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A Review on the Central Nervous System (CNS): Neurological Disorders and Plants with Therapeutic Effects on the CNS

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Abstract: The central nervous system (CNS) consists of the brain and the spinal cord. The central nervous system is a complex organ in the human being; it determines basic functions, such as consciousness, breathing, emotions and thoughts. Brain disorders can result directly from intrinsic dysfunction of the brain or complex interactions between the brain cells and the physical environment. A brain disorder associated with chronic break down and deterioration of neurons of the central nervous system is called a neurodegenerative disease. Statistics have shown that medicinal plants are being widely used in the treatment and management of diseases, such as malaria, diabetes, sickle-cell anemia and microbial infections. Some of these medicinal plants are also being used in the management of disorders of the CNS. These plants include *Ginkgo biloba* used in the management of symptoms associated with short term memory in Alzheimer's disease and also in anxiety. *Centella asiatica* is also used as an anxiolytic agent in the management of epileptic symptoms. *Piper methysticum* is used to manage hallucination and also as a sedative. Compared to synthetic drug use, medicinal plant treatment is almost free from side effects, when compared to synthetic drug treatment; therefore, it is preferred over synthetic drugs. In conclusion, it can be inferred that the CNS play a vital part in the human body by transmitting impulses via the nerve cells. But unlike other cells of the body which have regenerative properties, the nerve cells lack the ability to regenerate itself this makes a single damage to one or more of the nerve cells a fatal blow to the entire behavioural functions of the body and also treatment of this cell next to impossible. Thus treatment and management of these disorders is a lifetime commitment which makes it necessary to introduce medicinal plants with therapeutic properties into the treatment strategy in other to minimize long-term side effects of synthetic drugs.

Keywords: CNS, Medicinal Plant, Neurodegenerative Diseases, *Ginkgo biloba*, Alzheimers

1. Introduction

The spine and the brain make up the CNS [1]. The spine and brain share a common origin during embryo formation and also at adulthood. The human brain has developed far beyond the basic organization of the CNS by advancing its structure and function [2].

2. Central Nervous System

2.1. The Spinal Cord

The spine is present in vertebrae; it is in form of a long extension from the protective cover at the base of the skull down to the first lumbar vertebra. The spine is encased by triple layers of soft tissue. The outer layer which is the dura mater is a thick protective membrane it consists basically of collagen fibres. Beneath the dura mater is the arachnoid layer which has a cobweb-like mesh. The cerebrospinal fluid (CSF) is located between the dura mater and the spinal cord. There is a differentiation in length between the spine and the vertebral canal as a result of disparities between embryonic growth and the vertebral column [2].

2.2. The Brain

The brain is made up of the cerebrum, diencephal on which is subdivided into the thalamus and hypothalamus, cerebellum and the brain stem which is subdivided into the medulla, pons and midbrain [2].

2.2.1. Brainstem

The brain stem bears some similarities with the spinal cord. The brain stem is thought to be the evolutionary part of the brain, and it serves as a doorway for most cranial nerves [2].

2.2.2. Cerebellum

The cerebellum is formed from stem cells. It regulates morbidity. The cerebellum occupies 10% of the brain, but 50% of the brain neurons are present. The neurons are present in the cortex of the cerebellum. The cerebellum is sub-divided into three layers; the molecular layer, the outer layer, the granular layer, the innermost layer, and the Purkinje layer, which is the middle layer [1]. The cerebellum comprises nerve fibres bonded into three and are collectively called cerebellar peduncles. It is made up of inferior, middle and superior cerebellar peduncles. The inferior cerebellar peduncles carry sensory information to the joint from the muscles with the aid of the spine and medullar; the superior cerebellar peduncle carries information to the cerebrum from the cerebellum via the thalamus while the middle cerebellar peduncle carries impulses into the cerebellum from the cerebrum [2].

2.2.3. Hypothalamus

The hypothalamus is located underneath the thalamus, and it is present only in a minute portion of the brain [2]. The thalamus regulates activities such as reproduction [3], monitoring messages from the autonomic nervous system, controlling hormones, and regulating appetite and sleep [1]. Nuclei are predominantly present in the hypothalamus [2].

2.2.4. The Thalamus

The thalamus is the gateway to the cerebral cortex because most sensory information received in the body passes through the thalamus [2]. The sensory information passes through well-developed nuclei to the appropriate site in the thalamus. The thalamus is a small structure in the middle of the brain which plays a significant role in the brain [3].

2.2.5. Cerebrum

The cerebrum is the most significant part of the brain, and it comprises two hemispheres divided by a fissure called the corpus callosum. The first hemisphere is the cerebral cortex, and the second is the basal ganglia [1]. The cerebral cortex's external surfaces are wrinkled, which increases its surface area. The cortex is for high-level human functions, such as speech processing. The cortex has four lobes: frontal, parietal, temporal, and occipital. Each lobe is responsible for diverse motor and sensory functions [3]. The frontal is responsible for movement, planning and coordinating behaviour; the parietal is involved in speech and complex visual perception, attention, language and sensory processing. The temporal aids in auditory perception, and the occipitalis, the visual centre, plays a role in processing information [1].

2.2.6. Basal Ganglia

The basal ganglia are made up of masses of grey matter in each hemisphere; they contribute to the control of voluntary muscle movements [1].

3. Neuronal Physiology

The neuron also called the nerve cell is the basic functional and structural unit of the nervous system. They are the signalling cells of the nervous system and are involved in the generation of action potential and in transmitting nerve impulses across the whole length of the body. They are considered the oldest and longest cell in the body. Other cells of the brain are the non-neuronal glial cells. the glial cell provides support and protection to the nerve cells [4]. Nerve cells contain a nucleus, cell membrane, ribosomes, golgi apparatus and so just like every other animal cell. But unlike other cells, nerve cells possess axons and dendrites which are attached to their soma. Soma is also known as a cell body, this cell body is up to 10-100 mm in diameter, whereas the dendrites are branch-like and are thin and short while the axon forms a long tail-like structure which extends from the soma at a swollen point called the axon hillock. The axon is covered by a myelin sheath which is secreted by the Schwann cells (They are a type of glial cell). Axon ends in numerous small terminal buttons. Nerve impulses move from the axon of one neuron to the dendrite of another neuron through the synapse [5].

3.1. Functions of Nerve Cells

The basic function of nerve cells is to transfer electrochemical signals between other cells of the body. Signals are sent by the nerve cell by generation and a rise in spikes from the cell body down to the axon and finally to the terminal buttons. At the terminals, a neurotransmitter is released from the pre-synaptic neuron to trigger postsynaptic potential in the next nerve cell.

3.2. Classification of Neurons

A neuron can be classified based on its shape.

3.2.1. Unipolar

Axon or dendrite (either of them) emerges from the soma.

3.2.2. Pseudo Unipolar

Axon and dendrite emerge from the same side of soma.

3.2.3. Bipolar

Axon and dendrite emerge from the opposite ends of soma.

3.2.4. Multipolar

One axon and many dendrites emerge from the opposite ends of soma [6, 7].

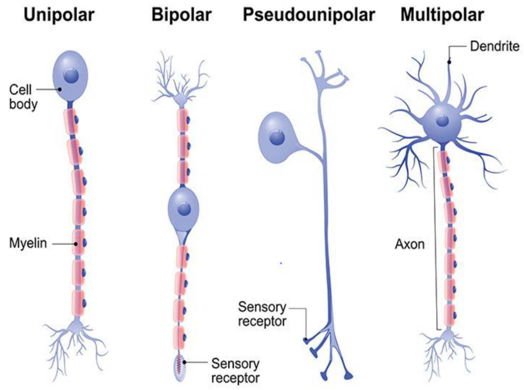

Figure 1. *Types of neurons [8].*

3.3. Neurotransmitters

Neurotransmitters can be defined as chemical messengers that transfer signals between the neurons of the central nervous system by crossing the synapse. They are stored in storage vesicles. When there is a signal, the neurotransmitter is released into the synapses where they bind to receptors in the synaptic membrane of the opposite neuron; this causes depolarization of the receptor resulting in an increased action potential. Some neurotransmitters cause hyperpolarization of the receptor site, which leads to an inhibition effect of the bound neuron [9].

3.4. Classification of Neurotransmitters

Neurotransmitters can be classified into3: the classical, biogenic amines and amino acid neurotransmitter.

3.4.1. Classical Neurotransmitters

Acetylcholine (ACh) was the first known neurotransmitter found at the peripheral synapses such as the cardiac muscles, visceral smooth muscle and the neuromuscular junction of the skeleton [2, 7]. It is classified as a classical neurotransmitter.

Figure 2. *Pathway for the synthesis of acetylcholine [10].*

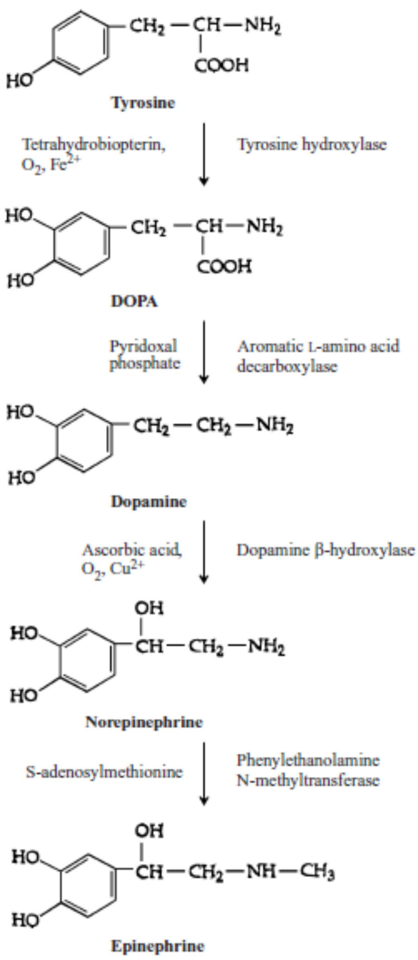

Figure 3. *Synthesis of the catecholamine transmitters [11].*

3.4.2. Biogenic Amines

There are 4 biogenic amines theses are serotonin, epinephrine, norepinephrine and dopamine. Epinephrine functions in mammals as a hormone. Norepinephrine and dopamine are called catecholamines, they are synthesized from tyrosine. The neurotransmitter norepinephrine is released from the ganglia neurons present in the autonomic nervous system. Dopamine has 5 known receptors namely D1, D2, D3, D4, and D5, they are bound to G-proteins which act as their second messenger [10].

3.4.3. Amino Acid Transmitters

The basic amino acid neurotransmitters are glutamate, γ-aminobutyric acid (GABA), and glycine. Glutamate is one of the most prevalent amino acid neurotransmitter present in the human brain, it is synthesized from γ-ketoglutarate arising from the citric acid cycle. Glutamate functions in peptide and protein synthesis, detoxification of ammonia in the brain and as a precursor of GABA which is an inhibitory neurotransmitter [11].

(i). Γ-aminobutyric Acid (GABA)

GABA is a major inhibitory neurotransmitter. GABAergic areas in the brain include the cerebellum, striatum, globus pallidus, olfactory bulb and spine. GABA have various receptors, the basic ones are the GABAA and GABAB. GABAA is a ligand-gated Cl+ channel while GABAB is a G-protein linked receptor [11].

(ii). Glycine

Glycine is a nonessential amino acid it is also an inhibitory neurotransmitter in the CNS. Glycine is majorly synthesized from serine. Glycine functions basically in the spinal cord it regulates glutaminergic receptor (NMDA) [11].

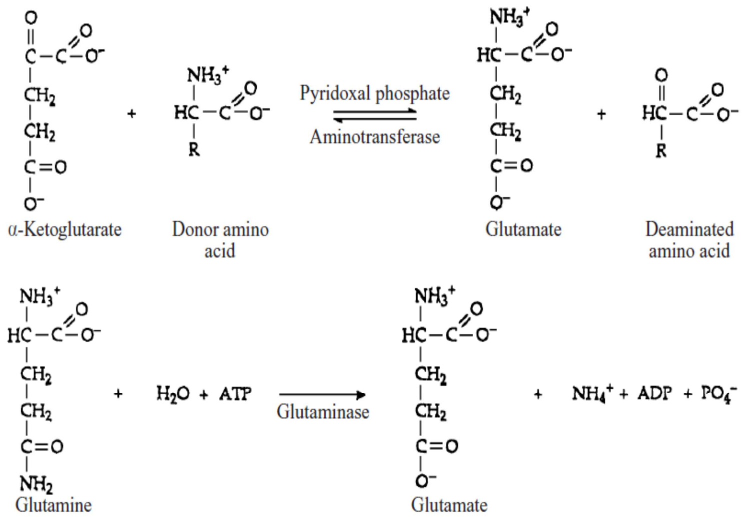

Figure 4. *Synthesis of glutamate from α-ketoglutarate [11].*

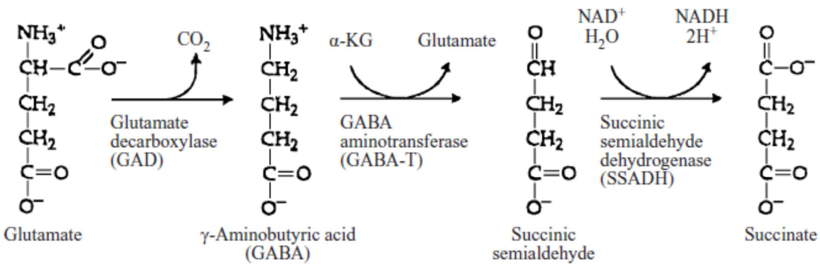

Figure 5. *Synthesis of GABA from glutamate [11].*

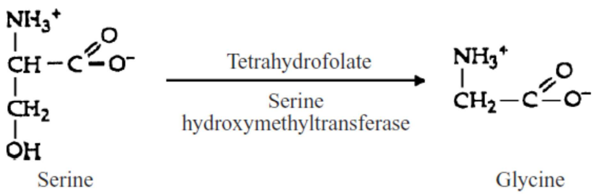

Figure 6. *Synthesis of Glycine from serine [11].*

4. Disorders of the CNS

A disorder of the CNS can also be called a brain disorder or mental disorder. Brain disorder is not limited to insanity it also cuts across emotional disorders. Abnormality in emotions can result in mental disorders. There are billions of nerve cells in the brain and they connect to form a network of communication. In other to function optimally, nerve cells supply, generate and receive energy. They also remove waste when the nerve system is disturbed. Various neurological diseases develop such disease including depression, anxiety, schizophrenia, epilepsy and also neurodegenerative diseases such as Alzheimer's, Parkinson's and Huntington's [12].

4.1. Neurological Diseases

Depression: Depression is a prevalent disorder associated with a mood disorder. Hallucinations and delusions accompany mood disorders. In this diseased state, there are elevated levels of some neurotransmitters in the brain; these include dopamine, acetylcholine and norepinephrine [13]. There are two types of depression: unipolar depression and bipolar depression. In unipolar depression, the mood swing experienced by the individual is in one direction, unlike bipolar depression, where the individual's mood alternates. The symptoms of this disease are sub-divided into2:

4.1.1. Biological Symptoms

It is associated with retarded thinking, distorted sleep, loss of libido and appetite.

4.1.2. Symptoms Associated with Mood

This is associated with guilty and incitement.

(i). Anxiety

Anxiety is characterized by some symptoms such as cognitive, emotional, somatic and behavioural factors. It is a psychological and physiological state. The combination creates an unpleasant feeling that leads to worry and fear, without being triggered by an identified threat. Anxiety differs from fear in the presence of an external threat. Anxiety results from presumed threat, while fear is triggered by avoidance or escape of a visible threat [14].

(ii). Epilepsy

Epilepsy is characterized by recurring unprovoked seizures.

Epilepsy is defined as a neuropsychological disorder that results from the discharge of neurotransmitters [15]. A seizure is a characteristic event in epilepsy. Seizure is a paroxysmal event due to abnormal excessive hypersynchronous discharge from an aggregate of central nervous system neurons. Epilepsy can be of two types, it can be partial epilepsy which is localized brain damage or generalized epilepsy associated with total brain damage [16].

(iii). Schizophrenia

Schizophrenia is a mental illness characterized by psychosis, apathy, social withdrawal and cognitive impairment. There are three types of schizophrenic symptoms, they are:

a) Positive Symptoms

The positive symptoms of psychosis are the presence of abnormalities such as delusions, hallucinations, and thought or Behavioural disorders. It begins during the youthful years of an individual and cognitive disorders are evident at an early age.

b) Negative Symptoms

weakened emotional responses and poor socialization is observed in this state. it is a result of increased neurotransmitters such as serotonin (5HT), acetylcholine, dopamine and norepinephrine in the brain. Synthetic drugs can reduce symptoms which include abnormal thinking, hallucination and delusion. Although some patients react to some of these drugs, they could suffer weight gain and tremors. Some of these drugs can interact with other medications or supplements [16].

c) Cognitive Symptoms

Long term cognitive impairment are disabling and persistent features of schizophrenia. It is characterized by problems with attention and concentration, psychomotor speed, impaired memory, and abstract thinking.

4.2. Neurodegenerative Diseases

Neurodegenerative diseases are several conditions that result from the deterioration or breakdown of neurons in the CNS [18]. Neurodegenerative diseases are predominant in elderly people. Neurodegenerative diseases are characterized by a gradual onset of progressive symptoms such as inability to handle complex tasks, impaired spatial orientation and abilities, language deficits and behavioural changes, loss of memory, tremor and difficulty in learning or assimilation [18]. Examples of neurodegenerative diseases include amyotrophic lateral sclerosis, spongiform encephalopathy, Alzheimer's disease (AD), Parkinson's disease, multiple sclerosis [19] with AD being the most prevalent [20, 21].

4.2.1. Alzheimer's Disease (AD)

Alzheimer's disease can be defined as presenile dementia. Presenile dementia is a progressive brain disorder with the primary symptom being the loss of intellectual abilities. Alzheimer's disease results from shrinkage of the brain and death of some neurons, primarily in the hippocampus and basal fore of the brain. AD is caused by extracellular amyloid plaques, consisting of β-amyloid protein deposits and intra-neuronal neurofibrillary tangles having filamentous phosphorylated microtubule proteins. The loss of memory experienced in AD patients results from loss of the neurotransmitter acetylcholine [23, 24].

4.2.2. Parkinson's Disease

Parkinson's disease is mainly associated with dementia and other symptoms such as tremor, which begins in the hands, rigid muscles in response to increased resistance of the limbic motor and hypokinesis resulting from suppressed voluntary movement of the muscles. Parkinson's disorder results from decreased neurotransmitters such as norepinephrine, dopamine, and soon [24]. These neurotransmitters are reduced basically in the carpus striatum and substantia nigra of the brain. A collection of nerve cells called the basal ganglia are seated deep within the brain; they help smoothen muscle movement and coordinate changes in posture. When impulses are initiated for muscle movement, the impulse passes through the basal ganglia. Neurotransmitters are released from the basal ganglia. These neurotransmitters trigger nerve cells (neurons); the active nerve cell triggers the next nerve cell. This follows a pathway of the continuous trigger of nerve cells, thus sending an impulse. Dopamine is predominant in the basal ganglia, and it functions to increase nerve impulses sent to the muscles. When the neuron presents in the basal ganglia degenerate, there is a production of less dopamine to transmit impulses to smoothen out the muscles. This leads to muscle dysfunction such as tremors, slow movement (bradykinesia), reduced movement (hypokinemia), loss of coordination and difficulty in walking and posture [25].

5. Plants with Therapeutic Effects on the CNS

Medicinal plants are herbs with compounds or properties that are useful in the therapeutic and synthesis of metabolites to produce drugs [26]. Medicinal plants include several herbs used in the treatment and management of diseases. Some of these plants have bioactive components that can be used in the development and synthesis of drugs. These plants also serve as good sources of nutrients for the human body [27]. Large populations of the world depend on traditional medicine as their primary treatment [28]. The rules guiding the adequate use of these plants involve proper characterization of the plant species, verification of the presence of the active compound, purification and lastly concentration of the required chemical compound [29]. Some of the active compounds in these medicinal plants are frequently used in the production of drugs such as laxatives, blood thinners, antibiotics and anti-malaria medications [27].

5.1. Hypericum Perforatum

Hypericum perforatum is classified under the Hypericaceae family [30]. It is most prevalent in the European parts of the world [31]. *H. Perforatum* is also called St John's wort. The active compounds present in *H. Perforatum* are xanthones, hypericin, and hyperforin [32]. *H. perforatum* functions as an anti-depressant by inhibiting the monoamine oxidase (MAO) enzyme, GABA, glutamate uptake [33] and binding serotonin, norepinephrine, and dopamine to neurons. It is also used as an anti-anxiety medication [34].

5.2. Piper Methysticum

Piper methysticum is also called kava, and it belongs to the Piperaceae family [12]. It is predominant in European countries and native to Poland [30, 35]. The primary compounds found in kava are mysthysticin, kava pyrenes and kavalactones. Kava pyrones inhibit Na+ channels, increase GABA-A receptor density, suppress glutamate release, and block norepinephrine [12]. Kavalactone inhibits some Cytochrome P450 (CYP450) enzymes, and it is used as an anti-seizure drug [30, 36].

5.3. Ginkgo Biloba

Ginkgo biloba is found in several countries, most prevalent in China and India. *Ginkgo biloba* belongs to the Ginkgoaceae family [12]. The active compounds in ginkgo leaves are flavonol glycosides, consisting of flavonol, mono-flavonol glycosides, isorhamnetin, triglycerides of kaempferol, and organic acids such as shikimic acid and benzoic acid [12, 37].

5.4. Panax Ginseng

Panax ginseng is commonly called ginseng root because the most used part of this plant is the root. Ginseng belongs to the Araliaceae family. It is used mainly in Asia, specifically in Korea, Japan and China [30, 38]. The primary bioactive compound in ginseng root is ginsenosides. According to a research carried out by Hu *et al.* on ginseng in 2011 [39], it was reported that ginseng extract stimulated the release of cytochrome C it also decreased the mortality of brain cells, prevented the production of free radicals, specifically reactive oxygen species, activated caspase-3 expression in 1-methyl-4-phenylpyridinium(MPP)(+)-treated SH-SY5Y human neuroblastoma cells and increased Bax/Bcl-2 ration. This thus aids the reduction of the symptoms of Parkinson's disease.

6. Conclusion

Disorders of CNS are several diseases which affect a large population of persons in several countries. Currently, there are no known drugs for treating these disorders but there are available drugs for their management. Medicinal plants have been recognized by the world health organization for their diverse role in the treatment of several diseases, as well as their use in the production of synthetic drugs. The use of synthetic drugs in the management of CNS disorders has shown to have an unpleasant after mass; this has caused a shift into the discovery of a better alternative, with a therapeutic role in CNS disorders. Thus the recent research focuses on some potential medicinal plants with anti-anxiety, anti-depressant and other bioactive compounds for the management of these disorders. Though some side effects have been observed in the use of these plants as a result of other compounds that are present in these plants or from an overdose. Notwithstanding, medicinal plants are more advantageous over synthetic drugs because, synthetic drugs have several side effects such as sleeping disorders, and withdrawal syndromes among others as a result of consistent use. Also, medicinal plants are readily available and the active constituents present in them can manage CNS disorders and also treat other diseases. Although there could be components present in some of these plants that could be toxic if consumed, it is advisable that in-depth research is conducted, to purify these extracts so they can be abducted as a means in the management and possibly treatment of CNS disorders.

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