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A Review on Role of Traditional Herbal Drugs in Treatment of Age-Related CNS Disorders

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ABSTRACT: Natural drugs have always been a part of Indian tradition as well as in developing countries around the world. Alzheimer's disease, Parkinson's disease, and Huntington's disease are neurodegenerative conditions primarily associated with ageing, cognitive decline, and mood disturbances. Conventional drugs often have numerous side effects, & high cost of modern medications makes them unaffordable for individuals with low incomes. Demand for alternative solutions that are effective, affordable, and safe is widespread. This review discusses the use of traditional herbal drugs for treating age-related central nervous system (CNS) disorders.

KEYWORDS: Neurodegenerative Disease, Nervous Disorder, Alzheimer's disease, Dementia.

I. INTRODUCTION

The central nervous system (CNS) is a crucial component of the nervous system, comprising the brain and spinal cord [1]. A CNS disorder is a condition that affects the structure or function of the brain (encephalopathy) or spinal cord (myelopathy), resulting in neurological, psychiatric, or neurodegenerative impairments. Neuroprotection refers to the implementation of strategies aimed at safeguarding the central nervous system (CNS) from various factors that can cause CNS disorders, including structural defects, infections, neuronal injury, autoimmune disorders, tumours, and neurodegeneration. In recent years, the prevalence of these disorders has been increasing as a result of the rise in life expectancy. Consequently, they impose a significant burden on families and social economies [2,3]. According to a recent report by the World Health Organisation (WHO), approximately one billion individuals globally are affected by neurological disorders, resulting in an annual mortality rate of 6.8 million people. Moreover, developing countries exhibit a higher prevalence of central nervous system (CNS) disorders compared to developed countries, with a ratio of approximately two to one [4].

Herbal remedies are widely utilised globally and their usage may be on the rise. These substances are consumed for various perceived advantages and to address specific medical conditions. The exploration of new pharmacotherapy options derived from medicinal plants for psychiatric disorders has made substantial advancements in the last ten years. The psychotherapeutic potential of numerous herbal preparations has been assessed in various animal models [5,6]. Herbal supplements have been utilised extensively in the treatment of neuronal and pathological disorders, offering a valuable alternative with minimal or no adverse effects. In recent years, there has been a global increase in the popularity of complementary and alternative medicine (CAM) [7]. Numerous plant species have been identified as herbal medicines, and their active constituents have been extensively studied through global scientific research. Complementary and alternative medicines (CAM) or traditional medicines are regarded as safe and efficacious in the treatment of complex and sensitive conditions such as central nervous system (CNS) disorders, with a lower incidence of adverse effects compared to synthetic compounds.

Oxidative stress refers to an imbalance between free radicals and antioxidants in the body, resulting in potential harm to cells and tissues [8,9]. Free radicals are oxygen-containing molecules with unpaired electrons that readily react with other molecules, leading to damage. Oxidative stress is a significant factor in the development of various diseases, including cancer, inflammation, metabolic disorders, and neurodegenerative conditions. Elevated levels of oxidative stress contribute significantly to the advancement of neurodegenerative disorders.Oxidative stress in the neuronal

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microenvironment leads to the oxidation of lipids, proteins, and DNA, resulting in the generation of various by-products such as alcohols, aldehydes, peroxides, cholesterol oxide, and ketones [10]. While it is not established that reactive oxygen species (ROS) directly cause neurodegenerative diseases, it is probable that oxidative damage, resulting from the interaction between ROS and mitochondria, can hasten the progression of these diseases. Brain tissues are highly vulnerable to oxidative damage because they consume a significant amount of oxygen, contain a high level of polyunsaturated membrane acids, and have a weak defence system against antioxidants. Mitochondrial dysfunction, caused by abnormal ROS development, is strongly linked to neurodegenerative diseases (NDD). ROS is present in the brain and acts on post-mitotic cells, glial cells, and neurons that are especially vulnerable to free radicals, resulting in neuronal harm. The body's inherent enzymatic and non-enzymatic antioxidant systems regulate the production of reactive oxygen species (ROS) in normal circumstances. Excessive production of reactive oxygen species (ROS) in both intra- and extracellular environments disrupts the equilibrium between pro-oxidants and antioxidants, leading to oxidative stress in the cells and tissues of the brain [6,10]. Hence, it is crucial to mitigate these effects through the utilisation of exogenous antioxidants. Furthermore, the prevention and treatment of neurodegenerative disorders face challenges such as the severe adverse effects associated with certain synthetic drugs, their high cost, lack of safety, poverty in certain circumstances, and inadequate accessibility for the global population. [7].

Ageing and neurodegeneration

Ageing is believed to be a stochastic process that involves both predictable and random effects. These effects contribute to the gradual accumulation of cellular damage that remains unrepaired over time. As a result, cellular repair and compensatory mechanisms become weakened. Lifestyle and environmental factors contribute significantly to the variation observed in the ageing process, while genetic factors only account for 25% of this variability. While brain cells are vulnerable to the cumulative impacts of ageing, it is important to note that neuronal death is not predetermined to happen at a specific time. The cellular and molecular changes associated with ageing are influenced by a combination of genetic factors and environmental influences. These factors collectively determine the differential ageing outcomes observed in cells, distinguishing between successful ageing and susceptibility to neurodegenerative processes. The mechanism behind selective vulnerability, which leads to distinct patterns of neurodegeneration in various diseases, remains unclear. Compensatory strategies that safeguard against cellular damage and death encompass mitochondrial oxygenation, ubiquitination, proteolysis by proteasomes, chaperone activity, and lysosome-mediated autophagy. Ageing is linked to mitochondrial dysfunction, heightened production of free radicals, and oxidative stress. These factors can result in genomic instability and DNA mutations. Additionally, shortened telomeres are associated with decreased survival. Age-related decline in proteasome activity results in the accumulation of damaged or ubiquitinated proteins, leading to abnormal deposition of brain proteins [8,9]. Age-related α -synuclein deposition is observed, but post-mortem studies indicate significantly lower levels in agematched controls compared to individuals with Parkinson's disease. These studies indicate that beta amyloid and a-synuclein pathology may coexist, suggesting potential shared pathogenic mechanisms between Alzheimer's disease and Parkinson's disease. Sirtuins, belonging to the histone deacetylase protein family, are involved in cell cycle regulation and cell survival promotion. Sirtuin inhibition has demonstrated the ability to alleviate α -synuclein toxicity in animal models, indicating a potential association between ageing and neurodegeneration. Ageing is characterised by diminished chaperone efficiency, disrupted autophagic recycling, altered inflammation, activated complement system, microglia activation, and impaired response to neurotrophic factors, all of which hinder the brain's capacity to recover from damage. Iron accumulates in the brain as a person ages, particularly in the substantia nigra. This accumulation makes the cells more vulnerable to toxins [11,12]. The insulin signalling pathway plays a crucial role in promoting longevity, as each tissue has its own specific critical level for optimal functioning. Decreased activity levels can disrupt metabolism and contribute to the development of diabetes, while increased activity levels in the brain during ageing can increase the risk of neurodegeneration. Age-related genetic changes occur in the substantia nigra as a result of the accumulation of mitochondrial DNA deletions during the ageing process. These changes lead to functional impairment of neurons. Deletions are common in Parkinson's disease (PD) and have an impact on neuronal function [22].

II. MORPHOLOGY OF PLANTS SHOWS CNS DISORDER

Datura Metel L.:

Interspecific hybrids of Datura with high scopolamine production have been successfully produced and selected. The tropane alkaloid concentrations in Datura metal leaves range from 0.2% to 0.5%, while the flowers contain 0.1% to 1.0% and the seeds contain 0.2% to 0.5%. Scopolamine is involved in important physiological processes in mature leaves. Other alkaloids present are hyoscyamine, norhyoscyamine, norscopolamine, hydroxyl-6-hyoscyamine, and metelodine. These substances elicit various physiological responses, including increased heart rate, muscle relaxation, inhibition, reduced secretions, and pupil dilation [13]. It is possible to synthesise scopolamine and hyoscyamine in vitro without significant financial resources. Datura metal root hairs demonstrate significant productivity in culture. The focus of this discussion is the urban resources found in tropical Africa. It is widespread in India. Datura plant leaves are used in the production of medicinal substances. Datura plants are known to contain tropane alkaloids, namely hyoscyamine and atropine.. [12,13].

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Rauwolfia serpentine L(Benth) ex Kurz:

Rauwolfia roots are utilised in the treatment of hypertension and mental disorders in humans. It is also employed for the treatment of central nervous system disorders, including anxiety and agitation. This substance is utilised for the treatment of insomnia, mental disorders, and aggressive behaviour. Benzodiazepines have a calming effect on the central nervous system, which helps to alleviate symptoms like anxiety, itching, and aggression. It is used in the treatment of schizophrenia, epilepsy, psychosis, and other psychiatric disorders. It is located in the Eastern and Western Ghats. The plant contains significant compounds, including desperpidine, indobine, reserpine, and serpentine. Rauvolfia serpentina possesses significant therapeutic properties.. [14,15].

Aegle marmelos L:

Aegle marmelos has been found to contain flavonoids in its phytochemical analysis. Flavonoids have been shown to exhibit anxiolytic properties through their interaction with benzodiazepine receptors [21]. The anxiolytic properties of Aegle marmelos may be ascribed to its flavonoids. Several studies have identified different phytochemicals in Aegle marmelos, such as tannic acid, phenols, marmesinin, ascorbic acid, eugenol, skimmianine, and saponin. These compounds have been proposed to have anxiolytic properties [16]. Aegle marmelos exhibits potential as a viable and effective therapeutic option for various anxiety disorders. The fruit contains extracts that are ethanolic in nature. These are employed to mitigate symptoms of fatigue, anxiety, and depression. The fruit contains steroids, coumarin, and alkaloids. The plant is located in Sri Lanka. The leaves possess bioactive compounds. The active constituents consist of aegeline, furocoumarins, and marmelosine. The compound exhibits significant potential for pharmaceutical applications! [17].

Embilica officinalis L:

Research has shown that it is advantageous in the treatment of several health conditions, including memory loss, mental fatigue, anxiety with mental irritability and restlessness, depression with aggressive reactions, and attention deficit hyperactivity disorder [20]. Amla has demonstrated potential benefits for a range of health conditions. Symptoms associated with the brain and nerves encompass headache with a burning sensation, migraine marked by pulsating and throbbing pain, memory impairment, cognitive exhaustion, and vertigo. Psychological disorders, such as anxiety and depression, are characterised by symptoms such as mental irritability, restlessness, aggressive reactions, insomnia, and violent mental agitation. Both dried and fresh fruit are used. It enhances cognitive functioning. The active components comprise embillicannin, ascorbic acid, polyphenols, and gallic aci. [18,19].

Table 1: List of Plants shows CNS Disorders:

Family	Plant Species	Geographical Location	Part Used	Use of the Plant
Poaceae	AvenasativaL.	Eurasia, Africa	seeds	Nervous disorder
Rutaceae	Aegle marmelos L.	India, Sri Lanka	Bark, leaf, flower, fiuit	Anxiety, depression
Acoraceae	Acorus calamus L.	Central Asia, Russia, Siberia	rhizome	Neuro protective
Solanaceae	Datura metel L.	North America	Seed, flower	Induce relaxation
Euphorbiaceae	Emblica officinalisL.	India	fiuit	epilepsy
Convolvulaceae	EvolvulusalsinoidesL.	East Asia	Whole plant	psychotropic
Apiaceae	FerulaasafoetidaL.	Iran	Gum, resin	epilepsy
Caprifoliaceae	Valeriana	Europe	root	sedative
Annonaceae	Annona squamosaL.	America	fiuit	depression
Plantaginaceae	Bacopa monieriL(Pennel)	Eastern India	Whole plant	insanity

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