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Effects of Polysaccharides in the Central Nervous System: A Literature Review

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ABSTRACT: Polysaccharides extracted from plants are molecules abundant in nature by structurally constituting the cell wall of plants. These compounds are provided with various biological activities and have low toxicity.In this perspective the polysaccharides of plants become promising for the development of drugs that can contribute to the therapy of disorders of complex etiology such as those that develop in the central nervous system. The objective of this review study was to carry out a survey of the literature data on the effects of plant polysaccharides on the central nervous system. This systematic review was carried out from studies published from January 2000 to September 2017 in scientific databases such as PubMed, Science Direct and CAPES journal portal. For this, the Health Sciences Descriptors (DeCS) and the Medical Subject Sections (MeSH) were used: "polysaccharides", "central nervous system" and "plants". After the search and sorting of the articles were identified 18 studies used in the preparation of this work. Biological activities of confirmed polysaccharides have been reported in studies demonstrating anti-inflammatory, antioxidant, neuroprotective, neurodepressive and antidepressant reduction activities, as well as the presence of mannose, rhamnose, xylose, arabinose, galactose, ribose and glucose in the structural composition of the polysaccharides. In addition, the medicinal use of polysaccharides is promising, as the pharmacological activities shown are significant and relevant from the perspective of drug development for the treatment of diseases affecting the central nervous system.

Keywords: polysaccharides, central nervous system, plants.

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I. RESUMO

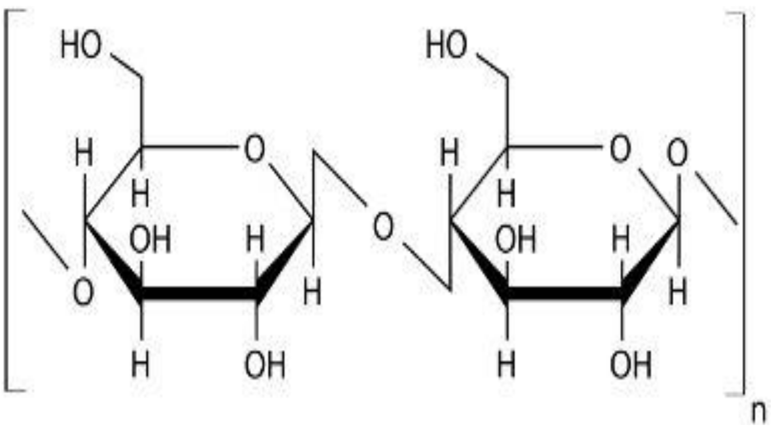
Os polissacarídeos extraídos de plantas são moléculas abundantes na natureza por constituírem estruturalmente a parede celular de vegetais. Esses compostos são providos de diversas atividades biológicas e possuem baixa toxicidade. Nessa perspectiva os polissacarídeos de plantas tornam-se promissores para o desenvolvimento de fármacos que possam contribuir com a terapêutica de distúrbios de etiologia complexa como os que se desenvolvem no sistema nervoso central. Objetivou-se nesse estudo de revisão realizar um levantamento acerca dos dados existentes na literatura sobre os efeitos de polissacarídeos de plantas no sistema nervoso central.Esta revisão sistemática foi realizada a partir de estudos publicados no período de janeiro de 2000 a setembro de 2017nas bases de dados científica como PubMed, Science Direct e portal de periódicos da CAPES. Para isso foi utilizado os Descritores das Ciências da Saúde (DeCS) e as Seções Médicas do Assunto (MeSH): "polissacarídeos", "sistema nervoso central" e "plantas". Após a busca e triagem dos artigos foram identificados 18 estudos utilizados na confecção deste trabalho. Foram relatadas atividades biológicas dos polissacarídeos confirmados por estudos que demonstraramatividades anti-inflamatórias, antioxidantes, neuroprotetora, redutora de déficits neuronais e antidepressivas, além da presença majoritária de moléculas como manose, ramnose, xilose, arabinose, galactose, ribose e glicose na composição estrutural dos polissacarídeos. Além disso, o uso medicinal dos polissacarídeos apresenta-se de modo promissor, pois as atividades farmacológicas evidenciadas são significativas e pertinentes na perspectiva do desenvolvimento de fármacos para o tratamento de doenças que acometem o sistema nervoso central.

Palavras chaves: polissacarídeos, cérebro, plantas.

II. INTRODUCTION

Central nervous system (CNS) disorders such as depression, anxiety, epilepsy, stroke and Alzheimer's arouse the interest of researchers around the world, as each year new cases arise, representing a serious public health problem, Besides compromising the individuals' quality of life (Kessler and Bromet, 2013).The pathophysiological mechanisms involved in these disorders correspond to a complex sequence of neurochemical events that can culminate in neuronal death, with the increase of reactive oxygen species (ROS), the proliferation of pro-inflammatory mediators, the development of beta-amyloid plaques, and of motor and cognitive alterations(Zhou et al., 2010, Yang et al., 2013, Lin et al., 2014).The drugs used in current clinical practice for the treatment of CNS disorders have numerous adverse effects, such as sleepiness, amnesia, tolerance and physical dependence, and they generally do not promote healing or delay the progression of the disease, presenting a more palliative approach Than curative (Alonso and Lépine, 2007). In this perspective, it is necessary the study of new substances, in particular those obtained from natural sources, with greater effectiveness and less adverse effects for the treatment of neurobehavioral disorders (Silva et al., 2014).The knowledge about medicinal plants has followed the evolution of man, since the civilizations realized the existence of potentialities in the plants taking into account the empirical understanding about the toxicity and curative effects demonstrated in the fight against several diseases (Araújo et al., 2007).From the popular knowledge of the therapeutic effects of several plants, scientists have been demanding efforts to elucidate the biological activities of various plant compounds through experimental studies such as polysaccharides (PL) that are extracted from different parts of plants, such as Leaves, roots, fruits and stems (Maciel et al., 2002).PLs are molecules abundant in nature and considered the main structural components of the cell wall of plant cells (figure 1). These are constituted of ten or more monosaccharide units linked by glycosidic bonds, differing in the type of monosaccharide residue, glycosidic bond, branching degree and chain size, presenting different structural characteristics (Pereira et al., 2002).

Figure 1. Structure of the cellulose, a polysaccharide.



http://brasilescola.uol.com.br/o-que-e/biologia/o-que-e-celulose.htm

The PL is presented as a promising tool for the scientific community by the proven spectrum of biological activities, such as: immunomodulatory (YI et al., 2011), anti-inflammatory (Pereira et al., 2012), analgesic (Wang et al., 2011), anticoagulant and antiplatelet (Yoon et al., 2002) additionally have low or no toxicity (Trombeta et al., 2014). In the CNS, are described with effects anti-inflammatories (Chen et al., 2011) antidepressive activities (Wang et al., 2010), neuroprotective (Zhou et al., 2010), reducing cerebral deficits (Lin et al., 2014) andantioxidant action (AI et al.,2013).From these findings, the importance of plant polysaccharides as an important tool for the study and/or treatment of diseases that affect the CNS is noticed. Therefore, it was aimed to perform a survey about the data already existent in the literature on the PL activities of plants in the CNS.

III. MATERIALS AND METHODS

The literature review was performed using the literature data on the effect and mechanisms of polysaccharides of medicinal plants in the CNS. To this, a search was made in the databases "PubMed", "Science Direct" and periodic portal of Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES). The time cut was from January 2000 to September 2017, in Portuguese and English. Initially, 2316 articles were identified. Editorials, review articles and short communications were excluded, remaining 82 articles that were read in full for selection of studies that addressed the biological activities of medicinal plant polysaccharides in the CNS. Subsequently, a sampling of 18 articles was selected (Table 1). In order to obtain the selected articles, the Health Sciences Descriptors (DeCS) and Medical Subject Headings (MeSH) were used: "polysaccharides", "central nervous system" and "plants". Data were presented descriptively and in tables on biological activities in the CNS.

(Table 1) After searching the literature for articles indexed in the databases over the last 17 years, 18 articles were identified that addressed more directly the biological activities of PL of medicinal plants in the CNS (Table 2).**(Table 2)**

IV. RESULTS AND DISCUSSION

4.1 Neuroprotective activity

In order to evaluate the neuroprotective effect and the degree of recovery before or after treatment with PL plants it is necessary to mimic the pathophysiological process with the objective of causing cerebral compromise in an animal model similar to those observed in humans. In this perspective, several models have been developed and are widely used to induce D-galactose-induced cognitive disorders (Lin et al., 2014), excitotoxicity induced by glutamate (Ho et al., 2009) And to simulate brain damage of ischemic origin with occlusion of the middle cerebral artery (Zhou et al., 2010);besides the stress caused to neurons with deprivation of oxygen and glucose (Chen et al., 2011). The PL obtained from*Lycium barbarum* (fruits) have monosaccharides of the arabinose, galactose, glucuronic acid and rhamnose type and were tested in a model of glutamate-induced neurotoxicity by activation of the N-methyl D-Aspartate receptor(NMDA).The results show a reduction in lactate dehydrogenase (LDH) release and caspase 3 activation, as well as the phosphorylation of the N-terminal c-Jun protein kinases (JNK1) in primary cortical neurons of rats (Yuan et al., 2016; Ho et al., 2009).The presence of the LDH enzyme in the blood is a tool used to evaluate the presence of lesions. In the CNS it is currently accepted as markers of acute or chronic cellular injury, since the cellular efflux of LDH present in the cytosol indicates lesions that affect the continuity of the membrane and thus its viability (Koh & Chol, 1987). Caspases are a group of essential proteases in the process of cellular apoptosis, in addition to exert functions in the immune system. In this context, proteins such as JNK are essential for the regulation of signaling that can initiate different cell death pathways(Pradeep et al., 2014)PL obtained from *Nerium indicum*(flowers) have in their chemical composition the monosaccharides rhamnose, arabinose, xylose and galactose and were tested in a model of beta-amyloid peptide-induced neurotoxicity, where they reduced LDH release, caspase 3 activation and phosphorylation of protein JNK, as well as stimulated the phosphorylation of other proteins such as pyruvate dehydrogenase kinase-1 (PDK-1) and protein kinase B (PKB / Akt) in primary cortical neurons of rats(Yu et al., 2007). The PL obtained from *Acanthopanax senticosus* (fruits), has in the chemical composition the monosaccharides rhamnose, xylose, glucose, mannose, arabinose, galactose and were tested in a model of glutamate-induced neurotoxicity and neuroinflammation with the lipopolysaccharide (LPS). Reduction of Oxigen-reactive species (ROS) and nitric oxide (NO) in microglia and hippocampal cells in vitro was achieved by increasing nuclear factors such as p38-CREB and Nrf2, which in turn produced the enzyme heme oxygenase 1 (HO -1), responsible for the reduction of expression of pro-inflammatory mediators, such as nitric oxide synthase (iNOS) and cyclooxygenase-2 (COX-2) (Jin et al., 2013).

The increase of nuclear transcription factors p38-CREB and Nrf2 correspond to the increase of transcription factors of genes that initiate the response to oxidative stress, specifically Nrf2 is responsible for promoting the transcription cascade of antioxidant genes and their proteins in response to stress. increased HO-1 provides protection against oxidative stress by decreasing the concentration of heme (pro-oxidant) and increasing the concentration of antioxidant substances and the ability to resist aggression in situations of oxidative stress, apoptosis and inflammation (Chen X et al., 2000).PL obtained from*Ipomoea tyrianthina*(Roots),present in their chemical composition the monosaccharides rhamnose and glucose, used in a model of hypnosis / sedation induced by phenobarbital. The increase in latency and sleep time, prevention of pentylenetetrazol-induced seizures and elevation of the extracellular concentrations of gamma-aminobutyric acid (GABA)in brain (Léon-Rivera et al., 2008From the stem of *Dendrobium nobile*, it was obtained that the PL in their chemical composition presented the monosaccharides rhamnose, arabinose, xylose, mannose, glucose and galactose(Luo et al., 2009). PLs after tested in a model of neuroinflammation and cognitive dysfunction induced by LPS, reduced tumor necrosis factor receptor 1 (TNFR1), nuclear factor kappa B (NF-KB) and mitogen-activated P38-protein kinases (p38 -MAPKs) in rat hippocampus (Li et al., 2011).From the stem of *Opuntia milpa* Alta, were isolated their PL that present in the chemical composition mannose, rhamnose, xylose, arabinose, galactose, ribose and glucose. When tested in a model of cerebral ischemia by deprivation of oxygen and glucose, it resulted in the reduction of LDH release, the intracellular influx of Ca^{2+}, the intracellular production of ROS, and prevented the increase of the extracellular concentration of glutamate in Primary cortical neurons of rats(Chen et al., 2011).Reducing blood flow to the neuronal tissue is one of the most common causes of acute cell injury. The most prominent biochemical alteration in hypoxic cells is the reduction of the generation of intracellular adenosine triphosphate (ATP).

The loss of ATP leads to failure of many systems including: ion pumps that lead to cellular swelling and calcium influx (Ca^{2+}),depletion of glycogen stores and accumulation of lactic acid, decreasing intracellular pH and reducing protein synthesis (Kumar et al., 2013).The PL obtained *Ganoderma lucidium*(fruits) presented in their chemical composition the monosaccharides glucose and galactose and were used in a model of cerebral ischemia by occlusion of the middle cerebral artery, obtaining the reduction of the area of cerebral infarction and the score of neurological deficits in a scale of 5 scores (Longa et al., 1989).The PL obtained from the fruits of *Euphoria longan*tested in a model of cerebral ischemia by occlusion of the middle cerebral artery, in which the reduction of cerebral infarct area, cerebral edema and the score of neurological deficits on a 5-point scale were observed. In addition, it reduced lipid peroxidation, myeloperoxidase activity (MPO), tumor necrosis factor-alpha levels (TNF-alpha) and interleukin IL-1 (alpha and beta) and Bax expression (pro-apoptotic enzyme), In addition increases the activity of superoxide dismutase (SOD), reduced glutathione (GSH), glutathione peroxidase (GPX) and Bcl-2 expression (anti-apoptotic enzyme) in rat ischemic brain tissue (Chen et al.,2011).

4.1Antioxidant activity

Production of ROS is associated with damage to cell structures and pathological conditions in the CNS, such as Parkinson's disease, stroke, dementia, and epilepsy (Adibhatla & Hatcher, 2008).ROS can be produced by different metabolic pathways, including the decoupled nitric oxide synthase (NOS) enzyme pathway (Porasuphatana et al., 2003), pathways such as xanthine oxidase (Kelley et al., 2010) and NADPH oxidase (Dworakowski et al., 2006), in addition to the mitochondria, where ROS are produced as a consequence of the release of electrons from the electron transport chain(Bordt & Polster, 2014).

The cells have a complex antioxidant system, distributed in different compartments inside the cell. Among the enzymatic antioxidants we can mention: SOD, Catalase (CAT), GPX, glutathione reductase (GR) and a second line of defense non-enzymatic substances that are strongly influenced by eating habits such as GSH, ubiquinone, melatonin, thioredoxin (TxR), lipoic acid, vitamins E, A, C and fatty acids (Campos et al., 2014).PL obtained from *Angelica sinensis*(roots) and their use in a reperfusion model of cerebral ischemia, reduced the production of nitric oxide (NO), as well as stimulated the activity of SOD, GSH, GPX, CAT and GR. In addition, it elevated levels of Na^+, K^+-ATPase, Ca^{2+}, Mg^{2+}-ATPase, glucose, acetylcholine (Ach) and reduced acetylcholinesterase (AChE)in cerebral ischemic brain tissue (Ai et al., 2013).PL obtained from*Salviamiltiorrhiza* (roots),have in their composition mannose, ribose, xylose, arabinose, glucose and galactose (Jiang et al.,2014), and when tested in a cerebral reperfusion ischemia model, the area of cerebral infarction, cerebral edema and the score of neurological deficits were reduced in a scale of 5 scores. In addition, they have reduced ROSand lipid peroxidation, as well as elevated SOD, CAT and GPX activity in rat ischemic brain tissue (Tuet al., 2013)PL obtained from the leaves of *Ginkgo biloba*present in the composition monosaccharide arabinose, mannose, galactose and glucose, and its use in a model of cerebral ischemia by middle cerebral artery occlusion, reduced cerebral infarction volume and neurological deficit score of 5 on a scale of scores.In addition, it reduced NO production, lipid peroxidation, MPO activity, and levels of TNF-alpha and IL-1 beta, as well as increased SOD activity and interleukin-10 (IL-10) levels in brain tissue Ischemic of rats (Yanget al., 2013).

4.2 Anti-inflammatory activity

The CNS is considered an immune privileged site due to the existence of the blood-brain barrier (BBB), which promotes unconventional lymphatic drainage and low density of monocyte and lymphocyte trafficking (Bucchieriet al., 2015The inflammatory process in the CNS promotes the increase of the production of cytokines by the endothelial cells of BBB, circulating immune cells, microglia and astrocytes, resulting in the positive regulation of adhesion molecules, activation of metalloproteinases and catabolism of arachidonic acid, resulting in BBB compromising increased permeability and consequent migration of leukocytes to the CNS (Vezzani & Granata, 2005). PL obtained from *Taraxacum officinale*(leaves, stem and flowers)were used in a model of LPS-induced neuroinflammation and reduced levels of TNF-alpha and IL-1 in primary rat astrocytes (Kim et al., 2000).PL obtained from roots, leaves and flowers of four plants of the genus *Pittocaulon*(praecox, bombycophole, hintonii, velatumandfilare)were used in models of paw edema induced by carrageenan andinduced by 12-O-tetradecanoylphorbol-13-acetate,where they reduced edema in both tests, as well as the levels of MPO in the ear of mice and lipid peroxidation in the rat brain, in addition to presenting antioxidant effect in tests with 2,2-diphenyl-1-picrylhydrazyl (DPPH) in vitro(Marín-Loaiza et al., 2013).The PL from *Panax ginseng* (roots), tested in a model of experimental autoimmune encephalomyelitis caused a decrease in the cellular proliferation and production of IFN-γ, IL-17 and TNF-α, besides altering the population of CD4 + T cells,CD11b+, macrophages and decrease CNS damage and dysmyelinazation (Bing et al. 2016).

4.3 Antidepressant activity

The depressive disorder is characterized by a depressed mood behavior during almost the whole period of the day with a frequency of two weeks, also characterized by the loss of interest or pleasure in daily activities (Bensaeed et al., 2014). One of the hypotheses studied (monoaminergic hypothesis) is that associated with a deficiency in the amount or activity of serotonin (5-HT), norepinephrine (NE) and dopamine (DA) in cortical and limbic areas (Köhler al., 2016). For the neurotrophic hypothesis there is evidence about the role played by nerve growth factors, such as brain-derived neurotrophic factor (BDNF), regulation of neural plasticity and neurogenesis, therefore, it is suggested that depression is associated with a loss of neurotrophic support (Filho Cet al., 2015).PL of the roots of *Aconitum carmichaeli*have mainly glucose residues in their composition, and when tested in a model of lymphocyte and splenocyte proliferation induced by LPS and lectin concanavalin A (ConA) increased the proliferation of these cells, besides the production of antibodies (Zhao et al., 2006). In addition, it reduces the time of immobility in the forced swim test, latency in the food suppression test for novelty, and reversed the stress-induced behavior of chronic social defeat as well as elevated levels of BDNF in hippocampus of mice (Yan et al., 2010).PL obtained from *Panax ginseng*(roots), In their chemical composition the residues of galactose, glucose, arabinose, rhamnose, galacturonic acid and glucuronic acid, and after being tested in a social interaction model, the time and number of interactions was increased, as well as the reduction of aggressive behavior and immobility time in the forced swimming test in mice (Wanget al., 2010).

4.4 Reducing effects of brain deficits

Cognitive deficits are changes in the way the individual processes information and especially in the development and execution of mental functions such as memory, language, logical and abstract reasoning, attention, perception, psychomotricity, visual ability and learning. In a simplified way, cognition is defined as the way the brain perceives, learns, remembers, and thinks about all information captured through the five senses (Hilkens & Weerd, 1995). The scale used delimits the score from 0 to 4 according to the degree of cognitive impairment of rats in the neurological findings, being the score attributed according to the following characteristics: the score zero the animal does not present neurological deficit, a point is considered deficit of focal neurological order, two points when there is moderate focal neurological impairment, three points there is a severe focal deficit and present cognitive impairment related to gait and primitive movements and the score 4 when the animals are unable to walk spontaneously and have a level of consciousness depressed (Bederson et al., 1986).

PL obtained from *Bacopa monnieri*(aerial parts) Present in their composition the saponinic glycosides that were tested in a model of cognitive deficit induced by the subchronic administration of phenylcyclidine, resulting in the reversal of the cognitive deficit by means of the increase of the expression of specific transporter proteins, such as vesicular carriers of glutamate type 2 (VGLUT2) in the pre-frontal cortex of rats (Piyabhan & Wetchateng, 2015).PLobtainedfrom*Millettia pulchra*(aerial parts, stem and root) presented in their chemical composite glucose and arabinose and, after being tested in a model of D-galactose-induced cognitive deficit, reverted to memory loss, as measured by the behavioral open-field, passive avoidance and Morris aquatic labyrinth tests. In addition, it reduced lipid peroxidation and NO levels, neuronal nitric oxide synthase (nNOS), SOD, GSH and GPX in mouse brain, as well as elevated levels of BDNF in the hippocampus (Linet al., 2014).

V. CONCLUSION

The biological effects of polysaccharides extracted from plants in the CNS demonstrate potentiality in preclinical trials. The most isolated molecules of medicinal plants were mannose, rhamnose, xylose, arabinose, galactose, ribose and glucose. In this regard, this review points to the need for studies that may elucidate the mechanisms involved in the effects of PL on the CNS. This study contributes with scientific evidence about the promising effects of these compounds on the CNS.

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Table 1. Articles found and selected in databases

*Data Base	Total articles	Excluded after application of the criteria	Read in full	Selected
PubMed	156	131	22	11
Science Direct	418	372	46	3
Newspapers from CAPES	1742	1728	14	4
Total	2316	2231	82	18

* Period from 2000 to 2017

Table 2. Activities and mechanism of PL action of medicinal plants in the CNS.

PL from medicinal plants	Biological activity	Mechanism of action	Reference
Lycium barbarum	Neuroprotective	↓release of lactate dehydrogenase. ↓of caspase activity 3. ↓of JNK protein phosphorylation.	Ho et al., 2009.
Nerium indicum	Neuroprotective	↓release of lactate dehydrogenase. ↓of caspase activity 3. ↑phosphorylation of PDK-1 and Akt. ↓of JNK protein phosphorylation.	Yu et al., 2004; Yu et al., 2007.
Acanthopanax senticosus	Neuroprotective	↓of the production of ROS and NO.	Jin et al., 2013.
Ipomoea tyrianthina	Neuroprotective	↑of the extracellular level of GABA.	León-Rivera et al., 2008.
Dendrobium nobile	Neuroprotective	↓expression of TNFR1.	Li et al., 2011.
Opuntia milpa Alta	NeuroprotectiveAntioxidant	↓release of lactate dehydrogenase. ↓of the production of ROS. ↓of the intracellular concentration of Ca^{2+}. ↓of the extracellular level of glutamate.	Chen et al., 2011.
Ganoderma lucidum	NeuroprotectiveBrain deficit reducer	↓release of lactate dehydrogenase. ↓of the activity of caspases 3, 8 and 9. ↓the expression of Bax and of Bcl-2. ↑ ↓of neurological findings on a 5-point scale.	Zhou et al., 2010.
Euphoria longan	Neuroprotective Antioxidant Anti-inflammatory Brain deficit reducer	↓ of lipid peroxidation. ↓the expression of Bax and of Bcl-2. ↑ ↑ of SOD, GSH and GPX activity ↓ of MPO activity. ↓levels of TNF-α and IL-1β.. ↓of neurological findings on a 5-point scale.	Chen et al., 2011.
Angelica sinensis	Antioxidant	↓of lipid peroxidation. ↓of the production of NO. ↑of SOD, GSH, GPX, CAT and GR activity. ↑ of Ach level andof AChE↓ ↑ levels of Na^{+}, K^{+}-ATPase, Ca^{2+}, Mg^{2+}-ATPase and glucose	Ai et al., 2013.
Salvia miltiorrhiza	AntioxidantBrain deficit reducer	↓ of the production of ROS. ↓ of lipid peroxidation. ↑of SOD, GPX and CAT activity. ↓ of neurological findings on a 5-point scale.	Tu et al., 2013.
Ginkgo biloba	Antioxidant Anti-inflammatoryBrain deficit reducer	↓ of lipid peroxidation. ↓of the production of NO. ↑ of SOD activity. ↓ of MPO activity. ↓levels of TNF-α and IL-1β andof IL-10. ↓of neurological findings on a 5-point scale.	Yang et al., 2013. ↑
Pittocaulon praecox	Antioxidant	↓ of lipid peroxidation. ↓ of the ROS concentration.	Marín-Loaiza et al.,2013.
Pittocaulon filare	Antioxidant	↓ of lipid peroxidation.	Marín-Loaiza et al., 2013.
Pittocaulon velatum	Anti-inflammatory Antioxidant	↓ oflipid peroxidation. ↓ of MPO activity. ↓ of the ROS concentration.	Marín-Loaiza et al., 2013.
Pittocaulon bombycophole	Anti-inflammatory Antioxidant	↓ of lipid peroxidation. ↓ of MPO activity. ↓ of the ROS concentration.	Marín-Loaiza et al., 2013.
Pittocaulon hintonii	Anti-inflammatory Antioxidant	↓ of lipid peroxidation. ↓ of MPO activity. ↓ of the ROS concentration.	Marín-Loaiza et al., 2013.
Taraxacum officinale	Anti-inflammatory	↓levels of TNF-α and IL-1.	Kim et al., 2000.
Aconitum carmichaeli Debx	Anti-inflammatory Antidepressant	↑Proliferation of splenocytes, lymphocytes and production of antibodies. ↑of BDNF expression.	Zhao et al., 2006; Yan et al., 2010.

Panax ginseng	Anti-inflammatory Antidepressant	↑ of neuronal plasticity. ↓ Cellular proliferation and production of IFN-γ, IL-17 and TNF-α. ↓ Population of CD4 + T cells,CD11b+ and macrophages. ↓ CNS damage and dysmyelination.	Wang et al, 2010; Bing et al. 2016.
Bacopa monnieri	Brain deficit reducer	↑ of VGLUT2 expression.	Piyabhan & Wetchateng, 2015.
Millettia pulchra	Brain deficit reducerAntioxidant	↓ of lipid peroxidation. ↓ of NO production and nNOS expression. ↑ of SOD, GSH and GPX activity. ↑ of Ach level and of AChE ↓	Lin et al., 2014.

Symbols: ↑ - elevation; ↓ - reduction.

*Dayanne Terra Tenório Nonato. "Effects F Polysaccharides in the Central Nervous System: A Literature Review." International Journal of Research in Engineering and Science (IJRES), vol. 05, no. 12, 2017, pp. 55–63.