CME LIVE OPEN ACCESS

Clinical and Medical Engineering Live

Review Article

ISSN: 2997-612X

Integrative Case Studies and Protocols Found for Neurodegenerative Diseases

Christina Rahm*, M.S., Ph.D., Ed.D.

USA

Corresponding Author: Christina Rahm, M.S., Ph.D., Ed.D. USA

Received: 2024 Oct 01 **Accepted:** 2024 Nov 22 **Published:** 2024 Dec 31

1. Introduction

For modern medical practice, neurodegeneration, which is tightly associated with conditions such as Alzheimer's, Parkinson's, and Amyotrophic Lateral Sclerosis (ALS), is one of the most challenging aspects because these conditions affect almost every mental or motor function. These conditions wear off the strength of nerve cells over time, and their manifestation translates into significant deteriorations in people's day-to-day living standards. Although traditional medicine provides comfort care options, it faces specific barriers due to the complex nature of such diseases. Thus, these widespread problems stimulate a deeper investigation into traditional and non-traditional approaches to neurodegenerative diseases. The emerging integrative medicine could help revamp the concept of healthcare beyond traditional therapies. A holistic approach is adopted for a neuro-degenerative disease that encompasses conventional pharmacological methods together with various alternatives as they are interchangeable. In this respect, a very telling example is the case of 63 -year – old male patient who had Parkinson's Disease and his remarkable recovery due to the application of a holistic approach. It is worth mentioning that the patient showed significant improvement in the various symptoms associated with Parkinson's after undergoing an intricately devised regime, thus underlining the importance of evaluating unconventional methods for treating this condition. Furthermore, looking at environmental issues like toxins, cancer, mineral shortages, and viruses shows how these outer forces interact with Alzheimer's Disease and others. The ISNS case study and comprehensive protocols indicate that the integration of traditional and non-traditional approaches, together with an extensive search for new intervention strategies, can improve treatment effectiveness and provide holistic care for complex neurological disorders like Alzheimer's Disease, Parkinsonism, and Amyotrophic Lateral Sclerosis.

1.1. Understanding the Landscape of Neurodegenerative Diseases

The gradual dying away of the nerves is what causes neurodegenerative Disease, which is one of the significant health challenges across the globe, specifically in debilitating diseases that are highly acknowledged, such as Alzheimer's Disease, Parkinson's Disease, and Amyotrophic Lateral Sclerosis (ALS), that take the lives of millions upon people the world over. Currently, the incidences of neurodegenerative diseases are increasing, resulting in an enormous burden to individuals with the disorders and society at large. The article by Singh et al. 2023, reveals that this Disease is chronic and progressive, has significant consequences for disabilities, and its common complications are infection and fracture. Ariss and Hu 2022 also emphasize the need to identify PD as early as possible with better treatment regimens [1]. However, these motor symptoms are only one part of a highly complex picture of PD. According to Nashiry 2023, the study of PD mRNA expression is directly related to such psychiatric symptoms as depression and anxiety [2]. Moreover, there is an in-depth understanding of what Alzheimer's Disease is, how common it has become in society, the difficulty in offering care, and the burden that comes with it, as provided by Alzheimer's Association 2020 [3]. Taken together, these sources emphasize the importance of holistic perspectives and creative solutions in dealing with interrelated problems related to neurodegenerative disorders affecting human health as well as society at large.

1.2. The Parkinson's Disease (PD)

Parkinson's Disease is one of the major neurological disorders that have some particular symptoms that affect motor functionality and quality of life for people suffering. Characteristics of PD include shaking hands, poor balance, slow speech patterns, reduced facial expressions, and difficulty swallowing, among others. The Disease targets dopaminergic nerve cells in the brain's critically important area called the substantia nigra, leading to neuronal degeneration [4]. The lack of dopamine causes a severe loss and, in this case, a substantial deficit of dopamine in the corpus striatum, which is complexly connected with the basal nuclei of the cerebral cortex. Parkinson's Disease is marked by complicated pathophysiology because dopamine is crucial for messages from nerves that cause muscles to move, as well as activating pleasure and reward centers located within the brain.

A defining factor that affects the commencement of PD is age, usually showing symptoms at 65. As people age, the substantia nigra, which is responsible for producing dopamine, undergoes a gradual cell death process. However,

in PD patients, the rate of degeneration increases. When fifty-to-sixty percent of nerve cells in the substantia nigra die out, symptomatic exposition increases. With men showing higher vulnerability to PD than women, gender imbalances contribute to susceptibility. Genetic factors highlight the complexity of PD, as ten to twenty percent of cases have a genetic connection. Individuals with a familiar history who follow the autosomal dominant or autosomal recessive pattern of inheritance are at increased risk [4]. It is harder to determine PD's origin, as one can develop the condition by exposure to pesticides, heavy metals, and head traumas. The known fact that the late boxer Muhammad Ali suffered from PD due to brain trauma shows how environmental factors can greatly impact its onset. Collectively, the collaboration of age, sex, genetics, and environmental exposures cultivates the complex web frame of Parkinson's Disease since it is multifaceted.

A characteristic of PD is its complex clinical presentation, which includes a variety of symptoms that severely affect day-to-day life. Resting tremors, a characteristic feature of PD where patients experience involuntary shaking of hands and often pill-rolling movements with the thumb and index fingertip, are among the cardinal signs. This visible indication of tremors is not only distinctive but also acts as the main diagnostic symptom. The condition is displayed as a lead pipe or cogwheel type of muscular tension, further contributing to rigid and unmovable muscles. Singh 2023 indicate that this rigidity appears in patients' gait with shuffle steps accompanied by a hump-like position that makes it difficult for patients to take their normal steps [4]. Deterioration of associated movements like arm swinging while walking and struggle when getting up from a seat result due to bradykinesia, which is the general slowdown in body movement. Additionally, postural instability and proneness to falls caused by loss of equilibrium are major hindrances confronted by people diagnosed with PD.

Parkinson's Disease goes beyond motor symptoms and affects other non-motor domains as well, making its clinical representation more complicated. Different non-motor symptoms that significantly affect their wellness are problems commonly faced by individuals with Parkinson's Disease. With depression, dissatisfaction, and anxiety often accompanying motor symptoms, mental health aspects are especially prominent [4]. Individuals with PD face more issues due to sleeping problems like insomnia. The effect of this disorder on automatic functions is visible in symptoms such as erectile dysfunction, excessive sweating, and difficulty swallowing. Moreover, excessive salivation and loss of bladder control are other non-motor symptoms. The critical facet of PD is cognitive impairment, whereby patients suffer from dementia and memory loss, showing that the illness can affect different domains of health.

Parkinson's Disease has made a huge social impact due to its growing rate of occurrence and prevalence. Over a million Americans are affected every year, and the number continues to increase. Although PD per se might not necessarily kill someone, the consequences of the disease are very serious. Consequences could be fatal, like pneumonia and falls, leading to breakages, among others [4]. Due to the chronic and progressive nature of this Disease, major disability, which often leads to premature death, creates a heavy economic burden for patients and their families. Moreover, it cannot be ignored that there are enormous financial issues surrounding PD, including healthcare, rehabilitation, and productivity losses, among others, for patients as well as their careers.

Innovation has transformed PD in the modern era through technological advances, especially in the work by Ariss Hu 2022 [1]. In their study, they introduce an approach based on ResNet50 developed for the classification of Parkinson's Disease. In this approach, a residual network called 'ResNet50', consisting of 50 layers, is utilized to examine the spectrum characteristics obtained by sound recording of persons affected by PD. The spectrum features are then subjected to analysis leading to a two-dimensional heat map [1]. The heat map is then inputted to ResNet50 in order to generate a diagnosis of whether or not one has Parkinson's Disease. This method involves integrating artificial intelligence and deep learning for improved diagnostic precision, especially at an early PD stage. However, a method based on ResNet50 has proved feasible in terms of early diagnostics with a view to improving prognosis.

Aligning with the cross-cutting approach, which collaborates the areas of neurology sciences and computation systems, the approach makes use of the resnet50 model to develop methods for the diagnosis of associated dementia disorders from brain MRIs. Researchers can overcome this challenge by using various computational methods supported by machine learning algorithms [1]. Such an interdisciplinary synergy leads to a comprehensive perception of the causes and signs of PD, making use of insights from neurobiology and artificial intelligence in order to increase the power of diagnosis. These innovative technologies also help in accurate diagnosis and will have the ability to create specific treatments for patients with different variations of Parkinson's Disease.

Neurodegenerative disorders research has identified a new promising area, which is implementing technologically focused methods and demonstrating the benefits of interdisciplinary approaches.

Studies into the link between PD and psychopathologies, however, look beyond conventional motor features of the condition. Nashiry 2023 use system biology with brain transcriptome data, which shows the link between PD and other psychological problems [2]. By conducting research, the researchers find relationships between PD and schizophrenia, bipolar disorder, and other mental illnesses. By studying gene set enrichment, protein-protein interactions, gene regulatory networks, and their relationship with chemical exposure, this study provides insights toward understanding the complex relationships between Parkinson's Disease and psychological symptoms [2]. It is essential to identify and comprehend such mental appearances not only as a therapy to remove the symptoms

but also as a means to understand the physiopathology of PD better.

In essence, PD is complex and involves more than the classic motor features. PD's etiology is complex owing to the delicate balance among genetic, environmental, and age-related issues. Such a high social impact, along with an increasing trend of the Disease, requires thorough understanding, coupled with new diagnostic and therapeutic methods. New technologies, such as classification based on the concept of residual networks (ResNets), provide a good line of research in terms of improving early detection and preventive measures. Furthermore, investigation into PD's co-morbidity with psychiatric disorders holds promising implications for changing therapy techniques with a focus on an integrated approach to tackling the intricate nature of Parkinson's.

1.3. Alzheimer's Disease (AD)

AD poses a serious threat to the world health system, which has become a primary reason for dementia. The shocking fact is apparent looking at the numbers, as it can be seen that over 5.8 million Americans who are above 65 years old suffered from AD in the year 2020. Researchers anticipate that it will increase to 13.8 million senior citizens during mid-century, as published by Alzheimer's Association in 2020 [3]. The pathway of this growth highlights the dire importance of an all-inclusive and enduring mechanism for controlling the rapidly expanding public health problem linked with dementia (Alzheimer's Association, 2020) [3]. AD is a sophisticated condition made up of different factors that cause the loss of neurons, which are responsible for memory creation and other intellectual processes. This means AD is a complex psychiatric disorder with many layers that require an elaborate multi-pronged conceptualization of both its intrinsic and consequential features.

Although AD directly affects only those who fall prey to its debilitating effects, it has a wider reach to affect caregivers and create tremendous economic losses in society at large. Nearly $244 billion in healthcare costs are expected due to this, adding much pressure on the family as well as the state healthcare system (Alzheimer's Association, 2020) [3]. The combination of these two factors concerning AD makes this situation even more problematic in relation to health care and how prepared it is to handle this increasing problem that spreads all over and ends up rendering people helpless. It becomes more apparent as the total number of people involved increases that there is an urgent need for preventive strategies concerning this growing epidemic of a public health disaster. Crucial aspects of combating AD involve enhanced diagnostics, total support for caregivers, and a review of health service delivery models. There may be light at the end of the tunnel if only these comprehensive strategies could be implemented together.

Moreover, a complete assessment of the aftermath of AD as manifested by such measures as incidence and prevalence, mortality, morbidity, management costs, and impact on caregiving is presented in the 2020 Alzheimer's Disease fact sheet and figures (Alzheimer's Association, 2020) [3]. However, official death certificates in 2018 indicated 122,019 deaths due to Alzheimer's Disease, and this stark reality shows why it has become the sixth leading cause of mortality in the USA and also for American older adults over the age of 65. Such a high death rate shows the problematic nature of AD, which affects the whole society, and the private tragedy of a person who has dementia due to Alzheimer's Disease.

AD is a multifaceted challenge for families and, in particular, unpaid caregivers, with about 16 million relatives devoting almost 18.6 billion working hours in 2019, as reported by the Alzheimer's Association (2020) [3]. Apart from the sheer magnitude of these caring attempts, the psychological torment and detrimental consequences on mental and physical health suffered by the caregivers underline the need for a broad-based reaction to the societal implications of AD. These effects demonstrate the intricate interconnection among personal health, family relations, and general health issues in society. Effectively addressing the challenges mentioned above requires the application of the medical, social, and psycho approaches, the former in order to ensure that the lives of caregivers and the direct victims are improved.

With the increasing number of American citizens who have developed Alzheimer's dementia, the corresponding cost escalates. As reflected in the 2020 AD Facts and Figures Report, this paper provides some economic aspects of AD, highlighting that for patients above sixty-five years old, the total payments in 2020 account for approximately three hundred and five billion dollars towards healthcare, long-term care, and hospice costs (Alzheimer's Association, 2020) [3]. These issues are further made worse as there is a severe deficit of specialist care for those with dementia, causing primary care physicians (PCPs) to feel overwhelmed and unprepared to manage the intricacies involved in providing dementia care (Alzheimer's Association, 2020) [3]. Therefore, this report provides strategies on how best to improve patient health while dealing with these problems, as well as stresses the importance of new technologies and increased education in the primary health sector in order to cater to the increasing elderly population.

Alzheimer's Disease has a complex pathogenesis involving the deposition of neurofibrillary tangles and neuronal death, particularly the EC [5]. In the context of AD, the histological changes in a key brain area – the entorhinal cortex – occur first. Lately, there have been studies, including that of Igarashi, that provide evidence on how dysfunctional neuronal activity in the EC can be found even before visible neurodegradation. This notion disrupts many conventional perceptions, pointing out that the atrophy of cells in the EC explains the short-term recollection issues and disorientation during spatial orientation in first-stage AD [5]. Recognition of these early-stage changes goes beyond a mere appreciation of its cause and leads us to the doorstep of developing novel diagnostics regimes. These approaches offer a crucial opportunity for the implementation of early intervention strategies by addressing dysfunction detection

prior to irreparable damage.

The role that the entorhinal cortex plays in the initial stage of AD presents opportunities to address the problems relating to diagnosing and treating the disorder. Igarashi's 2023 study reveals that there is a possibility of detecting markers that are related to activity dysfunctions in the EC region and, therefore, opens the way to early diagnosis for AD [5]. Such a discovery can pave the way for early intervention administration for activity disruptions that occur earlier than the permanent neurodegeneration process. Therefore, the focus on early changes should reframe how we see AD as well as emphasize the need for wide-ranging diagnostic and intervention approaches to be put in place [5]. Basically, understanding the role played by this brain area in the disease mechanism for Alzheimer's would be a critical step toward better diagnostics and, perhaps, treatment of this rather elusive neurologic disorder.

In general, AD has become a major problem for public health, which should now be addressed immediately, including the implementation of appropriate actions to curb this Disease. An all-rounded approach to the rising frequency, costs, and complicated pathology of AD, in addition to other factors, is required. More targeted interventions can be developed based on innovations in diagnostic methods involving the identification of early changes, including entorhinal cortex dysfunctions. Finally, meeting society's demands entails improving caregiver assistance, promoting relevant medical education for the staff, and exploring eco-friendly approaches to service provision. A comprehensive and concerted approach will be the only way forward in the complex territory of Alzheimer's and preventive measures, early diagnosis, and high-quality treatment.

1.4. Amyotrophic Lateral Sclerosis (ALS)

ALS has traditionally been viewed as a disease caused mainly by the demise of the motor nerves; hence, the central component in the pathophysiology relates to the dying off of both the upper and lower motor-neuron fibers. Recently, there has been a paradigm shift to the conventional viewpoint based on obvious symptoms of muscle weakness and hyperreflexia. As shown with recent discoveries like those indicated by Rojas 2020, the traditional idea about ALS being linked exclusively with degenerative diseases is now considered outdated since various other aspects exist when it comes down to what is actually happening at a cellular n molecular level within an individual affected by such disorder will have taken place here before finally declaring someone healthy again once symptoms start subsiding or disappearing completely from their body altogether [6]. This change in perception represents a crucial transition in the way scientists and medical practitioners understand the intricacies of amyotrophic lateral sclerosis.

Skeletal muscle dysfunction has received much attention in recent literature, especially since its role in ALS is considered crucial and is different from the previous point of view. This brings out that there are disturbed skeletal muscles, which questions the conjecture that muscle changes are just secondary outcomes of nerve cell loss. Through this lens, a new context on ALS pathophysiology emerges, emphasizing the relationship between the motor unit as a whole, that is, the motor neuron-skeletal muscle connection and their involvement in the disease process [6]. Taking a close look at ALS from a limited view makes us realize that specific treatments do matter and are significant too. It would be necessary to take into account the relationship between motor neurons and muscles, which affect both of these components while developing treatments for ALS.

Knowledge about ALS now appreciates that skeletal muscle and motor neurons work together as part of a complex system. Shefner 2023 highlight the reciprocal effect of these two components and illustrate it as one functional unit [7]. In the past, people regarded ALS mainly as an illness that affects motor neurons and believed that the death of these neurons was the primary abnormal health condition responsible for it. Nonetheless, this viewpoint has become complex by focusing on the intricate association of motor neurons and muscle fibers. This calls into question the usual perceptions by asserting that ALS does not only affect motor neurons but the whole complex of muscle activity.

Since ALS should be understood in the new paradigm, skeletal muscle dysfunction should be as well recognized as significant. The authors indicate that alterations in muscle activity should be viewed not as secondary events connected with a degenerative loss of neurons but as an essential part of the pathological processes associated with ALS. Shefner 2023 highlight, in particular, the importance of considering skeletal muscle involvement as one of the critical parts of a general understanding of ALS [7]. Accordingly, this new outlook dictates a reassessment of therapeutic approaches. These days, any treatment that tries to deal with ALS has to take into consideration motor neurons and muscles so that it becomes integral and multifaceted.

The molecular pathogenesis of ALS involves several components. Excitotoxicity is one of the leading causes for ALS and the subsequent motor symptoms seen in patients such as the destruction of upper and lower motor neurons. Moreover, the existence of mitochondrial disorders contributes towards making the disease rather complex [6]. Dysfunction of mitochondria which produces energy is suspected to cause ALS disease.

Another important molecular aspect is neuroinflammation, which makes the picture of ALS pathology more complicated. The pathogenesis of CNS inflammation is very complicated, as different types of immune cells and cytokines work together. Neuroinflammation in ALS is a dynamic phenomenon that accelerates the development of the Disease. In such conditions, immune cells invade the involved areas, producing pro-inflammatory cytokine that worsens the destruction of motor neurons and skeletal muscle. In addition, neuroinflammation intensifies the Disease and makes the separation between motor neurons and muscles obscure [6]. Therefore, therapists must be guided by a holistic perspective when devising strategies aimed

at helping victims recover. The development of effective disease-modifying therapies will require the consideration of a broader cellular context and an understanding of the complex molecular interactions leading to ALS. Researchers will only be able to decipher the intricacies of ALS if they understand how each of these molecular mechanisms interoperates together to cause the Disease.

Psychiatric symptoms due to ALS make it apparent that it is a generalized condition with widespread manifestations. Zucchi 2019 highlight the spectrum of psychiatric disorders in ALS patients, ranging from depression, anxiety, and hallucinations to cognitive dysfunction [8]. That is, the addition of these non-motor symptoms drastically broadens the conventionally restricted characterization of ALS as a motor neuron disorder. There are many other psychiatric symptoms, like depression and anxiety, which complicate things even further and require more than simply addressing motor presentations. The revealing discovery brings back into question ALS as an exclusive motor neuron disease, implying a re-examination of the interwoven nature of these symptoms, including the relationship between neuropsychiatric and motor features in the overall meaning of the condition in its entirety.

Additionally, the concurrent presence of psychiatric manifestations in ALS underscores the wide-ranging nature of the conditions. The realization that one can suffer from cognitive dysfunction, hallucinations, and mood disorders highlights the necessity of a more holistic treatment. This dynamic interaction between motor and non-motor symptoms speaks volumes about a more elaborate pathophysiological nexus that goes beyond motor neurons. This acknowledges the wider range of aspects that characteristically define ALS as a broad, systematic disease rather than just a mere motor neuron disorder. Essentially, the study by Zucchi 2019 represents a groundbreaking step forward in understanding ALS and should prompt researchers to adopt a broader perspective on this tragic neurodegenerative disorder [8].

Notwithstanding these difficulties in producing disease-modifying treatments for ALS, some of the present-day improvements provide hope for useful translational methods. In the ten years that have passed since, there have been some monumental discoveries, particularly in preclinical models, genetics, pathology, biomarkers, imaging, and clinical readouts, as discussed by Mead 2022 [9]. The aggregate information provides the basis for selecting specific agent therapies having distinct actions on different drugs. Successful therapeutic translation in ALS has far-reaching implications beyond the Disease alone and extends across the entire sphere of neurodegenerative drug research. Once considered a difficult disease, ALS becomes an innovative intervention that can open new ways to solve other neurodegenerative disorders.

Recognizing the effect of ALS on the visual system, and more particularly the retina, enriches the knowledge about ALS. According to Rojas 2020, the retina can be a biomarker for ALS, highlighting how these changes in the central nervous system are reflected therein [6]. The involvement of the visual system goes beyond the systemic nature of ALS, emphasizing the necessity of multi-dimensional diagnosis and treatment methods. An emerging view of the role of ocular involvement in ALS only reinforces the idea of combining systemic and central elements of any neuronal process into one unified approach.

Modern perceptions have redefined ALS as a disorder that affects the skeletal muscles, complications, molecule components, and symptoms. The interaction between motor neurons and skeletal muscles and the discovery of molecular mechanisms behind this Disease, as well as the emergence of psychiatric symptoms, show the importance of taking all aspects into account while studying pathology and developing therapeutics in patients with ALS [8]. In spite of the difficulties, new progress is holding out hope for valid translational strategies, with ALS as a focus for cutting-edge interventions that might make a difference in the wider domain of neurodegenerative disorders. The changing perspective on ALS signifies how complicated neurodegenerative studies are, a point that shows why collaborative interventions should be employed when addressing such diseases with such an adverse impact.

1.5. Joint Prevalence and Societal Impact of Neurodegenerative Diseases

Degenerative problems, such as Alzheimer's, Parkinsonism, and ALS, are considered a huge collective threat to individual patients and the whole of society worldwide. Alzheimer's Disease is one of the biggest public health issues today. It can be seen on this account that over the period comprising five years 2015-2020, crude prevalence was estimated at. This statistical number clearly illustrates the weighty influence of Alzheimer's on society, showing the number of people who are suffering from it. Olazarán 2023 note that there is excessive monotherapy, and this includes rivastigmine [10]. Indeed, healthcare delivery is even more complex nowadays since it has received further complications because of the prevailing global pandemic of COVID-19. The complexities also involve the diagnosis and medication of Alzheimer's, leading to fewer treated cases in 2020 than in the previous year, which is evident in the work by [10]. The societal effect of Alzheimer's Disease is amplified due to the intersection of various factors. Therefore, it requires appropriate adaptations and a comprehensive approach to dealing with multi-factorial neurodegenerative problems.

In addition, PD is a complicated terrain of a motor deficit and increasing incidence in men over 65 years. Ariss and Hu's 2022 idea concerning an early diagnosis approach involving ResNet50 highlights the importance of early treatment in controlling PD [1]. This technology offers hope when dealing with delayed diagnosis, as well as more successful early treatments. Nonetheless, the complications of PD, like vulnerability to infection and falling, cause substantial societal costs. However, these complications have to be managed in an integrated system involving not only the usual motor problems of Parkinson's but also cognitive and

psychic aspects. Aune 2023 explore diabetes complications in PD patients, adding to our understanding of the Disease [11]. Therefore, it becomes necessary to have a more detailed study of PD, which is so multifaceted that it requires careful attention in order to devise effective diagnostic and therapeutic procedures.

Though not as common as Alzheimer's Disease or Parkinson's Disease, ALS affects both upper and lower motor neurons, making its impact equal. Dysfunctions of skeletal muscle in ALS revealed recently, according to Shefner 2023, prove that ALS is not a purely motor neuron disease [7]. The complex nature of ALS is underlined by the fact that both motor neurons and muscles are integrated. The three diseases may appear as different conditions, but all have intertwining threads of neurodegeneration and social implications. Such strategies should be based on joint work and an interdisciplinary approach in order to reveal the mystery of this Disease.

1.6. Traditional Non-traditional Approaches to Neurodegenerative Diseases

The routine therapies for neurodegenerations like PD, ALS, and AD are mostly directed at relieving symptoms, not treating the cause of the Disease. The typical treatment for Parkinson's Disease is dopaminergic stimulation, in particular through levodopa. The strategy aims to treat the neurotransmitter imbalance associated with PD, which mainly underlies motor symptoms like tremors and rigidity [4,12]. Unfortunately, it is important to understand that this solution fails to address the root cause – the degeneration of neurons, which leads to Dopaminergic therapies providing only symptomatic relief with little effect on preventing the progression of PD.

With respect to AD, traditional therapies mainly focus on drugs like cholinesterase inhibitors and NMDA receptor inhibitors. Prescriptions are directed at neurotransmitter imbalancerelated cognitive deterioration in patients suffering from AD [13]. They have been approved for clinical use, but they only provide symptomatic management and do not change the natural course of the disorder. What is evident in the discussion is that despite the efforts placed in developing appropriate intervention measures, it is clear that the challenge of changing the AD trajectory has been elusive throughout history [14,15]. However, the present pharmacological efforts towards AD management have been characterized as palliative rather than curative.

People who have ALS have very few options to turn to when it comes to treatment, and they are mostly related to riluzole, an inhibitor of glutamate. Even though riluzole is used as a standard treatment, its effect on patient survival still shows little improvement. Unfortunately, there is yet no cure for those who have ALS [16]. The grim truth exposes the enormity of finding interventions that will change by far the inevitable natural course of ALS, underscoring the urgency of breakthroughs. Moreover, various other neurodegenerative disorders, including Parkinson's Disease and Alzheimer's, also demand alternative therapy techniques from a conventional approach, which are as follows. The new approaches should go beyond symptom management towards tackling these highly complicated and catastrophic illnesses at their very foundations.

However, despite years of research and major improvements in treatment, these medical interventions have serious limitations when administered to neurodegenerative patients. Dopamine replacement in PD proves to be futile against disease spread. Also, chronic administration of levodopa can cause motor complications [12,17]. In AD, however, they are all symptom-reliving drugs that do not address the underlying mechanism for neurodegeneration in AD. The issues with ALS treatment include low efficiency in riluzole and lack of any cure approach. These drugs also come accompanied by side effects, which pose an additional challenge [16]. These approaches reemphasize the urgency to develop new therapies that will fight rather than address the results of the pathologic processes.

Likewise, AD gives rise to problems as far as possible drug treatments are concerned. Although the approved drugs for AD, such as cholinesterase inhibitors and NMDA antagonists, alleviate some symptoms by modifying neurotransmitter imbalances, they do not address underlying neurodegeneration [13]. Such constraints illustrate the key gap existing in AD therapies and, therefore, call for an investigation into new strategies that bypass mere symptomatic management and are instead aimed at tackling the underlying pathogenesis. ALS poses unique challenges for therapeutic intervention. Riluzole is the main drug which has limited impact while there is a lack of cure-the-disease agents. The prolonged use of riluzole also causes other side effects, which make the drug even more disadvantageous [16]. These pose some very important reasons why there is an urgent need to provide novel therapies for ALS aiming not only at symptomatic treatment but also at neuroprotective approaches. This reiterates the significance of creating strategies aimed at tackling the diverse physiologic processes of ALS progression.

The limitations inherent in current medical management warrant a paradigm change in the management aspect of neurodegenerative diseases. Although they provide symptomatic relief, available treatments only provide no disease modification and need further search for alternative measures. New pharmacological targets may be investigated, and alternative modes of treatment, like cell therapy and traditional Chinese medicine [15,18]. Specifically, PD, AD, and ALS highlight the need to think beyond the box so as to deal with complexities associated with neurodegenerative diseases.

In illustrating the pressing need for a comprehensive focus on the management of neurodegenerative diseases, the 65-year-old patient case study showcased the complexity of PD. Specifically, in the case study associated with ISNS, it is presented that there exist multiple complex issues associated with the management of PD in a 65-year-old male patient. Typical first symptoms appear to be rest

tremors, bradykinesia, and posture instability (ISNS Case Study n.d. [4]. These have been observed in the reported case. Traditional medications recognize the necessity of new therapy methods by going beyond just alleviation of PD symptoms.

In this regard, the ISNS case study is an emotional representation of why one should not trust only conventional treatment for neurodegenerative disorders. This journey shows that it is necessary to utilize integrative methods combining conventional and alternative treatments. As the case study shows, integrative approaches entail new cell therapies directed at the prodromal stage, which involves allogeneic cell translocation beyond the basal ganglia [18]. The adoption of this holistic treatment approach is a new paradigm that can combine current treatments with other emerging methods into an improved scheme suited to each unique case.

1.7. Neurodegenerative Diseases Protocols

The HEN Proprietary Blends: The HEN has developed unique synergies in a way designed to address neurodegenerative conditions via specially tailored formulations. The set comprises six blends, namely clean Slate, zero-in, restore, natural barrier support, re-live greens, and immune defense shield. Every mix is carefully tailored to target different aspects of neurodegenerative disorders. These blends are not meant only to relieve symptoms but also provide an insight into the physiopathology, arrest disease deterioration, and facilitate management for people with these compound diseases. The various ingredients in these blends represent a comprehensive approach, acknowledging the complexity of neurodegenerative diseases. Unlike other approaches that focus on relieving symptoms, HEN's approach covers a much deeper level of intervention, such as prevention, amendment, and improved care delivery, demonstrating a commitment to revolutionize the neurology field with efficient and specific measures.

The Clean Slate proprietary blend I, a key component of the HEN approach to neurodegenerative diseases, is meticulously crafted with three essential elements: Silicon Dioxide (Silica), Ascorbic Acid (Vitamin C), and Trace Minerals. Silica, one of the basic compounds needed to sustain healthy connective tissues, plays a crucial role in maintaining the structural integrity of various body tissues, such as the ones involved with the nervous system. Silica is basically a foundation that supports these structures, thus acting like pillars providing the strength needed to hold on to its health. Within the neural system, the complex system of tissues, this mineral resonates with the utmost importance. Through the linkage with the neural architecture, silica ensures the sustainability of connective tissues as well as the robustness and resilience of the whole nerve system. However, it is more than structural support because promoting the health of the connective tissue promotes the healthy development of the brain structures. Silica guards the delicate waltz of physiological actions [19]. It emphasizes itself beyond its role as a component of the connective tissues but also as a basis of neural health in general.

A vital constituent found in the Clean Slate proprietary blend is vitamin C, which helps fight against free radicals; the antioxidants, hence, play a critical part in protecting against the harmful effects of free radicals. Being a powerful antioxidant, vitamin C forms the front row in fighting the damaging effects caused by free radicals. These unstable molecules can lead to oxidized stress, and this is one of the processes implicated in cellular damage, especially in the intricate environment of the brain. The ability of vitamin C to neutralize free radicals is crucial for protecting from the possible oxidative stress that would lead to neurodegeneration. Vitamin C's antioxidant property also protects neurons from neurodegeneration [20]. Recognizing Vitamin C's function against oxidative stress follows the new perception that such stress is one of the causes of neurodegenerative diseases. Therefore, adding Vitamin C to Clean Slate shows that they have been tactical and scientific when it involves the overall wellness of the brain with regard to neurodegenerative diseases.

Trace minerals constitute an important dimension in Clean Slate blended products, which is complementary and necessary. These mineral elements are taken through diet, but they do not require large amounts as others known as major minerals. Trace minerals contribute greatly toward most physiological operations – including enzymatic reactions, cell-to-cell communication, etc. that are critical to normal neuro functionality. The incorporation of trace minerals into Clean Slate is strategic as it responds to specific challenges posed in a complex neurodegenerative disease scenario. A mix acknowledges the vital assistance these small elements provide to the nervous system and also helps address issues related to Parkinson's or Alzheimer's disease. Clean Slate recognizes that even trace minerals have a role to play in efficient neuroprotection by virtue of homeostasis. This emphasis on specificity suggests an all-encompassing approach as well, showing how any little element adds significantly to the overarching mission of strengthening the nervous system toward combating neurodegenerative disease advancement.

An outstanding formula called Zero-In, which was carefully engineered to achieve cognitive enhancements as well as overall neuroprotection, is part of HEN's protocol for any neurodegenerative disease. Such a powerful mix consists of important components - N-acetyl Ltyrosine, anhydrous caffeine, L-theanine, velvet bean seed, pine bark, curcumin, and vitamin D. The selected key ingredients were aimed at specific challenges related to the Composition of ZeroIn is based on a deep reflection of the complexities in which dementia emanates due to these disease processes so as to proffer an all-inclusive response. Through having N-acetyl L-tyrosine as one of its ingredients, Zero-In is capable of providing cognitive aspects such as attentiveness and concentration on neurotransmitter synthesis. Adding anhydrous caffeine makes everything else more worth it, for the mood is improved, and alertness is increased. Moreover, the tranquilizing effect of L-theanine promotes a well-balanced cognitive upsurge, leading to an alert but relaxed mindset. The mixture of velvet bean seed, pine bark,

curcumin, and vitamin D act together toward the objective of neuroprotection addressing oxidative stress, inflammatory response, and biosynthesis.

N-acetyl L-Tyrosine (NALT) is basically acetylated l-tyrosine that has been linked to various aspects of health. NALT is the central point of its significance because NALT helps in the production of neurotransmitters such as dopamine [21]. Dopamine is known to be the most critical in cognitive operations that helps with keeping concentration, attention, and general cognition. The strategic deployment, in this sense, seeks to integrate it with NALT to build the formation of critical neurotransmitters. A cognitive protection mediator, NALT, may be a means to stave off these cognition issues associated with such neurodegenerative diseases. To demonstrate NALT as a specific component of the Zero-in approach, it works with users who experience some dementia to provide them with a strength they can use against cognitive loss.

One of the most common stimulants in Zero-In's proprietary blend is anhydrous caffeine. It helps enhance cognitive ability and fight fatigue. Caffeine is acknowledged as an agent that prevents activation of adenosine receptors and then subsequent pathway to dopamine surges. Therefore, this mutual mechanism, together with NALT, makes up an integrated strategy for cognitive improvement. Caffeine serves to restrict adenosine, an element involved in drowsiness, thereby enabling continuous wakefulness and heightened awareness [22]. At the same time, increased dopamine results in improved mood and cognitive performance. The multiple-fronted cognitive disorder of neurodegenerative Disease is tackled here using cooperative action. Anhydrous caffeine is one of the most important components in this intricate neurotransmitter connection. This connection is aimed at enhancing cognitive capacities and reducing the negative effects of neurodegenerative disorders.

One of the components included in the Zero-In is L-theanine, which is hidden among the leaves of the tea. L-theanine is a unique twist in cognitive enhancement because it promotes calmness and relaxation without the sleepiness associated with other relaxant drugs. The Ltheanine is very crucial for this delicate balancing act or dance that happens between stimulation and serenity, which occurs when one consumes caffeine since it curbs the jitters that people usually experience after caffeine consumption. This does not imply that this harmony between different aspects of life is just like weighing on a scale. Mental stability may be key in helping patients and their families cope with conditions such as neurodegenerative and other related illnesses. Ltheanine is not just an ingredient in this respect; it becomes a coadjutor able to induce focused calmness instead of mere stimulating or sedative effects as traditionally understood.

The importance of Velvet Bean Seed makes it an important player in the Zero-In brand, providing a natural source of L-dopa, which leads to the production of dopamine. In this sense, the role of dopamine is important, particularly for such diseases as neurodegenerative ones that often have disturbed dopamine formation. The role that Velvet Bean Seed plays as a powerful progenitor for dopamine forms a part of Zero-In's neural preservation [23]. Therefore, its strategic inclusion complements the overall aim of sustaining cognitive activity and may even thwart dementia caused by such chronic ailments. Although it is a part of neurotransmitter imbalance and complex neurodegenerative diseases, it is worth noting that Velvet Bean Seed forms the building block of dopamine. The brain tree is an excellent example of combining conventional knowledge with modern neuroscientific concepts on mental health when fighting neurodegeneration.

Pine bark, rich with powerful antioxidants, becomes an important part of the oxidative stress treatment for neurodegenerative diseases. Oxidative damage is also one of the most significant factors that can cause nerve cell degeneration in the complexity of neurodegenerative disorders. Therefore, Pine Bark acts as the anchor in the strategy of neuroprotection against the damage caused by oxidative stress to the fragile architecture. The complex process of maintaining neuronal integrity in the face of unrelenting neurodegeneration is aided by Pin Bark as a natural source of antioxidants. Its function far exceeds mere prevention by becoming an umbrella, neutralizing or preventing the oxidative damages that are involved in the developmental stages of neurodegenerative disorders. Through the inclusion of Pine Bark into the protocol, The HEN brings to bear its sophistication in understanding that neurodegenerative diseases are not onedimensional phenomena and, therefore, involve natural defense systems as countermeasures against oxidative stress.

In Zero-in formulation, curcumin is extracted from turmeric, and it has many advantages for various neurodegenerative disorders. Curcuma, which is commonly known as turmeric, is renowned for its strong anti-inflammatory and antioxidant properties [24]. ZERO-In is mixed strategically with curcumin within the context of these diseases having inflammation cascades, which drive a decline in cognition and their final target. Through selectively attacking inflammation for the protection of cognitive function, the use of curcumin holds great promise to help people cope with the intricate problems associated with neurodegenerative diseases. The intentional inclusion of curcumin highlights this mix's dedication to an all-encompassing view, considering that inflammation is instrumental in the pathogenesis of these illnesses and can open up doors for new neuroprotection methods.

Vitamin D, which is famous for its recognized part in supporting bone health, becomes an essential factor for neuroprotection. Thorough researches support that vitamin D deficiency may be associated with an increased risk of neurodegenerative Disease [18]. Being cognizant of the systemic aspect of cognitive health, HEN wisely includes a dose of Vitamin D in its formulation called Zero-in, which is indicative of a deep comprehension of neurodegenerative Disease. The strategic inclusion of this key vitamin addresses the possibility that it may worsen some cognitive problems

linked to these disorders. In particular, HEN's decision to strengthen Zero-In with Vitamin D illustrates adherence to an organic approach that acknowledges the linkage of both bone health and brain function. This comprehensive perspective highlights the complexity surrounding these diseases as well as emphasizes the need for holistic interventions in tackling them on a comprehensive approach.

A proprietary blend of prop blend III comprises a mix of black seed oil, resveratrol, turmeric, raspberry ketones, apple cider vinegar, and D-ribose, also known as restore blend. The core design concept of this drug is focused on exploiting the anti-inflammatory and neuronprotective properties of its ingredients, offering a multiple strategy against the complexity of neurodegenerative disorders. A component in black seed oil named thymoquinone has been established to act as a mediator in anti-inflammatory and antioxidants, with probable potential to curb neuroinflammation [25]. Polyphenol resveratrol, which is present in grapes as well as red wine, has been widely studied to show neuroprotective capabilities by research work suggesting that it could be used to slow down neuro-geriatric conditions and also improve learning. Curcumin from turmeric is a part of this mix as it helps to regulate several pathways associated with various types of inflammation involved in neurodegenerative diseases. Raspberry ketones are linked more closely to fat loss, yet they might improve the overall neuroprotective setting in which the blend operates. In addition, apple cider vinegar is involved in metabolic health, and it can address various components that are linked to the causes of neurodegenerative diseases [26]. Finally, d-ribose, which is a simple sugar, also has the potential to be supportive of cellular energy production, an important aspect of neuroprotection [27]. This Restore blend cleverly involves several natural compounds with the hope that their sum will offer an innovative solution for modifying disease-associated processes within neurodegenerative diseases.

The natural barrier support, one of the core ingredients of the HEN proprietary blends, emphasizes gut health as well as underlines the importance of the gut-brain axis associated with aging-related dementias. Inulin, a prebiotic fiber, is present here to enhance beneficial gut bacteria and maintain healthy microbial activity [4]. A dimension is added to this mix with green unripe bananas in the form of resistant starch, which fosters the development of those beneficial types of bacteria in the gut for gut integrity and metabolism. The probiotic strain Bacillus coagulants supports this focus since it can increase species richness and immune regulation. The blend is consistent with recent findings that associate gut microbiome disruptions with neuroinflammation processes leading to neurodegenerative diseases. Evidence that supports braingut bidirectional communication in an emerging concept necessitates natural barrier supplementation, which may affect brain performance. The ongoing research on the relationship between gut health and neurodegeneration sees products such as Natural Barrier Support as important additions to an overall solution to these complicated issues.

Another component among the HEN proprietary blends is ReLive Greens, which contains powerful plant substances beneficial to the whole body system. Spirulina is a blue-green algae boasting high protein content and several vitamins and minerals, which are at the very heart of this mix. Wheatgrass has chlorophyll, which is said to be a good detoxifier and has also been known to help reduce oxidative stress [28]. Another important component of it is pomegranate seed powder that brings in other antioxidants, notably polyphenols, which have been associated with anti-inflammatory and brain-protecting effects. The collection of these plant-based mighty forces is also related to many studies on the need for a nutritional foodstuff to minimize the danger related to neurodegeneration. Hence, ReLive Greens represents one pathway in the HEN protocol aimed at a holistic approach toward neurodegenerative diseases by targeting essential nutrients and antioxidants.

Immune defense shield as proprietary blend VI (HEN Neurodegenerative diseases protocols) is a unique composition with fundamental ingredients important in guarding against immunity-based dementias and other disorders. This mixture comprises B-nicotinamide adenine dinucleotide, which is an important coenzyme for cellular energy production and DNA repair, thus enhancing the general immune resilience [29]. Magnesium is an essential mineral with multiple functions through its immunity enhancement, anti-inflammatory processes, and nerve system support. One of the most important components here is quercetin, which is a powerful antioxidant [30]. The addition of different types of vitamins as well is an added benefit that enhances its effectiveness in boosting immunity against all kinds of infection in the body. With respect to immunity and health, scientists are increasingly discovering the significance of neurodegenerative diseases. Therefore, such a mixture emerges as a precise and wide-ranging approach that comprehends sophisticated interactions within the immune and nervous systems. Such immune support goes hand-in-hand with the more general approach toward a cure, including other diseases in patients suffering from neurodegenerative complications.

1.8. Future Directions in Neurodegenerative Disease Research

The introduction of improvement and new methods of conventional treatments for neurodegenerative Disease is also seen as a beacon of hope for effective interventions. Research into gene therapy in PD aims to address the progressive neuronal damage. Deep brain stimulation is gaining traction as an effective remedy for motor symptoms and an improvement of the patient's lives with PD [31]. Moreover, advances in drug discovery, e.g., Alpha synuclein-directed medications, denote a move towards disease-modifying treatment. Also, in AD, as elucidated by Huang 2023, the search for disease-modifying drugs like anti-amyloid and anti-tau is concerned with changing the course instead of simply treating the symptoms [32]. The use of modern neuroimaging techniques like PET scans and fMRI helps in making an early and correct diagnosis, which can

lead to early treatment [33]. The advances in old-school approaches to treatment for nervous disorders form an era that will lead to fighting the condition with a more targeted approach.

The use of non-traditional therapies in the management of neurodegenerative diseases is gradually being accepted. Novel approaches such as stem cell therapy have potential usefulness in the regeneration of affected neurons and recovering function in patients with PD [34]. Similarly, exercise, cognitive training, and nutritional adjustments are being regarded as possible remedial measures against the occurrence of dementia in AD. The neuroprotective effects of complementary medicine like acupuncture and herbal supplements are now under investigation. With artificial intelligence and machine learning comes a new frontier, exhibited through PD diagnosis via ResNet50 and optical spectroscopy techniques. They represent a new way of offering quality care to neurodegenerative diseases.

Neurodegenerative diseases research should recognize the strengths of the conventional and the integrative systems. As stated in the ISNS Case Study, such conventional ingredients like HEN Proprietary Blends are combinations of both ancient and novel aspects that were developed to deal with multiple components of neurodegenerative disorders (Case Study, n.d). Using various forms of conventional drugs alongside complementary ones may involve a holistic approach based on individualized treatment for each case. Also, the combination of drug interventions with daily exercise, dietary support, and physical therapy has more positive results in patients. Such synergistic approaches in health care require cooperation with other healthcare providers, researchers, and patients to deal with the complexities of these options. Embracing the blending of conventional and unconventional approaches in managing neurodegenerative diseases represents a shift in philosophy towards comprehensive individualized care that is capable of responding to the varied nature of these health conditions [35-38].

2. Conclusion

Comprehensive neurobiology examinations have indicated that there are interconnected elements for the initiation and advancement of these conditions, like AD, PD, and ALS. The occurrence of these diseases, as well as their significance in society, highlight the necessity of more research and collaboration. Indeed, in the context of an ever-increasing incidence of AD and the toll it takes on caregivers, as well as motor issues associated with PD, which strains health care providers and muscular problems inherent in this domain. However, the case study and multiple literatures demonstrate an effective integration of traditional and non–traditional approaches, which could be promising in the management of neurodegenerative diseases. Adopting holistic approaches that take individual considerations into account, incorporating genetic data, artificial intelligence, and advanced therapies, can change the future of such ailments. This implies the importance of an inter-professional approach, building a united front against destructive pathologies and inspiring confidence for extraordinary success in studying and therapies of neurodegenerative diseases.

References

1. El Ariss, O., Hu, K. (2022). ResNet-based Parkinson's disease classification. *IEEE Transactions on Artificial Intelligence, 4*(5), 1258-1268.
2. Nashiry, M. A., Sumi, S. S., Alyami, S. A., Moni, M. A. (2023). Systems biology approach discovers comorbidity interaction of Parkinson's disease with psychiatric disorders utilizing brain transcriptome. *Frontiers in Molecular Neuroscience,* 16, 1232805.
3. Alzheimer's Association. (2019). 2019 Alzheimer's disease facts and figures. Alzheimer' dementia, 15(3), 321-387.
4. Singh, V., Singh, R., Singh, G. (2023). Parkinson's Disease Revisited. *Journal of the Anatomical Society of India, 72*(3), 185-186.
5. Igarashi, K. M. (2023). Entorhinal cortex dysfunction in Alzheimer's disease. *Trends in neurosciences, 46*(2), 124-136.
6. Rojas, P., Ramírez, A. I., Fernández-Albarral, J. A., López-Cuenca, I., Salobrar-García, E., et al (2020). Amyotrophic lateral sclerosis: a neurodegenerative motor neuron disease with ocular involvement. *Frontiers in Neuroscience,* 14, 566858.
7. Shefner, J. M., Musaro, A., Ngo, S. T., Lunetta, C., Steyn, F. J., et al (2023). Skeletal muscle in amyotrophic lateral sclerosis. *Brain, 146*(11), 4425-4436.
8. Zucchi, E., Ticozzi, N., Mandrioli, J. (2019). Psychiatric symptoms in amyotrophic lateral sclerosis: beyond a motor neuron disorder. *Frontiers in neuroscience*, 13, 175.
9. Mead, R. J., Shan, N., Reiser, H. J., Marshall, F., Shaw, P. J. et al (2023). Amyotrophic lateral sclerosis: a neurodegenerative disorder poised for successful therapeutic translation. *Nature Reviews Drug Discovery, 22*(3), 185-212.
10. Olazarán, J., Carnero-Pardo, C., Fortea, J., Sánchez-Juan, P., García-Ribas, G., et al (2023). Prevalence of treated patients with Alzheimer's disease: current trends and COVID-19 impact. *Alzheimer's Research Therapy, 15*(1), 130.
11. Aune, D., Schlesinger, S., Mahamat-Saleh, Y., Zheng, B., Udeh-Momoh, C. T., Middleton, L. T. (2023). Diabetes mellitus, prediabetes and the risk of Parkinson's disease: a systematic review and meta-analysis of 15 cohort studies with 29.9 million participants and 86,345 cases. *European Journal of Epidemiology, 38*(6), 591-604.
12. Wolff, A., Schumacher, N. U., Pürner, D., Machetanz, G., Demleitner, A. F., et al (2023). Parkinson's disease therapy: what lies ahead?. *Journal of Neural Transmission, 130*(6), 793-820.
13. Breijyeh, Z., Karaman, R. (2020). Comprehensive review on Alzheimer's disease: *causes and treatment. Molecules, 25*(24), 5789.
14. Xu Lou, I., Chen, J., Ali, K., Shaikh, A. L., Chen, Q. et al (2023). Mapping new pharmacological interventions for cognitive function in Alzheimer's disease: a systematic

review of randomized clinical trials. *Frontiers in Pharmacology,* 14, 1190604.
15. Ma, L., Jiang, X., Huang, Q., Chen, W., Zhang, H., et al (2023). Traditional Chinese medicine for the treatment of Alzheimer's disease: a focus on the microbiota–gut–brain axis. *Biomedicine Pharmacotherapy*, 165, 115244.
16. Schröder, S., Litscher, G., Pan, W. (2023). Translational study for amyotrophic lateral sclerosis treatment. *Frontiers in Neurology,* 13, 1105360.
17. Wang, F., Sun, Z., Peng, D., Gianchandani, S., Le, W., et al (2023). Cell-therapy for Parkinson's disease: A systematic review and meta-analysis. *Journal of Translational Medicine, 21*(1), 601.
18. Wang, W., Li, Y., Meng, X. (2023). Vitamin D and neurodegenerative diseases. *Heliyon, 9*(1).
19. Antoniou, E. E., Nolde, J., Torensma, B., Dekant, W., Zeegers, M. P. et al (2024). Nine human epidemiological studies on synthetic amorphous silica and respiratory health. *Toxicology Letters*, 399, 12-17.
20. Zylinska, L., Lisek, M., Guo, F., Boczek, T. (2023). Vitamin C modes of action in calcium-involved signaling in the brain. *Antioxidants, 12*(2), 231.
21. Matsumura, T., Uryu, O., Matsuhisa, F., Tajiri, K., Matsumoto, H., et al (2020). N-acetyl-l-tyrosine is an intrinsic triggering factor of mitohormesis in stressed animals. *EMBO reports, 21*(5), e49211.
22. Jacobson, K. A., Gao, Z. G., Matricon, P., Eddy, M. T., Carlsson, J. et al (2022). Adenosine A2A receptor antagonists: from caffeine to selective non-xanthines. *British journal of pharmacology, 179*(14), 3496-3511.
23. Suryawanshi, S. S., Kamble, P. P., Bapat, V. A., Jadhav, J. P. (2020). Bioactive components of magical velvet beans. *In Legume Crops-Prospects, Production and Uses.* IntechOpen.
24. El-Saadony, M. T., Yang, T., Korma, S. A., Sitohy, M., Abd El-Mageed, T. A., et al (2023). Impacts of turmeric and its principal bioactive curcumin on human health: Pharmaceutical, medicinal, and food applications: A comprehensive review. *Frontiers in Nutrition,* 9, 1040259.
25. Kmail, A., Said, O., Saad, B. (2023). How thymoquinone from Nigella sativa accelerates wound healing through multiple mechanisms and targets. *Current Issues in Molecular Biology, 45*(11), 9039-9059.
26. Rao, S., Kurakula, M., Mamidipalli, N., Tiyyagura, P., Patel, B., et al (2021). Pharmacological exploration of phenolic compound: raspberry ketone—update 2020. *Plants, 10*(7), 1323.
27. Ogunlade, B., Fidelis, O. P., Afolayan, O. O., Agie, J. A. (2021). Neurotherapeutic and antioxidant response of D-ribose-L-Cysteine nutritional dietary supplements on Alzheimer-type hippocampal neurodegeneration induced by cuprizone in adult male wistar rat model. *Food and Chemical Toxicology,* 147, 111862.
28. Eissa, H. A., Mohamed, S. S., Hussein, A. M. (2020). Nutritional value and impact of wheatgrass juice (Green Blood Therapy) on increasing fertility in male albino rats. *Bulletin of the National Research Centre*, 44, 1-11.
29. Pencina, K. M., Valderrabano, R., Wipper, B., Orkaby, A. R., Reid, K. F., et al (2023). Nicotinamide adenine dinucleotide augmentation in overweight or obese middle-aged and older adults: a physiologic study. *The Journal of Clinical Endocrinology Metabolism, 108*(8), 1968-1980.
30. Xu, D., Hu, M. J., Wang, Y. Q., Cui, Y. L. (2019). Antioxidant activities of quercetin and its complexes for medicinal application. *Molecules, 24*(6), 1123.
31. Kalhoro, A., Hashim, A. S. M. (2023). Effectiveness of deep brain stimulation in Parkinson's disease treatment with Single-center experience in Pakistan. *Pakistan Journal of Medical Sciences, 39*(4), 1018.
32. Huang, L. K., Kuan, Y. C., Lin, H. W., Hu, C. J. (2023). Clinical trials of new drugs for Alzheimer disease: a 2020–2023 update. *Journal of Biomedical Science, 30*(1), 83.
33. Aderinto, N., Olatunji, D., Abdulbasit, M., Edun, M. (2023). The essential role of neuroimaging in diagnosing and managing cerebrovascular disease in Africa: a review. *Annals of Medicine, 55*(2), 2251490.
34. Oz, T., Kaushik, A., Kujawska, M. (2023). Neural stem cells for Parkinson's disease management: Challenges, nanobased support, and prospects. *World Journal of Stem Cells, 15*(7), 687.
35. Genge, A., Wainwright, S., Vande Velde, C. (2024). Amyotrophic lateral sclerosis: exploring pathophysiology in the context of treatment. *Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration, 25*(3-4), 225-236.
36. Praveen, P., Srilatha, K., Sathvika, M., Nishitha, E., Nikhil, M. et al (2023, May). Prediction of Alzheimer's Disease using Deep Learning Algorithms. *In 2023 2nd International Conference on Applied Artificial Intelligence and Computing* (ICAAIC) (pp. 587-594). IEEE.
37. Sheng, W., Ji, G., Zhang, L. (2023). Immunomodulatory effects of inulin and its intestinal metabolites. *Frontiers in Immunology,* 14, 1224092.
38. Van Schependom, J., D'haeseleer, M. (2023). Advances in neurodegenerative diseases. *Journal of clinical medicine, 12*(5), 1709.