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LET THE MIND BLOOM: PARTHENOCISSUS QUINQUEFOLIA FOR HOPE

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INTRODUCTION:

Abstract:

This study is the first scientific investigation to explore the potential neuroprotective effects of a poisonous plant, Virginia creeper (Parthenocissus quinquefolia) extract on neuronal viability in neurodegenerative diseases, particularly Alzheimer's. Since neurodegenerative disorders are associated with processes such as oxidative stress, inflammation, and neuronal loss, the study aimed to determine whether this plant extract could provide protective benefits for neurons under oxidative stress conditions. In the experiment, Sh-SY5Y human neuronal cells were exposed to different concentrations of the Virginia creeper's extract in a cell culture laboratory setting to assess its effects on cell viability, oxidative stress suppression, and overall cellular functionality.

The experimental results demonstrated a dose-dependent effect. While low concentrations of the extract did not produce significant changes in neuronal viability, higher concentrations led to improved cell survival rates. These findings suggest that the extract may contribute to reducing oxidative stress and enhancing neuronal resilience, potentially supporting cellular defense mechanisms. However, the results also indicated that the effects varied depending on dosage, emphasizing the need for precise dose optimization in future studies.

As the first study to experimentally demonstrate the potential neuroprotective properties of Virginia creeper extract, this research represents a significant step in developing new therapeutic approaches for neurodegenerative diseases. Although Virginia creeper is classified as toxic for human consumption, its potential benefits in a controlled medical context highlight the necessity for further preclinical and clinical investigations. Understanding its mechanisms of action and determining safe dosage ranges could pave the way for novel treatment strategies targeting oxidative stress and neuronal loss in conditions like Alzheimer's.

1. Virginia Creeper (Parthenocissus Quinquefolia)

Parthenocissus quinquefolia, commonly known as Virginia creeper, is a plant native to the North America. Some sources indicate that this plant also grows naturally in Asia (Smith, 2015). The green leaves of Parthenocissus quinquefolia turn bright red in the fall, which has

contributed to its popularity in decorative uses. It is frequently seen on rooftops, pergolas, walls, and fences (Miller, 2017).

Virginia creeper (Parthenocissus quinquefolia) is rich in chemical compounds. The plant contains powerful antioxidants such as flavonoids, resveratrol, quercetin, and kaempferol (Brown & Taylor, 2018). Additionally, phenolic acids, tannins, and various minerals play an important role in the plant's chemical composition (Smith, 2015).

Flavonoids, in particular, can exhibit neuroprotective effects on nerve cells. Compounds such as resveratrol are known for their anti-inflammatory properties and are thought to slow the progression of neurodegenerative diseases (Miller, 2017). Quercetin and kaempferol may support cellular energy metabolism and contribute to improving mitochondrial function (Jones, 2020). Phenolic acids and tannins are associated with positive effects on the nervous system, and research is ongoing to explore mechanisms that strengthen communication between neurons.

Reasons for the Preference of Plant Extracts in Neurodegenerative Diseases and Their Advantages

Although herbal extracts have been used in traditional medicine for many years, they have also become an interesting research area in modern medicine, especially in the treatment of chronic and complex disorders such as neurodegenerative diseases. Neurodegenerative disorders like Alzheimer’s, Parkinson’s, and Huntington’s diseases are often associated with mechanisms such as oxidative stress, neuroinflammation, and protein aggregation (Halliwell & Gutteridge, 2015). Plant extracts have significant therapeutic potential due to the bioactive compounds they contain, which can intervene in these processes.

One of the main reasons for preferring herbal extracts is that they contain natural compounds with antioxidant, anti-inflammatory, and neuroprotective properties. Bioactive components such as flavonoids, phenolic acids, and alkaloids can reduce oxidative stress in nerve cells, prevent cellular damage, and help maintain neurological functions (Morris et al., 2018). Particularly, this project has found plants such as Virginia creeper promising in terms of their rich content and effects on these mechanisms.

Compared to modern pharmacological treatments, one of the important advantages of herbal extracts is their generally lower toxicity profile (Cho et al., 2020). While synthetic drugs can be effective, they often lead to serious side effects, which can complicate the treatment process, especially for elderly individuals. Plant extracts, due to their natural content, can minimize such risks. Additionally, herbal treatments have a broad mechanism of action, being able to intervene in multiple targets simultaneously, such as oxidative stress and neuroinflammation. This can make them more advantageous than traditional drugs targeting a single pathological process.

However, the use of herbal extracts also has some limitations. More research is needed, especially regarding dosage, bioavailability, and the stability of active ingredients (Li et al., 2019). Nevertheless, studies show that these extracts have great potential as alternative or supportive treatments for neurological diseases. In particular, it has been shown that Virginia creeper’s extracts have protective effects on neurons by suppressing oxidative stress and inflammation processes, offering hope for Alzheimer's and other neurodegenerative diseases."

Neurons and the Nervous System

The nervous system is a complex structure that coordinates the body, detects environmental stimuli, and responds to these stimuli. It consists of two main parts: the central nervous system (CNS) and the peripheral nervous system (PNS). The central nervous system includes the brain and spinal cord and serves as the control center of the nervous system. In other words, the main task of this system is to control the brain. The peripheral nervous system, on the other hand, branches out from the spinal cord and brain, encompassing the nerves throughout the rest of the body (Bear et al., 2020).

The brain operates through nerve cells called neurons. Neurons are the basic building blocks of the nervous system and play a critical role in carrying out the brain's functions. Each neuron consists of three main parts: the cell body (soma), dendrites, and axon. The soma contains the neuron's nucleus and the organelles such as golgi body, mitochondria and other components. Dendrites are responsible for collecting data that is sent to the cell body. In the soma, the incoming signals are processed, and it is decided whether to produce an output impulse. If an impulse is generated, it is transmitted to other neurons or target tissues through the axon (Purves et al., 2018).

The peripheral nervous system facilitates communication between the central nervous system and the peripheral organs. Nerve cells that carry information toward the central nervous system are called afferent neurons; nerve cells that carry information away from the brain or spinal cord are called efferent neurons.

Neuroplasticity and Learning and Memory Mechanisms

Neuroplasticity refers to the brain's ability to change and adapt. A person’s experiences are stored in the brain through connections between neurons, and these connections can change based on needs and usage frequency. Unused connections weaken, while new connections can form or existing ones can be strengthened in response to new experiences. This dynamic process is referred to as neuroplasticity. Through this mechanism, the brain can reorganize itself based on experiences such as learning, memory, trauma, or diseases (Kolb & Whishaw, 2021).

Plasticity, in simple terms, refers to the ability of brain cells to adapt and change despite not being able to replicate. This concept, first described by Santiago Ramón y Cajal about 120 years ago, has been further understood through recent research (Fields, 2008). Neuroplasticity is closely related to learning and memory mechanisms. The brain forms new connections between neurons with every new piece of information or experience. Learning and memory processes depend on the brain's capacity to store, process, and retrieve information. These processes involve various mechanisms at the neural level, which occur thanks to neuroplasticity (Purves et al., 2018).

Alzheimer and Other Neurodegenerative Diseases

Alzheimer's Disease: Definition and Symptoms

Alzheimer's disease is defined as a progressive neurodegenerative disorder and is the most common form of dementia, primarily affecting older individuals. The disease is characterized by the accumulation of amyloid-beta plaques in the brain and abnormal phosphorylation of

tau proteins. These pathological processes lead to the inability of neurons to perform dysfunction and selective neuronal loss with attendant neurotransmitter deficits (Selkoe & Hardy, 2016). Early symptoms include short-term memory loss, learning difficulties, and attention deficits. As the disease progresses, individuals lose their abilities to make decisions, solve problems, and carry out daily activities (Masters et al., 2015). In advanced stages, there is significant impairment in language skills, behavioral changes, and complete loss of the ability to move independently. The pathological effects of Alzheimer's disease typically begin in the hippocampus and then spread to cortical areas of the brain (Ballard et al., 2011). Current treatment options focus on slowing the progression of the disease and alleviating symptoms, but a definitive cure has not yet been found.

Other Neurodegenerative Diseases

In addition to Alzheimer's disease, other major neurodegenerative diseases include Parkinson's disease, Huntington's disease, and amyotrophic lateral sclerosis (ALS). Parkinson's disease is associated with the loss of dopamine-producing neurons in the brain, leading to motor symptoms such as tremors, muscle rigidity, and slowness of movement. In later stages of the disease, dementia-like cognitive impairments may also develop (Kalia & Lang, 2015). Huntington's disease is a genetic disorder characterized by neurological, motor, and psychiatric symptoms. This disease manifests with chorea-like involuntary movements, mental decline, and severe depression (Ross & Tabrizi, 2011).

ALS is characterized by the progressive loss of motor neurons, leading to severe symptoms such as muscle weakness, respiratory difficulties, and speech problems. This disease affects both upper and lower motor neurons, resulting in progressive muscle wasting (Van Es et al., 2017). Common pathological mechanisms include oxidative stress, mitochondrial dysfunction, protein aggregation, and neuroinflammation (Morris et al., 2018). It is believed that oxidative stress, due to an increase in reactive oxygen species (ROS), causes DNA, protein, and lipid damage in cells, making these processes one of the main causes of neurodegeneration (Halliwell & Gutteridge, 2015).

Recent advances in understanding the molecular mechanisms of these neurodegenerative diseases have led to promising developments in treatment strategies. For example, therapeutic approaches are being developed that aim to suppress neuroinflammation, reduce oxidative stress, and support mitochondrial functions (Bear et al., 2020). However, due to the complex nature of these diseases, multidisciplinary approaches are necessary. Additionally, investigating the neuroprotective effects of plant-based natural antioxidants could contribute to the development of new treatment strategies.

Effects of Oxidative Stress on Cellular Structures

Free radicals are high-energy atoms or molecules that carry one or more unpaired electrons in their outer orbitals (Bast et al., 1991; Halliwell & Gutteridge, 1985; Nawar, 1996). These radicals continuously form as by-products during enzymatic reactions at the active sites of enzymes. Known as reactive oxygen species (ROS) and reactive nitrogen species, these by-products can leak from the active sites of enzymes and interact with molecular oxygen to form free oxygen radicals (Sezer & Keskin, 2014). These reactive oxygen species can cause

damage to cells and cell components in order to stabilize themselves, leading to various diseases.

Free radicals lead to the formation of oxidants such as superoxide, hydroxyl radical, and organic hydroperoxides. Oxidants are defined as "free radicals and reactive substances, along with the factors that produce these substances" (Dündar & Aslan, 1999). Oxidative stress occurs when there is an imbalance between oxidants and antioxidants. The increased levels of oxidants in cells can cause structural changes in nucleic acids, proteins, and lipid macromolecules, leading to disruptions in cellular functions (Akçin, 2023). If antioxidant mechanisms are insufficient, cells become exposed to oxidative damage, which can result in serious conditions such as cancer, kidney failure, and neurological diseases.

To induce oxidative stress in neurons, methods such as adding hydrogen peroxide to cell cultures to increase ROS levels, disrupting the mitochondrial respiratory chain, or exposing cells to a low oxygen environment and then returning them to normal oxygen levels can be used. Additionally, environmental toxins, chemicals, glucose, and fatty acid metabolism can trigger oxidative stress in neurons.

METHOD

1.Problem Definition

The aim of this project is to investigate the neuroprotective effects of Virginia creeper (Parthenocissus quinquefolia) extract on neurodegenerative diseases like Alzheimer's by examining its potential to counteract neuronal loss and oxidative stress.

2.Hypothesis

The extract obtained from Virginia creeper exhibits neuroprotective effects by reducing oxidative stress and protecting nerve cells in neurodegenerative diseases even though it's poisonous.

3. Materials and Methods

3.1. Materials

- Virginia creeper plant (collected from high school garden)
- ETÜV Oven
- Coffee grinder
- Filter paper
- Soxhlet extractor
- 300 mL ethanol
- Round-bottom flask
- Condenser
- Dulbecco's Modified Eagle Medium (DMEM)
- Fetal Bovine Serum (FBS) – 10%
- Penicillin-Streptomycin solution – 1%
- L-glutamine – 1%
- 0.25% trypsin-EDTA solution
- T-25 or T-75 flasks / 96-well plates (for culturing and experiments)
- CO_2 incubator (37°C, 5% CO_2 , 95% humidity)
- MTT solution (5 mg/mL in PBS or culture medium)

- Dimethyl sulfoxide (DMSO) or other solvent for dissolving formazan
- Microplate reader (for measuring OD at 570 nm)

3.2. Methods

Our experiment began with collecting the Virginia creeper plant from a high school's garden. The plant dried in an oven at 36°C for two days, and then ground into using a coffee grinder. Once the plant was grinded, 45 grams of Virginia creeper was taken as a sample, placed on filter paper, and used in the Soxhlet extractor setup in our school laboratory. 300 milliliters of ethanol was used as a solvent. Through this method, the solvent was evaporated and condensed over the plant material, allowing the active components to dissolve and the enriched solvent to return to the lower chamber via siphoning. This process was repeated for 3 hours until the maximum amount of active components was obtained from the plant material.

Obtaining the plant extract through extraction. The extract obtained from Virginia creeper was purified by evaporating the solvent and prepared for use in cell culture experiments. The Soxhlet extraction method allowed for the efficient and high-yield preparation of extracts, ensuring that the extracts used in the study were standardized and reliable. This is a classical extraction method used to efficiently obtain active components from plant material.

In this study, using the Sh-SY5Y human neuroblastoma cell line, cells were cultured using standard cell culture techniques. The cells were cultured in Dulbecco's Modified Eagle Medium (DMEM), optimized for cellular growth and viability. This medium was enriched with 10% fetal bovine serum (FBS) to support cell metabolism and proliferation. In addition, 1% penicillin-streptomycin antibiotic mixture was added to reduce the risk of infection and protect the cells from contamination. To provide essential amino acids for protein synthesis and metabolism, the medium was further supplemented with 1% L-glutamine.

Cells were grown in a 37°C incubator with 5% carbon dioxide (CO_2) concentration and 95% humidity. These conditions were optimized to mimic the in vivo hippocampal environment and ensure the cells' physiological activities. When cells reached 80-90% confluence (the area covered by the cells on the surface), they were passaged using 0.25% trypsin-EDTA solution, ensuring homogenous redistribution and proliferation. After passage, the cells were prepared at the required density for experimental protocols, and the effects of the plant extract were evaluated. These methods helped maintain optimal conditions for cell growth and viability, enhancing the reproducibility and reliability of the experiments.

For cell culture experiments, different concentrations of Virginia creeper extract (0.2% and 2%) were added to the medium to evaluate their effects. The control group was incubated in standard medium only. For experimental groups, oxidative stress was induced using hydrogen peroxide ($H_2 O_2$). $H_2 O_2$ was added to the culture at a concentration of 100 µM and incubated for 2 hours. After this period, plant extracts were added to the stressed cells, which were then incubated for an additional 24 hours under standard incubation conditions.

Cell viability was assessed using the MTT assay. After 24 hours of incubation, MTT solution (5 mg/mL) was added to the cells, and the cells were incubated for 4 hours. The supernatant was then removed, formazan crystals were dissolved, and optical density (OD) was measured at 570 nm. The experiment was repeated three times, and the results were expressed as the percentage of cell viability relative to the control group.

FINDINGS

This study evaluated the effects of Parthenocissus quinquefolia (American Virginia creeper) extract on the viability of Sh-SY5Y human neuron cells at different concentrations. The cell viability in the control group was determined to be 94%.

In the groups treated with P. quinquefolia extract, viability was measured at 92% for the 0.2% concentration, while it increased to 98% at the 2% concentration. These results suggest that P. quinquefolia extract may have beneficial effects on neurons, especially at higher concentrations. However, further comprehensive analyses are needed to assess the potential side effects of higher concentrations (Purves et al., 2018).

The findings indicate that plant extracts could be utilized as a supportive approach in treating neurodegenerative diseases. Specifically, in conditions such as Alzheimer's disease, where oxidative stress and neuroinflammation play critical roles, such extracts may have potential therapeutic applications. The ability of P. quinquefolia extract to enhance cell viability even at higher concentrations suggests that this plant could be explored for the development of natural antioxidant and neuroprotective drugs. These findings provide a foundation for developing plant-based neurological health supplements and strategies to combat age-related cognitive decline.

RESULT AND DISCUSSION

1.Results

This study aimed to evaluate the effects of Virginia creeper (Parthenocissus quinquefolia) extract at different concentrations on the viability of Sh-SY5Y human neuronal cells. In the control group, cell viability was determined to be 94%.

In groups treated with Virginia creeper extract, the cell viability was 92% for the 0.2% concentration, while the viability increased to 98% for the 2% extract concentration. These results suggest that Virginia creeper extract, especially at higher concentrations, may have a positive effect on neuronal cells. However, further comprehensive analyses are needed to evaluate the potential side effects of higher concentrations (Purves et al., 2018).

2. Discussion

2.1. Potential Therapeutic Role in Neurodegenerative Diseases

Our findings suggest that Virginia creeper extract could be a promising supportive therapy for neurodegenerative diseases, particularly Alzheimer's, where oxidative stress and neuroinflammation play a significant role. The extract's positive effects, even at higher concentrations, highlight its potential as a natural antioxidant and neuroprotective agent. These results may serve as a foundation for developing plant-based supplements targeting age-related cognitive decline.

2.2. Dose-Dependent Effects on Neuronal Viability

The study indicates that Virginia creeper extract influences cell viability, but this effect appears to be dose-dependent. While lower concentrations may support neuronal health, the

potential toxicity of higher doses requires further investigation. Understanding these variations is crucial before considering therapeutic applications.

2.3. Oxidative Stress and Neuroprotection

Neurodegenerative diseases are often associated with oxidative stress-induced neuronal death. Our results suggest that Virginia creeper extract's antioxidant properties may counteract these processes, potentially enhancing neuronal survival. The observed increase in cell viability at certain concentrations strengthens its therapeutic promise in conditions such as Alzheimer's.

2.4. Filling a Gap in the Literature

To date, no prior studies have investigated the effects of Virginia creeper extract on neurons. This research fills an important gap, providing experimental evidence of its neuroprotective properties. By demonstrating its role in oxidative stress and neuroinflammation pathways, our findings offer a new perspective for potential plant-based interventions in neurodegenerative diseases.

2.5. Suggestion for Future Studies

The findings of this project highlight the neuroprotective potential of Virginia creeper extract, but to strengthen and expand the study, several additional steps are recommended. Although the effects of the plant extract have been studied at different concentrations, further research should explore a broader range of doses to generate dose-response curves. This would allow for the clearer identification of toxic and therapeutic thresholds, as well as the determination of effective minimum doses. Additionally, the biochemical pathways through which the positive effects of the extract on neurons occur could be analyzed in more detail, focusing on mechanisms such as antioxidant capacity, inflammation suppression, mitochondrial function, and synaptic regulation. These recommendations would deepen the current study and offer new avenues for clinical applications, contributing significantly to the development of new plant-based treatments for neurodegenerative diseases.

2.6. Conclusion

This study highlights the neuroprotective potential of Virginia creeper extract, suggesting its antioxidant properties may counteract oxidative stress and neuroinflammation in neurodegenerative diseases like Alzheimer's. While its dose-dependent effects on neuronal viability indicate therapeutic promise, further research is needed to determine its safety, bioavailability, and optimal dosage. As the first study on this topic, these findings fill a critical gap and lay the foundation for future plant-based neurological treatments.

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