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Review

Role Of *Hypnea Spinella* On Alzheimer's Disease

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Abstract

The content examines the therapeutic potential of *Hypnea spinella*, a species of red algae, in managing Alzheimer's disease (AD). AD is the most prevalent cause of dementia globally, characterized by memory loss, cognitive decline, and behavioural changes, primarily affecting older adults. Despite extensive research into its genetic, environmental, and pathological underpinnings, effective disease-modifying treatments remain elusive. This study explores the bioactive compounds of *Hypnea spinella*, including sulfated polysaccharides, polyphenols, antioxidants, and other metabolites. These compounds exhibit neuroprotective, anti-inflammatory, and antioxidant properties that could target key mechanisms of AD pathology, such as amyloid plaque accumulation, tau protein dysfunction, oxidative stress, and neuroinflammation. The potential of these bioactive compounds to mitigate neurodegeneration and enhance cognitive health is highlighted. The document further provides an overview of AD's epidemiology, genetic risk factors, pathophysiology, and progression through its clinical stages. Current treatment strategies primarily focus on symptomatic relief rather than halting or reversing the disease process. Given the increasing global burden of AD and the limitations of existing treatments, *Hypnea spinella* emerges as a promising natural resource for developing innovative therapies. This research underscores the need for further studies to validate the efficacy and safety of its bioactive compounds for Alzheimer's disease management.

Keywords: Alzheimer's Disease, Neurodegenerative, *Hypnea spinella,* Beta-Amyloid receptor, Polysaccharides.

INTRODUCTION

Alzheimer's disease is a dynamic neurological clutter and the most common cause of dementia, especially among old aged peoples. It leads to memory misfortune, cognitive decay, and behavioural changes. The illness regularly starts with trouble recalling later occasions and slowly advances to extreme impedances in considering, thinking, dialect, and the capacity to perform ordinary tasks.

As Alzheimer's progresses, indications can incorporate dialect challenges, confusion (such as getting to be effectively misplaced), mood swings, misfortune of inspiration, self-neglect, and behavioural changes. In afterward stages, people frequently pull back from family and society, in the long run losing substantial capacities and requiring full-time care. The illness eventually leads to passing, in spite of the fact that the rate of movement changes between individuals.

Alzheimer's is characterized by the collection of amyloid plaques and neurofibrillary tangles in the brain. These irregular protein stores disturb neuron communication and lead to cell passing, causing the brain to shrivel over time. Whereas the correct cause remains vague, it is accepted to result from a combination of hereditary, natural, and way of life variables. Key chance variables incorporate maturing, family history, hereditary changes, and conditions like hypertension and diabetes [1].

Right now, there is no remedy for Alzheimer's disease, but medicines and way of life mediations can offer assistance oversee side effects and move forward quality of life. Continuous research aims to better understand the illness and create more compelling therapies.

All inclusive, Alzheimer's disease accounts for 60-70% of dementia cases. Around 6.5 million individuals aged 65 and more live with Alzheimer's in the United States, with over 70% being 75 years or more. Around the world, of the 55 million people living with dementia, a critical larger part have Alzheimer's disease [2].

Epidemiology

Alzheimer's disease (AD) is the leading cause of dementia, accounting for roughly 60% of cases in individuals over the age of 65. When combined with other brain pathologies, its prevalence among dementia patients increases to 80%. By 2050, Alzheimer's is expected to affect 85 million people worldwide, a dramatic rise from 26.6 million cases in 2006.

AD predominantly affects older adults. The global prevalence of dementia increased from 20.3 million in 1990 to 43.8 million in 2016, marking a 116% rise. Between 1990 and 2019, the incidence and prevalence of Alzheimer's disease and other dementias grew by 147.95% and 160.84%, respectively. Projections estimate that dementia cases will reach 150 million by 2050, a fourfold increase.

The incidence of Alzheimer's doubles approximately every five years after age 65. Age-specific rates rise significantly, from less than 1% annually before age 65 to 6% annually after age 85. Prevalence also increases sharply, affecting 10% of individuals over 65 and up to 40% of those over 85. Women, particularly those older than 85, are slightly more likely than men to develop Alzheimer's disease [3].

Etiology

The exact cause of Alzheimer's disease (AD) remains unknown, though various genetic and environmental factors have been identified as potential contributors.

1. Genetic Factors

Hereditary impacts have been connected to both early- and late-onset Alzheimer's disease:

- Early-Onset AD:
- More than half of early-onset familial Ad cases are related with modifications on chromosomes 1, 14, and 21.
- Mutations in a gene on chromosome 14, which encodes the presenilin-1 protein, are mindful for numerous forceful early-onset cases.
- A comparative protein, presenilin-2, is encoded by a gene on chromosome 1. Both presenilin-1 and presenilin-2 are membrane proteins included in the preparing of amyloid precursor protein (APP).
- Over 160 transformations in presenilin genes have been recognized, driving to decreased movement of γ-secretase, a chemical significant for creating beta-amyloid (Aβ) peptides.
- APP is encoded on chromosome 21, and a little number of early-onset Ad cases are connected to transformations in the APP gene, coming about in over the top Aβ generation or changed extents of Aβ forms.
- Late-Onset AD:
- Genetic helplessness is essentially related with the apolipoprotein E (APOE) gene.

- APOE has three major alleles: 2, 3, and 4. The presence of the APOE4 allele essentially increments the hereditary hazard for late-onset AD.
- Individuals with one APOE4 allele have a two- to threefold higher hazard, whereas those with two APOE4 alleles have a 12-fold higher hazard compared to people without the allele.
- APOE4 is too connected to prior onset of side effects. In any case, it is not one or the other symptomatic of Ad nor basic for the disease to develop.
- The correct component by which APOE4 contributes to Ad is vague, but it may include mitochondrial anomalies, cytoskeletal dysfunction, and disabled glucose metabolism.

2. Environmental and Other Factors

A few natural and way of life variables are related with an expanded chance of AD:

- Age: The rate of AD rises essentially with age.
- Brain Reserve: Components such as smaller brain estimate, lower instructive achievement, and decreased mental and physical action in afterward life increment vulnerability.
- Head Damage: Traumatic brain damage is connected to a higher chance of creating AD.
- Down Syndrome: People with Down syndrome are at a increased chance due to the inclusion of chromosome 21 in APP encoding.
- Medical Conditions: Sadness, gentle cognitive disability (MCI), and vascular chance variables such as high cholesterol, hypertension, atherosclerosis, coronary artery disease, smoking, hoisted homocysteine levels, weight, metabolic disorder, and diabetes have been related with AD [4].

Pathophysiology

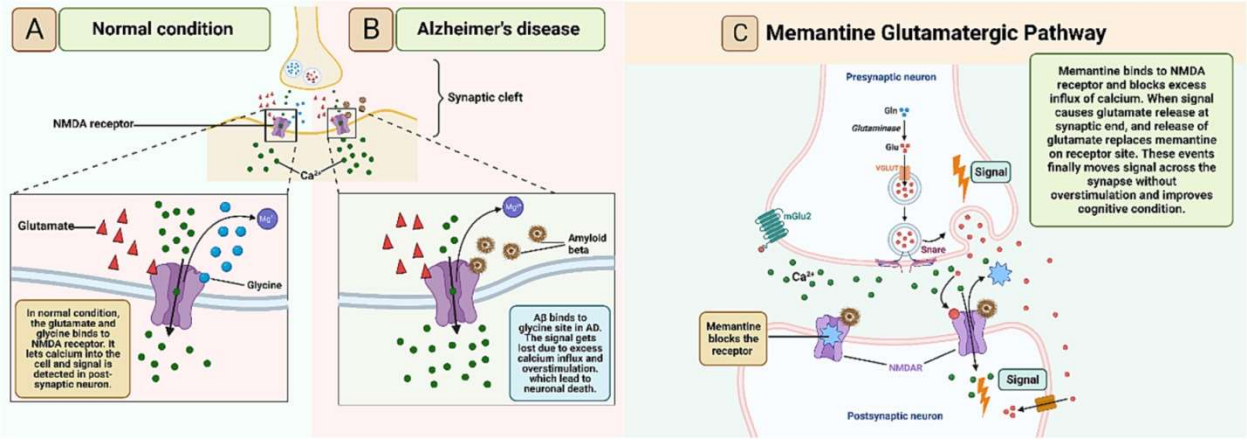

Fig 1: Pathophysiology of Alzheimer's Disease

The trademark injuries of Alzheimer's disease (AD) are amyloid plaques and neurofibrillary tangles (NFTs), fundamentally found in the brain's cortical zones and medial temporal lobe structures. A few components have been proposed to clarify the brain changes that result in AD indications, including:

- Protein Misfolding: Conglomeration and testimony of amyloid-beta (Aβ) proteins lead to plaque formation, while hyperphosphorylation of tau protein results in NFT development.
- Synaptic Brokenness: Disappointment of neural connections and consumption of neurotrophic variables and neurotransmitters.
- Mitochondrial Brokenness: Incorporates oxidative stretch, disabled affront signaling in the brain, vascular harm, irritation, calcium direction abandons, and anomalies in cholesterol digestion system [4].

Amyloid Cascade Hypothesis

Amyloid plaques are extracellular injuries found in brain tissue and cerebral blood vessels. They are fundamentally composed of Aβ peptides, which are inferred from the cleavage of amyloid antecedent protein (APP). Aβ42, in spite of the fact that less common than other Aβ shapes, is more inclined to conglomeration and plaque formation.

The amyloid cascade speculation proposes that a lopsidedness between the generation and clearance of Aβ peptides leads to their conglomeration, coming about in plaque collection and the movement of AD. Bits of knowledge from considers on early-onset AD and Down disorder contributed to the detailing of this speculation. Later overhauls to the theory propose that non-plaque Aβ drives the malady prepare. In any case, this demonstrate is most pertinent to early-onset, autosomal prevailing shapes of AD.

Neurofibrillary Tangles (NFTs)

In parallel with the recognizable proof of Aβ plaques, analysts found NFTs in the hippocampus and cerebral cortex of people with AD. NFTs are composed of strangely hyperphosphorylated tau protein, which ordinarily underpins microtubules in the cell's auxiliary and transport systems. When tau gets to be hyperphosphorylated, it can no longer tie to microtubules, causing them to collapse. This disturbance leads to cellular brokenness and inevitable cell passing. The thickness of NFTs unequivocally relates with the seriousness of dementia. Outstandingly, NFTs are too found in other dementias, recommending they may speak to a common pathway through which different triggers lead to neuronal death [5].

Inflammatory Mediators

Inflammation is progressively recognized as a noteworthy figure in Alzheimer's infection (AD) pathology, frequently connected to the amyloid cascade speculation. Amyloid-beta (Aβ) stores in the brain are related with neighborhood incendiary and resistant reactions, which a few analysts propose contribute to neurodegeneration.

The incendiary speculation sets that Aβ poisonous quality may not exclusively be coordinate but moreover a circuitous result of microglial enactment and astrocyte enrollment activated by Aβ protofibrils. Whereas this safe reaction may at first point to clear amyloid stores, it moreover leads to the discharge of cytokines, nitric oxide, responsive species, and complement variables, all of which can harm neurons and sustain aggravation. Hoisted levels of cytokines and chemokines have been watched in Advertisement brains, and certain pro-inflammatory quality variations are connected to expanded Advertisement chance. Epidemiological prove moreover recommends that long-term utilize of non-steroidal anti-inflammatory drugs (NSAIDs) may diminish the chance of creating AD.

The Cholinergic Hypothesis

Broad neuronal degeneration in Advertisement leads to neurotransmitter shortages, with cholinergic brokenness being especially unmistakable. Cholinergic movement misfortune relates with the seriousness of Advertisement. In progressed stages, the number of cholinergic neurons and nicotinic receptors in the hippocampus and cortex is altogether diminished. These presynaptic receptors control the discharge of acetylcholine and other neurotransmitters fundamental for memory and disposition, such as glutamate, serotonin, and norepinephrine.

The cholinergic theory recommends that cholinergic cell misfortune Is a major cause of memory and cognitive decay in Advertisement. Early medications pointed to boost cholinergic work to ease side effects. In any case, cholinergic cell misfortune is presently caught on to be a auxiliary result of Advertisement, not the essential cause. Whereas including acetylcholine cannot completely reestablish misplaced neurons and receptors, medications focusing on remaining neural connections point to upgrade neurotransmission and minimize indications [6].

Other Neurotransmitter Abnormalities

Beyond cholinergic brokenness, Advertisement moreover includes disturbances in other neurotransmitter system:

- Serotonin and Norepinephrine: Serotonergic neurons in the raphe cores and noradrenergic cells in the locus coeruleus are lost.
- Monoamine Oxidase (MAO): Action of MAO-B, which metabolizes dopamine, is expanded in the brain and platelets.
- Glutamate Dysregulation: Neuronal misfortune in cortical and limbic glutamate pathways has been connected to excitotoxicity. Glutamate, the brain's essential excitatory neurotransmitter, plays a basic part in learning and memory. Dysregulated glutamate movement is accepted to contribute to neuronal damage, in spite of the fact that its correct part in Advertisement remains hazy. Medicines focusing on NMDA receptors point to decrease glutamate movement at neural connections and possibly moderate neuronal damage.

Brain Vascular Infection and Tall Cholesterol

There is developing prove that cardiovascular illness and its chance variables, such as hypertension, hypercholesterolemia, and diabetes, are related with a higher chance of Advertisement. Brain vascular malady may compound cognitive decay by disabling supplement conveyance to neurons and diminishing the clearance of Aβ from

the brain. Broken blood vessels can compound the cognitive shortfalls caused by Advertisement pathology, highlighting the interconnecting of vascular wellbeing and neurodegeneration [7].

Stages of Alzheimer's disease

Alzheimer's disease can be understood as progressing through three stages:

Early Stage

This initial stage, often when the disease is first diagnosed, typically lasts from 2 to 4 years. During this phase, family and friends may start noticing subtle declines in the person's cognitive abilities. Common symptoms include difficulty retaining new information, solving problems, making decisions, managing finances, and expressing thoughts. The person may also withdraw socially, show reduced motivation, or have trouble with daily tasks. Misplacing items, getting lost, and struggling to navigate familiar places are also frequent signs.

Moderate Stage

Lasting between 2 to 10 years, this stage is often the longest. Memory loss becomes more pronounced, and patients may need assistance with daily activities. Symptoms include poor judgment, confusion about identifying family members, and disorientation in time and place. The individual may begin wandering, making it unsafe for them to be left alone. As memory loss deepens, patients may forget personal details and struggle with recognizing themselves.

Severe Alzheimer's Disease

The final stage of Alzheimer's disease is marked by a significant decline in cognitive function and severe physical limitations. This stage typically lasts between 1 to 3 years, and due to the increasing difficulty in providing care, many patients require placement in nursing homes or long-term care facilities. Common symptoms during this stage include the loss of the ability to communicate effectively. While patients may still speak in short phrases, they can no longer engage in coherent conversations. Individuals become increasingly dependent on others for basic personal care, such as eating, bathing, dressing, and toileting. Physical abilities are also severely compromised, with many patients unable to walk or sit independently. Muscular rigidity and difficulty swallowing are common as the disease progresses [8].

Risk Factors for Alzheimer's Disease

1. Age: Advancing age is the most significant risk factor for Alzheimer's. While it is not a part of normal aging, the likelihood of developing Alzheimer's increases with age. Studies show that the number of new diagnoses rises significantly with each decade. For those aged 65 to 74, there are 4 new diagnoses per 1,000 people; for those aged 75 to 84, 32 per 1,000; and for those 85 and older, 76 per 1,000.
2. Family History and Genetics: The risk of Alzheimer's is higher if a close relative (parent or sibling) has the disease. Although the genetic factors are complex and not fully understood, a well-known genetic variant is the apolipoprotein E (APOE) gene. APOE ε4 increases the risk of Alzheimer's, present in about 25-30% of the population, though not everyone with this variant will develop the disease. Rare genetic changes in three genes almost guarantee Alzheimer's but account for less than 1% of cases.
3. Down Syndrome: Individuals with Down syndrome often develop Alzheimer's due to an extra copy of chromosome 21, which is involved in beta-amyloid production. Symptoms appear 10-20 years earlier in people with Down syndrome than in the general population.
4. Sex: More women are affected by Alzheimer's, primarily because women tend to live longer than men.
5. Mild Cognitive Impairment (MCI): MCI is characterized by memory or cognitive decline that is greater than expected for a person's age but does not interfere significantly with daily functioning. However, people with MCI are at a higher risk of developing Alzheimer's. Those with memory-related MCI are particularly prone to progressing to dementia [9].
6. Head Trauma: People aged 50 and older who have experienced a traumatic brain injury (TBI) are at an increased risk of dementia and Alzheimer's, with the risk higher in cases of multiple or severe TBIs. The risk may be greatest within the first 2 years after the injury.
7. Air Pollution: Research in animals and humans shows that exposure to air pollution, particularly from traffic exhaust and burning wood, can speed up the breakdown of the nervous system and increase the risk of dementia.
8. Excessive Alcohol Consumption: Chronic heavy drinking can cause brain changes, and studies link alcohol use disorders to an increased risk of early-onset dementia.
9. Poor Sleep Patterns: Poor sleep, including difficulty falling asleep or staying asleep, has been associated with a higher risk of Alzheimer's disease.

10. Lifestyle and Heart Health: Risk factors for heart disease also increase the risk of dementia, possibly by worsening Alzheimer's brain changes or by affecting brain vascular health. These factors include:
    - Lack of exercise
    - Obesity
    - Smoking or exposure to second hand smoke
    - High blood pressure
    - High cholesterol
    - Poorly controlled type 2 diabetes

These factors are modifiable, and adopting healthier habits such as regular exercise and a diet rich in fruits, vegetables, and low in fat can reduce the risk of Alzheimer's.

11. Lifelong Learning and Social Engagement: Studies suggest that lifelong mental stimulation and social engagement can lower the risk of Alzheimer's. Having a low education level, such as less than a high school education, is considered a risk factor for the disease [10].

Hypnea spinella

Fig 2: ***Hypnea spinellla***

Taxonomical classification
Kingdom: Plantae
Subkingdom: Biliphyta
Phylum (Division): Rhodophyta
Subphylum (Subdivision): Eurhodophytina
Class: Florideophyceae
Subclass: Rhodymeniophycidae
Order: Gigartinales
Family: Cystocloniaceae
Genus: *Hypnea*
Species: *Hypnea Spinella*

Hypnea spinella is a red algae species commonly found in tropical and subtropical regions. Inherited from *Hypnea J.V. Lamouroux* are paraphyletic, with spawning fertilization on the female. Gamete types are oogamous, and the life cycle is haplodiplontic. They have an annual lifespan, and an erect body shape, and can be found in epilithic and epiphytic environments. These algae are non-unicellular with a branched body shape, and their dispersion mode is unknown. They do not reproduce asexually and are located in Europe, specifically in the Mediterranean Sea's Western Basin. These algae are non-calcified, have a dioicous gametophyte arrangement, and can grow to a maximum thallus length of 3 cm. They are also considered important to society for Fishery Statistics Purposes (FAO-ASFIS) [10].

Introduction and Origin
Native to Hawaii.
Hawaiian Distribution: Kauai, Maui, Oahu, Hawaii, Molokai Habitat Intertidal to subtidal, occasionally in turfs. In shallow, calm waters in the reef flat.
Environmental Effects: None documented. It is possible that, under favorable conditions, *H. spinella* may form

dense floating masses such as *H. musciformis* [11].
World Distribution*:* West Indies. Caribbean to Brazil, Hawaiiand Islands, Micronesia, Philippines, Japan, Tahiti.
Description: Plants develop in cushion-like growths with solitary, upright, branching axes sticking up from time to time; the top of the cushion has an uneven contour and is typically 2.5 cm high. The axons are cylindrical and have a diameter of less than 400 um in the middle, with most of the branches being dichotomous or unevenly split. If they exist, secondary attachments are often seen from the centre to the top parts of the thallus between branches. stubby, spine-like branches with somewhat truncated bases and sharply pointed apices, varying in abundance. Tetra sporangial sori can occasionally be seen prominently on the enlarged tips of branchlets, but it can also be found girdling branchlets toward the base of the same plant [12].

Bioactive Compounds Introduction

While detailed phytochemical studies specifically on *Hypnea spinella* may be limited, red algae, in general, are renowned for having a range of bioactive substances in them., including:

Polysaccharides

Such as carrageenan, which the food industry uses extensively as a thickening, stabilizing, and gelling ingredient.
Phenolic compounds: These support the antioxidant properties of the algae.
Proteins and peptides: Some of which may have potential antimicrobial and anti-inflammatory effects.
Lipids: Including essential fatty acids which are important for nutrition and health.
Vitamins and minerals: Algae are a source of various vitamins (e.g., vitamins C, and B vitamins) and minerals (e.g., calcium, magnesium, iron) [13,14].

Health Benefits of Red Algae

Antioxidant Activity: Rich in phenolic components and other antioxidants, red algae can reduce oxidative stress and potential cell damage by neutralizing free radicals. Antimicrobial Properties: Certain compounds in red algae exhibit antimicrobial activity against bacteria, fungi, and viruses, making them potential candidates for developing antimicrobial agents. Anti-inflammatory Effects: Red algae contain substances that may modulate inflammatory responses, which could be useful in treating inflammatory conditions. Anticancer Potential: Some studies have suggested that extracts from red algae could have anticancer properties, potentially inhibiting the growth of cancer cells. Anticoagulant Properties: Polysaccharides found in red algae, like carrageenan, have been reported to have anticoagulant effects, which might be useful in preventing blood clots Immunomodulatory Effects: Red algae may have an impact on the immune system, strengthening the body's defences against illness [15].

CONCLUSION

Research suggests that *Hypnea spinella*, a red algae species, holds potential as a therapeutic agent for Alzheimer’s disease (AD) due to its bioactive compounds. These compounds, such as sulphated polysaccharides, polyphenols, and antioxidants, have demonstrated neuroprotective properties in studies.

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