Review Article

Neuroprotective Effects, Biological Activities and Therapeutic Potential of Phytochemicals: A Comprehensive Review

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ABSTRACT

The incidence of neurological disorders is growing in the world together with an increased lifespan. Nowadays, there are still no effective treatments for neurodegenerative pathology, which make necessary to search for new therapeutic agents. Natural products, most of them used in phytochemicals from herbal medicine, are considered promising alternatives for the treatment of neurodegenerative diseases. Numerous herbs have been applied to neurodegenerative disease treatments as complementary and alternative medicines. In the 21st century, omics-coupled functional pharmacology was developed for neurodegenerative drug discovery from natural products. In this article, we firstly provide the latest understanding of neurological disorders on risk factors, category, diagnosis and treatment, and then specially present an overview of natural products in neuroprotective effects research from chemical biology to pharmacological targets, and also discuss the natural products application and future challenge.

Introduction

Neurological disorder is any disorder from nervous system, which most people in the world suffer from the problems and torment people of different age [1-2]. In the brain, spinal cord or nerves, structural, biochemical or electrical abnormalities lead to a range of symptoms including paralysis, myasthenia, poor coordination, interceptions, spasm, pain, altered consciousness and others [3-4]. Neurological disorders bring about a large burden on world-wide health, which is the main culprit of death or disability and the mortality is increasing year by year. Recent studies have demonstrated that the global burden such as Alzheimer’s disease, depression, stroke, Parkinson’s disease, multiple sclerosis, Huntington’s disease, traumatic brain injury and cerebral ischemia accounts for 3 percent of the worldwide burden of disease.

Although the overall percentage of neurological disorders seems relatively unimportant, dementia, epilepsy, migraine, and stroke are still in the top 50 causes of disability-adjusted life years [5].

In addition to migraine and epilepsy occupies more than a third of the neurological burden, the morbidity of neurodegenerative diseases such as dementia and Parkinson’s disease has greatly risen in the past decade. With population growth and ageing, the numbers and rates of years lived with disability have increased in the past two decades. Neurological disorder as one of the most common causes has not decreased [6]. Facing widespread, fatal, complex and exorbitant disease for patients, modern researches have been in progress in different race, age group and regions. It seems that neurological disorders are not frequent illness, but it is infrequently recognized in clinical practice and better understanding the early prevention, accurate diagnosis and prompt medical treatment.
Furthermore, there is the absence of substantial prospective methods and techniques to decrease its occurrence and development. Due to the non-communicable disorder becoming more serious and complex, rapid globalization, urbanization, the society faces new challenges and opportunities for innovative health care systems. Compared with currently available therapeutic options, natural products are becoming popular over the world and widely accepted as a conservative clinical therapy.

More public awareness and scientific interest has led to research towards the effect of natural products in the field of health promotion and disease treatment due to their effectiveness, convenience, less side-effects and relatively low cost [7, 8]. Growing evidence suggests that natural products, especially herbs and dietary supplements, have a major role for neurological disorders prevention, management, and treatment. Herbal and dietary supplements application for chronic disease states is increasing all over the United States. According to current circumstances, the reviews present new understanding and overview on neurological disorders, and then we pay particular attention to natural products for prevention, management, treatment of neurological disorders, and finally we probe into the future research directions and challenges.

**Overview of Neurological Disorders**

**I Risk Factors**

According to previous studies, various risk factors such as infection, poisoning, genetic defects, endocrine disorder and immunological injury have been led to a neurological disorder. It was showed that Coxsackievirus A16 is a major pathogen related to human hand, foot, and mouth disease in the Asia-pacific region, which lead to severe lesions or necrosis towards the skeletal muscle, spinal cord and brainstem in 21 days aged gerbils after five days infection [9]. In the Americas, Zika virus, as an arbovirus transmitted by mosquitoes, is now crazily spread and has proved to be detected in amniotic fluid, placenta and fetus brain tissue. A number of neurological disorders such as microcephaly, Guillain–Barré syndrome, meningoencephalitis and myelitis are associated with the virus infection [10]. Infection of HIV virus is often associated with neurological disease, the pathological mechanism will to be further studied [11]. Cigarette smoking and carbon monoxide are considered as a major risk factor in deteriorative process of various neurological disorders.

Chronic cigarette smoking-induced toxicity attribute to oxidative stress, which disrupts the brain’s protective mechanism and cause oxidative damage to the brain [12]. Under the influence of CO, the body cell respiration is inhibited. After hypoxia, the structure of the central nervous system (CNS) is usually susceptible to injury, the emergence of various pathological neurological symptoms [13]. Recent evidence suggests that sphingolipids, which contain a variety of molecules that can carry out N-acylated sphingosine-containing long-chain bases, are rich in the central nervous system, the genetic defects of synthesis and decomposition of intrathelial lipoproteins can cause undesirable consequences of brain physiology. These diseases are due to gene mutations in encode enzymes that catalyze maturation or degradation of simple sphingolipids such as ceramides or complex sphingolipids [14].

In addition, there are genes such as rs6094539 gene variant, ATP7B gene variants and apolipoprotein E gene associated with neurological diseases in recent study [15-17]. It has recently been noted that endocrine disrupting substances can cause increased neuropsychiatric disorders including autism, attention deficit, hyperactivity, learning disabilities and depression, which can lead to severe neurodegeneration. Meanwhile, compared with the same age healthy children, the morbidity of hyperthyroidism caused by endocrine disorders making sick children in a series of neurological disease is increasing [18, 19]. Autoimmune diseases are increasingly recognized as the main cause of some neurological disorders leading to clinical disability [20]. In addition, other risks contain nutritional disorders, congenital malformations, blood circulation disorders, abnormal hyperplasia, metabolic disorders, age and sex [21-25].

**II Category**

In the light of the primary position affected, the main type of dysfunction involved, or the main cause of disease, neurological disorders can be categorized different types in clinic. The nervous system includes the central nervous system and the peripheral nervous system, then the former contains the brain (cerebellum, brain, brain stem) and the spinal cord and the peripheral nervous system is composed of the brain and spinal nerve. Relevant research report lists brain, spinal cord and nervous disorders in the following categories [26-28]. Brain damage according to cerebral lobe: frontal lobe damage, parietal lobe damage, temporal lobe damage, occipital lobe damage. Brain dysfunction according to type: aphasia (language), dysgraphia (writing), dystarthritis (speech), apraxia (movements), agnosia (recognition), amnesia (memory). Spinal cord disorder according to pathology, injury, inflammation characteristics is divided into different types. Peripheral neuropathy system disorders: cranial nerve disorder such as Trigeminal neuralgia, autonomic nervous system disorder such as Dysautonomia, multiple system atrophy seizure disorders such as Epilepsy, movement disorders of the central and peripheral nervous system such as Parkinson’s disease, Amyotrophic lateral sclerosis, Multiple Sclerosis, Sleep disorders, migraines and other types.

**III Clinical Manifestation**

Typical symptoms of neurological disorders in clinic are muscle stiffness, trembling, slow movement, dysphagia, limb numbness, convulsions. In addition, it also presents speaking with a lisp, limb balance disorders, and loss of action capability. Sometimes, nervous system diseases continue to deteriorate leading to dementia [29, 30]. Different degree of depression is one of the common symptoms of nervous system, and it is often characterized by slow disease progression and symptoms mild at first which it is not easy to be found [31]. If not treated in time, the patient may have an accident in daily life. With the deterioration of the disease, the patient is in a greater risk of depression, which depression has become particularly serious in order that suffers lose the ability of independence in final [32]. Alzheimer’s disease (AD), a central nervous system disease, is the main culprit of dementia in elderly individuals around the world. Before symptoms of the disease emerge, individual had been in pathophysiological state of AD for many years. AD shows up prominent neuropsychiatric features including loss of memory, cognitive decline, language dysfunction closely, and
impairment of normal social and emotional behaviors such as depression, hallucinations, or agitation, even leading to death finally [33].

The key pathological changes of AD are increasing extracellular deposits levels of β-amyloid(AB) as diffuse and inflammatory plaques and abnormally neurofibrillary tangles (NFTs) resulting from hyper-phosphorylated tau (p-tau) accumulating intracellular and reduction in number of neurons [34]. Parkinson’s disease, as an incurable degenerative disorder, usually occurs in 1% population above the age of 65. It often damages movement and language skill of invalids and is accompanied by a series of the distinct symptoms of the disease such as still shaking, rigidity, bradykinesia, and loss of postural reflexes on account of head trauma or drug poisoning [35, 36]. Epilepsy is a disorder in brain, which it is generally recognized that the occurrence of two unprovoked seizures appearing more than 24 hours in addition to an enduring tendency to arise more serious seizures. When epilepsy occurs, patients lose consciousness suddenly and then come into being tonic clonic spasm accompanied by shouting, complexion colorless, urinary incontinence, biting tongue, foaming at the mouth, and other symptoms [37].

Depression is a clinical symptom of mood disorders with significant and persistent mental retardation, slow thinking, cognitive impairment, decreased will and physical symptoms as the principal clinical features [38]. Studies have shown that the prevalence rate of global depression and poor mood surveyed by WHO is 12.8% and predicted depression will become the world’s second medical in 2020 [39]. Scientific research found that approximately 17% of the population had at least one stroke in their life [40]. Not only do many stroke patients appear sudden faint, loss of cognitive ability, hemiplegia, mouth adverse symptoms, but they present sudden mental disorders, involuntary movement, memory decline, dizziness, walking instability, blurred vision and other clinical manifestations [41]. Multiple sclerosis, a chronic autoimmune inflammatory demyelination disorder, impairs the central nervous system and typically attacks people between 20 and 40 years of age [42, 43]. The main symptoms include limb numbness and tingling, balance disorders, blurred vision, bladder dysfunction. After repeated relapse and incomplete remission, the illness becomes more and more heavy leading to weakness, stiffness, sensory disturbances, physical instability, visual impairment and urinary incontinence for suffers.

IV Diagnosis

In clinical practice, diagnosis of neurological disorders includes location diagnosis, qualitative diagnosis and etiological diagnosis. Location diagnosis can provide information on lesions in specific parts of the nervous system on the basis of disease syndrome in different parts, which often contributes to the decision of the nature of the disease. What clinicians are often confused is the etiology of the patient is difficult to make due to incomplete understanding of disease. Using neurological examination mainly containing medical history, mental state assessment, physical examination and laboratory diagnostic examination in the diagnosis of neurological diseases can detect brain, nerve, muscle and spinal cord disease. In addition to medical history and physical examination, cerebrospinal fluid examination and other laboratory tests, electromyography, electroencephalogram also provide an important clue for clinical diagnosis [44, 45].

Neurological imaging examination plays a crucial role in the diagnosis of some related diseases, especially computed tomography and magnetic resonance imaging put into use, and positron emission computerized tomography, single photon emission computed tomography, transcranial doppler sonography, quantitative electroencephalogram, digital subtraction angiography, myelography and other new techniques are of value in the diagnosis of neurological diseases [46, 47]. The recent advances in high-throughput genome technologies leading to the rapid analysis and identification of millions of disease-related genes in thousands of patients has significantly promoted our understanding of the genomic underpinnings of neurological disorders susceptibility which are the result of mutations in genes involved in normal action of the brain, spinal cord, peripheral nerves or muscles [48]. The development has promoted the recognition of whole-genome structure and variation and research of its influence of human phenotypes.

Genome-wide association studies, which have offered information on the mechanism of risk factors for the development of neurological disorders caused by common genetic variability, discover emerging biological pathways related to disease pathogenesis after identification of disease-causing mutations [49]. In the last decade, the development of genomic technologies such as comparative genomic hybridization and genome-wide single nucleotide polymorphism arrays based on microarray-based techniques as substitute of cytogenetic testing and chromosomal microarray for screening copy number variants and long continuous stretches of homozygosity brings new era to interpretation individual’s genome in large scale[50]. Also, the emerging next-generation DNA sequencing platforms, coupling targeted capture and massively parallel DNA sequencing and whole-genome sequencing make the clinical diagnosis of neurological disorders more comprehensive, accurate and convenient [51-53].

V Intervention

In everyday clinical practice, drug intervention is more common applied than other clinical treatments such as genes, surgery, electrical stimulation and psychotherapy intervention, and the neurological disorders patient is more receptive and easier to use, which facilitates researchers to devote a lot of effort and research in recent years [54, 55]. It indicates that intrathecal baclofen treatment is used in children and young adult patients with spastic cerebral palsy, dystonic cerebral palsy and progressive neurological disease [56]. Some new drug is under clinical development for the neurological disorders treatment such as a class of tetracyclic butyrophenones that possess binding affinities to serotonin 5-HT and dopamine D2 receptors, and catechol-O-methyltransferase including neurotransmitters dopamine, epinephrine and norepinephrine as enzymes that catalyze the transfer of methyl from S-adenosyl methionine to catechol and catecholamines, which can be used for schizophrenia, Parkinson’s disease, bipolar disorder and many other neurological and mental disorders.

The new type of COMT inhibitor with good and safe therapeutic characteristics has been designed to replace previous inhibitors possessing high toxicity, short acting, poor bioavailability and
gastrointestinal side effects [57, 58]. The clinical development of metabotropic glutamate 5 (mGlu5) negative allosteric modulators, mGlu1 and mGlu5 PET ligands has also been shown outstanding advance as the potential treatment of Parkinson’s disease, autism, anorexia, depression, pain, levodopa-induced dyskinesia, however, it is reported that these modulators have some side effects and cytotoxicity [59, 60]. Due to dysfunction of the glutamatergic signaling pathway associated with the pathophysiology of mental and neurological pathophysiology, it has long been interested in scientists involved in drug research. The research of AMPAR positive allosteric modulators provides the chance to modulate rapid excitatory synaptic transmission and select emerging potential therapeutic agents for a series of neurological disorders [61].

As a significant potential for the treatment of neurological diseases, peptide therapeutic agents provide a new way to treat a wide variety of neurological disorders. However, clinic faces to many obstacles such as short half-life of the peptide, less passage through the blood-brain barrier, slowing through the extracellular space and rapid rinse of cerebrospinal fluid, which we studied stem cell-based cell therapy relying on the secretion of soluble factors as well as a new method of encapsulating genetically cells as peptide transfer vectors [62, 63].

Research confirmed that phospholipases A2 inhibitors and cannabinoids from plants are related to the pathogenesis of neurological disorders for treatment of oxidative stress and neuroinflammation [64, 65].

Gene therapy, as a powerful tool for treating neurological disorder such as central nervous system neoplasms, metabolic disorders and amyotrophic lateral sclerosis, inhibits the expression of toxic proteins and restore lost function [66-68]. Taking into account the instability of the gene and strong immunogenicity, selecting the appropriate carrier need to be further studied [69]. In addition, the clinical practice in the treatment of diseases also has surgery, electrical stimulation, psychological therapy and others [70-72]. With the advance of cell reprogramming technology and nanotechnology carriers, the laboratory has acquired new human cell sources such as iPSCs derived nerve cells that contribute to insight and treatment of early-onset neurological disorders, which not only to increase the potential for testing known drugs and recycle, but also to promote the clinical efficacy of new compounds and gene therapy [73, 74]. Compared to the delivery method of conventional drug, the nanotechnology carrier has the advantages such as high drug loading ability, targeting effect, low toxicity and increased therapeutic effect, and has established a new platform for clinical treatment (Figure 1) [75].

Herbal Products

Traditional Chinese medicine (TCM) which is equipped with complex recipes and formulae stem from historical and anecdotal evidence of ancient healer, has a long history for clinical practice through western drugs brought in China. With the development of economic modernization, TCM as a promising role bring an exploring trend of new therapeutic chemicals and drugs for disease, including neurological disorders. In researches of recent years, a great number of plant-derived herbs and prescription have been explored in the research of neurological disorders such as Tripterygium wilfordii Hook F, Ginseng, Valeriana amurensis, Ginko bilboa, Pueraria lobata and fig fruits, and prescription such as Di Dang soup, Xiao Yao san, Kai-Xin-San, Liwu Dihuang decoction, YQiFuMai and Tao hong si wu decoction [76-86]. Various active ingredients have been extracted from Chinese herbal extracts and then confirmed to have the characteristics of outstanding pharmacological effects in nervous system [87-89].

Polyphenols such as flavonoids, epigallocatechin gallate and epicatechin perfect learning and memory deficits in both animals and humans though acting on ERK/CREB pathway connected with synaptic plasticity and potentiation, and in vitro oxidative stress and in neurotoxicity cellular models’ polyphenols as the free radical scavengers reflects neuroprotective effects [90-92]. Curcumin referred to as anti-carcinogenic, antioxidant and anti-inflammatory resource is derived from turmeric. Results of vitro and animal studies indicated that curcumin alter Aβ metabolism and also affect brain work and the development of dementia in AD, which become promising mean of...
adjusting early AD pathology associated with new curcumin formulations to enhance bioavailability by comparing treating healthy, pre-clinical and mild cognitive impairment-period groups [93]. Resveratrol possesses various pharmacological effects such as anti-inflammatory, anti-apoptosis, antioxidation, antifungal and anticancer. As a polyphenolic compound naturally present in red wine and grapes, many researches have studied the use of resveratrol in PD and consider resveratrol related with neuroinflammation, apoptosis, and oxidative stress as neuro-protective role from many angles [94, 95].

In a recent research of probing the neuroprotective ability and underlying mechanisms of salvianolic acid B (Sal B), it is shown that pellium MDA level and the NOS activity of cerebral ischemia-reperfusion mice observably decreased and the activity of SOD and the T-AOC markedly increased in comparison of the model group (P<0.05 or P<0.01). Meanwhile, SalB inhibit neuronal loss, intensely accelerate expression of Bcl-2 protein (P<0.01) and prevented Bax protein expression by mitochondria-dependent pathway [96]. SalB also restrained NF-kB transcriptional activity and pro-inflammatory cytokine responses including IL-1β, IL-6, and TNF-α by blocking Toll-like receptor 4 in an oxygen-glucose deprivation and reoxygenation model [97]. As we all know, Ginseng is a famous invigorant in China, which saponin extract such as ginsenoside Rg1, Rg3, Rg5, RE and Rk1 was used in enhancing athletic performance and immune function, treating diabetes, erectile dysfunction, and male infertility [98, 99].

There is also increasing evidence that a range of saponin extracts from the plants are able to relieve deterioration and beneficial for the therapy of neurological disorder. Ginseng Fruit Saponins (GFS) plays an important role in regulating expressions of 5-HT and 5-HT2AR expressions after MI and depression [100]. A study evaluated GFS influence on the 5-HT system though comparing Myocardial Infarction depression, and MI + depression pointed that GFS decrease the reuptake of 5-HT from serum to platelet and the change in the brain is the opposite [101]. Salidroside inhibits cognitive deficit and ameliorated apoptosis in the hippocampal CA1 area in rats caused by chronic cerebral hyperperfusion, which is remarkably impeded the activation of caspase-3, up-regulated the ratio of Bax/Bcl-2 and reversed hippocampal neuronal loss [102]. The study also found that asiaticoside which come from herb Centella asiatica may alleviate the mitochondrial injuries, the activity of anti-inflammatory, and the influence on the apoptosis-associated proteins expression levels in AD [103].

The mechanism of ruscogenin on cerebral ischemia-induced blood-brain barrier dysfunction may reduce the brain infarction and edema, increased cerebral brain flow, improved neurological deficits, decreased evans blue (EB) leakage and promoted tight junctions’ expression [104]. In addition, the study also found that flavonoids from plants, alkaldoids, coumarins, terpenes, polysaccharides, volatile oils, anthraquinones such as puerarin, oxymatrine, daphnetin, oleanolic acid, crocin, physcion play important role in cerebral ischemia, encephalomyelitis, Alzheimer Disease, spinal injury, brain injury and other neurological diseases, and provides a valuable reference for the latter part of the study [105-114].

In another study by Lee SH et al., Cordyceps, a multifunctional natural products with various biological activities including nephroprotective, hepatoprotective, anti-inflammatory, antioxidative, and antiapoptotic roles, was named by the fungi on insects and suggest that Cordyceps overcomes cerebral ischemia-induced neuronal apoptosis by improving cerebral ischemia-induced short-term memory impairment in transient global ischemia in gerbils, inhibiting cerebral ischemia-induced cell proliferation in the hippocampal dentate gyrus and increasing the expressions of BDNF and TrkB in the hippocampus of ischemic gerbils [115]. Xyloketal B which shows protective effects against toxicity in neurodegenerative disease models such as PD and AD is a natural product from mangrove fungus as novel drug candidates for treating Huntington's disease in recent years. A study of screening potential neuroprotective molecules for Huntington's disease indicate that xyloketal B could bind to residues GLN369 and GLN393 of the mutant Htt protein, and then form a stable trimeric complex in case the formation of mutant Htt aggregates by molecular target analysis [116].

Animal Products

Bile acids possess a long history for medicine propose from intervention for primary ocular diseases as therapeutic agents in ancient times to using for liver diseases in approved way in modern, which is a specific structure related group of molecules related from cholesterol. Though data from models in vivo and in vitro and clinical experiments endorse neuroprotective role in treating a diverse spectrum of age-related neurodegenerative disorders, the origin and molecular mechanism of bile acids is little-known [117]. Taurochendodeoxycholic acid is considered as a promising role in reducing loss of dopaminergic neurons and dopaminergic fiber compared by MPTP which associate with ROS production and activation of JNK-mediated apoptosis [118]. Currently, arthropod venoms are recognized as an emerging source of bioactive compounds, which offer a platform for new neuroactive compounds discovery and provide novel and attractive chances for acting on the central nervous system by various neuronal targets.

There are some medications gained from venom proteins and derivatives including captopril, epitiobatide, tirofiban, bivalirudin, ziconotide, and exenatide. Some recent researches reported that peptides and acyl polypeptides isolated from arthropod venoms in mammalian CNS have analgesic, anxiolytic, antiplatelet and neuroprotective effects ability as inhibitors or stimulants for treating major existing neurological disorders such as stroke, Alzheimer's disease, epilepsy, Parkinson's disease, and pathological anxiety [119, 120]. Abundant source of structurally novel natural products derived from marine environment have markedly anti-cancer, anti-inflammatory, analgesic, immuno-modulatory, and neuroprotective ability. Previous studies have shown that some natural products from marine and their derivatives such as cytarabin, trabectedin, eribulin mesylate, and brentuximab vedotin using in cancer treatment approved by European national authority [121].

Phytochemical compounds which come out of microalgae and have neuroprotective potentials associated with the management and/or treatment of AD, are applied as pharmaceuticals, nutraceuticals and food supplements, and may possess neuroprotective potentials that are relevant to the management and/or treatment of AD [122]. Furthermore, some marine natural ingredients such as Omega-3-acid ethyl esters, ziconotide and iota-carrageenan have been proved to be therapeutically effective in clinical trial for neurologic diseases treatment, but the mechanism needs further study.
Dietary Supplements

Not only as nutrition in daily but also for medicinal application, dietary supplements have been widely used for a long time among the USA and the EU population [123]. The use of dietary supplements which have the ability to bring neuroprotective, neurotropic, and proneurogenic support occurs in fight of age-related illnesses and neurodegenerative diseases [124]. Several studies measured by real-time PCR have confirmed that vitamin A upregulate specific nuclear receptors such as Forkhead box P3 and transforming growth factor (TGF)-β gene expression in multiple sclerosis patients though retinoic acid as an active metabolite reestablishing the imbalance [125]. Complex of vitamin B such as B6, B12, and folic acid which associated with age-related cognitive fragility were found in plasma/serum of geriatric patients with cognitive impairment in lower level [126]. Vitamin B deficiency is common in invalids with neurological disorders suggesting its preventive and therapeutic potential [127, 128].

As one of the significant nuclear steroid transcription regulators, Vitamin D regulates a large number of genes transcriptions. In the recent study, Vitamin D may exert protective and neurotropic effects directly at the cellular level in different types of neurological disorders such as Parkinson’s disease and multiple sclerosis [129, 130]. In addition, vitamin D3 as an effective supplementary treatment beneficially improve clinical features of Huntington’s disease, which observably increased the lifespan of transgenic animals measured by Kaplan-Meier survival curves [131]. The deficiency of vitamin D is related with late depression and well-designed RCTs is needed to evaluate the prevention impact of vitamin D that seems as a risk factor for late-life depression [132]. Some experts believe that more trials are necessary to determine the appropriate vitamin E composition and dosage for AD treatment, because vitamin E in the proper dose prevents or delays AD, however, it also worsens the pathology in unusual dose by increasing the level of Aβ and decrease Aβ degradation [133].

Researchers have also evaluated the use of n-3 long chain polyunsaturated fatty acids (PUFAs) such as mega-3, docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA) in regulating neuronal membrane excitability and improving the capacity for neuronal transmission, which indicated that they prevent neuronal loss, cognitive decline stems and maintain membrane fluidity in preventing and/or slowing AD pathology [136, 137]. In early PD, inosine as a potential disease-modifying therapy was safe, tolerable, and effective in increasing urate levels of serum and cerebrospinal fluid. Compared with inosine groups, urate level in placebo groups was lower and has more disability chance [138]. Yu S et al. conducted cerebral ischemia experimental models in vitro and in vivo to explore neuroprotective role of Achyranthes bidentata Blume polypeptides (ABPks) isolated by reverse-phase HPLC [139]. ABPks promoted neuronal survival and inhibited ischemia-induced neuronal damage though modulating expression of apoptosis-related gene, regulating mitochondrial membrane potential for mitochondrial dysfunction, reducing and inhibiting harmful substances production and release (Figure 2).

A Kuopio Ischemic Heart Disease Risk Factor Study assessed the relationship between magnesium intake and unipolar depressive disorder by a 4-day food record of 2320 Eastern Finnish men aged 42-61 years old. Compared the lowest tertile of magnesium intake participants, the middle tertile has a statistically obviously decreased depression risk and present an inverse association between magnesium intake and the risk of depression. Further studies are necessary to explore whether magnesium intake have ability to prevent or treat depression [134]. Compared carotenoid and vitamin C intake associated with risk of amyotrophic lateral sclerosis (ALS) from different groups including the National Institutes of Health-Association of American Retired Persons Diet and Health Study, the Cancer Prevention Study II Nutrition Cohort, the Multiethnic Cohort, the Health Professionals Follow-up Study, and the Nurse Health Study, it has suggested that carotenoids intake reduce risk of ALS by restraining oxidative stress in the pathogenesis of ALS [135].

Conclusions and Future Directions

As a life threatening disorders with explosively increasing mortality and morbidity rate in populations worldwide, neurological disorders such as AD, PD and HD impose the high health impact not only to patients and their families, but also to society, which drive intense study for therapeutic alternatives of neurological disorders in consideration of fact that most of current chemical drugs are ineffective or only symptomatic treatment. The discovery and preparation of new drugs to cure them is highly demanding. Recently, natural products with their abundant source, low toxicity and side-effects have become a popular role when discussing methods for prevention and treatment of neurological diseases. It is necessary to conduct more clinical trials in design to improve the quality of evidence and the credibility of the beneficial effects of therapeutic supplements for neurological disorders.
disorders. In addition, especially, herbs possess various pharmacological activity such as antioxidant, anti-inflammatory, anti-apoptosis and free radicals-scavenging by a variety of mechanisms.

In this view, traditional Chinese herbs monomer and active ingredients with clear molecular structures attract a large number of scholar’s attention, but there exist some problems in the application of Chinese herbs. Some natural compounds which needs further exploration for necessary development due to many herbal produces lacking rigorous scientific further clinical observation and verification and still remaining in the stage of laboratory stage leading to serious toxic effects and drug-to-drug interaction have a vital role to perform neurological disorders management. We should reduce the efficacy difference between single use of monomers or active ingredients and herbal ingredients using in clinical and improve bioavailability of combination of various natural monomer and effective composition for better therapeutic effect.

The marine natural products could be a specially promising object to discover active ingredients with novel structures as potential drug for neurological disorders on account of high biodiversity, genetic uniqueness and severe competition for survival of marine organisms. Although medical research of neurological disorders is a long way to go for a large number of natural material, the discovery and application of natural products is still expected to endlessly made some progress with the help of rapidly evolving modern science and technology for improving the control system of natural medicine and promoting the modernization development of medicine.

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Competing Financial Interest

None.

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