapy in the treatment of epilepsy by drawing on influential research papers, clinical trials, and expert consensus statements in the area.

For patients with epilepsy who are not receptive to traditional therapy or who have severe side effects from drugs, the aforementioned cutting-edge approaches provide an option.However, in order to fully determine their efficacy, safety, and long-term effects, more study is necessary(Kryshtopava, Maryna.).

Energy-based therapies: These treatments make use of energy fields. Reiki and therapeutic touch are examples of biofield treatments that use the body's energy fields.

Reiki therapies :- Reiki is an alternative medicine that originated in Japan and is a pseudoscientific energy healing technique.[Belcaro, G.V. (2018)] Reiki practitioners employ a method known as palm

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healing, or hands-on healing, in which they believe a "universal energy" is transmitted to the client through the practitioner's palms in order to promote either physical or emotional recovery. Its foundation is qi ("chi"), which practitioners claim is a universal life energy despite the lack of factual proof for its existence.
The average length of a session is one hour. A "Level 1" practitioner spends a number of minutes placing one or more hands on or close to different body areas. It is intended for a vital energy to enter the client's body during this period from the practitioner. Another option is for "Level 2" practitioners to provide their services remotely, without making physical contact.[Russell J; Rovere A, eds. (2009)]

Reiki and homeopathy compete to be the "one quackery that rules them all" because to its "sheer ridiculousness and disconnect from reality," according to David Gorski.[Gorski DH (9 March 2020). "No, editors of The *Atlantic*, reiki does not work"] "Fraudulent misrepresentation" is how lawyer and alternative medicine critic Jann Bellamy has characterized reiki marketing.[Bellamy, Jann (12 June 2014). "Reiki: Fraudulent Misrepresentation". *Science-Based Medicine*. Archived from the original on 21 March 2021. Retrieved 21 April 2021.].

Aromatherapy:- There are several advantages to using essential oils. It contains emotional and spiritual components in addition to its ability to improve physical health. This can occasionally be fantastic, and other times it may not be.

Before starting any treatment, it is crucial to confirm that a person does not have epilepsy because some essential oils have the potential to cause an epileptic-like fit in those who are vulnerable. This is a question that a qualified aromatherapist will always ask before to the initial session.

Essential oils are safe as long as all known precautions are taken and they are utilized appropriately in the right proportions. specific oils should only be used sparingly since they can be harmful in specific situations, such as epilepsy and pregnancy.

The quantity and frequency of usage, along with the appropriate packaging (integral drop dispensers, for example), reduce the likelihood of any negative effects.
All individuals involved in the use of essential oils as therapeutic agents must prioritize safety; storage and transportation have an obligation to adhere to existing laws. In order to benefit from essential oils' therapeutic qualities, aromatherapists only utilize extremely little quantities of them.
Essential oils that can be used to diseases related to epilepsy

- Basil oil (Ocimum basilicum) • Bay Laurel oil (Laurus nobilis)
- Black Cumin oil (Nigella sativa)
- Cedar Himalayan oil (Cedrus deodara)
- Chamomile German oil (Matricaria recutita)
- Chamomile Roman oil (Anthemis nobilis)
- Clary Sage oil (Salvia sclarea flos, fol)
- French Lavender (Lavendula stoechas)
- Lemongrass oil (Cymbopogon citratus)
- Linden Blossom (Tilia europaea)
- Neroli oil (Citrus aurantium var. amara flos.)
- Petitgrain oil (Citrus aurantium var. amara)
- Spikenard oil (Nardostachys jatamansi)
- Sweet Marjoram oil (Origanum majorana)
- Valerian European oil (Valeriana officinalio)
- Valerian Indian oil (Valeriana wallichii rad.)

Ayurvedictherapy:- Ayurveda treats epilepsy in a variety of ways, including host-specific and disease-specific measures, as well as pharmacologic and nonpharmacologic methods. As to Ayurveda, when treating epilepsy, it is crucial to prioritize assurance, comorbidity control, and disease modification over

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merely managing seizures. Psychotherapy and other nonpharmacologic therapies are recognized by Ayurveda as being essential to the treatment of Apasmara. A typical Ayurvedic treatment approach for epilepsy is shown in Chart 1, which is based on Ayurvedic scriptures [Agnivesha, Charaka Samhita]. Sushrutha Samhita and Charaka Samhita of Agnivesha are the sources of this information. Sanskrit was the original language of these ancient books, which have now been translated into English and other languages and published in several versions.

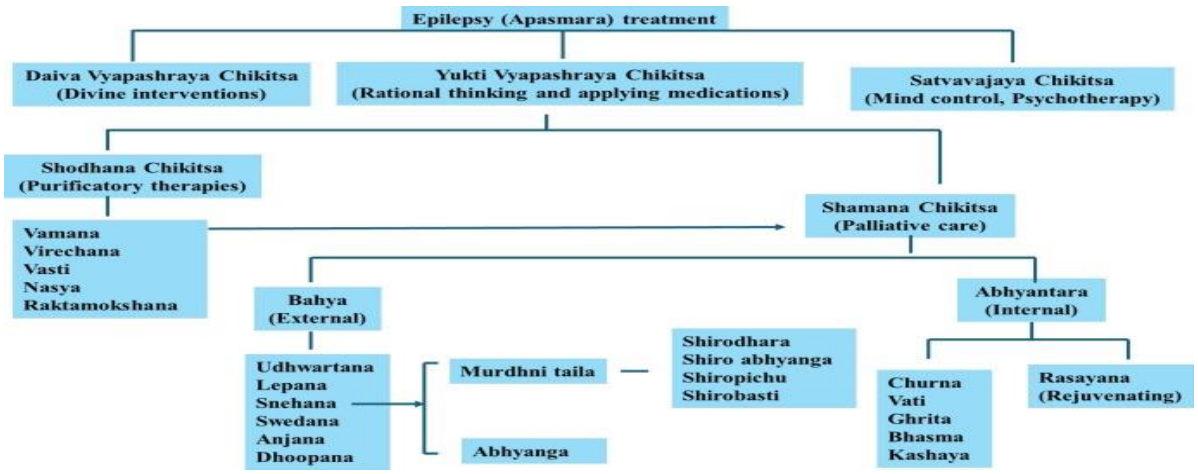

Figure- various therapy modalities used to treat epilepsy are demonstrated.

Three forms of treatments—daiva vyapashraya chikitsa, yukti vyapashraya chikitsa, and satvavajaya chikitsa—are often employed to control epilepsy, depending on the patient's condition [22]. Treatment is referred to as chikitsa.

Daiva vyapashraya chikitsa- These days, it is less customary to adopt the faith therapy known as Daiva Vyapashraya Chikitsa, which incorporates supernatural interventions.

Satvavajaya chikitsa- Using yoga, pranayama, spiritual knowledge, philosophy, and behavioral treatments, Satvavajaya Chikitsa is used to manage the mind in order to balance the functioning of the many mental qualities, such as intelligence, memory, fortitude, etc. [Agnivesha, Charaka Samhita]. Ashtanga yoga's pranayama focuses on breath control. By increasing vital energy and promoting lifespan, it can aid in the treatment of illnesses. Asanas, or bodily position, is the third phase of Ashtanga yoga. It usually refers to different meditation sitting postures. In order to prevent and cure illnesses, yoga practitioners can stay in a variety of comfortable positions.

A. **Yukti vyapashraya chikitsa**-The primary treatment is Yukti vyapashraya chikitsa, which consists of medication and therapy grounded on reason. Each patient is given a customized course of therapy depending on his or her body's dosha and the illness. Shodhana chikitsa (purificatory procedures) and shamana chikitsa (palliative care) are two tactics used in Yukti vyapashraya chikitsa.

i. Shodhana chikitsa-
A variety of shodhana chikitsa are accessible, such as rakta mokshana chikitsa, vasti (also known as basti) chikitsa, vamana chikitsa, virechana chikitsa, nasya chikitsa, and others []. Vamana chikitsa, also known as "emesis therapy," is a detoxification procedure that includes medically induced vomiting under strict supervision to rid the body of kapha dosha, which may otherwise lead to illness. The method known as Virechana Chikitsa involves carefully administering herbal purgatives to induce therapeutic purgation for a predetermined amount of time in order to eliminate pitta dosha from the body. The term "vasti" refers to the anal administration of drugs (enema) to eliminate the body's vata dosha and bio-purify the colons by draining out toxic waste. It comes in two varieties: a retention enema and an evacuator, both containing fat components and medicinal decoctions. Nasya chikitsa is the term used to describe giving a patient various

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medications via the nose (Fig. left panel). The therapeutic process of bloodletting is used in Rakthamokshana Chikitsa to eliminate circulating poisons that have been there for a long time.

Figure- Patients' manifestation of nasya, udhwartana, and shirodhara chikitsa.

ii. Chikitsa Shamana-There are two varieties of shamana chikitsa: abhyantara chikitsa (internal medication) and bahya chikitsa (external administration of medicaments).

a. Bahya chikitsa

Among the several forms of Bahya chikitsa are udhwartana, lepana, snehana, anjana, dhoopana, and others. Murdhini taila and abhyanga (massage treatment) are two forms of external therapy, or oleation. There are four varieties of murdhni taila, or oleation to the head: shirodhara, shirobasti, shiropichu, and shirodo abhyanga.

Whereas lepana chikitsa is applying herbal medications and medicinal oils to various body areas, udhwartana is a deep-tissue massage using herbal powders and oils. The internal administration of medicated lipid and external massage treatment can be used as a prelude to purification therapies in order to release the body's toxins and doshas. This is known as snehana or oleation therapy. As the only external primary therapy, snehana can be as simple as a massage with medicated oils that includes various oleation techniques for the head, such as shiroabhyanaga, shiropichu, shirodhara, and shirobasti, as well as simultaneous synchronized massaging of the entire body in the same direction. To soothe, relax, and reduce tension, Shiro Abhyanga applies a warm, herbal remedy with oil to the head and massages it gently. Shiro dhara chikitsa involves continuously applying a mixture of certain taila (oil) and other herbal remedies on an epileptic patient's forehead (Fig. 1, right panel). Shiro pichu chikitsa involves placing cotton swabs dipped in herbal oils over the head for a predetermined amount of time in order to alleviate tension and anxiety. To reduce tension and promote relaxation, medicinal herbal oils are applied to the head using a leather hat in shiro basti chikitsa.

b. Abhyantara chikitsa-

Oral medication consumption, including churna, vati, gritha, bhasma, kashaya, rasayana, and so on, is a component of abhyantara chikitsa. While vati refers to Ayurvedic medications in the form of tablets or pills, churna is a blend of finely powdered herbal remedies. Ghrita are ayurvedic medications made from ghee. Whereas water-based medicinal herb extracts are known as Kashaya, bhasma is an ash-based medication that contains mineral and botanical extracts. A rasayana is a concoction of many herbs and herbo-mineral formulas that is used to promote mental wellness and rejuvenation.

II. CONCLUSION

This data and various approaches for this prevention and treatment of epilepsy my be helpful and cosmetic in integrated in combination therapy as the many evidence for the treatment of epilepsy is very unique the cosmetically sensory stimulation approaches has been observed to minimise or get temporary treatment.

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