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# Revisión | Review Medicinal plants used in Brazil Public Health System with neuroprotective potential – A systematic review

[Plantas medicinales utilizadas en el Sistema de Salud Pública de Brasil con potencial neuroprotector – Una revisión sistemática]

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**Abstract:** Current pharmacological therapies to treat neurological diseases are at best palliative and manage only the symptoms. Unfortunately, few therapies can affect diseases outcomes and alternative strategies such as stem cell therapy, neurotransplantation and deep brain stimulation are still in progress. Diseases such as Alzheimer's and Parkinson's disease become major public health challenge worldwide. In this way, the interest in the development of neuroprotective drugs of natural origin grows. Hence, this systematic review has quantified the studies that refer neuroprotective potential of plants listed in the Brazilian National List of Medicinal Plants of Interest to the Unified Health System (RENISUS). Searches were performed in two scientific databases (PubMed and Science Direct) from 2010 to 2016. A total of 4.532 articles met the inclusion criteria. 445 studies were considered eligible and were reviewed as full text. Following full analysis, 63 studies were included in this review. The studies covered 12 of the 71 plants belonging to RENISUS. In addition, two species are currently available in the Brazilian public health system as herbal medicine. This review may encourage and contribute to the proper use of medicinal plants in public health system.

Keywords: Neurodegenerative disease, neuroprotection, natural products, public health.

**Resumen:** Las terapias farmacológicas actuales para tratar enfermedades neurológicas son, en el mejor de los casos, paliativas y sólo controlan los síntomas. Desafortunadamente, pocas terapias pueden afectar los avances de las enfermedades y las estrategias alternativas tales como terapia con células madre, neurotransplantate y la estimulación profunda del cerebro están todavía en curso. Enfermedades como el Alzheimer y la enfermedad de Parkinson se convierten en un reto importante para la salud pública en todo el mundo. De esta manera, crece el interés en el desarrollo de fármacos neuroprotectores de origen natural. Por lo tanto, esta revisión sistemática ha cuantificado los estudios que hacen referencia al potencial neuroprotector de las plantas incluidas en la Lista Nacional Brasileña de Plantas Medicinales de Interés para el Sistema Único de Salud (RENISUS). Las búsquedas se realizaron en dos bases de datos científicas (PubMed y Science Direct) de 2010 a 2016. Un total de 4,532 artículos cumplieron los criterios de inclusión. 445 estudios se consideraron elegibles y se revisaron como texto completo. Después del análisis completo, se incluyeron 63 estudios en esta revisión. Los estudios abarcaron 12 de las 71 plantas pertenecientes a RENISUS. Además, actualmente hay dos especies disponibles en el sistema de salud pública brasileño como medicina herbaria. Esta revisión puede alentar y contribuir al uso adecuado de las plantas medicinales en el sistema de salud pública.

Palabras clave: Enfermedad neurodegenerativa, neuroprotección, productos naturales, salud pública.

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#### **INTRODUCTION**

As human life expectancy has increased, also has increased the incidence of neurodegenerative diseases such as Alzheimer's and Parkinson's. These neurodegenerative pathologies comprise a large variety of disorders that result in the loss of functional neurons and synapses (Solanki *et al.*, 2016). Unfortunately, neurological disorders are becoming major public health challenge worldwide and major cause of death (Rios *et al.*, 2016).

The use of vegetal extracts and phytochemicals for medicinal purposes such as prevention, treatment and cure of disorders is one of the oldest practices of traditional folk medicine (Lin, 2011; Huppert et al., 2016). Despite the increased use of synthetic drugs in recent years, about 80% of the population in developing countries depend on medicinal plants as the only access to basic health care (Mendis et al., 2007; Cordell & Colvard, 2012). Increasing evidences suggest that natural products are able to attenuate neurotoxicity. In addition, plant extracts may have a complementary or alternative role in preventing and/or treating neurodegenerative diseases (Lin, 2011; Pandareesh et al., 2015). In view of that, the Brazilian public health system provides plant-derived phytomedicines to the population since 2007. In 2009, Brazil's Ministry of Health published the National List of Medicinal Plants of Interest to the Unified Health System (RENISUS) with the aim to encourage the use of complementary therapies in the Unified Health System (SUS), as well as to promote research on medicinal plants and to establish the correct and safe use of the same. It was prioritized the inclusion of native species of various biomes of the country. The plants were preselected by regions that alluded to its folk use. In addition, it was included plants whose effects have been scientifically proven. Currently, SUS offers the use of 12 herbal medicines (aloe, artichoke, cascara, cat's claw, devil's claw, espinheira-santa, guaco, mastic, mint, plantago, soy isoflavone and willow) derived from plants that belong to RENISUS (Marmitt et al., 2016). Therefore, the aim of the present systematic review was to quantify the scientific reports on RENISUS plants with neuroprotective potential.

#### **METHODS**

#### Search strategy

We conducted a search in PubMed and ScienceDirect databases in an attempt to cover all studies

investigated medicinal plants of RENISUS list that demonstrated neuroprotective potential. In this sense, we analyzed papers published since the creation of RENISUS in the period between January 2010 and December 2016. The keywords used to search were the scientific names of medicinal plants as described in RENISUS list.

### Inclusion and exclusion criteria

In order to be considered in this analysis, articles had to meet the following two inclusion criteria: the neuroprotective potential of the medicinal plant; and evidence in preclinical or clinical phase. All scientific papers available as full and open access texts were considered, regardless of the language. Reviews, semi-structured interviews and research articles that addressed the chemical constituents of the plants without the intention to demonstrate neuroprotective potential were excluded. In addition, papers that only mentioned the empirical use of plants were also excluded.

#### Study selection

Two reviewers independently reviewed the retrieved articles and the analysis of these studies was performed in three steps. The primary search comprised the screening of titles and selecting those with terms related to neuroprotective potential. After reading the abstract of the previous chosen reports, irrelevant or duplicated papers were excluded. The final search consisted of full reading and qualitative analysis of the selected papers in order to elect those that mentioned some evidence of neuroprotective potential.

#### RESULTS

The database search retrieved 4.532 records. Out of a total of 1.289 pre-selected papers, 844 articles that did not meet the inclusion criteria were excluded and the remaining 445 articles were assessed for eligibility. Afterwards, 63 full text articles (1,39% of all searched papers) were considered suitable for this review. All selected reports were written in English and involved in vitro (21 studies), in vivo treatments (41 articles) and preclinical in humans (three research). Figure N° 1 depicts an overview of the study selection procedure. The therapeutic effects attributed to the plants were analyzed according to Table N° 1.



Figure N° 1 Flowchart of the search strategy and study selection

Table Nº 1
Details on each study regarding methodological and outcome aspects of selected researches

Plant / family	Compound / plant part and concentration	Main results	Reference / country
Allium sativum L. (Amaryllidaceae)	Orally administered diallyl trisulfide (DATS) at 80 mg/kg body weight/day	DATS showed multifunctional neuroprotective effects in transgenic mice with amyotrophic lateral sclerosis (SOD1- G93A). Oral administration of the compound at the start of the clinical phase delayed the onset time of the disease. Treatment with the compound reduced the expression of	Guo <i>et al.,</i> 2011 China
		the glial fibrillic acid protein (GFAP) and induced heme oxygenase-1 (HO-1) in the lumbar spinal cord of rats	
Allium sativum L. (Amaryllidaceae)	Pretreated with S- Allylcysteine (SAC) (125 mg/kg intraperitoneal (i.p) daily for 17 days	<ul> <li>SAC induced neuroprotective effect against oxidative stress induced by 1-Methyl-4-phenylpyridinium (MPP (+) model used to evaluate neuroprotective agents for Parkinson's disease) in the striatum of mice. In animals treated with SAC there was attenuation of MPP(+)-induced loss of striatal dopamine (DA) levels. The neuroprotective effect was associated with blockade of lipid peroxidation and reduction of superoxide radical production (positive regulation of Cu-Zn-superoxide dismutase activity).</li> <li>Behavioral analyses showed that SAC improved MPP(+)-induced impairment of locomotion</li> </ul>	Rojas <i>et al.,</i> 2011 Mexico
Allium sativum L. (Amaryllidaceae)	Allicin (1, 10 and 50 mg/kg) by i.p injection per day, respectively for 2	Allicin significantly reduced the volume of the spinal cord infarctions, improved the histopathologic features and increased the number of motor neurons in a dose-	Zhu <i>et al.,</i> 2012 China

	weeks	dependent manner. Allicin also significantly suppressed the	
		accumulations of protein and lipid peroxidation products,	
		and increased the activities of endogenous antioxidant	
		enzymes, including catalase (CAT), superoxide dismutase	
		(SOD), glutathione peroxidase (GPX) and glutathione S-	
		transferase (GST). Allicin exerts neuroprotection against	
		spinal cord I/R injury in rabbits, which may be associated	
		with the improvement of mitochondrial function.	
Allium sativum L.	Garlic intake of the study	Daily consumption of garlic protects endothelial function in	Lau <i>et al.,</i> 2013
(Amarvllidaceae)	population (2.9 g/day) in	patients with ischemic stroke and may play a role in the	China
(	125 Chinese patients with	secondary prevention of atherosclerotic events through	
	prior ischemic stroke (ISS)	brachial artery flow-mediated dilatation (EMD). The daily	
		ingestion of garlic correlated significantly with FMD	
Allium sativum I	Diallyl trisulfide (DATS)	DATS induced increase in p21Waf1 expression (cvclin-	Wallace et al
(Amaryllidaceae)	$(10 \mu g/kg - 10 mg/kg)$	dependent n21 kinase inhibitor) which correlated with	2013
(/ and y madecae)	(10 µg/ kg 10 mg/ kg/	increased n53 expression and degradation of the MDM2	
		protein (n53 negative regulator) Compound reduced the	05/1
		tumor mass and the number of mitotic cells in the tumors	
		It decreased the activity of history deacetylase (HDAC)	
		pro-tumor markers (survivin Bcl-2 c-Myc mTOB EGER	
		VEGE) promoting apontotic factors (Bay mealnian	
		casnase-3) in mice DATS may be an effective therapeutic	
		agent in preventing tymor progression and inducing	
		agent in preventing tumor progression and inducing	
		apoptosis in numan dBivi in vivo without compromising	
Allium cativum I	Animals wore in treated	The with allicin treatment in a model of mean acclucion of	Lip at al 2015
Amum Sutivum L.	with 50 mg/kg alliain and	the corebral artery of rate reduced the volume of the	LIII et ul., 2015
(Amaryindaceae)	with 50 mg/kg amendadu	the cerebral aftery of rats reduced the volume of the	China
		levels of neurological deficits. Allicin increased neuropol	
	cortical neurons (50 µM)	ievels of neurological deficits. Afficin increased neuronal	
		viability, decreased lactate denydrogenase (LDH) release,	
		and inhibited apoptotic neuronal death following oxygen	
		deprivation. There was increased expression of	
		springosine kinase 2 (Sprk2) both in vivo and in vitro	71
Allium sativum L.	Allicin (50 mg/kg l.p.) was	Allicin protects the brain from cerebral I/R injury induced	Znang et al., 2015
(Amaryilidaceae)	administered 3 n after	by occlusion of middle cerebral artery occlusion (MCAO),	China
	daily reperfusion in rats	which can be attributed to its anti-apoptotic and anti-	
	for five consecutive days	inflammatory effects. Allicin reduced cerebral infarction	
		area, brain water content, neuronal apoptosis, tumor	
		necrosis factor- $\alpha$ (INF- $\alpha$ ) levels and myeloperoxidase	
		(MPO) activity in the serum	
Allium sativum L.	Ethanol extract (0.5 or 1.0	Extract and SAC, decreased cobalt chloride (CoCl <sub>2</sub> ) -induced	Orozco-Ibarra et
(Amaryllidaceae)	%) and S-allylcysteine	nypoxia in PC-12 cells, derived from a pheochromocytoma	ai., 2016
	(SAC) (5 or 10 mM)	of the rat adrenal medulia, a useful model for the study of	Mexico
		nerve cell differentiation. Treatment with extract and SAC	
		decreased reactive oxygen species (ROS) levels and the	
		amount of cells in the early and late phases of apoptosis,	
		this protective effect was associated with attenuation in	
		stabilization of the subunit of the hypoxia-inducible factor	

		(HIF-1α)	
Calendula	Compounds 28-O-β-D-	Compounds CS1 and CS2 exerted protection in mouse	Zaki <i>et al.,</i> 2016
officinalis L.	glucopyranosyl-oleanolic	melanoma cells (B16), rat neuroblastoma (neuro-2A) line,	Egypt, Japan and
(Asteraceae)	acid 3-O-β-D–	against hydrogen peroxide (H <sub>2</sub> O <sub>2</sub> ) induced toxicity. CS2	USA
	glucopyranosyl (1→3)-β-	exhibited melanin biosynthesis stimulatory activity. CS1	
	D-glucopyranosiduronic	showed a stimulatory effect for the production of	
	acid (CS1) and oleanolic	hyaluronic acid in human dermal fibroblasts (NHDF-Ad).	
	acid 3-O-β-D–	Both compounds did not show any inhibitory effect on	
	glucopyranosyl $(1\rightarrow 3)$ - $\beta$ -	both lipase and adipocyte differentiation. Compound CS2	
	D-glucopyranosiduronic	can protect neuro-2A cells and increase cell viability	
	acid (CS2) extracted from	against H <sub>2</sub> O <sub>2</sub>	
	the butanol fraction of		
	the seeds and tested in		
	concentration (2.5, 5 and		
	10 μg/mL)		
Curcuma longa L.	A combination	Curcumin combined with candersartan increases	Awad, 2011
(Zingiberaceae)	of candesartan 50 mg i.p	synergistically the inhibitory action of candesartan on	Egypt
	and curcumin 60 mg/kg	cerebral ischemia in rats by suppressing changes in blood	
	i.p	flow and oxidative stress via antioxidant properties,	
	10 days before MCAO in	suggesting beneficial and preventive effects in ischemic	
	mice	brain damage. The treatment restored levels of SOD and	
		glutathione-S-transferase (GST), thiobarbituric acid and	
		heart rate	
Curcuma longa L.	Curcumin (5, 10, 15, 20	Curcumin activates nuclear factor erythroid 2-related	Jiang <i>et al.,</i> 2011
(Zingiberaceae)	and 25 $\mu$ M) for 24 h	factor 2 (Nrf2) target genes in primary spinal cord	China
		astrocytes, decreases the level of intracellular ROS, and	
		attenuates oxidative damage and mitochondrial	
		dysfunction in vitro, which may serve as a therapeutic	
		strategy for neurodegenerative diseases	
<i>Curcuma longa</i> L.	Pretreated with curcumin	Parkinsonian model in rats induced by 6-hydroxydopamine	Khuwaja <i>et al.,</i>
(Zingiberaceae)	(80 mg/kg body weight	(6-OHDA) (10 $\mu$ g/2 $\mu$ l in 0.1% ascorbic acid–saline) the	2011
	orally, in 1% w/v sodium	behavioral activities were significantly preserved with	India
	carboxy methyl cellulose	curcumin pre-treatment (80 mg/kg for 21 days),	
	and 1% tween 80 in	attenuating levels of LPx, glutathione (GSH), GPX,	
	phosphate buffer saline)	glutathione reductase (GR), SOD, catalase (CAT) and	
	once daily for 3 weeks	tyrosine hydroxylase (TH). Curcumin is useful in preventing	
	followed by a single	and has therapeutic potential in attenuation the	
	injection of 6-OHDA in	Parkinson's disease	
	the striatum on the 22nd		
	day		
Curcuma longa L.	Curcumin (60 mg / kg)	Treatment with curcumin exerted a neuroprotective effect	Peeyush Kumar et
(Zingiberaceae)	suspension orally (0.5%	in the prevention of cortical dysfunction associated with	al., 2011
	(w/v) sodium	diabetes in mice. The antioxidant potential of curcumin	India
	carboxymethylcellulose)	attenuated cholinergic dysfunction and oxidative stress	
	daily for 14 days	and improved glucose transport and still delayed the	
		associated diabetic complications. I reatment induced	
		decreased gene expression of muscarinic M1, insulin	
		receptor, SOD, choline acetyl transferase and increased	

Curcuma longa L. [Zingiberaceae]         Curcumin (300 mg/kg, p. 0.) dissolved in DMSO (50%) was administered orally by gavage at volumes not greater than 1.0 m/100 g body weight         Co-administration of curcumin with fur antiepileptic drugs (sodium valproate, provide in DMSO (50%) was administered orally by gavage at volumes not greater than 1.0 m/100 g body weight         Reeta <i>et al.</i> , 2011 India           Curcuma longa L. (Zingiberaceae)         Curcumin (IC50=24.9 µM)         Diet containing curcumin with sub-therapeutic dose of advantation of curcumin with sub-therapeutic dose of advantation of curcumin with sub-therapeutic dose of advantation of curcumin and co-treatment with cisplatin or doxonbicin increased cytotoxicity and apoptosis was observed in human neuroblastoma cells, SK-N-AS and SK- N-BE. Apoptosis was associated with decreased the nuclear factor-xB (NF-xB) activity and a reduction in the expression of doxonbicin increased after 6-0HDA treatment. The preventive and protective effects of curcuma longa L. (Zingiberaceae)         Due t al., 2012 Curcumin (200 mg/kg twice a day for 24 days         Due t al., 2012 Crimin against 6-0HDA may be attributable to the irronchelating activity of curcumin to suppress the iron- induced degeneration of figral dopaminergic neurons         Due t al., 2012 China           Curcumin longa L. (Zingiberaceae)         Curcumin (20 µM)         Combination of 20 µM curcumin and 10 nM pacitized the advity of acetylotion factor (AIF). Combination of 80 µM genoptosis inducton factor (AIF). Combination of 80 µM genoptosis inducton factor (AIF). Combination therapy inhibited cell proliferation, reduced the expression of survival factors and also angiogenic factors         Jaques et al., 2012           Curcumin (12.5, 2 and 50 mutant and PTEM proficient) and U138MG (p53 mu			-	
Curcuma longa L.         Curcumin (300 mg/kg, p. 0) dissolver f3 (GLUT3) in cerebral cortex of diabetic rats         Reeta et al., 2011           (Zingiberaceae)         Curcumin (300 mg/kg, p. 0) dissolver fatter			gene expression of muscarinic M3, $\alpha$ 7-nicotinic	
Curcuma long L. (Zingiberaceae)         Curcumin (300 mg/kg) p.o.) dissolved in DMSO (50%) was administered orally by gavage at volumes not greater than 1.0 ml/100 g body weight 1.0 ml/100 g body weight         Co-administration of curcumin with four antiepilepits curcuma long L. (Zingiberaceae)         Reta et al., 2011           Curcuma long L. (Zingiberaceae)         Curcumin (ICSO=24.9 µM)         Diet containing curcumin and co-treatment with cisplatin or doxorubicin increased the latency to myoclonic jerks         Sukumari-Ramesh or doxorubicin increased the latency to myoclonic jerks           Curcuma longa L. (Zingiberaceae)         Curcumin (ICSO=24.9 µM)         Diet containing curcumia and co-treatment with cisplatin or doxorubicin increased cytotoxicity and apoptosis was observed in human neuroblastoma cells, SK-N-AS and SK- N-BE. Apoptosis was associated with decreased the nuclear factor-xB (Nr-KB) activity and a reduction in the expression         Sukumari-Ramesh USA           Curcumin longa L. (Zingiberaceae)         Curcumin pretreatment intragastric (200 mg/kg) twice a day for 24 days         Curcumin pretreatment intragastric (200 mg/kg) twice a day for 24 days         Curcumin against 6-OHDA may be attributable to the ironchelating activity of curcumin and 10 nM pacitaxel (PTX) worked synergistically therapeutic action in human brain tumor stem cells (HBTSC) and human glioblastoma LN18 (pS3 mutant and PTEN proficient) and UI3MG (pS3 mutant and PTEN mutant) cells, through induction of apoptosis, phosphorylation of Bcl-2 protein, cleavage of Bid to tBid, increase of Bax levels, mitochondrial release of cyctochrome c, and apoptosis induction factor factors         Jaques et al., 2012           Curcuma longa L. (Zingiberaceae)         Curcumin (12.			acetylcholine receptor, acetylcholine esterase and glucose	
Curcuma longa L. (Zingiberaceae)         Curcumin (300 mg/kg, p.) dissolved in DMSO (50%) was administered orally by gavage at volumes not greater than 1.0 ml/100 g body weight         Co-administration of curcumin with four antepleptic administration of curcumin with cour antepleptic curcuma longa L. (Zingiberaceae)         Reeta et al., 2011 India           Curcuma longa L. (Zingiberaceae)         Curcumin (IC50=24.9 µM)         Diet containing curcumin and co-treatment with cisplatin or doxorubicin increased cytotoxicity and apoptosis was observed in human neuroblastoma cells, SK-N-AS and SK- N-BE, Apoptosis was asociated with decreased the nuclear factor-KB (NF-kB) activity and a reduction in the expression of Bcl-2 and Bcl-XL         Sukumari-Ramesh et al., 2011           Curcuma longa L. (Zingiberaceae)         Curcumin pretreatment intragastric (200 mg/kg) twice a day for 24 days         Curcumin pretreatment intragastric (200 mg/kg) twice a day for 24 days         Curcumin apter base curcumin against 6-OHDA may be attributate to the irorochelating activity of curcumin to suppress the iron- induced degeneration of nigral dopaminergic neurons         Du et al., 2012 China           Curcuma longa L. (Zingiberaceae)         Curcumin (20 µM)         Curcumin apter base day for 24 days         Curcumin and 10 M pacitized in the striatum and the number of TH- immunoreactive neurons decreased after 6-OHDA treatment. The preventive and protective effects of curcuma longa L. (Zingiberaceae)         Du et al., 2012         Du et al., 2012           Curcumin (20 µM)         Curcumin and 10 M pacitized in the striatum of the suppressite iron- induced degeneration of nigral dopaminergic neurons         2012 <td< td=""><td></td><td></td><td>transporter 3 (GLUT3) in cerebral cortex of diabetic rats</td><td></td></td<>			transporter 3 (GLUT3) in cerebral cortex of diabetic rats	
(Zingiberaceae)       p. o.) dissolved in DMSO (50%) was administered orally by gavage at volumes not greater than 1.0 ml/100 g body weight       drugs (sodium valproate, phenytoin, phenobaritital and carbamazepine), acted as adjuvant in the epileptic seizure electroshock in mice. Co-administration increased of the three seight framents and reduced side effects. Co- administration of curcumin with sub-therapeutic dose of valproate significantly increased the latency to myoclonic jerks       India         Curcumo longa L. (Zingiberaceae)       Curcumin (IC50=24.9 μM)       Diet containing curcumin and co-treatment with cisplatin or doxorubicin increased cytotoxicity and apoptosis was observed in human neuroblastoma cells, SK-N-AS and SK- N-BE. Apoptosis was associated with decreased the nuclear factor-kB (N-kB) activity and a reduction in the serversion of Bc-2 and Bcl-xt.       Sukumari-Ramesh et al., 2011         Curcuma longa L (Zingiberaceae)       Curcumin pretreatment intragastric (200 mg/kg) twice a day for 24 days       Curcumin pretreatment increased after 6-OHDA treastment. The preventive and protective effects of curcumin against 6-OHDA may be attributable to the increased against 6-OHDA may be attributable to the increased against 6-OHDA treastment. The proficient) and U13MG (p33 mutant and PTEN proficient) and U13MG (p33 mutant and PTEN proficient) and U13MG (p53 mutant and PTEN proficient) and u13MG (p53 mutant and PTEN proficient) and allowing for expression of survival factors and also angiogenic factors       Jaques et al., 2012         Curcuma longa L (Zingiberaceae)       Curcumin (12.5, 2 and 50 mg/kg body weight) administred out once a day, 5 days each week, for 30 days       Exposure to cigarette smoke generated changes in the activity of acetyicholinesterse (AChE), influencing the los	Curcuma longa L.	Curcumin (300 mg/kg,	Co-administration of curcumin with four antiepileptic	Reeta <i>et al.,</i> 2011
(50%) was administered orally by gavage at volumes not greater than 1.0 ml/100 g body weight al.0 ml/100 g body weight       carbamazepine), acted as adjuvant in the epileptic seizure induced by pentylenetetrazol (PT2) or induced by electroshock in mice. Co-administration increased effectiveness of treatments and reduced side effects. Co- administration of curcumin with sub-therapeutic dose of valproate significantly increased the latency to myoclonic jerks         Curcuma longo L (Zingiberaceae)       Curcumin (IC50=24.9 µM)       Diet containing curcumin and co-treatment with cisplatin or doxorubicin increased cytotoxicity and apoptosis was observed in human neuroblastoma cells, SK-N-AS and SK- N-BE. Apoptosis was associated with decreased the nuclear factor-kB (Nr-kB) activity and a reduction in the expression of Bcl-2 and Bcl-xL       Sukumari-Ramesh <i>et al.</i> , 2011         Curcuma longo L (Zingiberaceae)       Curcumin pretreatment intragastric (200 mg/kg) twice a day for 24 days       Curcumin pretreatment induced degeneration of nigral dopaminergic neurons       Du <i>et al.</i> , 2012 China         Curcumin longo L (Zingiberaceae)       Curcumin (20 µM)       Combination of 20 µM curcumin and 10 nM pacitaxel (PTX) worked synergistically therapeutic action in human brain tumor stem cells (HBTSC) and human glioblastoma USA       Hossain <i>et al.</i> , 2012         Curcumin (12.5, 2 and 50 mg/kg body weight) administration of adays       Exposure to cigareter smoke generated changes in the activity of acetylcholinesterase (ACEE), influencing the loss of memory. Treatment with curcumin has bea involved in hereduceael curcumin 03 mark kg hordy       Jaques <i>et al.</i> , 2012         Curcumin (12.5, 2 and 50 mg/kg body weight) administration of curcumin with 6	(Zingiberaceae)	p.o.) dissolved in DMSO	drugs (sodium valproate, phenytoin, phenobarbital and	India
curcuma longo L.       Curcumin (ICS0=24.9 µM)       induced by pentylenetertazol (PTZ) or induced by electroshock in mice. Co-administration increased         Curcuma longo L.       Curcumin (ICS0=24.9 µM)       Diet containing curcumin and co-treatment with cisplatin or downbicin increased cytotoxicity and apoptosis was observed in human neuroblastoma cells, SK-N-AS and SK-N-BE. Apoptosis was associated with decreased the nuclear factor-кB (NF-κB) activity and a reduction in the expression of Bcl-2 and Bcl-xL       Sukumari-Ramesh et al., 2011         Curcuma longo L.       Curcumin pretreatment       Curcumin pretreatment in rats the DA content       Due et al., 2012         Curcuma longo L.       Curcumin (20 µM)       Curcumin pretreatment in rats the DA content       Du et al., 2012         Curcuma longo L.       Curcumin (20 µM)       Combination of 20 µM curcumin and the number of TH-immunoreactive neurons decreased after 6-0HDA treatment. The preventive and protective effects of curcumin against 6-0HDA may be attributable to the ironchelating activity of curcumin and 10 nM paclitaxel (PTX) worked synergistically therapeutic action in human brain tumor stem cells (HBTSC) and human glioblastoma USA       Hossain et al., 2012         Curcuma longo L.       Curcumin (12.5, 2 and 50 mg/kg) body weight) administration of survival factors and also angiogenic factors       Hossain et al., 2012         Curcuma longo L.       Curcumin (12.5, 2 and 50 mg/kg body weight) administration of courcumin again Starbophylation of BL-2 protein, clavage of Bid to tBid, increase of Bax levels, mitochondrial release of cytochrome c, and apoptosis, induction factor (AFF).       Jaque		(50%) was administered	carbamazepine), acted as adjuvant in the epileptic seizure	
volumes not greater than 1.0 ml/100 g body weight       electroshock in mice. Co-administration of curcumin with sub-therapeutic dose of valproate significantly increased the latency to myoclonic jerks         Curcuma longa L (Zingiberaceae)       Curcumin (IC50=24.9 µM)       Diet containing curcumin and co-treatment with cisplatin or doxorubicin increased tyotoxicity and apoptosis was observed in human neuroblastoma cells, SK-N-AS and SK. N-BE. Apoptosis was associated with decreased the nuclear factor-xB (NF-kB) activity and a reduction in the expression of Bcl-2 and Bcl-xL       Sukumari-Ramesh et al., 2011         Curcuma longa L (Zingiberaceae)       Curcumin pretreatment intragastric (200 mg/kg) twice a day for 24 days       Curcumin pretreatment reestablished in the striatum and the number of TH- immunoreactive neurons decreased after 6-0HDA treatment. The preventive and protective effects of curcumin against 6-0HDA may be attributable to the ironchelating activity of curcumin and 10 nM paclitaxel (PTX) worked synergistically therapeutic action in human brain tumor stem cells (HBTSC) and human glioblastoma LN18 (p53 mutant and PTEN proficient) and U138MG (p53 mutant and PTEN mutant) cells, through induction of apoptosis, phosphorylation of Bcl-2 protein, cleavage of Bid to tBid, increase of Bax levels, mitochondria release of cytochrome c, and apoptosis induction factor (AIF). Combination therapy inhibited cell proliferation, reduced the expression of survival factors and also angiogenic factors       Jaques et al., 2012         Curcuma longa L (Zingiberaceae)       Curcumin (12.5, 2 and 50 mg/kg body weight) administred out once a day, 5 days each week, for 30 days       Exposure to cig		orally by gavage at	induced by pentylenetetrazol (PTZ) or induced by	
1.0 ml/100 g body weight       effectiveness of treatments and reduced side effects. Co- administration of curcumin with sub-therapeutic dose of valproate significantly increased the latency to myoclonic jerks       Sukumari-Ramesh         Curcuma longa L. (Zingiberaceae)       Curcumin (IC50=24.9 µM)       Diet containing curcumin and co-treatment with cisplatin or doxorubicin increased cytotoxicity and apoptosis was observed in human neuroblastoma cells, SK-N-AS and SK- N-BE. Apoptosis was associated with decreased the nuclear factor-k8 (NF-k8) activity and a reduction in the expression of BcI-2 and BcI-xt.       Sukumari-Ramesh et al., 2011         Curcuma longa L. (Zingiberaceae)       Curcumin pretreatment intragastric (200 mg/kg) twice a day for 24 days       Curcumin pretreatment in rats the DA content reestablished in the striatum and the number of TH- immunoreactive neurons decreased fler 6-OHDA treatment. The preventive and protective effects of curcumin against 6-OHDA may be attributable to the ironchelating activity of curcumin on Un paclitaxel (PTX) worked synergistically therapeutic action in human brain tumor stem cells (HBTSC) and human glioblastoma LN18 (p53 mutant and PTEN proficient) and U138MG (p53 mutant and PTEN mutant) cells, through induction of apoptosis, phosphorylation of Bcl-2 protein, cleavage of Bid to Bid, increase of Bax levels, mitochondrial release of cytochrome c, and apoptosis induction factor (AIF). Combination therapy inhibited cell proliferation, reduced the expression of survival factors and also angiogenic factors       Jaques et al., 2012         Curcuma longa L. (Zingiberaceae)       Curcumin (12.5, 2 and 50 mg/kg body weight) administred out once a day, 5 days each week, for 30 days       Exposure to cigarette smoke generated changes in the activity of acetylcholinesteras		volumes not greater than	electroshock in mice. Co-administration increased	
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(Lingiberaceae)       administred out once a day, 5 days each week, for 30 days       of memory. Treatment with curcumin has been involved in the modulation of cholinergic neurotransmission, improved cognitive deficits induced by smoke, exerted a protective effect on learning and memory and decreases cholinergic alterations in rats exposed to smoke       Brazil         Curcuma longa L.       Oral administration of curcumin (30 mg/kg body       Supplementation of 0.05% in rats for 30 days showed a significant       Jena <i>et al.,</i> 2012a	(Zingiberaceae)	mg/kg body weight)	activity of acetylcholinesterase (AChE), influencing the loss	2012
day, 5 days each week, for 30 days       the modulation of cholinergic neurotransmission, improved cognitive deficits induced by smoke, exerted a protective effect on learning and memory and decreases cholinergic alterations in rats exposed to smoke         Curcuma longa L. (Zingiberaceae)       Oral administration of curcumin (30 mg/kg body       Supplementation of curcumin with 6-propyl-2-thiouracil (PTLI) of 0.05% in rats for 30 days showed a significant       Jena <i>et al.</i> , 2012a	(8.20100000)	administred out once a	of memory. Treatment with curcumin has been involved in	Brazil
for 30 days       improved cognitive deficits induced by smoke, exerted a protective effect on learning and memory and decreases cholinergic alterations in rats exposed to smoke         Curcuma longa L.       Oral administration of curcumin (30 mg/kg body)       Supplementation of curcumin with 6-propyl-2-thiouracil       Jena et al., 2012a		day, 5 days each week.	the modulation of cholinergic neurotransmission.	DIGEN
Curcuma longa L.       Oral administration of       Supplementation of curcumin with 6-propyl-2-thiouracil       Jena et al., 2012a		for 30 days	improved cognitive deficits induced by smoke exerted a	
Curcuma longa L.       Oral administration of Curcumin (30 mg/kg body)       Supplementation of Curcumin with 6-propyl-2-thiouracil       Jena et al., 2012a			protective effect on learning and memory and decreases	
Curcuma longa L.       Oral administration of       Supplementation of curcumin with 6-propyl-2-thiouracil       Jena et al., 2012a         (Zingiberaceae)       curcumin (30 mg/kg body       (PTU) of 0.05% in rats for 30 days showed a significant       India			cholinergic alterations in rats exposed to smoke	
(Zingiberaceae) curcumin (30 mg/kg body (PTLI) of 0.05% in rats for 30 days showed a significant India	Curcuma longa L	Oral administration of	Supplementation of curcumin with 6-propyl-2-thiouracil	lena <i>et al.</i> , 2012a
	(Zingiberaceae)	curcumin (30 mg/kg body	(PTU) of 0.05% in rats for 30 days showed a significant	India
weight) in drinking water reduction in the level of linid peroxidation (IPx) in brain	(	weight) in drinking water	reduction in the level of lipid peroxidation (IPx) in brain	in ord
The curcumin modulates the expression of superoxide			The curcumin modulates the expression of superovide	
The carcanin modulates the expression of superovide			dismutase in rat brain cortex and cerebellum under PTU-	
	1		dismutase in rat brain cortex and cerebellum under PTU-	

		induced hypothyroidism	
Curcuma longa L.	Oral administration of	The decreased activity of superoxide dismutase (SOD) and	Jena <i>et al.,</i> 2012b
(Zingiberaceae)	curcumin (30 mg/kg body	protein expression of SOD1 in cerebellum of T4-treated	India
	weight) in drinking water	rats were ameliorated after pretreatment administration	
		of curcumin, which also induced a decrease in LPx levels.	
		The regulation of expression of SOD by curcumin in	
		different regions (cerebral cortex and cerebellum) of rat	
		brain is different under hyperthyroidism	
Curcuma longa L.	Curcumin (50 mg/kg) was	Curcumin exhibited neuroprotective effect against toxicity	Mansouri <i>et al.,</i>
(Zingiberaceae)	injected during 10 days	exerted by the intracerebroventricular administration of	2012
	(i.p.)	homocysteine, and consequently improved locomotor	Iran
		function in animals and preventing the onset of Parkinson's	
		disease	
Curcuma longa L.	Bisabolene	Bisabolene sesquiterpenoids exhibited anticonvulsant	Orellana-Paucar
(Zingiberaceae)	sesquiterpenoids	activities in a PTZ -induced seizure assay in larval zebrafish	et al., 2012
	extracted of dried	and rats showing possible neuromodulatory activity	Belgium
	rhizome powder		
Curcuma longa L.	Curcumin (20 μmol/L)	Curcumin protects against staurosporine (STS)-induced	Qin <i>et al.,</i> 2012
(Zingiberaceae)		cytotoxicity in rat hippocampal neurons in primary culture	China
		assay in vitro. Caspase-3, heat shock protein 70, Akt and	
		reactive oxygen species (ROS) activation may be involved	
		in this protection	
Curcuma longa L.	Curcumin C3 Complex <sup>®</sup>	Oral administration of C3 Complex <sup>®</sup> was associated with	Ringman <i>et al.,</i>
(Zingiberaceae)	per day in two divided	reduction of hematocrit and increase of glucose levels in a	2012
	doses for 24 weeks (2 gm	group of 36 patients with Alzheimer's disease, with good	USA
	or 4 gm)	tolerance and limited bioavailability to compound	
Curcuma longa L.	Curcumin (100 mg/kg,	Curcumin protected against biochemical changes and	Sankar <i>et al.,</i>
(Zingiberaceae)	orally) daily for 28 days	oxidative damage induced by cypermethrin (CYP) in rats.	2012
		Curcumin treatment decreased levels of biochemical	India
		markers and lipid peroxidation in the blood and increased	
		levels of GSH, CAT and GPX, preserving the normal	
		histological architecture of the liver, kidney and brain	
Curcuma longa L.	Curcumin (30 and 60	Treatment with curcumin showed protective effect and	Tiwari y Chopra,
(Zingiberaceae)	mg/kg; oral gavage)	reversed cognitive déficits associated with increased AChE	2012
		activity, neuroinflammation (oxidative-nitrosative stress,	India
		TNF- $\alpha$ , interleukins-1 $\beta$ (IL-1 $\beta$ ) and TGF- $\beta$ 1) and neuronal	
		apoptosis (NF-кB and caspase 3) in the cerebral cortex and	
		hippocampus of mice pups postnatally exposed to etanol	
Curcuma longa L.	Tetrahydrocurcumin	THC decreased oxidative damage and ameliorated the	Tyagi <i>et al.,</i> 2012
(Zingiberaceae)	(THC) (25mg/kg/day 0.1%	homocysteinylation of cyto-c in-part by metalloproteinase-	USA
	DMSO dose) was given	9 (MMP-9) activation which leads to autophagy in I/R	
	for 3 days by i.p injection	groups as compared to sham operated groups. This study	
	in mice atter 30 min of	suggests a potential therapeutic role of dietary THC in	
	ischemia induction	cerebral ischemia. The size of edema and cerebral	
		Infarction was reduced in animals treated with THC	
Curcuma longa L.	I en days atter glioma	Curcumin is a potential agent against the human (U138MG,	Zanotto-Filho et
(Zingiberaceae)	implantation (C6),	U87 and U373) malignant glioblastomas (GBM) cell lines	ai., 2012
	animals were trated with	and glioma implantation (C6) in rat. In vitro, curcumin	Brazil

	(50 mg/kg/day curcumin solubilized in sterile DMSO) were administered intraperitoneal (i.p) for 10 days	inhibited proliferation, migration and induced cell death in GBM growth models. In U138MG, curcumin decreased the constitutive activation of PI3K/Akt and the NF-κB pathway, inducing mitochondrial dysfunction as a prelude to apoptosis. In mice implanted with C6, curcumin decreased the volume of brain tumors by 81.8%. No tissue evidence of metabolic transaminases (creatinine and alkaline phosphatase) (cholesterol and glucose), oxidative damage or toxicity was observed	
Curcuma longa L.	Curcumin (50, 100, or	Curcumin exhibited antidepressant effect through	Hurley et al.,
(Zingiberaceae)	200 mg/kg) i.p. injection	neurotrophic activity and increased brain-derived	2013
		neurotrophic factor (BDNF) (antidepressant) in rat	USA
		hippocampus. There was a dose-dependent reduction of	
		immobility in the forced swim test (FST)	L'
(Zingiboracoaa)	Curcumin (1 µM)	Curcumin selectively inhibited L-type Ca <sup>21</sup> channels in cell	Liu <i>et al.</i> , 2013
(Ziligiberaceae)		bigh voltage gated $Ca^{2+}$ channel (HVGCC) currents (IPa)	China
		induced by the intracellular application of the PKC-A	
		pentide inhibitor or by the PKC-A knockdown siRNA in rat	
		hippocampal neurons. In these neurons, new PKC isoforms	
		including PKC-δ, PKC-ε and PKC-θ were endogenously	
		expressed. Compound inhibited the PKC-θ dependent	
		IBavia pathway, which could contribute to its	
		neuroprotective effects on rat hippocampal neurons	
Curcuma longa L.	Combination extract of	The combination of extracts containing C. longa rhizomes	Shi <i>et al.</i> , 2013
(Zingiberaceae)	four plants traditional	showed a neuroprotective mechanism in the prediction of	China
	chinese medicine,	Alzheimer's disease through inhibition of protein	
	longa at concentrations	expression and also in immunohistochemical analysis of	
	(0.075  g/kg-1 x day-1)	the 3p glycogen synthase-kinase (A-GSK-3p) target in the	
	0.15 g/kg-1 x day-1, 0.30	cerebral cortex of transgenic fince (APPV7171)	
	g/kg-1 x day-1) for 4 or 8		
	months		
<i>Curcuma longa</i> L.	Curcumin (2,5 $\mu$ M and 5	Neprilysin (NEP) is a poorly expressed metallopeptidase in	Deng <i>et al.</i> , 2014
(Zingiberaceae)	μινι) ior 24 e 48 h	the brain. Treatment with curcumin induced NEP gene	China
		concomitant with Akt inhibition. NE vP suppression and	
		nroinflammatory cytokines, cyclooxygenase 2 (COX-2)	
		inducible nitric oxide synthase (iNOS) in rat neuroblastoma	
		cells (N2a), which suggests potential for treatment of	
		Alzheimer's disease	
Curcuma longa L.	Compound (ar-)	Compound induced proliferation of neural stem cells (NSC)	Hucklenbroich et
(Zingiberaceae)	turmerone at serial	from fetal rats. In vitro and in vivo, turmerone promoted	<i>al.</i> , 2014
	concentrations of 1.56 to $25 \text{ mm}^{T}$	the neuronal differentiation of NSC. In vivo, after	Germany
	25 µg/mL	intracerebroventricular (i.c.v.) injection of the compound,	
		there was greater proliferation of NSC from the	
		suprentricular zone (SVZ) and hippocampus of adult rats. It	
		the regeneration of neurological disease	
	1		1

Curcuma longa L. (Zingiberaceae)	Curcuminóides diarylalkyls curcumin (CCN), demethoxycurcumin (DMCCN) and bisdemetoxicurcumina (BDMCCN) extracted from rhizomes and tested at concentrations (200, 500, and 1000 µM)	The human β-amyloid enzyme (BACE-1) is a key enzyme responsible for the production of amyloid plaques, which implies the progress and symptoms of Alzheimer's diseas. Curcuminoids CCN, DMCCN and BDMCCN inhibited the activity of BACE-1 in the Drosophila model. Structural features, such as degrees of saturation, functional group and hydrophobicity, appear to be involved in the inhibitory action of curcuminoids against BACE-1	Wang <i>et al.</i> , 2014 Republic of Korea
Curcuma longa L. (Zingiberaceae)	Curcumin (10 µM)	Curcumin improved microglial viability against amyloid $\beta$ (A $\beta$ 42) and suppressed the expression of A $\beta$ 42-induced CD68 glycoprotein. It decreased the levels of IL-1 $\beta$ and interleukin-6 (IL-6) and TNF- $\alpha$ induced by A $\beta$ 42. It exerted an inhibitory effect on the phosphorylation of the ERK1/2 MAPK and p38 MAPK pathways induced by A $\beta$ 42 in the microglia, thus attenuating the inflammatory responses of the cerebral microglia	Shi <i>et al.</i> , 2015 China
<i>Curcuma longa</i> L. (Zingiberaceae)	Pretreatment with curcumin (2,5–20 μmol/L) for 24 h	Curcumin supressed induced apoptosis through the overexpression of appoptosin in cells of dopaminergic neurons SH-SY5Y (human neuroblastoma). It induced a positive regulation of HO-1 expression, reducing the production of intracellular heme and ROS, preventing loss of mitochondrial membrane potential (ΔΨm)	Zheng <i>et al.</i> , 2015 China
<i>Curcuma longa</i> L. (Zingiberaceae)	Curcumin intragastrically administered (100 mg/kg) twice a day for 50 days	Curcumin attenuated oxidative damage such as rotenone- induced dopaminergic neuronal loss in the central nervous system (SNpc) of rats through the activation of the Akt / Nrf2 signaling pathway. Curcumin relieved motor dysfunction, increased GSH levels, and reduced ROS activity and malondialdehyde (MDA) content. Increase suppressed tyrosine hydroxylase (TH) activity in the SNpc of rotenone (ROT)-injured rats. Treatment with the compound restored levels of HO-1 and expression of NADPH	Cui <i>et al.</i> , 2016 China
<i>Curcuma longa</i> L. (Zingiberaceae)	Ethanolic extract	KCHO-1 is a product composed of 30% of ethanolic extracts obtained from the leaves of nine plants, including C. Longa. Preparation showed direct neuroprotective effects on mouse hippocampal cells (HT22). KCHO-1 suppressed levels of cellular damage and generation of ROS induced by glutamate and H2O2. KCHO-1 increased the mRNA and protein expression levels of HO-1, induced the extracellular activation of ERK and increased nuclear translocation of Nrf2	Lee <i>et al.</i> , 2016 Republic of Korea
<i>Curcuma longa</i> L. (Zingiberaceae)	Curcumin at a dose of 200 mg/kg/day or 300 mg/kg/day via gavage for 2 weeks	Compound protects neuronal cells against status epilepticus-induced hippocampal neuronal damage in the lithium-pilocarpine-induced status epilepticus in rat model through induction of autophagy and inhibition of necroptosis. Results have demonstrated an alteration in expression of Beclin-1 and Microtubule-associated protein	Wang <i>et al.</i> , 2016 China

		1A/1B-light chain 3 (LC3) proteins for autophagy and mixed lineage kinase domain-like (MLKL) protein and protein kinase-1 (RIP-1) for necroptosis in almost all four regions	
		(CA1, CA3, DG, and H) of rat hippocampus	
<i>Glycine max</i> (L.) Merr. (Eabaceae)	Compound soyasaponin I (5, 10, and 20 mg/kg-1)	Oral administration of soyasaponin I exhibited significant	Hong <i>et al.</i> , 2013 Republic of Korea
Wien. (Pabaccac)	(3, 10, and 20 mg kg-1)	memory-emancing effects in the passive avoluance, Y-	Republic of Rolea
	once a day for 4 weeks	maze, and Morris Water maze tests in rats. Orai	
	once a day for 4 weeks	administration of soyasaponin l increased the amount of	
		neural precursor cells (NPCs), cell proliferation markers (Ki-	
		67), and neuronal differentiation (NeuN, TUJ1, and MAP2).	
		The compound also increased neurite prolongation and the	
		number of neurites during the differentiation of NPCs.	
		Soyasaponin I can enhance learning and protect memory	
		impairment by promoting the proliferation and	
		differentiation of NPCs in the hippocampus by facilitating	
		neuronal regeneration and minimizing neuroinflammation	
Matricaria	Hydroalcoholic extract	Administration of extract before formalin injection showed	Abad <i>et al.</i> , 2011
chamomilla L.	leaves (25 mg·kg- <sup>1</sup> , i.p.)	decrease of pain responses in both phases of formalin test	Iran
(Asteraceae)		and showed has anti inflammatory effects in the second	
		phase of formalin. Injection of extract and cisplatin	
		together have shown that extract is able to decrease the	
		second phase of cisplatin-induced pain. Extract have	
		analgesic and painful neuropathic effects, is able to	
		decrease cisplatin-induced pain and inflammation better	
		than morphine.	
Matricaria	Compound Apigetrin	Compound reduced mRNA expression and secretion of	Lim et al., 2016
chamomilla L.	(12.5, 25, 50, or 100 µM)	inflammatory cytokines, TNF- $lpha$ and IL-6, prostaglandin E2	Republic of Korea
(Asteraceae)	for 24 h	(PGE2) level, suppressed expression of NF-kB, all	
		stimulated by lipopolysaccharide (LPS), besides nitric oxide	
		(NO) production, as well as expression of COX-2 and iNOS	
		in BV-2 mouse micróglia. Apigetrin enhanced expression of	
		antioxidant enzymes, HO-1 and Nrf2 in BV-2 cells.	
		Compound also increased 2,20-azinobis-(3-	
		ethylbenzothiazoline-6-sulfonic acid) (ABTS) radical	
		scavenging activity, indicating antioxidative activity. Finaly,	
		apigetrin inhibited H2O2-induced cell death in HT22	
		hippocampal cells	
Mentha piperita	Aqueous extract from	Extract activity reduced gamma radiation-induced	Hassan <i>et al.</i> ,
L. (Lamiaceae)	leaves was administered	neuronal injury in rats. The biochemical analysis registered	2013
	to rats by oral gavages at	a decrease in GR and SOD levels after treatment with	Egypt
	a dose of 1 g/kg body	extract. Several histopathological changes were detected	
	weight/day for seven	in rat brain tissues, such as pyrolysis signals in pyramidal	
	consecutive days	cells of the cortex, nuclear vacuolization, apoptosis and	
		neural degeneration. In the rats irradiated with gamma	
	1		1
		rays pretreated with the extract, there was an	
		rays pretreated with the extract, there was an improvement in all the parameters tested above by means	
		rays pretreated with the extract, there was an improvement in all the parameters tested above by means of a state of homeostasis and stabilization of the DNA cycle	

Mikunia laevigata         Ethanolic extract leaves (40 µl/ml.)         Collago et al., Pretreatment of extract To 30 min before includation with Asteraceae)         Collago et al., 2012         Collago et al., 2012           (Asteraceae)         (40 µl/ml.)         Pretreatment of extract To 30 min before includation with Asterace precision. The extract protected against venom-included muscle damage by 80.3% and 60.4% in PND and BC, respectively, and prevented TN-Fa and interferon gamma (IFNy) expression. The extract protected against venom-included muscle stracts on damage, and neurological inflammatory effects of <i>P. olfersii</i> venom (6.5 g powder:100 g of freeh juice). The powder so obtained was oral administrated in diabetic mice (200-800 mg/kg, p.o., o.d.)         The cerebral oxidative stress and damage, and neurological deficits were dose dependently attenuated. Moreover, pre-treatment with the lyophilized from leaves (65% EOH at 4°C, EDH at 4°C. EDH at 4°C. (Forwillations of ethanolic agueous, dried leaves: 65% EOH at 4°C. (Forwillations of ethanolic agueous, dried leaves: 65% EOH at 4°C. (FOR Hardee C. (Forwillations of theore also administration in the dimining water (1000 mg furccer driid extract/kg/day: equivalent to betwee 4.2 and 13 g of dry herb/kg/day depending on preparation method) for one week agueous, chick leaves: 65% EOH at 4°C. (Forwillation in the dimining water (1000 mg furccer driid extract/kg/day: equivalent to betwee 4.2 and 13 g of dry herb/kg/day depending on preparation method) for one week agueous; chick leaves: 65% EOH at 4°C. (Forwillation in the definition and ordernaline leaves (150, 300, and 600 mg/kg body weight (hwi) for 7 weeks         Extract suppressed PTZ-induced seizures and improved the severity of epileptic seizures in a dose-dependent maner and also attenuated serotonin and nordernaline leavels in the brain. With better action than the antieplepti			· · · · ·	
Mikania lacvigata Sch.Bip. ex Baker (Asteraceae)       Ethanolic extract leaves (40 µl/mL)       Pretreatment of extract for 30 min before incubation with (Sugmit) completely protected mouse phrenic nerve-diaphragm (PND) from neuromuscular blockade and delayed the blockade in chick biventer cervicis (BC). Pretreatment of the preparations with extract protected against venom induced muscle damage by 80.3% and 60.4% in PND and BC, respectively, and prevented TNF-a and interferon gamma (IFNV) expression. The extract protected nerve-muscle preparations against the myotoxic, neurotoxic and inflammatory effects of P. olfersil venom       Malik et al. 2011         Momordica charantia L. (Courubiaceae)       1.yophilized fruit juice (6.5 g powder/100 g of firsh juice). The powd so bitained was oral administrated in diabetic mice (200-800 mg/kg, p.o., o.d.)       The cerebral oxidative stress and damage, and neurological deficits were dose dependently attenuated. Moreover, pre-treatment with the lyophilized luce also exhibited dose dependent antihyperglycemic activity in diabetic mice dependent direct GABA, receptor currents in hippocampal slices. Aqueous extracts of fresh leaves and drined leaves defineteraroile (PT2)-induced convulsions in CF-1 mice. Anxiogenic effects in the elevated plus maze were seen in mice receiving any of the five Possiflora extracts in witro assays       Elsas et al., 2010         Passiflora incernatia L., (Passifloraceae)       Ethanol extract from leaves (150, 300, and 600 mg/kg i.p.)       Extract suppressed PT2-induced seizures and improved be severity of epiletic seizures in a dos-dependent maner and also attenuated sertonin and noradrenaline levels in the brain, With better action the anteipleptic drig datapamin method) for one weeks receiptors, which is the main inhibitory neurotinsmitter in theoratia L. (Passifloraceae) <t< td=""><td></td><td></td><td>and in the defense system antioxidant</td><td></td></t<>			and in the defense system antioxidant	
Sch.Bip. ex Baker (Asteraceae)       (40 µJ/mL)       Philodryas offessi venom (50 µg/mL) completely protected mouse phrenic nerve-diaphragm (PND) from neuromuscular blockade and delayed the blockade in chick biventer cervicis (BC). Pretreatment of the preparations with extract protected agains venom-induced muscle damage by 80.38 and 60.4% in PND and BC, respectively, and prevented TN-ra and interferon agama (IFNy) expression. The extract protected nerve-muscle preparations against the myotoxic, neurotoxic and inflammatory effects of <i>P. olfersii</i> venom       Mulik <i>et al.</i> , 2011         Momordica charantia L. (Cucurbitaceae)       Lyophilized fruit juice (6.5 g powder/100 g of fresh juice). The powder so obtained was oral administrated in diabetic mice (200-800 mg/kg, p.oo.d.)       Whole Passiflora extract protected preminent, dose- dependent direct GABA, receptor currents in hippocampal slices. Aqueous extracts of fresh leaves and dried leaves 65% ErOH at 4° C, ErOH 65% ErOH 65% ErOH 65% ErOH 65% ErOH 6	Mikania laevigata	Ethanolic extract leaves	Pretreatment of extract for 30 min before incubation with	Collaço <i>et al.</i> ,
(Asteraceae)       mouse phrenic nerve-daphragm (PRD) from neuromuscular blockade in delayed the blockade in chick biventer cervicis (BC). Pretreatment of the preparations with extract protected against venom-induced muscle damage by 80.3% and 60.4% in PRD and BC, respectively, and prevented TNF-a and interferon gamma (IFNV) expression. The extract protected nerve-muscle preparations against the myotoxic, neurotoxic and inflammatory effects of P. offersil venom       Malik et al., 2011         Momordica charantia L. (Cucurbitaceae)       Lyophilized fruit juice charantia L., (Courbitaceae)       Lyophilized fruit piace charantia (5.5 g powder:100 g of frush juice). The powder so obtained was oral administrated in diabetic mice (200-800 mg/kg, p.o., o.d.)       Whole Passiflora extract induced prominent, dose- des dependent attityperglycemic activity in diabetic mice so (5% EOI H at 4° C, EOH 65% EIOH at 4° C, EOH 65% EIOH 65% EIOH at 4° C, EOH 65% EIOH at 4° C, EOH 65% EIOH 65% E	Sch.Bip. ex Baker	(40 µl/mL)	Philodryas olfersii venom (50 µg/mL) completely protected	2012
Momordica charantia L. (Cheurbitaceae)Lyophilized fruit juice (6.5 g powder/10 g of fresh juice). The powder so obtained was oral administrated in diabetic mice (200-800 mg/kg, p.o. o.d.)The cerebral oxidative stress and damage, and neurological damage by 80.3% and 60.4% in PND and BC, respectively, and prevented TN-and interferon gamma (IFNy) expression. The extract protected nerve-muscle preparations against the mytoxic, neurotoxic and inflammatory effects of <i>P. olfersii</i> venomMalik <i>et al.</i> , 2011 IndiaMomordica charantia L. (Cheurbitaceae)Lyophilized fruit juice (6.5 g powder/10 g of resh juice). The powder so obtained was oral p.o. o.d.)The cerebral oxidative stress and damage, and neurological deficits were dose dependently attenuated. Moreover, p.c. o.d.)Malik <i>et al.</i> , 2011 IndiaPassiflora inccarnata L., (Passiflora extract from leaves 65% EIOH at 4° C, EIOH of 5% EIOH at 4° C, EIOH of the the cycle of the divide anticomvulsant effects against freeze dried extract by loby weight (Obt mice. Anxiogenic effects in the elevated plus maze were seen in mice receiving any of the five Passiflora extracts in vitro assaysSingh <i>et al.</i> , 2012Passiflora incernata L., (Passifloraceae)Hydroethanolic extract mechanistration in the administration in the anyeks; i.p.)Extract suppressed PTZ-induced seizures and improved by ext-ictal depression associated. The treatment reduced drug diageamSingh <i>et al.</i> , 2012Passiflora incernata L., (Passifloraceae)Ethanol extract from leaves (30, 100 at 300 mg/kg i.p.)Extract suppressed PTZ-induced seizures and improved the servity of epiletic seizures in a diso-dependent manner and also attenuated serotonin and norad	(Asteraceae)		mouse phrenic nerve-diaphragm (PND) from	Brazil
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and prevented INd and interfering and interior and interfering and interfering and interding and interfering and interding and interding and interding			ualitage by 80.5% and 00.4% in FND and BC, respectively,	
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charannia L. (Cucurbitaceae)       (6.5 g powder/100 g of fresh juice). The powder so obtained was oral administrated in diabetic mice (200-800 mg/kg, p.o., o.d.)       deficits were dose dependently attenuated. Moreover, pre-treatment with the lyophilized juice also exhibited dose dependent antihyperglycemic activity in diabetic mice incurnata L., (Passifloraceae)       India         Passiflora incurnata L., (Passiflora cate)       Formulations of ethanolic extract from leaves: (S% EtOH and aqueous, dried leaves: 65% EtOH at 4° C. EtOH 65% at 100° C and aqueous, dried leaves: 65% at 010° C and aqueous) continuous administration in the drinking water (1000 mg freeze dried extract/kg/day; equivalent to between 4.2 and 13 g of dry herb/kg/day depending on preparation methool) for one week       Extract suppressed PTZ-induced seizures and improved post-ictal depression associated. The treatment reduced manner and also attenuated serotoni and noradrenaline leaves (150, 300, and 600 mg/kg; i.p.)       Singh et al., 2012         Passiflora incurnata L., (Passiflora incurnata L., (Passiflora i	Momordica	Lyophilized fruit juice	The cerebral oxidative stress and damage, and neurological	Malik <i>et al.</i> , 2011
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IOF / Weeks       hippocampus. The results partially confirmed the proposed mechanism of action of <i>P. incarnata</i> involving GABA receptors, which is the main inhibitory neurotransmitter in the brain         Punica granatum       Pomegranate peel         L. (Lythraceae)       Extract (200         Chloride-induced oxidative stress in in brain of female rats, 2012	(Passifioraceae)	mg/kg body weight (bw))	the content of glutamic acid and cortical serotonin in the	Poland
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Punica granatum       Pomegranate peel       Extract attenuated neurotoxicity by decreasing aluminum       Abdel Moneim,         L. (Lythraceae)       methanolic extract (200       chloride-induced oxidative stress in in brain of female rats,       2012			mechanism of action of <i>P. incarnata</i> involving GABA	
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	L. (Lythraceae)	methanolic extract (200	chloride-induced oxidative stress in in brain of female rats.	2012
mg/kg bwt) and these effects may be related to the stimulation of anti-		mg/kg bwt)	and these effects may be related to the stimulation of anti-	Spain

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		apoptotic protein (Bcl-2) and antioxidant activities	
Punica granatum	P. granatum peel	Administration of the extract decreased the oxidative	Middha et al.,
L. (Lythraceae)	methanolic extract (75	stress in the brain of diabetic mice induced by aloxane,	2012
	and 150 mg of kg body	regulating the antioxidant defense mechanism, attenuating	India
	weight) administred for	the lipid and protein oxidation. Supplementation with the	
	45 days	extract showed increased SOD and GPX activity and	
		decreased MDA, with the most evident changes in the	
		hippocampus region	
Punica granatum	Extract of fruits from	Extract treatment exhibited neuroprotective effects in rats	Celik <i>et al.</i> , 2013
L. (Lythraceae)	pomegranate (225 mg/kg)	by attenuating oxidative stress and inflammatory response	Turkey
	for seven days once a day	in the sciatic nerve, increasing total antioxidant canacity	101110 9
	through orogastric gavage	and decreasing levels of TNE-α. IL-18 and MDA	
Punica aranatum	Eruit Seeds Essential Oil	Nouroprotective effect of the essential oil reversed	Al Sababi <i>at al</i>
I (I vthraceae)	(2.0  mg/mL)	system of the second colls (PC12) induced by 2	2014
L. (Lyunaceae)	(2,0 mg/mL)	cytotoxicity in neuronal cells (PC12) induced by 3-	Lndia
		af the silts sector (3-NP), which may be due to the ability	maia
		of the off to neutralize ROS, NO, LPX and LDH generated by	
		neurotoxicity induced by 3-NP (100 mivi), increasing levels	
D		of antioxidant enzymes	
Punica granatum	Pomegranate seed oil	Nano-PSO delayed the development of Alzheimer's disease	Mizrahi <i>et al.</i> ,
L. (Lythraceae)	(PSO) was unlimitedly	when given in mice TgMHu2ME199K (exhibit typical	2014 Jamaal
	administered; and ater-	pathological features of human CJD, Creutzfeldt Jacob	Israel
	from DSO (Nano DSO)	disease, and of general neurodegeneration) and postponed	
	administered either by	the worsening of the disease in already sick animals.	
	gavage 5 times a week	Analysis of brain samples revealed that the treatment	
	(150  ul/day)	reduced lipid oxidation and neuronal loss, indicating a	
	(150 µi/day),	neuroprotective effect	
Punica granatum	Juice of the pomegranate	Pomegranate juice exhibited neuroprotective effects in a	Tapias <i>et al.</i> ,
L. (Lythraceae)	fruits (6.5–7.5 mL of fluid	rat model of rotenone that induces Parkinson's Disease.	2014
	per day) administered in	Oral administration juice of the pomegranate fruits did not	USA
	their drinking water for	mitigate or prevent experimental Parkinson's disease, but	
	two weeks	instead increased nigrostriatal terminal depletion, DA	
		neuron loss, the inflammatory response and caspase	
		activation, thereby heightening neurodegeneration.	
		Observed increased nitrotyrosine levels, inducible nitric	
		oxide synthase, and activated caspase-3 expression in	
		nigral DA neurons is consistent with potential pro-oxidant	
		activity of Pomegranate juice	
Ruta graveolens	Aqueous extract of leaves	Extract induced cell death in glioblastoma lines (U87MG,	Gentile et al.,
L. (Rutaceae)	(0,01,0,1,1  and  10)	C6 and U138), through the activation of the pathways by	2015
	mg/mL) for 24, 48 and 72	ERK1/2 and AKT. Interestingly, the rutin compound,	Italy
	hours	isolated from the aqueous extract, does not induce cell	-
		death, suggesting that rutin alone is not responsible for the	
		neuroprotective effects	
Zingiher	Compound 6-shogaol (1	6-shogaol suppressed the activation of LPS-induced	Ha et al 2012
officinale Roscoe	5 and 10 µM) and doses	microglia in neuronal-glia cortical primary culture and	Republic of Korea
(Zingiberaceae)	of 5 mg/kg and 20 mg/kg	showed neuroprotective effects in an in vivo	T
	once per day for 3 days in	neuroinflammatory model acting on transient global	
	model in mice	ischemia through inhibition of microglia. It has been shown	
1		ischenna an oagh mhibhan of microglia. It has been showl	1

sulets of powder of er rhizome (250 mg) only one ulet upon headache onset bound 6-gingerol (25 M) trated for 24 h	system of multiple sclerosis patients, implicating that IL-33 may participate in the pathogenesis of multiple sclerosis) (down-regulated) in the spinal cord of mice in an experimental autoimmune encephalomyelitis (EAE) model Capsule administered in a randomized, double-blind clinical trial with 100 patients who had acute migraine was shown to be effective in the treatment of migraine attacks, with effect comparable to the drug sumatriptan. Capsule administration had a lower incidence of side effects than the drug 6-gingerol induced cell death of meningioma (IOMM-Lee and CH157MN cells) by apoptosis with phosphorylation of	Maghbooli <i>et al.,</i> 2014 Iran Das <i>et al.,</i> 2015 USA
sulets of powder of er rhizome (250 mg) only one ulet upon headache onset	system of multiple sclerosis patients, implicating that IL-33 may participate in the pathogenesis of multiple sclerosis) (down-regulated) in the spinal cord of mice in an experimental autoimmune encephalomyelitis (EAE) model Capsule administered in a randomized, double-blind clinical trial with 100 patients who had acute migraine was shown to be effective in the treatment of migraine attacks, with effect comparable to the drug sumatriptan. Capsule administration had a lower incidence of side effects than the drug	Maghbooli <i>et al.</i> , 2014 Iran
sulets of powder of er rhizome (250 mg) only one ulet upon headache onset	system of multiple sclerosis patients, implicating that IL-33 may participate in the pathogenesis of multiple sclerosis) (down-regulated) in the spinal cord of mice in an experimental autoimmune encephalomyelitis (EAE) model Capsule administered in a randomized, double-blind clinical trial with 100 patients who had acute migraine was shown to be effective in the treatment of migraine attacks, with effect comparable to the drug sumatriptan. Capsule administration had a lower incidence of side effects than	Maghbooli <i>et al.,</i> 2014 Iran
sulets of powder of er rhizome (250 mg) only one ulet upon headache	system of multiple sclerosis patients, implicating that IL-33 may participate in the pathogenesis of multiple sclerosis) (down-regulated) in the spinal cord of mice in an experimental autoimmune encephalomyelitis (EAE) model Capsule administered in a randomized, double-blind clinical trial with 100 patients who had acute migraine was shown to be effective in the treatment of migraine attacks, with effect comparable to the drug sumatriptan. Capsule	Maghbooli <i>et al.,</i> 2014 Iran
sulets of powder of er rhizome (250 mg) only one	system of multiple sclerosis patients, implicating that IL-33 may participate in the pathogenesis of multiple sclerosis) (down-regulated) in the spinal cord of mice in an experimental autoimmune encephalomyelitis (EAE) model Capsule administered in a randomized, double-blind clinical trial with 100 patients who had acute migraine was shown to be effective in the treatment of migraine attacks,	Maghbooli <i>et al.,</i> 2014 Iran
sulets of powder of er rhizome (250 mg)	system of multiple sclerosis patients, implicating that IL-33 may participate in the pathogenesis of multiple sclerosis) (down-regulated) in the spinal cord of mice in an experimental autoimmune encephalomyelitis (EAE) model Capsule administered in a randomized, double-blind clinical trial with 100 patients who had acute migraine was	Maghbooli <i>et al.</i> , 2014
sulets of powder of	system of multiple sclerosis patients, implicating that IL-33 may participate in the pathogenesis of multiple sclerosis) (down-regulated) in the spinal cord of mice in an experimental autoimmune encephalomyelitis (EAE) model Capsule administered in a randomized, double-blind	Maghbooli <i>et al.</i> ,
	system of multiple sclerosis patients, implicating that IL-33 may participate in the pathogenesis of multiple sclerosis) (down-regulated) in the spinal cord of mice in an experimental autoimmune encephalomyelitis (EAE) model	
	system of multiple sclerosis patients, implicating that IL-33 may participate in the pathogenesis of multiple sclerosis) (down-regulated) in the spinal cord of mice in an	
	system of multiple sclerosis patients, implicating that IL-33 may participate in the pathogenesis of multiple sclerosis)	
	system of multiple sclerosis nationts implicating that II-22	
	were eievaleu in the venuely and ut the tentral Helvuus	
¥ J · · · ·	were elevated in the periphery and of the central perious	
i.p. injection	repaid(yies, endothenal cells, neurons, B cells drid NK cells) (un-regulated) and II-33 (reported that II-33 levels	
day) for 30 days by	cells, such as i cells, monocytes, dendritic cells, mast cells,	11 a 11
90 mg/kg bw every	a variety of immune and non-immune	2014 Iran
o-alconolic extract of	Extract modulated the expression of IL-27 (is expressed by	Jararzadeh <i>et al.</i> ,
	which was largely owing to 10-gingerol	Teferment 1 de T
treatment	exhibited a significant anti-neuroinflammatory capacity,	
$20 \mu\text{M}$ for 20 h of	proinflammatory gene expression. Fresh ginger extract	
8-gingerol,	underlying mechanism responsible for inhibiting the	
nL) and compounds	activated BV2 microglia. Blocking NF-KB activation was the	
ktract (0.125–0.5	IL-6 and TNF- $\alpha$ as well as their mRNA levels in LPS-	Taiwan
sh ginger ethanolic	Compounds inhibited the production of nitric oxide, IL-1 $\beta$ ,	Ho et al., 2013
	and terpenoids	
	of phytochemicals such as flavonoids, alkaloids, tannins	
	lipid peroxidation, which can be attributed to the presence	
	sodium nitroprusside (SNP) and quinoline (QA) induced by	Nigeria
izomes (100 $\mu$ L)	in vitro models. The extract inhibited the activity of AchF.	2012b
ous extract of ginger	Extract exerted anti-Alzheimer properties in the rat brain in	Oboh <i>et al.</i>
	managed/prevented by dietary intake of ginger	
	or the prain of mice in a dose-dependent manner. The	
	extract caused a significant decrease in the MDA contents	TAISCHA
rnizomes	lipid peroxidation in rat brain homogenates in vitro. The	2012a Nigeria
eous extract of the	Extract showed protective properties against Fe <sup>2+</sup> -induced	Oboh <i>et al.</i> ,
	GPX, both cerebral cortex and hippocampus	
14 days after the	pharmacopuncture presented increased levels of CAT and	
us point for a period	mice. Animals submitted to ginger treatment with	Thailand
s injected into the	cerebral ischemia induced by occlusion of the MCAO in	2012
mes (0.1 mL/kg bw)	cognitive function and decreases oxidative stress after	Wattanathorn,
eous extract of the	Extract co-administered to pharmacopuncture improves	Jittiwat &
	PGE2, IL-1 $\beta$ , TNF- $\alpha$ , p38 MAPK and NF- $\kappa$ B	
	neurodegenerative diseases by inhibiting the production of	
	to be an effective therapeutic agent for the treatment of	
16	cous extract of the	to be an effective therapeutic agent for the treatment of neurodegenerative diseases by inhibiting the production of PGE2, IL-1β, TNF-α, p38 MAPK and NF-κB

	downregulation of tetraspanin protein (TSPAN12), survival	
	proteins (Bcl-XL and Mcl-1), and overexpression apoptotic	
	factors (Bax and caspase-3)	

From the selected articles in the two databases (Figure N° 2), more than a third of the publications occurred in 2012 (34.92%). Curcuma

*longa* L. (turmeric) was the medicinal plant with the highest number of published data totalizing 30 studies (47,62% of all selected articles).



#### Figure N° 2 Number of publications with neuroprotective potential distributed between 2010 and 2016, between RENISUS and C. Longa plants, plant with the largest amount of research.

Out of the 63 articles, only three studies were developed by Brazilian institutions (Jaques et al., 2012; Zanotto-Filho et al., 2012; Collaço et al., 2012). We would have expected an increase in Brazilian scientific research after the creation of RENISUS, although that was not the case here. In terms of the 71 medicinal herbs of RENISUS, only 12 plant species were reported within the scope of our review. Out of 12 plants with neuroprotective potential, two species, Glycine max L. (soy) and Mentha piperita L. (pepper mint), is currently available at SUS as phytotherapy. In addition, Mikania laevigata Sch.Bip. ex Baker (guaco) and Passiflora incarnata L. (passion fruit) are representative Brazilian plants.

It is worthy to highlight that this systematic review evaluated so only a period of scientific production after the creation of RENISUS. Nevertheless, it is noteworthy that before and after that period numerous plant species have been scientifically proven for their neuroprotective potential including *Panax ginseng* C.A. Mey. (Chinese ginseng) (Van Kampen *et al.*, 2014), *Ginkgo biloba* L. (ginkgo) (Saleem *et al.*, 2008), *Salvia officinalis* L. (sage) (Eidi *et al.*, 2006), *Hypericum perforatum* L. (St John's wort) (Silva *et al.*, 2004), *Morus alba* (white mulberry) (Kang *et al.*, 2006) and *Bacopa monnieri* L. (Brahmi) (Calabrese *et al.*, 2008).

#### DISCUSSION

The present systematic review identified 63 reports on the effects of 12 medicinal herbs listed in RENISUS on neuroprotective potential. Neuroprotective properties are defined here as the ability to counteract and attenuate mechanisms that may contribute to the pathogenesis and progression of neurodegenerative disorders. The pooled data revealed that the identification and characterization of new phytochemicals extracted from medicinal plants are vital for the development of new drugs for the treatment of neurological diseases such as the neurodegenerative ones. The potential of plants is justified by their importance in the most different medical applications. In addition, several plants traditionally used that were not the object of our study may also offer a great field for research to proving the efficacy and safety of their administration (Bolson *et al.*, 2015; Adebayo *et al.*, 2015).

One of the most active compounds studied was curcumin, which is a polyphenol antioxidant of low molecular weight. It was first extracted from *C. longa* rhizomes thousands of years ago by Asians (Srivastava *et al.*, 1985). Curcumin is one of the active phytochemicals found in high concentration in species of Zingiberaceae family and it has an exceptional safety profile and a number of pleiotropic actions with potential neuroprotective efficacy that can be achieved at submicromolar level (Chin *et al.*, 2013). All these facts corroborate with the number of studies on turmeric and ginger found in this review.

As demographics move towards an aging population, neurological pathologies become one of the main challenges to the modern health care system. Therefore, the zeal directed by public health agencies for the use of medicinal plants has increased substantially. Since 1978, the World Health Organization (WHO) has been funding significant public investment in projects related to medicinal plants. Consequently, an increase in public interest in natural therapies can be seen in developing and developed countries resulting in growing acceptance of herbal medicines by health professionals and the population in general (Calvo & Cavero, 2015).

Despite the abundance of Brazilian flora, the therapeutic profile of innumerous plants has not been properly explored (Oliveira *et al.*, 2013; Martins *et al.*, 2016). Seeking to enhance the knowledge of existing natural products in the country, since 2012, Brazil's Ministry of Health launches funds focused on projects and research on medicinal plants. Since the creation of the fund, 66 projects in the country were awarded with budgets that totalize US\$ 7 million (Brazil, 2015). In this context, in order to guide and encourage professionals to prescribe plants and herbal medicines, ANVISA published in June 2016, the Herbal Memento, which gathers detailed information on numerous RENISUS plants, containing data on contraindications, precautions for use, adverse effects, drug interactions, routes of administration and dosage (Brazil, 2016).

## CONCLUSION

In conclusion, the outcomes of this systematic review have disclosed the neuroprotective potential of 12 selected plant species of RENISUS. Data from preclinical studies showed that medicinal herbs might have potential benefit for the management of neurodegenerative diseases. In addition, the abovementioned beneficial properties of RENISUS plants contribute substantially to the medicinal knowledge of potentially important species, and this review can be used as a guide to new researches in the neurological field.

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## REFERENCES

- Abad ANA, Nouri MHK, Gharjanie A, Tavakoli F. 2011. Effect of Matricaria chamomilla Hydroalcoholic Extract on Cisplatin-induced Neuropathy in Mice. **Chin J Nat Med** 9: 126 - 131.
- Abdel Moneim AE. 2012. Evaluating the potential role of pomegranate peel in aluminuminduced oxidative stress and histopathological alterations in brain of female rats. **Biol Trace Elem Res** 150: 328 -336.
- Adebayo SA, Dzoyem JP, Shai LJ, Eloff JN. 2015. The anti-inflammatory and antioxidant activity of 25 plant species used traditionally to treat pain in southern African. **BMC Complement Altern Med** 15: 159.
- Al-Sabahi BN, Fatope MO, Essa MM, Subash S, Al-Busafi SN, Al-Kusaibi FS, Manivasagam T. 2014. Pomegranate seed oil: Effect on 3-nitropropionic acid-induced neurotoxicity in PC12 cells and elucidation of unsaturated fatty acids composition. Nutr Neurosci 20: 40 48.
- Awad AS. 2011. Effect of combined treatment with curcumin and candesartan on ischemic brain damage in mice. J Stroke Cerebrovasc 20: 541 - 548.

- Bolson M, Hefler SR, Dall'Oglio Chaves EI, Gasparotto Junior A, Cardozo Junior EL. 2015. Ethno-medicinal study of plants used for treatment of human ailments, with residents of the surrounding region of forest fragments of Parana, Brazil. J Ethnopharmacol 161: 1 - 10.
- Brazil. Ministério da Saúde. Portal da Saúde. Edital SCTIE Nº 2/2015, de 24 de agosto de 2015. 2015.

http://portalsaude.saude.gov.br/images/pdf /2015/agosto/26/edital-sctie-2-2015disposicoes-gerais.pdf

Brazil. Ministério da Saúde. Memento Fitoterápico. 2016.

http://portal.anvisa.gov.br/documents/338 32/2909630/Memento+Fitoterapico/a80ec4 77-bb36-4ae0-b1d2-e2461217e06b

- Calabrese C, Gregory WL, Leo M, Kraemer D, Bone K, Oken B. 2008. Effects of a standardized *Bacopa monnieri* extract on cognitive performance, anxiety, and depression in the elderly: a randomized, double-blind, placebocontrolled trial. J Altern Complement Med 14: 707 - 713.
- Calvo MI, Cavero RY. 2015. Medicinal plants used for neurological and mental disorders in Navarra and their validation from official sources. **J Ethnopharmacol** 169: 263 - 268.
- Celik F, Gocmez C, Bozkurt M, Kaplan I, Kamasak K, Akil E, Dogan E, Guzel A, Uzar E. 2013. Neuroprotective effects of carvacrol and pomegranate against methotrexate-induced toxicity in rats. **Eur Rev Med Pharmacol Sci** 17: 2988 - 2993.
- Chin D, Huebbe P, Pallauf K, Rimbach G. 2013. Neuroprotective properties of curcumin in Alzheimer's disease--merits and limitations. **Curr Med Chem** 20: 3955 - 3985.
- Collaco RC, Cogo JC, Rodrigues-Simioni L, Rocha T, Oshima-Franco Y, Randazzo-Moura P. 2012. Protection by *Mikania laevigata* (guaco) extract against the toxicity of *Philodryas olfersii* snake venom. **Toxicon** 60: 614 - 622.
- Cordell GA, Colvard MD. 2012. Natural products and traditional medicine: turning on a paradigm. **J Nat Prod** 75: 514 - 525.
- Cui Q, Li X, Zhu H. 2016. Curcumin ameliorates dopaminergic neuronal oxidative damage via

activation of the Akt/Nrf2 pathway. **Mol Med Rep** 13: 1381 - 1388.

- Das A, Miller R, Lee P, Holden CA, Lindhorst SM, Jaboin J, Vandergrift WA 3rd, Banik NL, Giglio P, Varma AK, Raizer JJ, Patel SJ. 2015. A novel component from citrus, ginger, and mushroom family exhibits antitumor activity on human meningioma cells through suppressing the Wnt/β-catenin signaling pathway. **Tumour Biol** 36: 7027 - 7034.
- Deng Y, Lu X, Wang L, Li T, Ding Y, Cao H, Zhang Y, Guo X, Yu G. 2014. Curcumin inhibits the AKT/NF- $\kappa$ B signaling via CpG demethylation of the promoter and restoration of NEP in the N2a cell line. **Am Assoc Pharm Scient J** 16: 649 - 657.
- Du XX, Xu HM, Jiang H, Song N, Wang J, Xie JX. 2012. Curcumin protects nigral dopaminergic neurons by iron-chelation in the 6hydroxydopamine rat model of Parkinson's disease. **Neurosci Bull** 28: 253 - 258.
- Eidi M, Eidi A, Bahar M. 2006. Effects of *Salvia officinalis* L. (sage) leaves on memory retention and its interaction with the cholinergic system in rats. **Nutrition** 22: 321 326.
- Elsas SM, Rossi DJ, Raber J, White G, Seeley CA, Gregory WL, Mohr C, Pfankuch T, Soumyanath A. 2010. *Passiflora incarnata* L. (Passionflower) extracts elicit GABA currents in hippocampal neurons in vitro, and show anxiogenic and anticonvulsant effects in vivo, varying with extraction method. **Phytomedicine** 17: 940 - 949.
- Gentile MT, Ciniglia C, Reccia MG, Volpicelli F, Gatti M, Thellung S, Florio T, Melone MA, Colucci-D'Amato L. 2015. *Ruta graveolens* L. induces death of glioblastoma cells and neural progenitors, but not of neurons, via ERK 1/2 and AKT activation. **PLoS One** 10: e0118864.
- Guo Y, Zhang K, Wang Q, Li Z, Yin Y, Xu Q, Duan W, Li C. 2011. Neuroprotective effects of diallyl trisulfide in SOD1-G93A transgenic mouse model of amyotrophic lateral sclerosis. Brain Res 1374: 110 - 115.
- Ha SK, Moon E, Ju MS, Kim DH, Ryu JH, Oh MS, Kim SY. 2012. 6-Shogaol, a ginger product, modulates neuroinflammation: a new approach to neuroprotection. Neuropharmacology 63: 211 - 223.

- Hassan HA, Hafez HS, Goda MS. 2013. *Mentha piperita* as a pivotal neuro-protective agent against gamma irradiation induced DNA fragmentation and apoptosis: Mentha extract as a neuroprotective against gamma irradiation. **Cytotechnology** 65: 145 - 156.
- Ho SC, Chang KS, Lin CC. 2013. Antineuroinflammatory capacity of fresh ginger is attributed mainly to 10-gingerol. **Food Chem** 141: 3183 - 3191.
- Hong SW, Heo H, Yang JH, Han M, Kim DH, Kwon YK. 2013. Soyasaponin I improved neuroprotection and regeneration in memory deficient model rats. **PLoS One** 8: e81556.
- Hossain M, Banik NL, Ray SK. 2012. Synergistic anti-cancer mechanisms of curcumin and paclitaxel for growth inhibition of human brain tumor stem cells and LN18 and U138MG cells. **Neurochem Int** 61: 1102 -1113.
- Hucklenbroich J, Klein R, Neumaier B, Graf R, Fink GR, Schroeter M, Rueger MA. 2014. Aromatic-turmerone induces neural stem cell proliferation *in vitro* and *in vivo*. **Stem Cell Res Ther** 5: 100.
- Huppert D, Oldelehr H, Krammling B, Benson J, Brandt T. 2016. What the ancient Greeks and Romans knew (and did not know) about seasickness. **Neurology** 86: 560 - 565.
- Hurley LL, Akinfiresoye L, Nwulia E, Kamiya A, Kulkarni AA, Tizabi Y. 2013.
  Antidepressant-like effects of curcumin in WKY rat model of depression is associated with an increase in hippocampal BDNF.
  Behav Brain Res 239: 27 30.
- Jafarzadeh A, Mohammadi-Kordkhayli M, Ahangar-Parvin R, Azizi V, Khoramdel-Azad H, Shamsizadeh A, Ayoobi A, Nemati M, Hassan ZM, Moazeni SM, Khaksari M. 2014. Ginger extracts influence the expression of IL-27 and IL-33 in the central nervous experimental autoimmune system in encephalomyelitis and ameliorates the clinical symptoms of disease. J Neuroimmunol 276: 80 - 88.
- Jaques JA, Rezer JF, Carvalho FB, da Rosa MM, Gutierres JM, Goncalves JF, Schmatz R, de Bairros AV, Mazzanti CM, Rubin MA, Schetinger MR, Leal DB. 2012. Curcumin protects against cigarette smoke-induced cognitive impairment and increased

acetylcholinesterase activity in rats. **Physiol Behav** 106: 664 - 669.

- Jawna-Zboińska K, Blecharz-Klin K, Joniec-Maciejak I, Wawer A, Pyrzanowska J, Piechal A, Mirowska-Guzel D, Widy-Tyszkiewicz E. 2016. *Passiflora incarnata* L. improves spatial memory, reduces stress, and affects neurotransmission in rats. **Phytother Res** 30: 781 - 789.
- Jena S, Anand C, Chainy GB, Dandapat J. 2012a. Induction of oxidative stress and inhibition of superoxide dismutase expression in rat cerebral cortex and cerebellum by PTUinduced hypothyroidism and its reversal by curcumin. **Neurol Sci** 33: 869 - 873.
- Jena S, Dandapat J, Chainy GB. 2012b. Curcumin differentially regulates the expression of superoxide dismutase in cerebral cortex and cerebellum of L-thyroxine (T(4))-induced hyperthyroid rat brain. **Neurol Sci** 34: 505 -510.
- Jiang H, Tian X, Guo Y, Duan W, Bu H, Li C. 2011. Activation of nuclear factor erythroid 2related factor 2 cytoprotective signaling by curcumin protect primary spinal cord astrocytes against oxidative toxicity. **Biol Pharm Bull** 34: 1194 - 1197.
- Jittiwat J, Wattanathorn J. 2012. Ginger pharmacopuncture improves cognitive impairment and oxidative stress following cerebral ischemia. J Acupunct Meridian Stud 5: 295 - 300.
- Kang TH, Oh HR, Jung SM, Ryu JH, Park MW, Park YK, Kim SY. 2006. Enhancement of neuroprotection of mulberry leaves (*Morus alba* L.) prepared by the anaerobic treatment against ischemic damage. Biol Pharm Bull 29: 270 274.
- Khuwaja G, Khan MM, Ishrat T, Ahmad A, Raza SS, Ashafaq M, Javed H, Khan MB, Khan A, Vaibhav K, Safhi MM, Islam F. 2011. Neuroprotective effects of curcumin on 6hydroxydopamine-induced Parkinsonism in rats: behavioral, neurochemical and immunohistochemical studies. Brain Research 1368: 254 - 263.
- Lau KK, Chan YH, Wong YK, Teo KC, Yiu KH, Liu S, Li LS, Shu XO, Ho SL, Chan KH, Siu CW, Tse HF. 2013. Garlic intake is an independent predictor of endothelial function

in patients with ischemic stroke. J Nutr Health Aging 17: 600 - 604.

- Lee DS, Ko W, Song BK, Son I, Kim DW, Kang DG, Lee HS, Oh H, Jang JH, Kim YC, Kim S. 2016. The herbal extract KCHO-1 exerts a neuroprotective effect by ameliorating oxidative stress via heme oxygenase-1 upregulation. **Mol Med Rep** 13: 4911 - 4919.
- Lim HS, Kim OS, Kim BY, Jeong SJ. 2016. Apigetrin from *Scutellaria baicalensis* Georgi inhibits neuroinflammation in BV-2 microglia and exerts neuroprotective effect in HT22 hippocampal cells. **J Med Food** 19: 1032 - 1040.
- Lin B. 2011. Polyphenols and neuroprotection against ischemia and neurodegeneration. **Mini Rev Med Chem** 11: 1222 1238.
- Lin JJ, Chang T, Cai WK, Zhang Z, Yang YX, Sun C, Li ZY, Li WX. 2015. Post-injury administration of allicin attenuates ischemic brain injury through sphingosine kinase 2: *In vivo* and *in vitro* studies. **Neurochem Int** 89: 92 100.
- Liu K, Gui B, Sun Y, Shi N, Gu Z, Zhang T, Sun X. 2013. Inhibition of L-type Ca(<sup>2+</sup>) channels by curcumin requires a novel protein kinasetheta isoform in rat hippocampal neurons. **Cell Calcium** 53: 195 - 203.
- Maghbooli M, Golipour F, Moghimi Esfandabadi A, Yousefi M. 2014. Comparison between the efficacy of ginger and sumatriptan in the ablative treatment of the common migraine. **Phytother Res** 28: 412 - 415.
- Malik ZA, Singh M, Sharma PL. 2011. Neuroprotective effect of *Momordica charantia* in global cerebral ischemia and reperfusion induced neuronal damage in diabetic mice. **J Ethnopharmacol** 133: 729 -734.
- Mansouri Z, Sabetkasaei M, Moradi F, Masoudnia F, Ataie A. 2012. Curcumin has neuroprotection effect on homocysteine rat model of Parkinson. **J Mol Neurosci** 47: 234 - 242.
- Marmitt DJ, Bitencourt S, Silva AC, Rempel C, Goettert MI. 2016. Scientific production of plant species included in the Brazilian national list of medicinal plants of interest to the unified health system (RENISUS) from 2010 to 2013. J Chem Pharm Res 8: 123 -132.

- Martins FJ, Caneschi CA, Vieira JLF, Barbosa W, Raposo NRB. 2016. Antioxidant activity and potential photoprotective from amazon native
- potential photoprotective from amazon native flora extracts. **J Photochem Photobiol B** 161: 34 - 39. Mendis S, Fukino K, Cameron A, Laing R, Filipe Jr.
- A, Khatib O, Leowski J, Ewen M. 2007. The availability and affordability of selected essential medicines for chronic diseases in six low- and middle-income countries. **Bull World Health Organ** 85: 279 - 288.
- Middha SK, Usha T, RaviKiran T. 2012. Influence of *Punica granatum* L. on region specific responses in rat brain during Alloxan-Induced diabetes. **Asian Pac J Trop Biomed** 2: S905 S909.
- Mizrahi M, Friedman-Levi Y, Larush L, Frid K, Binyamin O, Dori D, Fainstein N, Ovadia H, Ben-Hur T, Magdassi S, Gabizon R. 2014. Pomegranate seed oil nanoemulsions for the prevention and treatment of neurodegenerative diseases: the case of genetic CJD. **Nanomedicine** 10: 1353 - 1363.
- Oboh G, Akinyemi AJ, Ademiluyi AO. 2012a. Antioxidant and inhibitory effect of red ginger (*Zingiber officinale* var. *Rubra*) and white ginger (*Zingiber officinale* Roscoe) on Fe(<sup>2+</sup>) induced lipid peroxidation in rat brain in vitro. **Exp Toxicol Pathol** 64: 31 - 36.
- Oboh G, Ademiluyi AO, Akinyemi AJ. 2012b. Inhibition of acetylcholinesterase activities and some pro-oxidant induced lipid peroxidation in rat brain by two varieties of ginger (*Zingiber officinale*). **Exp Toxicol Pathol** 64: 315 - 319.
- Oliveira AA, Segovia JF, Sousa VY, Mata EC, Gonçalves MC, Bezerra RM, Junior PO, Kanzaki LI. 2013. Antimicrobial activity of amazonian medicinal plants. SpringerPlus 2: 1 - 6.
- Orellana-Paucar AM, Serruys AS, Afrikanova T, Maes J, De Borggraeve W, Alen J, Leon-Tamariz F, Wilches-Arizabala IM, Crawford AD, de Witte PA, Esguerra CV. 2012. Anticonvulsant activity of bisabolene sesquiterpenoids of *Curcuma longa* in zebrafish and mouse seizure models. **Epilepsy Behav** 24: 14 - 22.
- Orozco-Ibarra M, Muñoz-Sánchez J, Zavala-Medina ME, Pineda B, Magaña-Maldonado R, Vázquez-Contreras E, Maldonado PD,

Pedraza-Chaverri J, Chánez-Cárdenas ME. 2016. Aged garlic extract and S-allylcysteine prevent apoptotic cell death in a chemical hypoxia model. **Biol Res** 49: 7.

- Pandareesh MD, Mythri RB, Srinivas Bharath MM. 2015. Bioavailability of dietary polyphenols: Factors contributing to their clinical application in CNS diseases. **Neurochem Int** 89: 198 - 208.
- Peeyush Kumar T, Antony S, Soman S, Kuruvilla KP, George N, Paulose CS. 2011. Role of curcumin in the prevention of cholinergic mediated cortical dysfunctions in streptozotocin-induced diabetic rats. **Mol Cell Endocrinol** 331: 1 - 10.
- Qin XY, Lv JH, Cui J, Fang X, Zhang Y. 2012. Curcumin protects against staurosporine toxicity in rat neurons. **Neurosci Bull** 28: 606 - 610.
- Reeta KH, Mehla J, Pahuja M, Gupta YK. 2011. Pharmacokinetic and pharmacodynamic interactions of valproate, phenytoin, phenobarbitone and carbamazepine with curcumin in experimental models of epilepsy in rats. **Pharmacol Biochem Behav** 99: 399 -407.
- Ringman JM, Frautschy SA, Teng E, Begum AN, Bardens J, Beigi M, Gylys KH, Badmaev V, Heath DD, Apostolova LG, Porter V, Vanek Z, Marshall GA, Hellemann G, Sugar C, Masterman DL, Montine TJ, Cummings JL, Cole GM. 2012. Oral curcumin for Alzheimer's disease: tolerability and efficacy in a 24-week randomized, double blind, placebo-controlled study. Alzheimers Res Ther 4: 43.
- Rios JL, Onteniente M, Picazo D, Montesinos MC. 2016. Medicinal plants and natural products as potential sources for antiparkinson drugs. Planta Med 82: 942 - 951.
- Rojas P, Serrano-García N, Medina-Campos ON, Pedraza-Chaverri J, Maldonado PD, Ruiz-Sánchez E. 2011. S-Allylcysteine, a garlic compound, protects against oxidative stress in 1-methyl-4-phenylpyridinium-induced parkinsonism in mice. J Nutr Biochem 22: 937 - 944.
- Saleem S, Zhuang H, Biswal S, Christen Y, Dore S. 2008. Ginkgo biloba extract neuroprotective action is dependent on heme oxygenase 1 in

ischemic reperfusion brain injury. **Stroke** 39: 3389 - 3396.

- Sankar P, Telang AG, Manimaran A. 2012. Protective effect of curcumin on cypermethrin-induced oxidative stress in Wistar rats. **Exp Toxicol Pathol** 64: 487 -493.
- Shi J, Tian J, Zhang X, Zeng C, Wei M, Wang P, Wang Y. 2013. A combination extract of Renshen (Panax Ginseng), Yinyanghuo (Herba Epimedii Brevicornus), Yuanzhi (Radix Palygalae) and Jianghuang (Rhizoma Curcumae Longae) decreases glycogen synthase kinase 3beta expression in brain cortex of APPV7171 transgenic mice. J Tradit Chin Med 33: 211 - 217.
- Shi X, Zheng Z, Li J, Xiao Z, Qi W, Zhang A, Wu Q, Fang Y. 2015. Curcumin inhibits Aβ-induced microglial inflammatory responses *in vitro*: Involvement of ERK1/2 and p38 signaling pathways. **Neurosci Lett** 594: 105 - 110.
- Silva BA, Dias AC, Ferreres F, Malva JO, Oliveira CR. 2004. Neuroprotective effect of *H. perforatum* extracts on beta-amyloid-induced neurotoxicity. **Neurotox Res** 6: 119 - 130.
- Singh B, Singh D, Goel RK. 2012. Dual protective effect of *Passiflora incarnata* in epilepsy and associated post-ictal depression. J Ethnopharmacol 139: 273 - 279.
- Solanki I, Parihar P, Parihar MS. 2016. Neurodegenerative diseases: From available treatments to prospective herbal therapy. **Neurochem Int** 95: 100 - 108.
- Srivastava R, Dikshit M, Srimal RC, Dhawan BN. 1985. Anti-thrombotic effect of curcumin. **Thromb Res** 40: 413 - 417.
- Sukumari-Ramesh S, Bentley JN, Laird MD, Singh N, Vender JR, Dhandapani KM. 2011. Dietary phytochemicals induce p53- and caspase-independent cell death in human neuroblastoma cells. **Int J Dev Neurosci** 29: 701 710.
- Tapias V, Cannon JR, Greenamyre JT. 2014. Pomegranate juice exacerbates oxidative stress and nigrostriatal degeneration in Parkinson's disease. **Neurobiol Aging** 35: 1162 - 1176.
- Tiwari V, Chopra K. 2012. Attenuation of oxidative stress, neuroinflammation, and apoptosis by curcumin prevents cognitive deficits in rats

postnatally exposed to ethanol. **Psychopharmacology** 224: 519 - 535.

- Tyagi N, Qipshidze N, Munjal C, Vacek JC, Metreveli N, Givvimani S, Tyagi SC. 2012. Tetrahydrocurcumin ameliorates homocysteinylated cytochrome-c mediated autophagy in hyperhomocysteinemia mice after cerebral ischemia. J Mol Neurosci 47: 128 - 138.
- Van Kampen JM, Baranowski DB, Shaw CA, Kay DG. 2014. Panax ginseng is neuroprotective in a novel progressive model of Parkinson's disease. **Exp Gerontol** 50: 95 - 105.
- Wallace GC 4th, Haar CP, Vandergrift WA 3rd, Giglio P, Dixon-Mah YN, Varma AK, Ray SK, Patel SJ, Banik NL, Das A. 2013. Multitargeted DATS prevents tumor progression and promotes apoptosis in ectopic glioblastoma xenografts in SCID mice via HDAC inhibition. **J Neurooncol** 114: 43 -50.
- Wang X, Kim JR, Lee SB, Kim YJ, Jung MY, Kwon HW, Ahn YJ. 2014. Effects of curcuminoids identified in rhizomes of *Curcuma longa* on BACE-1 inhibitory and behavioral activity and lifespan of Alzheimer's disease Drosophila models. BMC Complement Altern Med 14: 88.
- Wang J, Liu Y, Li XH, Zeng XC, Li J, Zhou J, Xiao B, Hu K. 2016. Curcumin protects neuronal

cells against status-epilepticus-induced hippocampal damage through induction of autophagy and inhibition of necroptosis. **Can J Physiol Pharmacol** 95: 501 - 509.

- Zanotto-Filho A, Braganhol E, Edelweiss MI, Behr GA, Zanin R, Schroder R, Simoes-Pires A, Battastini AM, Moreira JC. 2012. The curry spice curcumin selectively inhibits cancer cells growth in vitro and in preclinical model of glioblastoma. **J Nutr Biochem** 23: 591 -601.
- Zaki A, Ashour A, Mira A, Kishikawa A, Nakagawa T, Zhu Q, Shimizu K. 2016. Biological activities of oleanolic acid derivatives from *Calendula officinalis* seeds. **Phytother Res** 30: 835 841.
- Zhang B, Li F, Zhao W, Li J, Li Q, Wang W. 2015. Protective effects of allicin against ischemic stroke in a rat model of middle cerebral artery occlusion. **Mol Med Rep** 12: 3734 - 3738.
- Zheng KM, Zhang J, Zhang CL, Zhang YW, Chen XC. 2015. Curcumin inhibits appoptosininduced apoptosis via upregulating heme oxygenase-1 expression in SH-SY5Y cells. Acta Pharmacol Sin 36: 544 - 552.
- Zhu JW, Chen T, Guan J, Liu WB, Liu J. 2012. Neuroprotective effects of allicin on spinal cord ischemia-reperfusion injury via improvement of mitochondrial function in rabbits. Neurochem Int 61: 640 - 648.