**ABSTRACT: -**

The role of Spirulina, a type of cyanobacterium, in treating neurodegenerative disorders, which are caused by damage or death to neurons in the central nervous system. Neurodegenerative disorders often occur in elderly individuals and include Parkinson’s disease, Alzheimer’s disease, and motor neuron disease. Oxidative stress and inflammation play a major role in the development of these disorders. The review highlights Spirulina’s neuroprotective and antioxidant properties which have been shown to reduce oxidative stress and improve neurological function in various studies. Spirulina is rich in nutrients, such as proteins, vitamins, minerals, and essential fatty acids, and contains various antioxidants and anti-inflammatory compounds. Its composition makes it useful in preventing memory loss, promoting neurogenesis, and boosting cell survival in neurodegenerative disorders. This article points out the need for better medications and nutraceuticals for treating neurological conditions and emphasizes the potential of Spirulina as a natural medication option. Additionally, Spirulina has a positive impact on the immune system, DNA repair, and inflammatory markers in aging rats and can be a promising therapeutic agent for treating a range of neurological conditions.

**INTRODUCTION: -**

A class of illnesses known as neurodegenerative disorders (ND) cause damage or death to neurons in the central nervous system, leading to severe impairments and, in the worst cases, death. Most of the time, they are seen in elderly folks. On the other hand, illness could strike sooner. Recent years have seen a marked increase in their occurrence, and as people age, this tendency is anticipated to continue. (Chaki & Woźniak, 2023). Numerous illnesses, such as Parkinson's disease, motor neuron disease, and Alzheimer's disease, are classified as neurological disorders. These illnesses have an impact on life expectancy and quality of life, and oxidative stress is thought to play a role in their etiology.(Houldsworth, 2023). For most brain-related illnesses, neurodegeneration has been found to be the primary pathophysiological alteration. Modern science has worked tirelessly to provide a medicinal or surgical remedy, but the results have not been promising. For most elderly people, neurodegenerative illnesses (NDs) including dementia and Alzheimer's remain a clinical issue. The extremely effective blood–brain barrier (BBB) nevertheless poses a significant obstacle to the proper management of NDs. Although numerous successful procedures and extremely evasive approaches have been established, their clinical adoption is limited because of differing concerns regarding their long-term value due to possible brain barrier injury. (Lamptey *et al.*, 2022). Any pathological condition that primarily affects neurons is referred to as neurodegeneration.(W. Zhang *et al.*, 2023). NDs are disorders that impact not just the brain but also the nerves throughout the entire body. Many symptoms can be brought on by structural, electrical, or metabolic abnormalities in the brain or other nerves. Muscle weakness, paralysis, poor coordination, convulsions, loss of feeling, confusion, pain, and altered states of awareness are a few of the symptoms.(Chaki & Woźniak, 2023). The diverse range of conditions known as neurodegenerative illnesses is characterised by significant changes in cognitive function. The hippocampus and prefrontal cortex (mPFC), two regions of the central nervous system (CNS) involved in learning and memory, have increased oxidative and inflammatory processes because of the aberrant activation of microglia cells. These changes are caused by a variety of mechanisms.(Martin *et al.*, 2023)

The cyanobacterium Arthrospira (Spirulina) platensis (SP) has garnered interest due to its pharmacological and nutritional qualities.(Pérez-Juárez *et al.*, 2016). Nutrient-rich and flamentous, Spirulina platensis (SP) is a cyanobacterium with a range of medicinal applications. Naturally occurring antioxidants and free radical scavengers found in SP include tocopherol, γ-linolenic acid, β-carotene, phycocyanin, and phenolic compounds.(Behairy *et al.*, 2024). A tiny, filamentous cyanobacterium known as spirulina thrives in alkaline water sources. Because of its high concentration of useful chemicals, including phycocyanins, phenols, and polysaccharides, which have anti-inflammatory, antioxidant, and immunomodulating qualities both in vivo and in vitro, it is widely used as a nutraceutical dietary supplement worldwide. (Trotta *et al.*, 2022). Spirulina has been shown in numerous studies over the past few years to have neuroprotective benefits by reducing oxidative stress and having antioxidant qualities, in addition to being advantageous for the development of the neurological system. It contains high concentrations of PCB, an inhibitor of NADPH oxidase that may contribute to oxidative stress in a range of neurodegenerative and neurological illnesses. The usual defense mechanisms against oxidative stress and inflammation are diminished with age and neurodegeneration, leaving the brain more vulnerable to the harmful consequences of this type of stress. In fact, age-related inflammation and/or an increase in oxidative stress are the root causes of many neurological illnesses, including senility, inflammatory injuries, Parkinson's disease, and Alzheimer's disease (AD). It has been shown that feeding aged rats’ diets rich in spirulina boosts levels of the antioxidant glutathione (GSH) in the cerebellum, lowers levels of malondialdehyde, lowers pro-inflammatory cytokines, and improves both motor and spatial learning. Spirulina treatment demonstrated neuroprotective effects in cerebral ischemia, a condition characterized by cerebral hypoxia, the production of free radicals, ROS, or reactive nitrogen species, and an energy crisis. TUNEL positive cells and caspase-3 activity in the ischemic hemisphere gradually decreased. Spirulina supplementation showed an improvement in the fine ultrastructure of spinal cord grey matter in Sprague Dawley rats with partial crush injury induced at the level of T12 when compared to the control group, indicating the neuroprotective potential of spirulina in reducing the effects of spinal cord injury and promoting functional recovery. (Trotta *et al.* 2022).

**ROLE OF SPIRULINA IN NEURODEGENERATIVE DISORDERS: -**

Spirulina species are frequently used as functional foods whose consumption benefits human health and improves physical and mental performance because they contain significant amounts of proteins, essential amino acids, vitamins, carotenoids, minerals, essential fatty acids, polysaccharides, glycolipids, etc. In experimental models of neurodegenerative illnesses, spirulina has also been demonstrated to have neuroprotective properties. Treatment with spirulina platensis water extract was proposed to prevent memory loss in a mouse model of Alzheimer's disease by decreasing the amount of amyloid β-protein deposited in the brain and increasing glutathione peroxidase and catalase activity, which are antioxidants. In an alternative model where mice were injected with amyloid β1-42 ICV, treatment with ethanol extract of spirulina maxima prevented increased phosphorylation of glycogen synthase kinase-3, increased glutathione, and triggered the BDNF/phosphatidylinositol-3 kinase/serine/threonine-protein kinase signaling pathway, which in turn improved cognitive impairments. (Sorrenti *et al.*, 2021).

The central nervous system may be affected by the protective effect of SP, which may be utilized to treat neurodegenerative conditions like Alzheimer's, and Parkinson’s damage to the nigrostriatal dopamine system, models of cerebrovascular accidents, and neurotoxicity caused by the generation of free radicals to maintain stratum dopaminergic neurotransmission in vivo. Additionally, SP can aid in defending against the harmful consequences of inflammation brought on by a lipopolysaccharide insult in the brain's neurogenic area. Since kainic acid (KA) activates kainite glutamate receptors, which are known to be overstimulated and associated with the excitotoxicity process, KA is an often-used experimental technique. When KA is administered systemically, it selectively causes neuronal cell death in the CA1 and CA3 hippocampal areas, which raises reactive oxygen species and activates microglia.(Pérez-Juárez *et al.*, 2016).

Iron is one of the most significant nutrients for the generation of oxidative stress and the reduction in brain activities. Increased iron accumulation in particular brain regions appear to play a role in the neuropathology of several neurodegenerative diseases, including AD and PD. Iron-dependent oxidative stress causes the brain's antioxidant reserves to be depleted, despite the fact the exact cause of neurodegenerative illnesses is yet unknown. The effects of the S. platensis protein extract on iron-induced oxidative stress in a neuroblastoma cell line (SH-SY5Y) are demonstrated by the reduction of GSH, the increase in the glutathione disulfide (GSSG)/GSH ratio, and the exhaustion of GSH pathway enzyme activities. The antioxidant enzyme glutathione peroxidase (GPx) converts H2O2 to H2O and oxidises it to GSSG, which is then reduced to GSH by glutathione reductase (GR). GSH is an antioxidant enzyme. Fe2+ can result in the creation of hydroxyl or alkoxy radicals, which can be neutralized by phycocyanin and the protein extract from S. platensis, maintaining the activity of antioxidant enzymes. Moreover, it has been demonstrated that spirulina functions as an iron chelator, blocking reactions with peroxides or oxygen. This work shows that the iron chelator property and free radical scavenger activity of S. platensis protein extract enhance decreased GSH and protect the activity of total GPx, GPx-Se, and GR, hence boosting cell survival.(Trotta *et al.* 2022).

Cell damage and eventual cell death can occur when the body's natural antioxidant systems are overwhelmed by the generation of free radicals. In test animals, *Arthrospira platensis* decreased neuronal death. As previously mentioned, *Arthrospira platensis* guards against the negative neurobehavioral effects of kainic acid and lowers oxidative stress in the hippocampal regions. It is unknown, nevertheless, if these outcomes are connected to a decline in hippocampal neuronal damage. Rats in the teenage stage (PNDs 30–40) underwent 10 days of 2 hours per day of restraint stress. After giving *Arthrospira platensis* (200 mg/kg/day) to the animals for 15 days (PNDs 41–55), the animals' basolateral amygdala was examined morphologically, biochemically, and by molecular means. As a non-pharmacological intervention in adolescence, *Arthrospira platensis* can prevent chronic stress-induced neuroanatomical, biochemical, and molecular impairments in adulthood, hence mitigating the development of stress-related illnesses. Due to their antioxidant, anti-inflammatory, immunomodulatory, and cholesterol-lowering qualities, marine algae (such as fecosterol) have been studied for a wide range of health benefits, including antidiabetic, anti-obesity, anti-Alzheimer's, antiaging, anticancer, and hepatoprotection. These benefits suggest that marine algae may be useful as therapeutic leads. *Arthrospira platensis* combats memory loss and strengthens the microglial cell activity's resilience to oxidative stress. The neuroprotective effects of *Arthrospira platensis* on the body are achieved by the reduction of oxidative stress and the increase of molecules with antioxidant capabilities in the body. found that *Arthrospira platensis* enriched in selenium markedly increased neuronal survival (from 57.2% to 94.5%) and prevented apoptosis in primary neurons treated with oxygen glucose deprivation (OGD) (from 45.6% to 6.3%). These effects were accompanied by better neuronal shape and caspase activity.(Gentscheva *et al.*, 2023).

Oxidative stress and inflammation are the main causes of ageing and neurodegeneration. Ageing and neurodegeneration both cause a decrease in the body's natural defense mechanisms against oxidative stress and inflammation, which leaves the brain more vulnerable to its harmful consequences. Most neurological conditions (AD, PD, HD, ALS, inflammatory traumas, and senility) are caused by oxidation and/or inflammation, according to a substantial body of research. Numerous medicines and nutraceuticals have had their anti-inflammatory and antioxidant properties thoroughly studied. Nutraceuticals: It has been claimed that a few dietary supplements, such as spirulina, spinach, and blueberries, protect the central nervous system (CNS) by lowering oxidative stress and inflammatory indicators and so lessening neurological impairments. Aside from these health benefits, consuming spirulina also lengthens life span in Drosophila melanogaster DJ-1βΔ93 flies (a model of Parkinson's disease), enhances locomotor activity, and lowers HSP70 (an indicator of cellular stress) and Jun-N-terminal kinase signaling (JNK signaling involved in modulating the life span).(Sinha *et al.*, 2018).



Fig1 : Spirulina effects in Glial cells (Trotta *et al.* 2022).

**NUTRITIONAL COMPOSITION OF SPIRULINA: -**

One of the most powerful nutritional sources is spirulina. Spirulina's protein concentration ranges from 60 to 70 percent of its dry weight. In addition, it contains various mineral substances (iron, calcium, phosphorus, magnesium, and trace minerals), vitamins (B-12, beta carotene, and E), polysaccharides (rhamnose and glycogen), glycolipids and sulfolipids, essential fatty acids (gamma-linoleic acid, palmitic acid, linoleic acid, oleic acid, etc.), enzymes (SOD, which neutralises free radicals), and a variety of pigments (phycocyanin, chlorophyll, carotenoids, etc.). The protein complex known as phycocyanobilin inhibits the activity of NADPH oxidase. This enzyme contributes to oxidative stress in a few different neurological conditions. Thus, consuming spirulina reduces NADPH oxidase activity and can be used as a treatment for a variety of vascular illnesses, malignancies, diabetes, and inflammatory and neurological diseases. It has been demonstrated that the presence of carbohydrates in spirulina promotes the synthesis of DNA repair molecules and the activity of cell nucleus enzymes, especially endonucleases. Additionally, it has a favorable impact on cell-mediated immunity (T cells and macrophages) as well as humoral immunity (cytokines and antibodies). Rats fed a high-spirulina diet showed downregulation of oxidative stress and inflammatory markers in both neurodegenerative diseases and ageing, suggesting that spirulina may be a better natural medication option for treating neurological conditions.(Sinha *et al.*, 2018).

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| --- | --- | --- | --- |
| **S. No.** | **Phytochemicals** | **Aqueous Extract** | **Ethanolic Extract** |
| 01 | Catalase(U/g) | 120.827±0.672 | 79.907±0.447\* |
| 02 | SOD(U/g) | 4.735±0.179 | 2.009±0.305\* |
| 03 | GPx (U/g) | 211.098±0.563 | 157.878±0.790\* |
| 04 | Vitamin C (mg/g) | 0.128±0.005 | 0.111±0.003\* |
| 05 | Vitamin E (mg/g) | 0.152±0.010 | 0.264±0.163\* |
| 06 | Reduced GSH (nm/g) | 122.758±0.793 | 42.081±0.913 |
| 07 | T. Phenol (mg/g) | 9.919±0.449 | 3.476±0.362 |
| 08 | Flavonoid (mg/g) | 1.047±0.004 | 0.585±0.054\* |
| 09 | Tannin (mg/g) | 0.792±0.006 | 0.568±0.061\* |
| 10 | Carbohydrates (g/g) | 0.153±0.008 | 0.248±0.009 |
| 11 | Protein (g/g) | 0.707±0.046 | 0.775±0.047\* |

Table.1: Phytochemicals of Spirulina(A. Kumar *et al.*, 2022)

**SPIRULINA ROLE IN NEUROPROTECTANT: -**

* **Parkinson’s Disease: -**

The cyanobacterium Spirulina platensis (SPI) possesses notable anti-inflammatory and antioxidant properties. Given the pivotal role of inflammation and oxidative stress in Parkinson's disease (PD), the neuroprotective potential of SPI was assessed in a PD model.(Lima *et al.*, 2017). The motor symptoms observed in this condition stem from a specific brain pathology involving the degeneration of dopaminergic neurons in the substantia nigra (SN). These neurons typically transmit signals via the medial forebrain bundle (MFB) to the striatum, where dopamine is released. The reduction in dopamine levels caused by the loss of these neurons leads to the characteristic motor symptoms. Additionally, within the surviving SN neurons, a distinctive pathological feature known as Lewy bodies (LB) can be identified as intracellular inclusions.(Burke & O’Malley, 2013). Initially, the predominant emphasis in polysaccharide research centered on those sourced from botanical origins, notably astragali and Ganoderma. Nevertheless, there has been a discernible shift towards heightened interest in polysaccharides extracted from Spirulina platensis in recent times. The water-soluble and non-toxic heteropolysaccharide derived from Spirulina platensis, known as PSP, exhibits potential neuroprotective properties. Although its specific impact on dopamine neurons remains uncertain, findings suggest promising outcomes. Notably, administration of PSP at its highest dosage effectively counteracted the loss of TH-positive neurons induced by MPTP in the substantia nigra. Additionally, PSP mitigated the decline in TH and DAT expression caused by MPTP, alongside preserving dopamine levels, and curbing the escalation of dopamine metabolism rates in MPTP-treated mice. Furthermore, PSP demonstrated protective effects against the depletion of SOD and GSH-px induced by MPTP. These results imply PSP's potential in safeguarding dopamine neurons and combating the neurotoxic effects triggered by MPTP exposure.(F. Zhang *et al.*, 2015). Spirulina demonstrated a noteworthy neuroprotective effect in halting neuronal death at 1 and 4 months after the α-synuclein-induced injury. (Pabon *et al.*, 2012). Metabolic dysfunction and neuroinflammation play increasingly significant roles in Parkinson’s disease (PD). Elevated levels of G6PD were observed in both LPS-treated midbrain neuron-glia cultures (an in vitro PD model) and the substantia nigra of four different in vivo PD models. This elevation correlated positively with both microglial activation and dopaminergic neurodegeneration. Moreover, when G6PD was inhibited by 6-aminonicotinamide and dehydroepiandrosterone, or when microglial G6PD was knocked down, there was a reduction in LPS-induced chronic dopaminergic neurodegeneration.(Tu *et al.*, 2019).

Fig. 2: Floe chart of Parkinson’s treatment with Spirulina

* **Alzheimer’s Disease: -**

In Alzheimer's disease (AD), oxidative stress and elevated cytoplasmic calcium are important mediators of the deleterious effects on neuronal survival and function. The mechanisms via which these disruptions occur, hinder the development of dendritic spines, encourage tau hyperphosphorylation, intensify the production of amyloid β, and trigger the death of neurons are explained.(McCarty *et al.*, 2021). The secondary validation using the MoCA-K confirmed that there was a statistically significant difference in the vocabulary findings between the groups. Since there were no physiological alterations or clinically noticeable negative reactions, it was concluded that SM70EE consumption was safe for human health. Consequently, clinical studies were the first to indicate that SM70EE ingestion increased memory function activity. Patients with early AD, such as MCI, also confirmed that consistent SM70EE intake may improve vocabulary and visual memory. (Choi *et al.*, 2022).

* **Amyotrophic Lateral Sclerosis: -**

In recent times, there has been increasing attention paid to the impact of mitochondrial disruptions on the development of neurodegenerative diseases. ALS, a fatal condition characterized by the targeted degeneration of voluntary motor system neurons, has garnered particular interest. The prevalence of ALS is estimated to be around 1–2 cases per 100,000 individuals.(Manfredi & Xu, 2005). It has been demonstrated that nutritional treatments may be beneficial in the treatment of ageing and neurodegenerative illnesses. Vegetables and fruits offer a variety of compounds that have several functions. The Aztecs utilized spirulina, a blue-green algae, as sustenance for thousands of years. It is known to contain significant levels of β-carotene and numerous phycocyanin’s, which have strong anti-inflammatory and antioxidant properties. In the G93A SOD1 mouse model of ALS. In G93A mice, nutritional supplements containing spirulina effectively preserved body weight and the extension reflex while lowering inflammatory markers and motor neuron degeneration. For ALS patients, a diet high in spirulina may be an alternative or complementary treatment. (Garbuzova-Davis & C. Bickford, 2010). The impact of the Wnt signaling pathway on oxidative stress, mitochondrial dysfunction, autophagy, and apoptosis is a subject of significant research interest. However, despite advancements in this field, the underlying cause of motor neuron degeneration remains elusive.(Soumya *et al.*, 2023). Spirulina has been shown to enhance the activity of the Wnt signaling pathway, which is involved in regulating cell proliferation, differentiation, and apoptosis. Activation of the Wnt pathway has been linked to various beneficial effects, including promoting tissue repair and regeneration.(Liu *et al.*, 2019).

* **Spirulina as Anti-stress Agent: -**

The hypothalamus, a key region of the brain, assumes the crucial role of regulating diverse stress responses. Upon initiation of a stress response, signals are relayed from the hypothalamus to the pituitary gland and the adrenal medulla. Specifically, the pituitary gland is prompted by the dynamic activity within the brain to secrete adrenocorticotropic hormone (ACTH). The adrenal gland is prompted to generate corticosteroid hormones, notably cortisol, as they traverse the bloodstream toward the adrenal cortex. Cortisol, a pivotal stress hormone, facilitates the maintenance of steady blood sugar levels within the body. Adequate and stable blood sugar levels empower individuals to effectively manage prolonged stress and facilitate their physiological recovery from it. These stress responses are regulated by corticotrophin-releasing hormone neurons.(Lee *et al.*, 2014). The remarkable antioxidant capabilities found in blue-colored cyanobacteria have sparked significant interest in the cosmetic industry. These pigments serve as natural colorants for cosmetic formulations such as eyeliner and lipstick, while also doubling as potent antioxidants, shielding the skin against harmful UV radiation.(Ragusa et al., 2021). Spirulina stands out as a nutritional powerhouse, boasting a rich profile of essential components vital for overall health. Notably, it is abundant in all nine indispensable amino acids, constituting a protein content that is nearly 60% complete and remarkably easy to digest. Beyond its protein content, spirulina emerges as an unparalleled source of gamma-linolenic acid (GLA), surpassing other foods in beta-carotene content and offering substantial doses of B vitamins, minerals, trace elements, chlorophyll, and enzymes. Additionally, its nutrient spectrum encompasses a diverse array of compounds such as carotenoids, sulfolipids, glycolipids, phycocyanin, superoxide dismutase, RNA, and DNA.(Li *et al.*, 2005).

The intricate landscape of serotonin (5-HT) receptors encompasses seven families denoted as 5-HT1 through 5-HT7, further divided into 14 distinct receptor subtypes. Apart from the 5-HT3 receptor, which operates as a ligand-gated ion channel, all identified 5-HT receptors are G-protein coupled. Among these, the 5-HT1A receptor holds significant prominence, particularly in the realm of neuropsychiatric disorders such as anxiety and Major Depressive Disorder (MDD).(Lee *et al.*, 2014). Its distribution spans critical regions including the limbic system, cortical regions, and the dorsal and median raphe nucleus. Functionally, 5-HT1A receptors interface with the Gi/Go pathways, exerting regulatory control by inhibiting adenylyl cyclase to attenuate cyclic adenosine monophosphate (cAMP) levels and activating G-protein inward rectifying potassium (GIRK) channels. This receptor type serves a dual role, operating both as presynaptic auto-receptors and postsynaptic heteroreceptors, transmitting signals across diverse and occasionally opposing pathways. In the pursuit of therapeutic interventions, phycocyanin, a photosynthetic pigment sourced from spirulina, emerged as a lead compound targeting 5-HT1A receptors. This selection was informed by its capacity to modulate the Gi/Go pathways, thereby modulating adenylyl cyclase activity and GIRK channel activation. Such molecular insights underpin the potential of spirulina-derived compounds as anti-stress agents, highlighting the intricate interplay between serotonin receptor signaling and pharmacological interventions.(Mishra *et al.*, 2023).

* **Spirulina in Neurotoxicity: -**

Spirulina platensis contains a protein called selenium, which showed novel antioxidant activity as well as it is also give activity to neurotoxicity. (Song *et al.*, 2021). Selenium (Se) stands as a crucial micronutrient vital for maintaining human health, renowned for its potent antioxidant, antitumor, and immunomodulatory properties. It has been harnessed in diverse medical contexts, serving in both disease prevention and treatment endeavors. (Fan *et al.*, 2012; Lipinski, 2019). Se-SP exhibited notable enhancements in neuronal viability and suppression of apoptosis in primary neurons, accompanied by improvements in neuronal morphology and modulation of caspase activation. Concurrent treatment with Se-SP effectively mitigated DNA damage accumulation in neurons. Furthermore, Se-SP co-treatment significantly ameliorated mitochondrial dysfunction by restoring balance in the expression of Bcl-2 family proteins. Moreover, the inhibition of mitochondrial permeability transition pore (MPTP) using CsA, a potent MPTP inhibitor, substantially mitigated reactive oxygen species (ROS) generation, oxidative damage, loss of mitochondrial membrane potential (MPP), and ultimately reversed neuronal toxicity and apoptosis induced by oxygen-glucose deprivation (OGD). (Song *et al.*, 2021). Studies have shown that spirulina may help mitigate neurotoxicity induced by various agents such as heavy metals, pesticides, and environmental toxins. Its antioxidant properties help neutralize reactive oxygen species (ROS) and reduce oxidative stress, which is a common mechanism underlying neurotoxicity.(Mallamaci *et al.*, 2023).

* **In Brain Inflammation: -**

Spirulina, a cyanobacterium, is characterized by its microscopic size and filamentous structure, earning its name from the spiral or helical shape of its filaments. This superfood has a rich culinary history, with records dating back to its use in the Aztec civilization. (Karkos *et al.*, 2011). Spirulina supplementation may decrease markers of inflammation in the brain and improve cognitive function in animal studies. Additionally, some human studies have shown promising results in reducing inflammation and improving symptoms in conditions associated with brain inflammation, such as neurodegenerative diseases and mood disorders.(S. Kumar *et al.*, 2024). In Sprague Dawley rats subjected to partial crush injury at the T12 level, administration of Spirulina supplements resulted in an improvement in the fine structural integrity of the gray matter in the spinal cord compared to the control group. This suggests that Spirulina possesses neuroprotective properties capable of attenuating the consequences of spinal cord injury and promoting functional recovery. (Abdullahi *et al.*, 2020). In the neuroblastoma cell line (SH-SY5Y), the S. platensis protein extract was observed to mitigate oxidative stress induced by iron. This oxidative stress was characterized by a depletion in the enzymatic activities associated with the glutathione (GSH) pathway, resulting in a decrease in GSH levels and an elevation in the glutathione disulfide (GSSG)/GSH ratio. Glutathione (GSH) functions as an antioxidant enzyme, wherein it acts as a substrate for the enzyme glutathione peroxidase (GPx) to convert hydrogen peroxide (H2O2) into water (H2O) while becoming oxidized to GSSG. GSSG is subsequently reduced back to GSH by the enzyme glutathione reductase (GR).(Opara, 2006).

**FUTURE ASPECTS: -**

* **Therapeutic Development:**

Continued research into Spirulina's bioactive compounds could lead to the development of novel therapies for neurodegenerative disorders. This could involve isolating and studying specific compounds within Spirulina that demonstrate neuroprotective effects.

* **Nutritional Supplements:**

Spirulina's rich nutritional profile makes it a promising candidate for inclusion in dietary supplements aimed at supporting brain health and mitigating the risk of neurodegenerative diseases. Future studies may explore the optimal dosages and formulations for maximum efficacy.

* **Neuroprotective Mechanisms:**

 Further investigation into the underlying mechanisms of Spirulina's neuroprotective effects is warranted. Understanding how Spirulina interacts with biological pathways involved in neurodegeneration could pave the way for targeted therapeutic interventions.

* **Clinical Trials:**

Rigorous clinical trials are essential to validate the efficacy and safety of Spirulina-based interventions for neurodegenerative diseases. Future research should focus on conducting well-designed studies to assess Spirulina's potential as a therapeutic agent in real-world settings.

* **Combination Therapies:**

Exploring the synergistic effects of Spirulina with other neuroprotective compounds or conventional treatments could enhance therapeutic outcomes for neurodegenerative diseases. Combinatorial approaches may offer greater efficacy or reduce the risk of adverse effects.

* **Personalized Medicine:**

Tailoring Spirulina-based interventions to individual patients based on genetic predispositions, disease stage, and other factors could optimize treatment outcomes. Personalized approaches may enhance the effectiveness of Spirulina-based therapies in addressing the diverse manifestations of neurodegenerative diseases.

**CONCLUSION: -**

In conclusion, Spirulina, a type of cyanobacterium, has shown promise in treating neurodegenerative disorders like Alzheimer's disease, Parkinson's disease, and motor neuron disease. These disorders are often characterized by oxidative stress and inflammation, contributing to neuronal damage or death in the central nervous system. Spirulina's neuroprotective and antioxidant properties have been shown to reduce oxidative stress, promote neurogenesis, and improve neurological function in various studies. The rich nutrient composition of Spirulina, including proteins, vitamins, minerals, essential fatty acids, antioxidants, and anti-inflammatory compounds, makes it beneficial in preventing memory loss, boosting cell survival, and enhancing immune system function. Additionally, Spirulina has been linked to DNA repair, reduced oxidative stress, and improved inflammatory markers in aging models, suggesting its potential as a natural medication option for a range of neurological conditions. Tailoring Spirulina-based interventions to individual patients based on genetic predispositions and disease stage could optimize treatment outcomes. Overall, Spirulina's ability to combat oxidative stress, promote cellular survival, and enhance neuroprotective effects makes it a promising therapeutic agent for neurodegenerative disorders and other neurological conditions. Further research and clinical trials are necessary to explore the full potential of Spirulina in the treatment and management of various neurological diseases.

**REFERENCE: -**

1. Abdullahi, D., Ahmad Annuar, A., & Sanusi, J. (2020). Improved spinal cord gray matter morphology induced by *Spirulina platensis* following spinal cord injury in rat models. *Ultrastructural Pathology*, *44*(4–6), 359–371. https://doi.org/10.1080/01913123.2020.1792597
2. Behairy, A., Elkomy, A., Elsayed, F., Gaballa, M. M. S., Soliman, A., & Aboubakr, M. (2024). Antioxidant and anti-inflammatory potential of spirulina and thymoquinone mitigate the methotrexate-induced neurotoxicity. *Naunyn-Schmiedeberg’s Archives of Pharmacology*, *397*(3), 1875–1888. https://doi.org/10.1007/s00210-023-02739-4
3. Burke, R. E., & O’Malley, K. (2013). Axon degeneration in Parkinson’s disease. *Experimental Neurology*, *246*, 72–83. https://doi.org/10.1016/j.expneurol.2012.01.011
4. Chaki, J., & Woźniak, M. (2023). Deep learning for neurodegenerative disorder (2016 to 2022): A systematic review. *Biomedical Signal Processing and Control*, *80*, 104223. https://doi.org/10.1016/j.bspc.2022.104223
5. Choi, W.-Y., Lee, W.-K., Kim, T.-H., Ryu, Y.-K., Park, A., Lee, Y.-J., Heo, S.-J., Oh, C., Chung, Y.-C., & Kang, D.-H. (2022). The Effects of Spirulina maxima Extract on Memory Improvement in Those with Mild Cognitive Impairment: A Randomized, Double-Blind, Placebo-Controlled Clinical Trial. *Nutrients*, *14*(18), 3714. https://doi.org/10.3390/nu14183714
6. Fan, C., Jiang, J., Yin, X., Wong, K.-H., Zheng, W., & Chen, T. (2012). Purification of selenium-containing allophycocyanin from selenium-enriched Spirulina platensis and its hepatoprotective effect against t-BOOH-induced apoptosis. *Food Chemistry*, *134*(1), 253–261. https://doi.org/10.1016/j.foodchem.2012.02.130
7. Garbuzova-Davis, S., & C. Bickford, P. (2010). Short Communication: Neuroprotective Effect of Spirulina in a Mouse Model of ALS. *The Open Tissue Engineering and Regenerative Medicine Journal*, *3*(1), 36–41. https://doi.org/10.2174/1875043501003010036
8. Gentscheva, G., Nikolova, K., Panayotova, V., Peycheva, K., Makedonski, L., Slavov, P., Radusheva, P., Petrova, P., & Yotkovska, I. (2023). Application of Arthrospira platensis for Medicinal Purposes and the Food Industry: A Review of the Literature. *Life*, *13*(3), 845. https://doi.org/10.3390/life13030845
9. Houldsworth, A. (2023). Role of oxidative stress in neurodegenerative disorders: A review of reactive oxygen species and prevention by antioxidants. *Brain Communications*, *6*(1), fcad356. https://doi.org/10.1093/braincomms/fcad356
10. Karkos, P. D., Leong, S. C., Karkos, C. D., Sivaji, N., & Assimakopoulos, D. A. (2011). *Spirulina* in Clinical Practice: Evidence-Based Human Applications. *Evidence-Based Complementary and Alternative Medicine*, *2011*, 1–4. https://doi.org/10.1093/ecam/nen058
11. Kumar, A., Ramamoorthy, D., Verma, D. K., Kumar, A., Kumar, N., Kanak, K. R., Marwein, B. M., & Mohan, K. (2022). Antioxidant and phytonutrient activities of Spirulina platensis. *Energy Nexus*, *6*, 100070. https://doi.org/10.1016/j.nexus.2022.100070
12. Kumar, S., Saha, S., Singh, K., Singh, T., Miahra, A. K., Dubey, B. N., & Singh, S. (2024). Beneficial Effects of Spirulina on Brain Health: A Systematic Review. *Current Functional Foods*, *02*. https://doi.org/10.2174/0126668629269256231222092721
13. Lamptey, R. N. L., Chaulagain, B., Trivedi, R., Gothwal, A., Layek, B., & Singh, J. (2022). A Review of the Common Neurodegenerative Disorders: Current Therapeutic Approaches and the Potential Role of Nanotherapeutics. *International Journal of Molecular Sciences*, *23*(3), 1851. https://doi.org/10.3390/ijms23031851
14. Lee, M.-S., Kim, Y. H., Lee, B., Kwon, S.-H., Moon, W.-J., Hong, K.-S., Song, Y. S., Morita, K., Hahm, D. H., Shim, I., & Her, S. (2014). Novel Antidepressant-Like Activity of Caffeic Acid Phenethyl Ester Is Mediated by Enhanced Glucocorticoid Receptor Function in the Hippocampus. *Evidence-Based Complementary and Alternative Medicine*, *2014*, 1–10. https://doi.org/10.1155/2014/646039
15. Li, B., Zhang, X., Gao, M., & Chu, X. (2005). Effects of CD59 on antitumoral activities of phycocyanin from Spirulina platensis. *Biomedicine & Pharmacotherapy*, *59*(10), 551–560. https://doi.org/10.1016/j.biopha.2005.06.012
16. Lima, F. A. V., Joventino, I. P., Joventino, F. P., De Almeida, A. C., Neves, K. R. T., Do Carmo, M. R., Leal, L. K. A. M., De Andrade, G. M., & De Barros Viana, G. S. (2017). Neuroprotective Activities of Spirulina platensis in the 6-OHDA Model of Parkinson’s Disease Are Related to Its Anti-Inflammatory Effects. *Neurochemical Research*, *42*(12), 3390–3400. https://doi.org/10.1007/s11064-017-2379-5
17. Lipinski, B. (2019). Redox-Active Selenium in Health and Disease: A Conceptual Review. *Mini-Reviews in Medicinal Chemistry*, *19*(9), 720–726. https://doi.org/10.2174/1389557517666161104125022
18. Liu, P., Choi, J.-W., Lee, M.-K., Choi, Y.-H., & Nam, T.-J. (2019). Wound Healing Potential of Spirulina Protein on CCD-986sk Cells. *Marine Drugs*, *17*(2), 130. https://doi.org/10.3390/md17020130
19. Mallamaci, R., Storelli, M. M., Barbarossa, A., Messina, G., Valenzano, A., & Meleleo, D. (2023). Potential Protective Effects of Spirulina (Spirulina platensis) against In Vitro Toxicity Induced by Heavy Metals (Cadmium, Mercury, and Lead) on SH-SY5Y Neuroblastoma Cells. *International Journal of Molecular Sciences*, *24*(23), 17076. https://doi.org/10.3390/ijms242317076
20. Manfredi, G., & Xu, Z. (2005). Mitochondrial dysfunction and its role in motor neuron degeneration in ALS. *Mitochondrion*, *5*(2), 77–87. https://doi.org/10.1016/j.mito.2005.01.002
21. Martin, M., Pusceddu, M. M., Teichenné, J., Negra, T., Connolly, A., Escoté, X., Torrell Galceran, H., Cereto Massagué, A., Samarra Mestre, I., Del Pino Rius, A., Romero-Gimenez, J., Egea, C., Alcaide-Hidalgo, J. M., & Del Bas, J. M. (2023). Preventive Treatment with Astaxanthin Microencapsulated with Spirulina Powder, Administered in a Dose Range Equivalent to Human Consumption, Prevents LPS-Induced Cognitive Impairment in Rats. *Nutrients*, *15*(13), 2854. https://doi.org/10.3390/nu15132854
22. McCarty, M. F., DiNicolantonio, J. J., & Lerner, A. (2021). A Fundamental Role for Oxidants and Intracellular Calcium Signals in Alzheimer’s Pathogenesis—And How a Comprehensive Antioxidant Strategy May Aid Prevention of This Disorder. *International Journal of Molecular Sciences*, *22*(4), 2140. https://doi.org/10.3390/ijms22042140
23. Mishra, P., Kumar, S., & Malik, J. K. (2023). Molecular Mechanistic Insight Spirulina as Anti-stress Agent. *Middle East Research Journal of Pharmaceutical Sciences*, *3*(02), 25–30. https://doi.org/10.36348/merjps.2023.v03i02.003
24. Opara, E. C. (2006). Oxidative Stress. *Disease-a-Month*, *52*(5), 183–198. https://doi.org/10.1016/j.disamonth.2006.05.003
25. Pabon, M. M., Jernberg, J. N., Morganti, J., Contreras, J., Hudson, C. E., Klein, R. L., & Bickford, P. C. (2012). A Spirulina-Enhanced Diet Provides Neuroprotection in an α-Synuclein Model of Parkinson’s Disease. *PLoS ONE*, *7*(9), e45256. https://doi.org/10.1371/journal.pone.0045256
26. Pérez-Juárez, A., Chamorro, G., Alva-Sánchez, C., Paniagua-Castro, N., & Pacheco-Rosado, J. (2016). Neuroprotective effect of *Arthrospira* (Spirulina) *platensis* against kainic acid-neuronal death. *Pharmaceutical Biology*, *54*(8), 1408–1412. https://doi.org/10.3109/13880209.2015.1103756
27. Ragusa, I., Nardone, G. N., Zanatta, S., Bertin, W., & Amadio, E. (2021). Spirulina for Skin Care: A Bright Blue Future. *Cosmetics*, *8*(1), 7. https://doi.org/10.3390/cosmetics8010007
28. Sinha, S., Patro, N., & Patro, I. K. (2018). Maternal Protein Malnutrition: Current and Future Perspectives of Spirulina Supplementation in Neuroprotection. *Frontiers in Neuroscience*, *12*, 966. https://doi.org/10.3389/fnins.2018.00966
29. Song, X., Zhang, L., Hui, X., Sun, X., Yang, J., Wang, J., Wu, H., Wang, X., Zheng, Z., Che, F., & Wang, G. (2021). Selenium-containing protein from selenium-enriched *Spirulina platensis* antagonizes oxygen glucose deprivation-induced neurotoxicity by inhibiting ROS-mediated oxidative damage through regulating MPTP opening. *Pharmaceutical Biology*, *59*(1), 627–636. https://doi.org/10.1080/13880209.2021.1928715
30. Sorrenti, V., Castagna, D. A., Fortinguerra, S., Buriani, A., Scapagnini, G., & Willcox, D. C. (2021). Spirulina Microalgae and Brain Health: A Scoping Review of Experimental and Clinical Evidence. *Marine Drugs*, *19*(6), 293. https://doi.org/10.3390/md19060293
31. Soumya, B. S., Shreenidhi, V. P., Agarwal, A., Gandhirajan, R. K., Dharmarajan, A., & Warrier, S. (2023). Unwinding the role of Wnt signaling cascade and molecular triggers of motor neuron degeneration in amyotrophic lateral sclerosis (ALS). *Cellular Signalling*, *110*, 110807. https://doi.org/10.1016/j.cellsig.2023.110807
32. Trotta, T., Porro, C., Cianciulli, A., & Panaro, M. A. (2022). Beneficial Effects of Spirulina Consumption on Brain Health. *Nutrients*, *14*(3), 676. https://doi.org/10.3390/nu14030676
33. Tu, D., Gao, Y., Yang, R., Guan, T., Hong, J.-S., & Gao, H.-M. (2019). The pentose phosphate pathway regulates chronic neuroinflammation and dopaminergic neurodegeneration. *Journal of Neuroinflammation*, *16*(1), 255. https://doi.org/10.1186/s12974-019-1659-1
34. Zhang, F., Lu, J., Zhang, J., & Xie, J. (2015). Protective effects of a polysaccharide from Spirulina platensis on dopaminergic neurons in an MPTP-induced Parkinson′s disease model in C57BL/6J mice. *Neural Regeneration Research*, *10*(2), 308. https://doi.org/10.4103/1673-5374.152387
35. Zhang, W., Xiao, D., Mao, Q., & Xia, H. (2023). Role of neuroinflammation in neurodegeneration development. *Signal Transduction and Targeted Therapy*, *8*(1), 267. https://doi.org/10.1038/s41392-023-01486-5