

Animal Galectins and Plant Lectins as Tools for Studies in Neurosciences

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Abstract: Lectins are proteins or glycoproteins of non-immunological origin capable of reversibly and specifically binding to glycoconjugates. They exist in free form or associated with cells and are widely distributed in nature, being found in plants, microorganisms, and animals. Due to their characteristics and mainly due to the possibility of reversible binding to glycoconjugates, lectins have stood out as important tools in research involving Neurobiology. These proteins have the ability to modulate molecular targets in the central nervous system (CNS) which may be involved with neuroplasticity, neurobehavioral effects, and neuroprotection. The present report integrates existing information on the activity of animal and plant lectins in different areas of Neuroscience, presenting perspectives to direct new research on lectin function in the CNS, providing alternatives for understanding neurological diseases such as mental disorders, neurodegenerative, and neuro-oncological diseases, and for the development of new drugs, diagnoses and therapies in the field of Neuroscience.

Keywords: Lectin, carbohydrate, neurobiology, neurosciences, neurobehavioural, neurological diseases.

1. INTRODUCTION

Lectins are an important group of proteins which have been widely studied since the 19th century [1] and are defined as distinct glycoproteins of immunoglobulins that contain at least one non-catalytic domain which allows them to selectively recognize and bind in a reversible way to specific glycoconjugates without causing structural modifications [2]. They are widely distributed in nature, being found in a variety of organisms such as plants, microorganisms, and invertebrate [3] and vertebrate animals [4-6].

These proteins are classified on the basis of functional and structural criteria and are subdivided into four classes: merolectins (possessing at least one carbohydrate-binding domain and therefore being unable to bind cells because they are monovalent), hololectins (formed by two or more carbohydrate-binding domains, but contain at least two such domains which are identical or very similar), chimerolectins (having at least one carbohydrate-binding domain and an unrelated domain, with well-defined catalytic activity or other biological activities), and superlectins (having at least two binding domains of carbohydrates that present different specificities) (Fig. 1) [7, 8].

Lectins have been used as pharmacological tools in several areas and have presented antimicrobial [9-11], anti-inflammatory [12-14], antitumor [15-17], antinociceptive [18-20], healing [21-23], and neuroprotective effects [24-26]. Scientific studies with lectins are very relevant as they have several and important applications, constituting one of the most versatile groups of proteins that are used in basic and applied biomedical and biological research.

In the field of Neurobiology, lectins demonstrated a potent molecular modulating capacity in the central nervous system (CNS), presenting responses involved in behavioral regulation, neuroprotection, and neuroplasticity [26, 27]. These effects may occur through the interaction of these lectins with glycoconjugates present on cell surfaces in the CNS, which act as cellular regulators and are actively involved in signal transduction modulation [28]. These interaction mechanisms are the subject of neuropharmacological studies with neurodegenerative and neuro-oncological diseases, epilepsy syndromes, and mental disorders [26, 29-31].

Though a variety of applications of lectins have been reported in different research and review papers, the application of lectins as tools for neuroscience has not yet been systematically addressed before. Considering the importance of new studies in the Neurobiology field and the growing investigations on the biochemical and pharmacological properties of lectins, this review presents information and perspectives

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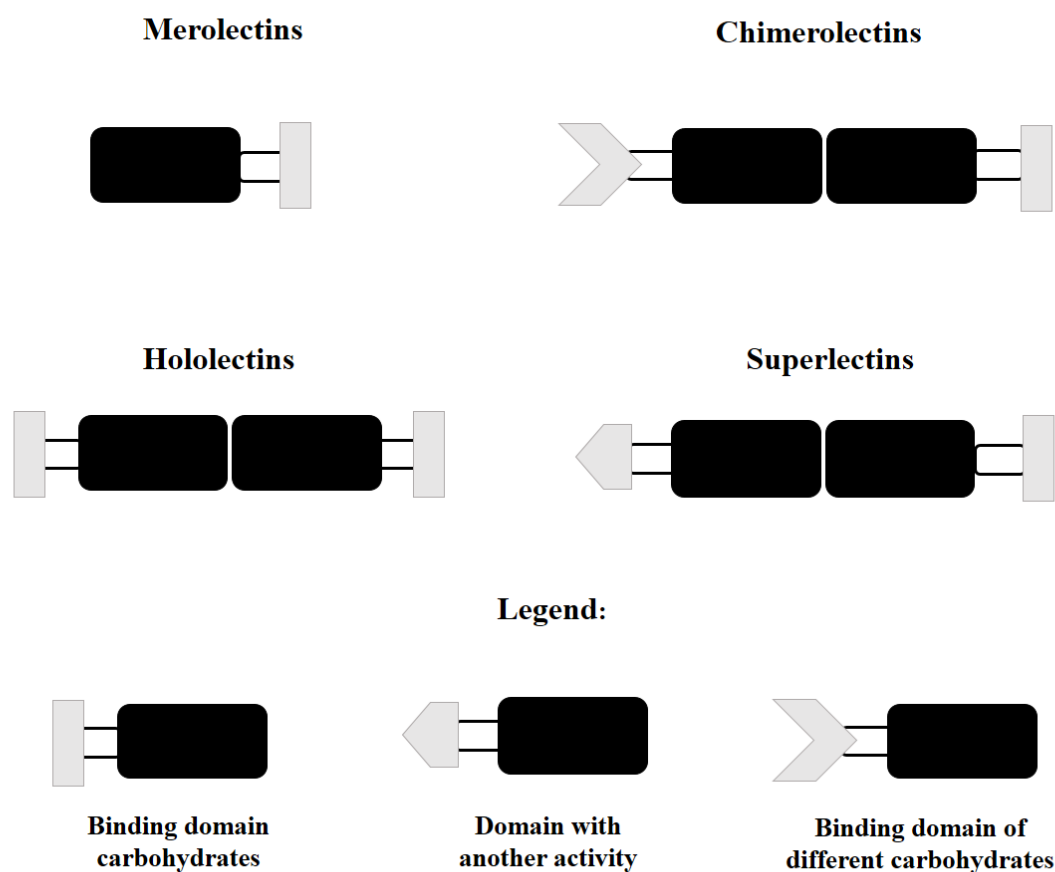


Fig. (1). Lectin classification by structure. Adapted from Peumans *et al.* [7]. (A higher resolution / colour version of this figure is available in the electronic copy of the article).

on the effect of lectins in the CNS to direct new scientific research in the field of Neurosciences.

2. PLANT LECTINS

One of the pioneering studies involving plant lectins was performed by Hermann Stillmark in 1888 [32], which identified that *Ricinus communis* seed extracts caused agglutination of erythrocytes, thus initiating the term hemagglutinin. Then it was in 1954 that the term lectin was introduced by Boyd and Shapleigh to emphasize the ability of plant agglutinins to differentiate red blood cells from ABO due to reactions with the different sugar residues present in these erythrocytes [33, 34].

Lectins are found in many plant families, including monocotyledons and dicotyledons, but most were first detected in Leguminosae [35]. Most plant lectins are present in seed cotyledons, where they can be found in the cytoplasm or in protein bodies, although they have also been found in roots, stems, leaves, fruits, or flowers and other tissues [36]. It has already been shown that lectins found in leaves have similar properties to those obtained from seeds of the same plant [37]; therefore, lectins found in distinct plant tissues may have similar properties.

According to Van Damme *et al.* (1998), plant lectins are classified into seven families: legume lectins, mannose-binding monocotyledone lectins, hevein domain lectins, ri-

bosome-inactivating proteins (RIPs) type 2, lectins related to jacalin, amarantin and phloem lectins from Cucurbitaceae [35].

The use of these plant proteins in the area of neurobiology has grown in recent years and deserves more attention, considering that there is little research on this subject when compared to other areas. The importance of new studies in this area is due to the fact that plant lectins have demonstrated several modulatory effects on the central nervous system (CNS) [26].

3. POTENTIAL OF PLANT LECTINS IN NEUROSCIENCES

Many studies have been developed to elucidate neurochemical bases in neurological diseases and investigation of neuropathological processes has gained increasing attention [38-40]. The drugs available for the treatment of many of these diseases have reasonable efficacy and many side effects [41, 42]. These factors stimulate scientific research that looks for new molecules, especially from natural sources in order to increase the effectiveness of the therapies and to reduce the adverse effects. Plant lectins have gained prominence in neurobiological modulation studies, being promising biomolecules that have effects on the CNS, demonstrating responses that are involved in behavioral regulation, neuroplasticity, and neuroprotection (Table 1).

Table 1. Applications of plant lectins in neurosciences.

Vegetal Source	Lectin	Binding Affinity	<i>In Vitro</i> Activity	<i>In Vivo</i> Activity	Refs.
<i>Artocarpus incisa</i> L	FTL	Galactose	Reversal of glutamatergic excitotoxicity in hippocampal slices	Antidepressant-like effect	[52, 56]
<i>Canavalia ensiformes</i>	ConA	Glucose/ mannose	Neurite growth; Axonal regeneration; Neuroplasticity effects; Anti-gliomas properties	Not reported	[43, 44, 45, 46, 47, 48, 60]
<i>Canavalia brasiliensis</i>	ConBr	Glucose/ mannose	Reversal of glutamatergic excitotoxicity in hippocampal slices	Antidepressant-like effect; Anticonvulsive effect	[26, 53, 54, 55]
<i>Bauhinia bauhinioides</i>	BBL	Galactose	Reversal of glutamatergic excitotoxicity in hippocampal slices	Not reported	[52]
<i>Dioclea lasiophylla</i>	DVL	Glucose/ mannose	Anti-gliomas properties	Not reported	[59]
<i>Dioclea violácea</i>	DlyL	Manose	Anti-gliomas properties	Not reported	[58]
<i>Parkia pendula</i>	PpeL	Glucose	Meningiomas Diagnosis	Not reported	[62]
<i>Vatairea macrocarpa</i>	VML	Galactose	Modulation of the expression of proteins related to inflammation and glial reactivity	Depressant-like effect	[57]

Abbreviations: FTL: frutalin, ConA: Concanavalin A lectin, ConBr: *Canavalia brasiliensis* lectin, BBL: *Bauhinia bauhinioides* lectin, DVL: *Dioclea lasiophylla* lectin, DlyL: *Dioclea violácea* lectin, PpeL: *Parkia pendula* lectin, VML: *Vatairea macrocarpa* lectin.

3.1. Neuroplasticity Effects

The lectin Concanavalin A (ConA) extracted from *Canavalia ensiformes* (Fabaceae family) seeds has glucose/mannose-binding specificity, and has been used as a tool in studies on neural function and neuroplasticity, showing improvement in neurite growth, axonal regeneration, changes in the specificity and blockage of synaptic connections, and modulation of neurotransmitter responses and mechanisms [43-46]. It has also been used in studies on neurochemical aspects involved in the neurotransmission and plasticity of the CNS through functional and biochemical properties of ionotropic glutamate receptors, AMPA and kainate [47, 48].

3.2. Neuroprotective Effects

ConBr is a lectin extracted from *Canavalia brasiliensis* [49] seeds which presents 99% similarity in the amino acid sequence of ConA and the same glucose/mannose-binding specificity [50], and presented a neuroprotective effect in the model of convulsions induced by quinolinic acid, inhibiting the severity of convulsions in mice [26] and presented *in vitro* neuroprotective effect against ischemia in organotypic culture of the hippocampus in rats [51].

A screening of lectin neuroprotective activity in hippocampal slice models of mice treated *in vitro* with glutamate was performed *via* the MTT viability test [52]. ConBr and CGL lectins (obtained from *Canavalia gladiata* seeds) having glucose/mannose-binding affinity, and Frutalin (FTL) (obtained from *Artocarpus incisa* seeds), BBL (obtained from *Bauhinia bauhinioides*), and VGL (obtained from seeds of *Vatairea guianensis*) which have galactose binding affinity were used. ConBr, FTL, and BBL were able to significantly reverse glutamatergic excitotoxicity *in vitro*, suggesting a neuroprotective potential for these lectins against glutamate neurotoxicity [52, 53].

3.3. Neurobehavioral Effects

The neurobehavioral effects of ConBr were also analyzed. ConBr presented an antidepressive-like effect in mice in the forced swimming test and was dependent on the activation of the serotonergic (5HT1 and 5HT2 receptors), adrenergic (α 1-adrenergic receptor), and dopaminergic (D2 receptor) systems [54]. Other studies also demonstrated that antidepressive-like action can also be mediated by the glutamatergic system through NMDA receptors [55].

Our research group screened neurobehavioral models with Frutalin (FTL), lectin α -D-galactose ligand, obtained from *Artocarpus incisa* L seeds. The neuropharmacological characterization of FTL was performed through neurobehavioral models of anxiety and depression. FTL presented a possible anxiogenic-like effect observed in the high plus-maze test and an antidepressive-like effect in the tail suspension test and forced swimming test in mice. The antidepressant-like effect was dependent on carbohydrate interaction and protein structure integrity and mediated by the glutamatergic system through NMDA receptors and the L-Arginine/NO/cGMP pathway observed *in vivo* using antagonist drugs and enzymatic inhibitors, and *in silico* through molecular docking [56].

VML isolated lectin from *Vatairea macrocarpa* seeds (as well as FTL) also has galactose binding affinity but had inverse effects to those demonstrated by FTL. VML presented depressant action, inducing depressive-like behavior in mice, in addition to increasing the expression of proteins related to inflammation and glial reactivity, presenting potentially toxic effects on the hippocampus of mice, apparently involving neuroinflammatory responses [57]. Interesting results were observed for FTL and VML involving plant lectins with galactose binding affinities, but they had opposite effects in the forced swimming test in mice, and the double

role of plant lectins with an affinity for galactose in neural function could be suggested [56, 57].

3.4. Applications in Neuro-oncology

Some plant lectins have also been studied in the induction of cell death in cancer cell lines. The lectins DVL, glucose/mannose-binding extracted from *Dioclea violacea*, and DlyL, mannose-binding extracted from *Dioclea lasiophylla*, showed antitumor effects on rat C6 gliomas through the induction of autophagy and cell death *via* caspase 3 [58, 59]. The lectin ConA also showed autophagic effects in glioblastoma lines [60, 61].

The use of plant lectins as immunohistochemical biomarkers in brain tumors has also been studied, such as PpeL, glucose binding ligand extracted from *Parkia pendula*, which was used for characterizing and diagnosing meningiomas [62].

4. ANIMAL LECTINS

Bovine conglutinin was one of the earliest reports of lectins isolated from animal species, identified in the works of Bordet and Gay in 1906, since many other lectins of animal origin have been identified [63].

The animal lectins were initially divided into two groups, C-type and S-type lectins [64]. Many other characteristics have arisen with the growth of research involving isolation and characterization by chromatographic methods and sequencing, and the lectins of animal origin today are classified according to their structural characteristics, dividing them into five main families: C-type lectins (need disulfide bonds in their structure and the presence of Ca^{2+} ions for their activity), P-type lectins (formed by the calcium-dependent mannose-6-phosphate receptor and the insulin-like growth factor

II/mannose-6-phosphate receptor), I-type lectins or selectins (they are immunoglobulin-like, structurally belonging to the immunoglobulin family and perform functions in the immune system), S-type lectins or galectin (gal) (thiol/sulfhydryl-dependent, specific for β -galactosides), and pentraxins (they form pentamers, are Ca^{2+} ligands and include C-reactive protein, playing a crucial role in the immune system) [65-67]. These lectins have similar sequences and structural properties [68]. Other types of animal lectins have been found, including M-type, L-type, chitinase-type, and F-type lectin, among others [69].

In the mammalian central nervous system (CNS), endogenous lectins with glucose, mannose, or galactose affinity have been highlighted as important molecules modulating the neural function and may play important physiological roles, with galectins being the most studied class of animal lectins in the field of Neurosciences [70-73].

5. POTENTIAL OF GALECTINS IN NEUROSCIENCES

Galectins are the most studied mammalian lectins, have a permanent carbohydrate recognition domain (CRD) sequence consisting of approximately 130 amino acids, an affinity for β -galactosides and are involved in several cellular processes [5, 74, 75].

Isolation and identification studies of this class of proteins presented approximately 15 types and were classified according to the amount and disposition of the CRDs in three subgroups: prototypic galectin, which has a single CRD (gal-1, -2, -5, -7, -10, -11, -13, -14, and -15); tandem-repeat-type galectin having 2 homologous CRDs in a single polypeptide chain (gal-4, -6, -8, -9, and -12); and chimeric-type galectin (gal-3) containing a non-lectin N-terminal region (with proline, glycine and tyrosine residues) bound to 1 CRD (Fig. 2) [21, 76-79].

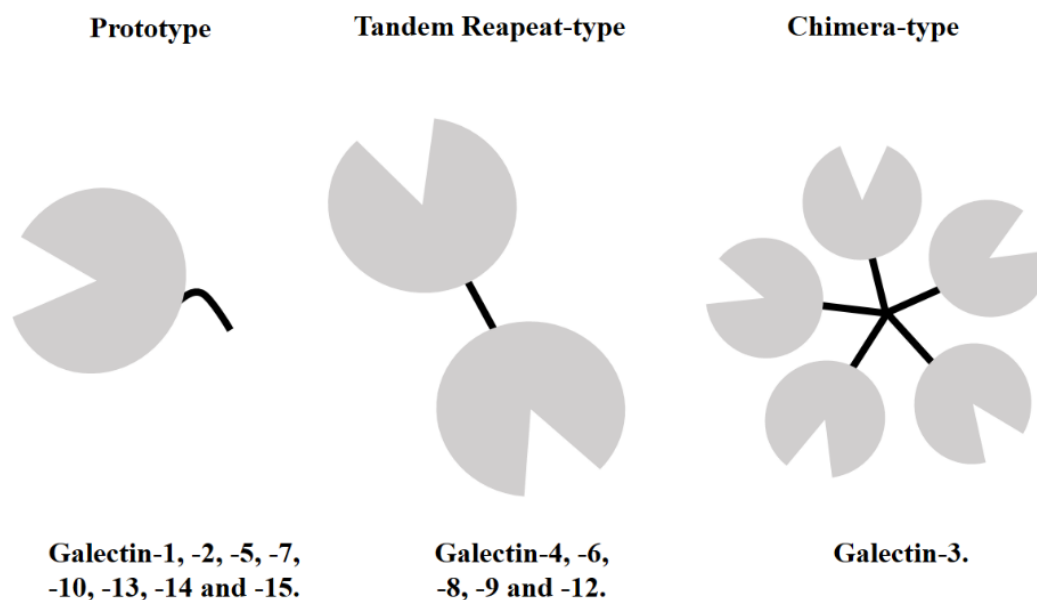


Fig. (2). Overview of the three types of galectins, divided by structure. The Prototype galectins contain a single conserved carbohydrate-recognition domain (CRD) (gal-1, -2, -7, -10, -13, and -14), which can form homodimers. The Tandem repeat-type consists of two linked CRDs (gal-4, -8, -9, and -12). The Chimera-type is characterized by several single CRD's which are fused together to form a pentamer (gal-3). Adapted from Van der Hoeven *et al.* [79].

Galectin functions correlate with their expression patterns. Some galectins (gal-1 and -3) have wide tissue distribution, while others (gal-4, -7, -8, -9 and -12) are more specifically distributed [80]. The major galectins expressed in the CNS are gal-1, -3, -4, -8, and -9 [81]. Gal-1 is found in olfactory receptor neurons (ORNs) and in the subventricular zone (SVZ) of the lateral ventricles [82, 83]. Gal-3 is found in the corpus striatum and microglia [84, 85]. Gal-4 is expressed in immature neurons and oligodendrocytes in the olfactory system [86]. Gal-8 and -9 were detected in astrocytes, but their tissue distribution in the brain is still not well understood [87, 88].

Although the exact physiological roles are not well understood, this class of proteins is present in several cellular compartments, and can be found in the intra and/or extracellular environment, in which they interact with ligands present on the surface of other cells or in the extracellular matrix components [21, 89, 90].

Among the studied functions, galectin has been shown to participate in cell homeostasis through regulation of cell growth, adhesion and cell proliferation, modulation of apoptosis, signal transduction and synthesis of inflammatory mediators such as cytokines, prostaglandins, and nitric oxide, and modulation of neural function [91-96]. The effects of galectins in the CNS have been extensively studied, especially studies with gal-1 and gal-3 (Table 2).

5.1. Effects on Neuronal Development

Neural tissues contain large amounts of glycoconjugates that are important for development in the nervous system

and several specific galactosamine lectins have been found in the brains of animals [97-99].

Gal-1 is a non-covalent homodimeric protein with a galactose-binding CRD and is present in the intra and extracellular media [100, 101]. This galectin exerts physiological and biochemical functions by participating in cell differentiation in myoblasts, hematopoietic mesenchymal cells and is widely distributed through the central and peripheral nervous system [102, 103]. It has been shown that gal-1 presents several important roles in the neural network formation, in addition to in the olfactory system, being widely expressed in nervous tissues in embryonic stages, as well as in adult organisms, being found in sensory and motor neurons, pia mater, choroid plexus, pineal gland, astrocytes, and Schwann cells [104-107].

5.2. Nerve Regeneration

By binding to endogenous glycans, galectins can contribute to cell-cell, cell-matrix interactions, and modulate cellular functions. In addition, intracellular galectin may (as in the case of gal-3) regulate cellular activities, thereby contributing to fundamental processes such as pre-mRNA processing, exhibiting a marked functional diversification in immunological homeostasis and studies with tissue regeneration [108, 109].

In addition, gal-3 is also involved in neuroinflammatory processes, shown by its absence in knockout mice, reduced neuroinflammation and protected the retina and the optic nerve of diabetic mice [110]; improved functional results preserving spinal cord tissue after injury, promoting a better

Table 2. Applications of galectin-1 and galectin-3 in Neurosciences.

Galectins	<i>In Vitro</i> Activity	<i>In Vivo</i> Activity	Refs.
Galectin-1	Neuroplasticity (cell formation and differentiation; expression in the central nervous system)	Development of the olfactory system in mice	[104, 102, 106, 107]
	Nerve regeneration (central and peripheral nerves)	Recovery of locomotor function in mice	[102, 116, 119, 120]
	Neuroprotection (increased myelination)	Neuroprotective effect in models of amyotrophic lateral sclerosis (ALS)	[129, 130]
	Increased expression after cerebral ischemia; Increased of BDNF; Reduction of neuronal apoptosis	Neuroprotection in cerebral ischemia models	[30, 139-142]
	Increased expression in brain tumors and tumor angiogenesis; Biomarker in brain tumors	Induction of tumor growth in mice	[155, 156, 161, 170, 171]
Galectin-3	Absence of gal-3 reduced neuroinflammation	Absence of gal-3 induced motor recovery in mice	[110, 111]
	Gal-3 promoted neurites growth, axonal growth, and functional reinnervation	Improved locomotor activity of mice	[80, 112, 113]
	Biomarker in neurodegenerative diseases (Alzheimer's disease and ALS)	Neuroprotective effect in ALS models in mice	[85, 132, 133, 135]
	Increased gal-3 expression promoted beneficial effects in ischemic brain injury; Biomarker in the prognosis of stroke patients	Gal-3 reduced ischemic brain injury in mice	[144, 147-150]
	Increased expression in neurogliomas; Tumor biomarker for diagnosis of neurogliomas	Anti-gliomas properties	[151, 163, 169]

Abbreviations: ALS: amyotrophic lateral sclerosis, galectin-1: gal-1, galectin-3: gal-3.

recovery of locomotor function [111]; and showed a faster regeneration associated with increased growth of Schwann cells, favoring rapid myelination and neuron survival, thus promoting better morphological and functional results [109]. In contrast, studies have shown gal-3 as a molecule that promotes neural cell adhesion, neurite outgrowth, axonal growth, and functional reinnervation [80, 112, 113].

Gal-1 is expressed in dorsal root ganglia neurons and motor neurons, with immunoreactivity restricted to neuronal cell bodies, axons, and Schwann cells of animals [80, 114, 115]. Gal-1 in reduced and oxidized forms promoted axonal growth and regeneration in central and peripheral nerves [116-122]. Although the mechanisms for gal-1 regeneration actions are not well understood, studies have indicated that macrophages can be target cells, which are stimulated by gal-1 to secrete some neurotrophic molecules, which in turn increase neurite regeneration and the migration of Schwann cells [121, 123, 124].

Studies have also presented gal-4 as required for the growth of axons. It is expressed in hippocampal and cortical neurons, and its reduction inhibits the synthesis of the promoter and functional molecules in the plasma membrane that are necessary for adequate axon growth [125]. Gal-4 also had a regulatory effect on the differentiation of oligodendrocytes, and consequently on myelination [86].

5.3. Neuroprotective Effect in Neurodegenerative Diseases

Galectin has been studied in neurological diseases. Studies have demonstrated that the expression of gal-1 in neuronal and glial cells is related to regenerative processes after injury, being studied in demyelinating diseases [102, 126, 127]. Moreover, the level of gal-1 autoantibodies found in patients with multiple sclerosis is higher than the level found in healthy people [128].

Gal-1 has been studied in amyotrophic lateral sclerosis (ALS). Biochemical and immunohistochemical methods showed the accumulation of gal-1 in axonal spheroids (pathological alteration in the spinal cord) and in degenerate motor neurons of patients with ALS [129]. It has also been observed that gal-1 immunoreactivity is reduced in the skin of patients with ALS, suggesting that cutaneous gal-1 is involved in the pathological process of the disease [126]. In preclinical models of ALS with transgenic mice, oxidized gal-1 improved motor activity, delayed onset of symptoms, prolonged survival of animals, and preserved spinal motor neurons [130, 131].

The effects of gal-3 have also been observed in studies with neurodegenerative diseases, which presented a functional role in microglial neuroinflammation, demonstrating a neuroprotective response in transgenic mice submitted to ALS models [85]. Recent studies have also presented gal-3 as an important molecule for studies of pathogenic mechanisms in neurodegenerative diseases, acting as a possible biomarker observed in the serum, plasma, bone marrow and/or cerebrospinal fluid of patients with Alzheimer's disease [132, 133], ALS [133-135], and Parkinson's disease [136].

5.4. Effects on Cerebral Ischemia

Gal-1 is expressed in neural stem cells (NSCs), in neurons, and in the subventricular zone (SVZ) in the normal adult brain [82, 83]. However, under pathological conditions such as cerebral ischemia, gal-1 levels have been shown to increase in NSCs and in injured cells [137, 138]. The natural increase in gal-1 after an injury has been the target of studies indicating compensatory mechanisms in the self-defense of the organism that suffered cerebral ischemia [30, 139].

Administration of human recombinant gal-1 significantly increased brain-derived neurotrophic factor (BDNF) expression and secretion, reduced neuronal apoptosis, improved motor and cognitive recovery, and decreased the volume of infarcted area in rodents submitted to ischemic models, thus presenting as a promising molecule in brain damage caused by stroke [140-142].

Gal-3 has also presented important roles in studies of cerebral ischemia [143]. Increased expression is related to the performance of crucial roles in the mediation of microglial activation and proliferation induced by ischemic brain injury, with effects observed both *in vitro* [84, 144] and *in vivo* [145-148]. Gal-3 has also been indicated as a biomarker for the prognosis of patients who have suffered from stroke [149, 150].

5.5. Applications in Neuro-oncology

Many studies have highlighted the importance of galectins in the biology of tumors in the central nervous system (CNS) [29, 89, 151-153]. Most of the studies demonstrate the relationship between increased galectin expression and the malignant potential of brain tumors [151, 154-158]. Increased galectin expression has been observed in gliomas [159], astrocytomas [160], oligodendrogliomas [161], ependymomas [162], and meningiomas [163].

The involvement of galectins in the malignant progression of gliomas may be involved in different progression stages such as migration, angiogenesis, or chemoresistance [70, 164-167]. The correlation between galectin expression and tumor progression and metastasis makes these proteins an important target in studies with tumor markers for prognosis and new therapies [159, 168-171].

6. CLINICAL APPLICATIONS

There is a diversity of plant-origin lectins which have already been isolated, characterized and are commercially available. Based on their carbohydrate-binding properties, these proteins have been used for histochemical and cytochemical analyses [172]. Lectin from *Ulex europaeus*-Atto 488 conjugate (19337) was taken for the detection of α -L-fucose by microscopy, flow cytometry and fluorescence *in situ* and hybridization [173]; WGA, Alexa Fluor 488 Conjugate (W11261) was taken for the detection of N-acetylglucosamine and sialic acid residues by microscopy and flow cytometry, and was also used as an *in vivo* neuron marker for neuroanatomical studies [173, 174].

Lectin microarrays have recently been used as a promising tool for research and clinical applications [175]. In this technology, several lectins with known specificity are im-

mobilized as microdots on a solid surface. These lectin microarrays provide a powerful tool for glycosylation determination, drug discovery, and biomarker development [176].

The diagnostic and prognostic relevance of galectins has also been demonstrated [177]. A series of experimental and clinical evidence has correlated high galectin expression with neoplastic progression, and therefore galectins play an important role as potential biomarkers which can help identify numerous diseases and serve as a therapeutic target [178-181].

Among the strategies used, inhibition of carbohydrate recognition domains of galectins has become a target for the action of antagonist molecules, which are being tested in human clinical trials [182]. Traditional small molecule drugs, antibodies, and natural products have been used as galectin antagonists and have shown effects on fibrotic diseases and different cancers [182-185].

Plant lectins and galectins have become validated pharmaceutical targets, increasing the interest of pharmaceutical companies to increasingly exploit the potential of these proteins through preclinical and clinical trials as powerful tools for discovering new therapies and diagnostics [173, 182].

CONCLUSION AND FUTURE DIRECTIONS

Several psychological, biological, and pharmacological studies are developed to understand the neurobiological and neurochemical bases of neurological diseases, often being involved with functional deficits of neurotransmission systems, neuronal degeneration, and growth of brain tumors [186-190]. Research into these pathological processes has gained increasing attention, bearing in mind that many of the treatments are ineffective and the drugs available for treatment of many of these diseases are associated with adverse side effects and may result in other problems such as heart disease, sedation, discharge toxicity, and addiction, among others [41, 42].

Lectins stand out as promising biomolecules, having presented many applications in several areas and are essential tools for neurobiological studies. They are bioactive molecules that are characterized by their ability to recognize glycoconjugates in animal cells. This is one of the lectin properties that demonstrate potential molecular modulation capacity in the central nervous system (CNS) which may be involved in behavioral regulation, neuroplasticity, and neuroprotection [27]. These proteins have been used as tools in basic and applied research, and may provide alternatives for the understanding of neurological diseases such as mental disorders, neurodegenerative, and neuro-oncological diseases, and the search for new therapeutics for the diagnosis and treatment of these diseases [54, 56, 141, 149, 153].

The number of lectin studies and their biological and pharmacological potentials have increased in recent years. Studies on the function of these proteins in neurosciences have been increasingly supported by the aforementioned potentials, but further studies are still needed to deepen their molecular mechanisms in the animal brain since the biomedical potential of these incredible proteins must be widely explored.

Unraveling the neurobiology and molecular mechanisms underlying neurological diseases may contribute to developing new therapies that can promote a better quality of life for patients around the world. In light of this, this review presented a wealth of information and evidence on the role of lectins of animal and vegetable origin in the field of neurobiology, offering subsidies for new biological and pharmacological studies of lectins which are promising possibilities for discovering new treatments for neurological diseases. Most importantly, there is a lack of a systematic summary of the application of these lectins in neurology to which researchers could easily refer when they want to choose them properly for a neuroscience study.

LITERATURE SURVEY AND DATA COLLECTION

Scopus, Web of Science and PubMed databases were searched in April 2019 using the following combination of keywords: (lectin OR plant lectin OR galectin-1 OR galectin-3) AND (neuroscience OR neuroprotection OR neurobehavior OR neuro-oncology OR neurochemistry OR neuronal). From each study, the following information was retrieved: plant lectins (vegetal source, binding affinity, *in vitro* and *in vivo* activity); animal galectins (galectin-1, galectin-3, *in vitro* and *in vivo* activity). All the articles in English, regardless of the time of publication, text availability, and species included were initially accepted. Only original studies were selected that included preclinical and/or clinical data. Reviews, editorials, letters to the editor, and studies with other types of diseases were excluded from the study.

CONSENT FOR PUBLICATION

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CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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