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Ethnopharmacology and Neurodegenerative Disorders

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Abstract

Neurodegenerative disorders, exemplified by Alzheimer's and Parkinson's diseases, significantly affect both individuals and healthcare systems. Despite continuous research endeavors, there are no definitive cures for these conditions, and existing treatments merely alleviate symptoms. An intriguing avenue for investigation is ethnopharmacology, a field that draws inspiration from traditional healing practices across the globe to identify natural compounds potentially capable of protecting neurons. These substances, derived from plants and other origins, offer potential advantages like antioxidative and anti-inflammatory properties. Nevertheless, they necessitate rigorous examination and confirmation of their safety and effectiveness. Natural products possess varied chemical structures, enabling them to interact with diverse molecular targets involved in the functioning and preservation of neurons, whereas synthetic drugs provide specificity and potency. The selection between these approaches depends on their respective merits and drawbacks, warranting thorough assessment within the context of neurodegenerative disorders. This review provides an overview of current and future trends in ethnopharmacology, as well as the exploration of natural products and synthetic drugs for these conditions, emphasizing the potential benefits and challenges, and underscoring the importance of a well-balanced research approach and integration in the quest for effective treatments.

Keywords: Ethnopharmacology, herbal medicine, Neurodegenerative Disorders

1.Introduction

Neurodegeneration is a term that describes the loss of structure and function in the nerve cells of the brain and spinal cord, which can cause problems with thinking, movement, and behavior. Some examples of neurodegenerative diseases are Alzheimer's disease (AD), which affects memory and cognition; Parkinson's disease (PD), which causes tremors and stiffness; Huntington's disease (HD), which leads to involuntary movements and personality changes; amyotrophic lateral sclerosis (ALS), which affects the muscles and breathing; and multiple sclerosis (MS), which damages the protective layer of the nerve fibers. (1) . Many people around the world suffer from diseases that affect their brain and nervous system, and reduce their quality of life.

in vitro or in animal models fail to reach the brain effects in humans. To overcome this challenge,
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There is still no way to cure or prevent these brain and nervous system diseases, even though many researchers and developers are working hard on this problem. The treatments that exist today can only help with some of the symptoms and make the patients more comfortable, but they are not very effective or safe(Hartman, Jenkinson et al. 2020).Click or tap here to enter text.
Finding new and better ways to discover and develop drugs that can protect the brain and nervous system is very important, because there is no cure or prevention for these diseases yet. One of the possible ways to do this is to study how different people and cultures use plants and other natural products as medicine. This is called ethnopharmacology, and it can help us learn from the traditional wisdom, practices, and beliefs of various communities about how to use natural products to treat and prevent different diseases, including brain and nervous system disorders(Cavalcante e Costa, Nishijo et al. 2018).
Moreover,ethnopharmacology can facilitate the identification, isolation, characterization, and validation of bioactive compounds and extracts from natural sources that have potential neuroprotective effects against different mechanisms and pathways involved in neurodegeneration.

This review aims to give a detailed and critical summary of the current and future trends of eth

nopharmacology and brain and nervous system disorders. In particular, this review will focus on these topics: the definition, scope, and significance of ethnopharmacology and neurodegenerative disorders;

The current challenges and limitations in the treatment and prevention of neurodegenerative disorders

The brain and nervous system are made up of neurons, which are cells that communicate with each other and perform various functions. Neurodegenerative disorders, such as Alzheimer's disease (AD) and Parkinson's disease (PD), are diseases that cause neurons to gradually die and lose their functions. These diseases affect the lives of many people around the world, and have a negative impact on their health, well-being, and society. There is still no way to cure or prevent these diseases, even though many researchers and developers are working hard on this problem. The treatments that exist today can only help with some of the symptoms and make the patients more comfortable, but they are not very effective or safe(Passeri, Elkhoury et al. 2022).
The causes and processes of neurodegenerative disorders are very complicated and varied. These diseases affect different parts of the brain and nervous system in different ways, depending on many factors. Some of these factors are related to the molecules and cells in the brain, such as how proteins fold and stick together, how cells cope with damage and stress, how cells communicate and work together, and how cells die. Other factors are related to the genes and environment of the patients, such as what they inherit from their parents and what they are exposed to in their life (Asil, Ahlawat et al. 2020). These diseases also have similar symptoms and signs, which makes it hard to tell them apart and find them early. This is why we need to find reliable ways to measure and track these diseases, such as biomarkers that can show the start and change of these diseases in the body. We also need to find new and powerful drugs that can target the specific causes and effects of these diseases and change the way they progress (Livingston, Huntley et al. 2020).
Another major challenge in the treatment and prevention of neurodegenerative disorders is the delivery of drugs to the central nervous system (CNS). The blood-brain barrier (BBB), which protects the brain from harmful substances in the blood, also limits the penetration of most drugs into the brain.

at sufficient concentrations or with minimal side effects in humans. To overcome this challenge, various strategies have been explored, such as modifying the physicochemical properties of drugs, using invasive or non-invasive routes of administration, and employing nanotechnology-based drug delivery systems(Nance, Pun et al. 2022).Click or tap here to enter text.
Neurodegenerative disorders can be treated and prevented by using nanotechnology, which can improve the drug properties and delivery to the brain. Nanomaterials, such as liposomes, exosomes, nanoparticles, and nanofibers, can carry or attach drugs and transport them through the BBB and to the specific brain regions. Nanomaterials can also help to visualize the brain and track the drug effects and distribution. However, nanotechnology also has some drawbacks and challenges, such as the possible harmful effects of nanomaterials, the lack of consistent methods for their testing and assessment, and the ethical and regulatory issues related to their use(Ngowi, Wang et al. 2021).
They need a team of experts from different fields to work together. To find new and better ways to diagnose and cure these disorders, we need to learn more about how they affect the brain cells and molecules. We also need to find reliable signs that can detect them early. We need to make sure that the drugs can reach the right places in the brain. We need to use nanotechnology and other new technologies to help us.

the potential role and benefits of natural products derived from traditional medicinal plants for neurodegeneration

Neurodegenerative diseases are disorders that damage neurons in the brain, causing irreversible cognitive decline. Examples are Alzheimer's, Parkinson's, Huntington's, and ALS. Their causes and mechanisms are unclear, but oxidative stress, inflammation, mitochondrial dysfunction, protein aggregation, and genetic mutations may contribute. There is no cure, only treatments that relieve symptoms and slow down disease progression.
Natural products derived from traditional medicinal plants have been used for centuries to treat various ailments, including neurological disorders. Natural products are rich sources of bioactive compounds that can modulate multiple molecular pathways and exert neuroprotective effects against neurodegeneration. Some of the potential benefits of natural products for neurodegeneration are:Antioxidant activity: Natural products can protect neurons and biomolecules from oxidative damage by eliminating free radicals and reactive oxygen species, lowering lipid peroxidation, and boosting the endogenous antioxidant defense system. For example, cur cumin, a turmeric polyphenol, has been shown to improve cognitive function and decrease oxidative
stress in Alzheimer's disease models(Mohd Sairazi and Sirajudeen 2020).
Anti-inflammatory activity: Natural products can reduce neuroinflammation and neurodegeneration by blocking the activation of microglia and astrocytes, the production of pro-inflammatory cytokines and chemokines, and the signaling pathways of NF-κB and MAPK. For example, resveratrol, a grape polyphenol, has been shown to lower the expression of iNOS and COX-2 and the levels of IL-1β and TNF-α in Parkinson's disease models (Wang, Yu et al. 2005).
Neurogenesis and synaptic plasticity: Natural products can boost the neurogenesis and synaptic function in the brain by promoting the growth and differentiation of neural stem cells, the survival and development of neurons, and the synaptic communication and plasticity. For example, ginseng, a traditional herbal medicine, has been shown to enhance the memory and learning and increase the expression of BDNF and neurogenesis in the hippocampus in Alzheimer's disease models (Appleby, Kempermann et al. 2011, Ávila-González, Romero-Morales et al. 2023).
Protein homeostasis: Natural products can maintain the balance and function of proteins in the brain by regulating their production, folding, aggregation, and degradation, and avoiding the accumulation of harmful protein deposits. For example, ashwagandha, an ayurvedic herb, has been shown to lower the levels of Aβ and tau proteins and prevent the formation of amyloid plaques and neurofibrillary tangles in Alzheimer's disease models (Sharma, Srivastava et al. 2021).
Apoptosis and autophagy: Natural products can control the balance between apoptosis and autophagy, and avoid the excessive or improper activation of cell death pathways, thereby keeping the neurons alive and functional. For example, bacopa monnieri, a brain-boosting herb, has been shown to protect the neurons from apoptosis and enhance autophagy by inhibiting the activation of caspase-3 and PARP and inducing the expression of beclin-1 and LC3-II in Huntington's disease model (Okouchi, Ekshyyan et al. 2007).
Natural products from medicinal plants may slow down or prevent neurodegeneration by affecting various molecular targets and mechanisms. However, more research is needed to understand how they work, how they are absorbed and metabolized, how safe and effective they are in humans.

The types, sources, chemistry, pharmacology, mechanisms, safety, and clinical evidence of natural products with neuroprotective effects against different neurodegenerative disorders

Biological substances that come from plants, animals, fungi, or microorganisms and have therapeutic potential are called natural products. Some natural products can protect neurons from various harmful factors, such as oxidative stress, inflammation, excitotoxicity, protein aggregation, and apoptosis. These are known as neuroprotective natural products. They have been studied for their possible roles in preventing and treating different neurodegenerative disorders, which are diseases that cause progressive loss of neuronal structure and function. Examples of neurodegenerative disorders are Alzheimer's disease, Parkinson's disease, Huntington's disease, amyotrophic lateral sclerosis, and stroke (Cavalcante e Costa, Nishijo et al. 2018).

Natural products are biological substances that come from plants, animals, fungi, or microorganisms and have therapeutic potential. They can be grouped into different types based on their chemical structures, such as polyphenols, flavonoids, terpenoids, alkaloids, steroids, fatty acids, peptides, and polysaccharides. Some of these natural products can protect neurons from damage and dysfunction caused by various factors, such as oxidative stress, inflammation, excitotoxicity, protein aggregation, and apoptosis. These are called neuroprotective natural products. Examples of neuroprotective natural products are curcumin, resveratrol, epigallocatechin -3-gallate, ginkgo biloba, huperzine A, omega-3 fatty acids, and melatonin(Passeri, Elkhoury et al. 2022).

Various natural sources, such as fruits, vegetables, herbs, spices, nuts, seeds, mushrooms, algae, marine organisms, and traditional medicines, can provide natural products that have neuroprotective effects. These natural products can protect neurons from damage and dysfunction caused by various factors, such as oxidative stress, inflammation, excitotoxicity, protein aggregation, and apoptosis. Some natural sources that contain neuroprotective natural products are turmeric, grapes, green tea, ginkgo tree, Chinese club moss, fish oil, and cherry (She, Jo et al. 2017).Click or tap here to enter text.

The chemical structures of natural products with neuroprotective effects are diverse and complex, which affect their physical and chemical properties, absorption, breakdown, and interactions with biological targets. Some natural products have more than one active component, while others have only one or a main component. Some natural products can be changed or made artificially to enhance their stability, solubility, or strength. Some examples of changes made to natural products with neuroprotective effects are curcumin analogs, resveratrol derivatives, and synthetic huperzine A(Mohd Sairazi and Sirajudeen 2020).

Natural products that have neuroprotective effects can affect various processes and molecules that are involved in keeping neurons alive, functioning, and adapting. They have different pharmacological actions and mechanisms, which can change the way various signals, receptors, enzymes, transcription factors, and genes work in neurons. Some natural products can pass through the blood-brain barrier and enter the brain, while others can work indirectly through the connection between the gut and the brain or the whole body. Some natural products can work together or against each other or with conventional drugs. Some examples of how natural products with neuroprotective effects work are antioxidant, anti-inflammatory, anti-apoptotic, anti-amyloidogenic, anti-tau, cholinergic, dopaminergic, glutamatergic, and neurotrophic effects(Griñán-Ferré, Bellver-Sanchis et al. 2021, Gomez-Verjan, Zepeda-Arzate et al. 2023).

Natural products that have neuroprotective effects are usually safe and well-tolerated, with little or no adverse effects. However, some natural products can be harmful, interact with other drugs, or be unsuitable for some people at high doses, long-term use, or in certain conditions. Therefore, natural products with neuroprotective effects should be tested carefully before using them in clinical settings. Some examples of problems that can arise from natural products with neuroprotective effects are liver damage from kava, bleeding risk from ginkgo biloba, and low blood pressure from resveratrol(Uddin, Mamun et al. 2021).

Natural products are biological substances that come from plants, animals, fungi, or microorganisms and have therapeutic potential. They can protect neurons from various harmful factors, such as oxidative stress, inflammation, excitotoxicity, protein aggregation, and apoptosis. These are called neuroprotective natural products. They have been studied for their possible roles in preventing and treating different neurodegenerative disorders, which are diseases that cause progressive loss of neuronal structure and function. Examples of neurodegenerative disorders are Alzheimer's disease, Parkinson's disease, Huntington's disease, amyotrophic lateral sclerosis, and multiple sclerosis. Natural products with neuroprotective effects have shown promising results in laboratory studies using cells and animals with neurodegeneration. . However, the results from human studies are still limited and unclear, because of the differences, inconsistencies, and weaknesses of the methods used. Therefore, more careful, large-scale, and long-term human studies are needed to confirm the effectiveness

and safety of natural products with neuroprotective effects in patients with neurodegenerative disorders. Some examples of human studies of natural products with neuroprotective effects are curcumin in Alzheimer's disease, omega-3 fatty acids in Parkinson's disease, and melatonin in Huntington's disease(González-Fuentes, Selva et al. 2018, Al-Shami, Essawy et al. 2023, Merighi, Travagli et al. 2023).

the comparison and contrast of the advantages and disadvantages of natural products versus synthetic drugs for neurodegeneration

Neurodegenerative diseases are conditions that cause the gradual loss of neurons in the brain and nervous system, leading to problems with thinking, memory, movement, and life span. Some common neurodegenerative diseases are Alzheimer's disease, Parkinson's disease, Huntington's disease, amyotrophic lateral sclerosis, and multiple sclerosis. These diseases have many different causes, such as genes, environment, and metabolism, as well as factors that damage neurons, such as oxidative stress, inflammation, excitotoxicity, mitochondrial dysfunction, protein aggregation, and apoptosis. There is no cure for these diseases, and the current drugs can only relieve some symptoms and have limited effects and side effects. Therefore, finding new and effective drugs for these diseases is very important.

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Two kinds of substances that have been used to prevent and treat neurodegenerative diseases are natural products and synthetic drugs. Natural products are biological substances that come from plants, animals, fungi, or microorganisms and have therapeutic potential. They have been used for centuries in traditional medicine systems, such as traditional Chinese medicine, Ayurveda, and Unani, to treat various diseases, including neurodegenerative diseases. Synthetic drugs are substances that are made or changed in the laboratory, usually by chemical or biological processes. They are designed to copy or improve the effects of natural products or substances that are naturally produced in the body, such as neurotransmitters, hormones, or enzymes.

Natural products have diverse and complex chemical structures, which enable them to interact with multiple molecular targets and signaling pathways involved in neuronal survival and function. Many natural products have shown neuroprotective effects against different neurodegenerative diseases by modulating various mechanisms, such as antioxidant, anti-inflammatory, anti-apoptotic, anti-amyloidogenic, anti-tau, cholinergic, dopaminergic, glutamatergic, and neurotrophic effects. Some examples of natural products with neuroprotective effects are curcumin, resveratrol, epigallocatechin-3-gallate, ginkgo biloba, huperzine A, omega-3 fatty acids, and melatonin(Assi, Farrag et al. 2023).

Synthetic drugs have specific and defined chemical structures, which allow them to have high selectivity and potency for their intended targets and actions. Many synthetic drugs have shown neuroprotective effects against different neurodegenerative diseases by targeting various mechanisms, such as acetylcholinesterase inhibition, monoamine

oxidase inhibition, dopamine receptor agonism, N-methyl-D-aspartate receptor antagonism, and amyloid precursor protein cleavage inhibition. Some examples of synthetic drugs with neuroprotective effects are donepezil, rasagiline, pramipexole, memantine, and semagacestat(Pommier, Gomez et al. 2004) .

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Natural products come from natural sources, such as plants, animals, fungi, or microorganisms, which may make them more acceptable and accessible. They also have multiple effects and mechanisms, which may make them more effective and versatile for complex and multifactorial diseases, such as neurodegenerative diseases. However, natural products have variable and unpredictable compositions, which may affect their quality, stability, absorption, breakdown, and interactions. They also have limited and unclear evidence from human studies, due to the differences, inconsistencies, and weaknesses of the methods used. Therefore, natural products need to be tested carefully before using them for neurodegeneration(Maurya, Bhattacharya et al. 2021).

Synthetic drugs are substances that are made or changed in the laboratory, usually by chemical or

biological processes. They are designed to copy or improve the effects of natural products or substances that are naturally produced in the body, such as neurotransmitters, hormones, or enzymes. Synthetic drugs have some advantages for the prevention and treatment of neurodegeneration, which is the progressive loss of neurons in the brain and nervous system. advantages of synthetic drugs have specific and defined chemical structures, which allow them to have high selectivity and potency for their intended targets and actions. This may reduce the risk of unwanted side effects or interactions with other drugs or biological systems. It also have consistent and conclusive results in preclinical studies using in vitro and in vivo models of neurodegeneration. This may increase the reliability and validity of their effects and mechanisms. However, synthetic drugs also have some disadvantages for the prevention and treatment of neurodegeneration, such as, they are unnatural and foreign to the body, which may make them less compatible and tolerable to patients and practitioners. This may cause allergic reactions, immune responses, or organ damage and They have single or dominant pharmacological actions and mechanisms, which may make them less effective and adaptable for complex and multifactorial diseases, such as neurodegenerative diseases. This may limit their scope and diversity of action, or cause tolerance or resistance(Ratheesh, Tian et al. 2017, Mallah, Couch et al. 2020).

Natural products and synthetic drugs have both advantages and disadvantages for the prevention and treatment of neurodegeneration. They have different types, sources, chemistry, pharmacology, mechanisms, safety, and clinical evidence, which can be compared and contrasted based on various criteria. The optimal use of natural products and synthetic drugs for neurodegeneration requires a comprehensive understanding of their benefits and risks, as well as a rational integration of their complementary and synergistic effects.

Conclusion

Neurodegenerative diseases continue to be a significant public health concern, with the number of affected individuals expected to rise substantially in the coming decades. Despite the substantial efforts invested in research and drug development, a cure or effective prevention strategy for these conditions remains elusive. Ethnopharmacology provides a valuable platform for exploring novel therapeutic options. Traditional knowledge from diverse cultures can guide the development of natural products derived from traditional medicinal plants, which offer the potential for neuroprotection. These natural products have demonstrated various mechanisms of action, from antioxidative and anti-inflammatory effects to the promotion of neurogenesis and synaptic plasticity.

In contrast to natural products, synthetic drugs have well-defined structures and specific pharmacological actions, which make them suitable for targeting particular disease mechanisms. Nonetheless, they may come with a higher risk of side effects and a limited scope of action, necessitating a careful balance between natural and synthetic approaches. In summary, the complex nature of neurodegenerative disorders demands a multidisciplinary and comprehensive strategy, combining insights from traditional medicine, advancements in drug delivery technology, and a thorough understanding of the advantages and limitations of natural products and synthetic drugs. Further research and clinical studies are required to unlock the full potential of these approaches and bring effective treatments within reach for the millions of individuals affected by neurodegenerative diseases.

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