

A Review on “Plant – Based Probiotics from *Spathodea campanulata* Nectar and their role in Neuroprotection”

Vinitha S¹, Madumitha G², Monica S³, Harshavardhini V S⁴, Ramya S⁵

¹ Assistant Professor, Department of Biotechnology – Sri Shakthi Institute of Engineering and Technology, Coimbatore, India
^{2,3,4,5} Students of Department of Biotechnology – Sri Shakthi Institute of Engineering and Technology, Coimbatore, India

Abstract: Neurodegenerative disorders, such as Alzheimer’s and Parkinson’s diseases, involve the gradual loss of neurons, often caused by oxidative stress, inflammation, and imbalances in neurotransmitters. Current treatments offer limited benefits, making it crucial to explore new approaches for protecting the brain. Probiotics are beneficial microbes that have gained attention for their ability to influence the gut–brain connection and support brain health through antioxidant and anti-inflammatory effects, as well as regulation of neurotransmitters. One promising source of such probiotics is the nectar of *Spathodea campanulata*, also known as the African tulip tree, which is rich in bioactive compounds and hosts diverse microbial communities. Emerging research suggests that probiotics from this nectar may help protect neurons by reducing oxidative stress and inflammation. This review brings together current knowledge on the neuroprotective roles of nectar-derived probiotic strains, explaining how they work and their potential therapeutic benefits. It also highlights areas where more research is needed and discusses the future possibilities of using these natural probiotics to help prevent or manage neurodegenerative diseases in a safe and multi-targeted way.

Keywords: Probiotics, *Spathodea campanulata*, Neuroprotection, Antioxidant activity, Anti-inflammatory activity, Neurodegeneration, Gut-brain axis.

INTRODUCTION

Neurodegenerative disorders, including Alzheimer’s and Parkinson’s diseases, slowly damage the brain’s neurons, leading to memory loss, difficulty in thinking, and problems with movement. These conditions develop due to a mix of factors such as oxidative stress, long-term inflammation, and abnormal protein buildup in the brain. Current treatments mostly ease symptoms rather than stop the disease, which has sparked interest in natural approaches. In particular, compounds from plants and beneficial microbes, or probiotics, are showing promise in protecting neurons and slowing down disease progression.

Neurodegenerative Disorders

Neurodegeneration refers to progressive degeneration in the neurons of the brain leading to a loss in neuronal functions and structures. Diseases that are considered as neurodegenerative disorders include Alzheimer’s disease, Parkinson’s disease, Huntington’s disease, and Amyotrophic lateral sclerosis (ALS). Neurodegenerative diseases lead to cognitive decline, memory deficits, motor impairment and have a negative impact on the quality of life of affected individuals (Przedborski et al., 2016; Dugger & Dickson, 2017). The prevalence of neurodegenerative diseases is increasing worldwide as a consequence of aging of populations. These diseases have different causations including oxidative stress, chronic inflammation, mitochondrial dysfunction, and accumulation of abnormal proteins in the case of Alzheimer’s disease (DeTure & Dickson, 2019; Wang et al., 2020). Of these factors, oxidative stress is central, and it refers to the production of ROS in excess of the protective antioxidant systems. The human brain is vulnerable to oxidative stress because of its high energy consumption and fatty composition (Singh et al., 2019).

Importance of Natural Therapeutics

Natural medicines have come into the limelight as more viable alternatives to man-made drugs. The bioactives present in plants like polyphenols, flavonoids, alkaloids, and terpenoids possess antioxidative, anti-inflammatory, and neuroprotective activities (Pohl & Kong Thoo Lin, 2018; Sharifi-Rad et al., 2020). Such bioactives function through various means that include scavenging of radicals, regulation of signaling pathways, and strengthening of endogenous antioxidant systems. Their multitarget actions make them ideal for conditions like neurodegeneration that cannot be easily managed by drugs with single targets (Cummins 2023). This approach to health care is reflective of the global trend toward prevention-oriented approaches that involve searching for new sources like plant probiotics.

Role of Probiotics in Human Health

Probiotics are live microorganisms with beneficial effects for human health at appropriate levels. Historically linked to gut health, probiotics ensure microbial equilibrium, digestion improvement, and nutrient uptake (Hill et al., 2017). In addition, probiotics can modulate immunity, stimulating both innate and adaptive immune systems. Probiotics create bioactive substances, such as SCFAs, vitamins, and antimicrobial peptides, supporting general health (Sanders et al., 2019). New scientific evidence indicates the importance of probiotics for metabolic regulation and brain functioning. Finally, probiotics can eliminate oxidative stress and inflammation, leading causes of chronic conditions, including neurodegeneration (Cryan et al., 2020).

Need for Plant-Based Probiotic

The majority of traditional probiotics come from dairy products; however, plant-based probiotics have gained popularity due to their

benefits. They are isolated from fruits, vegetables, cereals, and floral habitats (Marco et al., 2017). These probiotics are recommended for lactose-intolerant and vegan individuals and are more environmentally friendly. Fruits and vegetables are rich in nutrients, such as vitamins, minerals, fibers, and phytochemicals, which facilitate the survival and functioning of microorganisms (Filannino et al., 2018). It has been demonstrated that plant-based probiotics are tolerant of low pH levels and bile acids, hence, have a higher probability of surviving the gastrointestinal tract. Nonetheless, little is known about plant-based probiotics, particularly floral nectar – derived strains.

Significance of *Spathodea campanulata* Nectar

Spathodea campanulata (African tulip tree) is a plant found in tropical regions, with medicinal applications. Different portions of the plant have antibacterial, antioxidative, anti-inflammatory, and anticancer effects because of bioactive compounds such as flavonoids and phenolics (Akinmoladun et al., 2018). The nectar from the *S. campanulata* tree contains sugars, amino acids, vitamins, and minerals, providing conditions that favor microbial development. As a result, there are different microbial populations, which include probiotics (Herrera et al., 2017). Nectar from flowers is a distinctive ecological habitat that is home to microbes that can produce beneficial substances. Such microbes might have probiotic properties, including resistance to acid, antimicrobial behavior, and antioxidation.

Scope and Objective of the Review

The objective of this review is to give a thorough analysis on the isolation and neuroprotective effects of probiotic strains from the *Spathodea campanulata* nectar. The review will focus on the significance of using plant probiotics as a means of neurodegenerative diseases prevention. This paper will bring into light the nectar microbiota as a new source of useful microorganisms, as well as their ability to produce anti-oxidants and anti-inflammatories. Moreover, the paper will point out the importance of the gut-brain axis for the occurrence of neuroprotection.

2 PROBIOTICS

2.1 Definition

According to the WHO and FAO, probiotics are “live microorganisms which when administered in adequate amounts confer a health benefit on the host” (Hill et al., 2017). This is a broad classification of probiotics and stresses the importance of vitality, dosage, and scientific proof of health benefits of the probiotics. The probiotics, which are normally non-pathogenic and useful microorganisms that assist in the maintenance of normal microbiota of hosts, are mainly extracted from fermented foods and milk products, and, more recently, from plant materials like fruits, vegetables and floral nectar.

2.2 Classification

Probiotics may be grouped according to their taxonomy, origin, functions, and generation. These organisms comprise bacteria including *Lactobacillus* and *Bifidobacterium*, as well as yeasts including *Saccharomyces*. When classified based on origin, they consist of probiotics that are dairy-derived or plant-based probiotics. In terms of function, probiotics can be classified as digestive probiotics, immunomodulatory probiotics, and neuroactive probiotics affecting the brain-gut connection. Additionally, probiotics may be classified as conventional probiotics or next-generation probiotics having target-based therapeutic effects (O’Toole et al., 2017). An ideal probiotic must resist the acidic environment of the stomach and bile salts, adhere to cells lining the intestine, possess antibacterial effects, and benefit the host’s health.

2.3 Types of Probiotic Microorganisms

2.3.1 *Lactobacillus*

Among the most extensively researched probiotics are those belonging to the genus *Lactobacillus*. Gram-positive rod-like bacteria, they are naturally occurring inhabitants of the digestive tract and reproductive organs. In terms of gut health, their importance comes from their ability to produce lactic acid, resulting in an acidic environment within the digestive tract that prevents the growth of other harmful bacteria (Zhang et al., 2018). Additionally, they have antimicrobial properties through the production of bacteriocins and hydrogen peroxide, furthering their beneficial nature. Some common species of *Lactobacillus* include *Lactobacillus acidophilus*, *Lactobacillus rhamnosus*, *Lactobacillus plantarum*, and *Lactobacillus casei*. They have multiple applications in food products and supplements, where they are recognized for improving digestion, boosting immunity, and minimizing oxidative stress and inflammation (Markowiak & Śliżewska, 2017).

2.3.2 *Bifidobacterium*

Bifidobacteria are the most abundant bacteria in the human colon and are critical for maintaining gut health. This genus of Gram-positive, anaerobic bacteria converts food fibers into short-chain fatty acids (SCFA) including acetate, propionate, and butyrate (O’Callaghan & van Sinderen, 2016). SCFAs are an energy source for gut cells, help maintain the integrity of the gut wall, and lower inflammation levels. Some common species of Bifidobacteria are *Bifidobacterium bifidum*, *Bifidobacterium longum*, and *Bifidobacterium breve*. They play a significant role in childhood by enhancing the immune response and preventing infections. Emerging research suggests that Bifidobacteria can also affect the gut-brain axis, improving brain functions and lowering anxiety and depression (Cryan et al., 2020)

2.3.3 Yeasts

Apart from bacteria, some yeasts have probiotic characteristics as well. *Saccharomyces boulardii* is one such probiotic yeast that is extensively utilized clinically. This organism does not cause any disease and is also resistant to antibiotics, which makes it suitable for use when people undergo treatment with antibiotics (Kelesidis & Pothoulakis, 2012). The probiotic yeasts can tolerate extreme conditions in the stomach and work through inhibiting pathogenic microorganisms, improving the barrier function of the gut,

and regulating immunity.

2.4 Mechanisms of Action

- **Gut Microbiota Modulation** - The probiotics influence their activities mainly through manipulating the intestinal flora. They support the maintenance of microbial balance through competition against pathogens, production of antimicrobial substances, and the stimulation of microbial growth (Zmora et al., 2018). This mechanism prevents the colonization of pathogenic microbes and the restoration of microbial balance after disruption due to antibiotics, infections, or dietary imbalances.
- **Immune Regulation** - The probiotics have an effect on the gut-associated lymphoid tissue (GALT), controlling immune response functions. They improve innate and adaptive immunity, stimulating the immune response cells and antibodies' production (Plaza-Diaz et al., 2019). They control the synthesis of cytokines, lowering the inflammatory reactions while increasing the production of anti-inflammatory compounds.
- **Antioxidant Activity** - The probiotics have antioxidant effects, which contribute to minimizing oxidative stress, one of the leading causes of chronic and neurodegenerative diseases. In addition to producing antioxidants, they scavenge free radicals and improve endogenous antioxidant defense mechanisms like glutathione (Wang et al., 2017). This ensures that their antioxidation benefits are utilized to minimize cell damage.

2.5 Health Benefits of Probiotics

- **Digestive Health** - Probiotics have been highly acclaimed for the benefits they provide to the gastrointestinal system. This is because they promote balance of gut flora, improve digestion, and avoid gastrointestinal diseases like diarrhea, constipation, and IBS (Didari et al., 2015). Moreover, they also assist in increasing nutrient absorption and maintaining the integrity of the intestinal wall, thus reducing bloating and pain.
- **Immune Enhancement** - The role of probiotics in boosting immunity is accomplished through increasing resistance against infections and immune response regulation. Respiratory and gastrointestinal infections are less common among people consuming probiotics, and allergic reactions can be controlled using probiotics (Lehtoranta et al., 2020).
- **Neurological Benefits** - The significance of probiotics for brain function has been recently demonstrated through the gut-brain axis. Probiotics are able to produce neurotransmitters, such as serotonin, dopamine, and GABA, responsible for regulation of emotional responses and cognitive abilities (Dinan & Cryan, 2017). In addition, probiotics are capable of decreasing inflammation and oxidative stress within the brain and promoting good mental well-being (Cryan et al., 2019).

3. PLANT-BASED PROBIOTICS

3.1 Concept and Importance

In relation to plant-based products, probiotics represent beneficial microorganisms occurring naturally in plants' material like fruits, vegetables, cereals, flowers, and nectar. As opposed to conventional probiotics obtained from the dairy industry, probiotics occur naturally in a variety of plants, providing an abundant source for microbial strains (Marco et al., 2017). In the last years, there was an increase in the number of studies concerning plant-based probiotics due to increased health consciousness, dietary preferences, and environment sustainability issues. Lactose intolerance and milk allergy problems affect a considerable portion of the world's population, which cannot benefit from dairy-based probiotics. Thus, plant-based probiotics offer an advantageous way of solving these problems, being especially suitable for those following vegan diets (Filannino et al., 2018). The reason why plants provide a natural environment for bacteria and fungi relies on the high content of nutrients such as carbohydrates, dietary fibers, vitamins, minerals, and phytochemicals, promoting microbial growth and activity. Additionally, microorganisms present in plants have adapted to withstand environmental stress factors such as pH variation, osmotic pressure, and temperature changes, leading to enhanced resistance throughout gastrointestinal transit (Behera et al., 2020). One of the features of plant-based probiotics is their ability to interact with plant compounds such as polyphenols or flavonoids, providing them with enhanced antioxidant, antimicrobial, and anti-inflammatory effects (Panghal et al., 2018). Thus, the interaction between probiotics and plant compounds can promote their application for functional food or nutraceuticals production. Apart from health concerns, plant-based probiotics offer solutions for environmental sustainability because producing them does not imply using much more natural resources. Therefore, the utilization of plant-based probiotics fits the trend of ecofriendly solutions in medicine (Swain et al., 2016)

3.2 Source of Plant-Derived Probiotics

Nectar - The floral nectar is a complex secretion produced by plants, containing sugars like glucose, fructose, and sucrose, amino acids, vitamins, and minerals. Such a composition ensures optimal conditions for microbial colonization and proliferation (Herrera et al., 2017). The floral nectar contains a variety of microbes, which include different bacteria and yeasts, entering into the nectar via pollination or the environment. These microorganisms are adapted to thrive in high sugar concentration and high osmotic pressure conditions, being therefore resilient and functionally relevant (Vannette & Fukami, 2018). The nectar microbiota has shown to have several probiotic activities, namely the resistance to acidic and bile environments, antimicrobial activity, and biosynthesis of bioactive metabolites with antioxidant properties (Gonzalez-Teuber et al., 2015). Thus, the floral nectar represents an underinvestigated source of probiotics with beneficial properties. Moreover, the nectar derived from medicinal plants presents even more advantages since

bioactive compounds are present that may contribute to improving microbial functionalities (Akinmoladun et al., 2018). The combination of phytochemicals and microbial metabolites may lead to synergistic activities, including increased antimicrobial, antioxidant, and neuroprotective effects (Akinmoladun et al., 2018).

4. Advantages Over Dairy-Based Probiotics

- **Lactose-Free** Among some of the main challenges associated with using dairy products as probiotics is the fact that they cannot be consumed by those who are lactose intolerant or have an allergic reaction to milk. Many people worldwide do not have the enzymes needed to break down the sugar found in milk. In other words, plant probiotics provide a viable solution to this challenge (Marco et al., 2017).
- **Natural Microbial Diversity** The microbial community present in the plant habitat is much more diverse than that in dairy products. Such diversity increases the chances of discovering new probiotics with unique biological functions (Behera et al., 2020). Bacteria found in plants exhibit high stress resistance, higher survival rates within the gut environment, and a variety of metabolic activities. The interaction of bacteria with plant phytochemicals enhances the functionality of bacteria, making them suitable for various medical treatments, including antioxidative and neuroprotection.
- **Better Safety Profile** Plant probiotics tend to have a better safety aspect than dairy probiotics. There is a reduced chance of containing allergens in plant-based probiotics and minimize chances of contamination by some harmful pathogens found in dairy-based probiotics. The plant-based probiotics do not contain any form of hormones or antibiotics that are used on farm animals, hence making it easier for them to be safe. Environmentally wise, there are more sustainable, use less energy, and produce lower carbon emissions than dairy probiotics (Swain et al., 2016).

5. BOTANICAL AND PHYTOCHEMICAL PROFILE OF *Spathodea campanulata*

5.1 Taxonomy - The *Spathodea campanulata*, which belongs to the family Bignoniaceae, is known for its ornamental and medicinal properties. This plant is popularly known as the African tulip tree because of its tulip-like flowers and native habitat in Africa. The importance of this plant has transcended its use in the ornamental world and has found recognition in the field of medicine as well (Akinmoladun et al., 2018; Padhy et al., 2021).

5.2 Morphology The *Spathodea campanulata* is an evergreen tree that grows rapidly up to a height of 20-25 meters. It has a robust trunk and a dense canopy. The leaves of this species are large and pinnate. The *Spathodea campanulata* can be identified from its bright orange-red bell-shaped flowers that appear in clusters. Nectar produced by the flowers is high in sugar content, thus facilitating the growth of microbes. Such nectar forms a unique habitat for many types of microorganisms such as bacteria and yeasts (Herrera et al., 2017).

5.3 Geographic Distribution - Though endemic to tropical Africa, this species has spread widely throughout Asia, South America, and the Pacific region. It prefers warm, humid conditions and can be grown extensively in tropical and sub-tropical areas. This particular species is often planted in India for ornamental purposes in gardens and on college campuses because of its tolerance and fast-growing nature. The wide distribution of *S. campanulata* allows easy access for study purposes and increases the chances of being a sustainable source in nature (Orwa et al., 2019).

5.4 Phytochemical Composition The various biological activities of the *Spathodea campanulata* plant may arise due to presence of various bioactive phytochemicals in it. Various part of the plant such as leaves, bark, flower and nectar produce several kinds of bioactive molecules namely flavonoids, phenols, alkaloids, glycosides, tannins, saponins etc. (Padhy, 2021). Flavonoids present in the plant have been proved to have strong antioxidant and anti-inflammatory activity due to the reason that they are free radical scavenging in nature and phenols have well proven work in antioxidants where they neutralize free radicals and prevent the damage due to oxidation (Sharifi-Rad et al., 2020) thus resulting in good amount of potential for antioxidant properties in the plant. Extracts of *S. Campanulata* have been experimentally proved to have strong free radical scavenging activities.

5.5 Medicinal Properties

- **Anti-inflammatory Activity** - *Spathodea campanulata* exhibits potent anti-inflammatory activity, because of the active compounds that can be obtained from this plant, i.e., flavonoids and phenolic compounds. These compounds inhibit pro-inflammatory cytokines synthesis, which is one of the major inflammatory process mediators. Inhibition of the inflammation of the plant can contribute to protect neurons from neurodegenerative disease, because the chronic inflammation of this kind disease plays an important role in its pathogenesis (Akinmoladun et al., 2018).
- **Antioxidant Activity** - The plant has substantial antioxidant capacity through eliminating free radicals and reducing oxidative stress. It is especially important because such activity helps protect neurons against damage linked to the development of neurodegeneration. In addition, the interaction between phytochemicals from *Spathodea campanulata* and metabolites of microorganisms contained in the nectar makes it a promising source of antioxidants (Sharifi-Rad et al., 2020).
- **Functional Role of Nectar as a Microbial Niches** - The nectar of *Spathodea campanulata* can be considered as a rich source of nutrients, creating favorable conditions for microbial growth. The content of sugar, amino acids, and other mineral substances enables the microorganism to adapt well to living in such an environment. Isolated from nectar, microorganisms can possess various probiotic properties, including the ability to survive in acidic environments, antibacterial activity, and antioxidant activity (Vannette & Fukami, 2018).

6. Nectar Microbiome and Its Importance

6.1 Microorganisms in Flower Nectar

The chemical constituents of floral nectar primarily composed of the sugars (glucose, fructose and sucrose), amino acids and micronutrients make it a rich medium and ideal for microbial proliferation. The nectar is known to harbor diverse microbial species like bacteria and yeast carried there by pollinators and the ecosystem (Herrera et al. 2017). Some of the bacterial genera normally found are *Lactobacillus*, *Bacillus* and *Pseudomonas*, also yeasts are predominantly found in nectar which belong to *Saccharomyces*. Nectar inhabitants possess highly tolerant natures toward high osmotic pressure and acidity thereby them robust. Microbes of the nectar depend on plants type, ecosystem, pollinator's activities, etc. For *S. Campanulata* the nectar is rich so it is source of useful microbe

6.2 Role of Nectar Microbiota

The function of nectar microbiota is critical in terms of its ecological functions and health-related applications for humans. Ecologically, the presence of nectar microbiota impacts the relationship between plants and their pollinators through the modification of nectar content, thus affecting the efficiency of pollination. Health-wise, nectar microbiota shows probiotic qualities such as resistance to acid and bile, adhesiveness, and antimicrobial potential. The nectar microbiota also produces metabolites that exhibit antioxidant and anti-inflammatory effects (Dinan and Cryan, 2017). Neurobiologically, nectar microbiota may be involved in gut-brain axis modulation by influencing the makeup of the gut microbiota, degree of inflammation and production of neurotransmitters.

6.3 Benefits of Natural Microflora

The nature-based microflora, that can be sourced from plants such as nectar, has several beneficial properties that is due to its high variety, high adaptability and safety of the organisms. Natural microflora has an extremely high capacity of adapting in harsh environmental conditions and hence is also likely to survive within the human gut (Behera et al. 2020). Different bio active components such as antioxidants, antimicrobial agents, anti-inflammatory agents etc. Can be produced by these microflora and help maintain good health by relieving oxidative stress, reducing harmful pathogen levels in the gut and controlling the inflammation caused by the immune response. It also helps in the proper functioning of the other parts of the body, such as the brain and also aids in preventing intestinal dysbiosis which occurs with the depletion of healthy gut microflora. In *Spathodea campanulata* there is a synergetic effect produced between the phytochemicals found in the plant and the bioactive compounds derived from the microbial strains used. This synergy produces different health benefits such as improved antioxidant properties, reducing inflammatory factors, preventing oxidative cell damage etc.

7. PROBIOTIC POTENTIAL OF NECTAR-DERIVED MICROORGANISMS

Floral nectar provides a unique environment where different types of microorganisms can grow and survive. These microbes are naturally exposed to high sugar concentrations, osmotic stress, and varying environmental conditions. As a result, they develop strong adaptive features that make them suitable for probiotic applications. Because of these properties, nectar-derived microorganisms are now being considered as potential probiotic sources with possible benefits in improving human health and treating diseases (Herrera et al., 2017; Vannette & Fukami, 2018).

7.1 Survival in Gastrointestinal Conditions

In order for a microorganism to function as a probiotic, it must endure the challenging conditions present in the human digestive system, including acidic pH levels, digestive enzymes, and bile salts. Microbes that are extracted from floral nectar frequently exhibit significant resistance to these conditions, primarily because they have adapted to thrive in demanding nectar environments. Research has indicated that numerous bacteria and yeasts associated with nectar can endure highly acidic environments akin to those found in the stomach (pH 2–3), which facilitates their successful passage through the gastric phase (Behera et al., 2020). Furthermore, these microorganisms are capable of withstanding bile salts through mechanisms such as bile salt hydrolase activity, which aids in preserving their cellular stability (Hill et al., 2017). They may also generate stress-related proteins and protective substances that enhance their survival in the face of gastrointestinal stress. Given these characteristics, microbes derived from nectar are regarded as appropriate candidates for oral probiotic applications, as they can survive the digestive process and effectively reach the intestine.

7.2 Adhesion Properties

In order for probiotics to function effectively, they must adhere to the inner lining of the intestine. This adherence enables them to remain in the gut for an extended period, allowing them to perform their functions adequately. Microorganisms derived from nectar appear to possess this capability, primarily due to the substances found on their surfaces, such as proteins and polysaccharides (Lebeer et al., 2018). This attachment facilitates direct interaction with the body, which can aid in preventing harmful microbes from adhering to the gut, enhancing the integrity of the intestinal barrier, and bolstering the immune system. Additionally, some of these nectar-derived microbes are capable of forming biofilms, which increases their stability and enables them to persist in the gut for a longer time.

7.3 Safety and Non-Pathogenic Nature

Safety is an aspect that must not be overlooked regarding probiotics. Microorganisms derived from nectar are typically regarded as safe due to their origin from natural plant sources. The majority of these microorganisms fall into benign categories such as lactic acid bacteria and specific yeasts, which do not generate toxins or induce disease. In comparison to microbes sourced from clinical environments, these are generally less hazardous and often do not exhibit antibiotic resistance (Sanders et al., 2019). However, they cannot be utilized directly without prior verification. Thorough testing is essential, both under laboratory conditions and within living systems, to ensure their safety for use in food or medical purposes.

7.4 Functional Properties

The usefulness of probiotics in medicine is not decided just by how safe they are or how well they survive in the body. What really

matters is what they actually do inside the body. Microorganisms isolated from nectar have shown different beneficial effects, and these activities can support overall health in several ways.

7.5 Antioxidant Activity

Oxidative stress is one of the key reasons for cell damage and is strongly connected with many long-term diseases, especially those affecting the brain. Microorganisms obtained from nectar have been reported to show good antioxidant activity, which helps in protecting cells and lowering oxidative stress levels (Wang et al., 2017). These microbes work in different ways. They produce enzymes like superoxide dismutase and catalase, help in neutralizing free radicals, and also support the body's own antioxidant system. On top of that, the interaction between microbial compounds and plant-based phytochemicals present in nectar further improves its overall antioxidant capacity (Sharifi-Rad et al., 2020). Because of this, their antioxidant effect becomes very important in neuroprotection, as it helps in reducing damage to neurons caused by oxidative stress.

7.6 Anti-Inflammatory Effects

Chronic inflammation is one of the main reasons behind many health issues, especially problems related to metabolism and the brain. Microorganisms taken from nectar have shown that they can help in reducing this inflammation by keeping the immune system balanced. They tend to increase helpful anti-inflammatory cytokines like IL-10, while reducing harmful ones such as TNF- α and IL-6 (Plaza-Diaz et al., 2019). They also play a role in maintaining the gut barrier. When this barrier is strong, harmful substances cannot easily enter the body and cause inflammation. By controlling both general inflammation and inflammation in the brain, these microbes may help in protecting body tissues and could even slow down the progression of neurodegenerative diseases (Cryan et al., 2019).

8. GUT–BRAIN AXIS AND PROBIOTICS

The gastrointestinal system and the central nervous system are connected by the intricate bidirectional communication network known as the gut-brain axis. It affects immunity, digestion, and neurological function and is essential for preserving physiological homeostasis. Probiotics are a key area of study in neuroprotection since there is growing evidence that gut microbiota influences brain function (Cryan et al., 2019; Morais et al., 2021).

8.1 Concept of Gut–Brain Axis

The gut–brain axis integrates various neural, endocrine, immune, and metabolic signalling pathways that connect the gut and the brain. This interaction links the central nervous system (CNS) with the enteric nervous system (ENS), commonly referred to as the “second brain” (Dinan & Cryan, 2017). Communication takes place through several pathways. The vagus nerve serves as the primary neural link, conveying signals from the gut to the brain and impacting mood and cognition. Hormonal signalling is also significant, as the gut generates neurotransmitters like serotonin, which is a key regulator of emotional and physiological functions. Immune pathways that involve gut-associated lymphoid tissue (GALT) manage inflammation, which has a direct effect on brain health. Furthermore, microbial metabolites, including short-chain fatty acids (SCFAs), affect neural signalling and can interact with the blood–brain barrier (Cryan et al., 2019). Disruptions in this system, referred to as dysbiosis, are linked to neurological disorders such as anxiety, depression and neurodegenerative diseases.

8.2 Microbiota Influence on Brain Function

The gut microbiota is composed of trillions of microorganisms that have a profound impact on brain function and behavior. These microbes synthesize neurotransmitters and neuromodulators, including serotonin, dopamine, and gamma-aminobutyric acid (GABA), which are crucial for regulating mood, cognition, and emotional responses (Strandwitz, 2018). They also play a role in modulating immune responses by influencing cytokine production, thus controlling inflammation. Chronic inflammation is closely associated with neurological disorders, making the maintenance of immune balance vital for brain health (Morais et al., 2021). Another significant mechanism is the production of short-chain fatty acids (SCFAs) such as acetate, propionate, and butyrate. These metabolites are essential for preserving the integrity of the intestinal and blood-brain barriers while also providing anti-inflammatory and neuroprotective benefits (Dalile et al., 2019). Furthermore, gut microbiota affect the hypothalamic-pituitary-adrenal (HPA) axis, which is responsible for regulating stress responses. Dysregulation of this axis can result in heightened stress, anxiety, and depression. Moreover, an imbalance in microbial populations can lead to increased intestinal permeability, permitting harmful substances to enter the bloodstream and incite systemic inflammation, potentially affecting brain function.

8.3 Role of Probiotics in Neuroprotection

Probiotics serve as modulators of the gut–brain axis by restoring microbial equilibrium and enhancing gut health. Their neuroprotective effects are facilitated through various mechanisms. Probiotics assist in maintaining the balance of gut microbiota, diminishing harmful bacteria while promoting beneficial species, which is crucial for effective gut–brain communication (Sanders et al., 2019). They also regulate immune responses by lowering pro-inflammatory cytokines and boosting anti-inflammatory pathways, thus mitigating neuroinflammation. Additionally, probiotics demonstrate antioxidant properties by decreasing reactive oxygen species and strengthening host antioxidant defenses. They can affect the production of neurotransmitters such as serotonin, dopamine, and GABA, which are vital for cognitive function and emotional regulation (Dinan & Cryan, 2017). Moreover, probiotics fortify the intestinal barrier, preventing toxins from entering the bloodstream and alleviating systemic inflammation. Furthermore, they modulate the HPA axis, aiding in the regulation of stress responses and enhancing mental well-being. Recent evidence indicates that probiotics may enhance cognitive performance, alleviate symptoms of anxiety and depression, and potentially slow the progression of neurodegenerative diseases (Cryan et al., 2019).

9. NEUROPROTECTIVE MECHANISMS OF PROBIOTICS

Probiotics offer neuroprotection by addressing various pathological pathways, such as oxidative stress, inflammation, neurotransmitter imbalance, and neurotoxicity.

9.1 Antioxidant Activity - Oxidative stress plays a significant role in neuronal injury and neurodegenerative conditions. Probiotics demonstrate antioxidant properties by neutralizing reactive oxygen species and bolstering antioxidant defenses (Wang et al., 2017). They generate antioxidant enzymes like superoxide dismutase and catalase, eliminate free radicals, and diminish lipid peroxidation. Furthermore, probiotics activate endogenous antioxidant mechanisms, aiding in the protection of neuronal cells from oxidative harm.

9.2 Anti-inflammatory Effects - Persistent inflammation is a major contributor to neurodegeneration. Probiotics assist in modulating immune responses by lowering pro-inflammatory cytokines such as TNF- α and IL-6, while enhancing anti-inflammatory agents like IL-10 (Plaza-Diaz et al., 2019). This immunomodulatory action mitigates systemic inflammation and prevents neuroinflammation, thus safeguarding neuronal tissues and decelerating disease advancement.

9.3 Neurotransmitter Modulation - Probiotics affect the synthesis and regulation of neurotransmitters, including serotonin, dopamine, and GABA. These neurochemicals are crucial for mood stabilization, cognitive function, and neural communication (Strandwitz, 2018). They also influence tryptophan metabolism, which in turn affects serotonin production. This modulation leads to enhanced mental well-being and a decreased likelihood of neurological disorders.

9.4 Reduction of Neurotoxicity - Neurotoxicity resulting from toxins, heavy metals, and the accumulation of abnormal proteins significantly contributes to neurodegenerative disorders. Probiotics assist in diminishing neurotoxicity by fortifying the intestinal barrier, inhibiting the entry of toxins, and improving detoxification mechanisms. Additionally, they aid in preserving the integrity of the blood-brain barrier and decreasing the generation of detrimental metabolites. Collectively, these effects safeguard the brain against toxic harm and promote overall neurological well-being (Cryan et al., 2019).

10. POTENTIAL OF *Spathodea campanulata* NECTAR PROBIOTICS IN NEUROPROTECTION

The nectar derived from *Spathodea campanulata* serves as a promising and relatively unexplored reservoir of probiotic microorganisms that possess enhanced therapeutic capabilities. The interaction between plant-based bioactive compounds and microbes found in nectar establishes a synergistic environment that could significantly aid in neuroprotection (Akinmoladun et al., 2018; Herrera et al., 2017).

10.1 Bioactive Compounds and Their Role

Spathodea campanulata is abundant in bioactive compounds, including flavonoids, phenolics, alkaloids, glycosides, and tannins, all of which demonstrate potent antioxidant and anti-inflammatory effects (Sharifi-Rad et al., 2020). Flavonoids and phenolic substances are essential in counteracting free radicals, alleviating oxidative stress, and regulating inflammatory processes. These functions are particularly vital for safeguarding neuronal cells against oxidative harm and inflammation, which are critical contributors to neurodegenerative disorders. The presence of these compounds in nectar amplifies the functional attributes of the associated microorganisms, thereby enhancing their probiotic efficacy.

10.2 Synergistic Effects of Plant and Microbes

A significant benefit of probiotics derived from nectar is the synergistic relationship between plant phytochemicals and microbial metabolites. This relationship enhances the biological efficacy of both elements, leading to improved antioxidant, antimicrobial, and anti-inflammatory properties (Panghal et al., 2018). Microorganisms leverage nutrients from plants to generate additional bioactive substances, thereby increasing their therapeutic capabilities. Furthermore, this synergy enhances the stability and functionality of probiotic strains, rendering them more effective in promoting health and preventing illness.

10.3 Evidence from Previous Studies

While the study of nectar-derived probiotics is still in its early stages, investigations into plant-associated microorganisms have revealed considerable health advantages. These benefits encompass robust antioxidant and antimicrobial properties, modulation of gut microbiota, and regulation of immune responses (Behera et al., 2020). Research focusing on *Spathodea campanulata* has underscored its antioxidant and anti-inflammatory characteristics, indicating its potential role in neuroprotection (Santos et al., 2020). Although specific research on its nectar microbiota is scarce, the available evidence strongly indicates that it may provide a source of innovative probiotic strains with therapeutic promise. These results highlight the necessity for further research to thoroughly investigate and confirm the neuroprotective applications of probiotics derived from nectar.

11. APPLICATIONS AND FUTURE PERSPECTIVES

11.1 Functional Foods Development

Probiotics are extensively utilized in the creation of functional foods that provide health advantages beyond basic nutrition. Plant-derived probiotics, including those sourced from nectar, can be integrated into beverages, fermented plant products, and dietary supplements (Marco et al., 2017). These products offer a natural and convenient method for delivering probiotics while catering to the increasing demand for vegan and lactose-free options. The addition of plant-based probiotics also improves the nutritional and therapeutic properties of food items.

11.2 Pharmaceutical Applications

Probiotics are being increasingly investigated in pharmaceutical formulations due to their capacity to influence the gut-brain axis. They can be formulated into capsules, tablets, and synbiotic combinations that merge probiotics with prebiotics (Sanders et al., 2019). Their neuroprotective characteristics render them promising candidates for treating neurological disorders. Probiotic-based treatments present a safer and more natural alternative to traditional medications, with reduced side effects.

11.3 Need for Further Research

In spite of encouraging results, additional research is necessary to fully harness the potential of nectar-derived probiotics. Critical areas include the identification and characterization of new strains, understanding molecular mechanisms, and performing clinical trials to confirm efficacy (Cryan et al., 2019). The standardization of probiotic formulations is also vital to guarantee consistency, safety, and effectiveness. A multidisciplinary approach that combines microbiology, biotechnology, and clinical research will be essential for progressing in this domain.

12. LIMITATIONS OF CURRENT STUDIES

Despite the considerable potential of probiotics, various limitations hinder their extensive use. Most research, especially concerning nectar-derived probiotics, is confined to laboratory and animal studies, with a notable absence of well-structured human clinical trials (Sanders et al., 2019). Floral nectar is still an inadequately explored source of probiotics, and the diversity and functionality of microorganisms associated with nectar are not yet completely understood. Furthermore, there is a deficiency of standardized protocols for isolation, characterization, and formulation, which impacts reproducibility and the feasibility of large-scale applications. It is crucial to address these limitations to effectively translate research outcomes into practical therapeutic interventions.

13. CONCLUSION

13.1 Summary of Findings

This review underscores the considerable potential of probiotics, especially those derived from plants, in enhancing human health and preventing diseases. Their antioxidant, anti-inflammatory, and neuroprotective attributes render them significant in the management of complex conditions such as neurodegenerative disorders (Cryan et al., 2019).

13.2 Importance of Plant-Based Probiotics

Plant-based probiotics present benefits such as safety, sustainability, and greater accessibility. Natural sources, including fruits, flowers, and nectar, offer a diverse array of beneficial microorganisms with improved functional characteristics (Filannino et al., 2018). The nectar from *Spathodea campanulata* stands out as a unique and promising source of probiotic strains due to its abundant phytochemical composition and the synergistic interactions between plant compounds and microbes.

13.3 Future Potential in Neuroprotection

Probiotics are vital in regulating the gut-brain axis, alleviating oxidative stress, and managing inflammation, all of which are critical for neuroprotection. With additional research and clinical validation, probiotics derived from nectar may become effective therapeutic agents for neurodegenerative conditions. Incorporating plant-based probiotics into contemporary healthcare signifies an innovative and promising approach to creating safe, natural, and effective treatments for neurological disorders.

REFERENCES

1. Przedborski, S. (2016). Neurodegeneration. In *Neuroimmune Pharmacology* (pp. 345-354). Cham: Springer International Publishing.
2. Dugger, B. N., & Dickson, D. W. (2017). Pathology of neurodegenerative diseases. *Cold Spring Harbor perspectives in biology*, 9(7), a028035.
3. DeTure, M. A., & Dickson, D. W. (2019). The neuropathological diagnosis of Alzheimer's disease. *Molecular neurodegeneration*, 14(1), 32.
4. Wang, X., Zhou, Y., Gao, Q., Ping, D., Wang, Y., Wu, W., ... & Shao, A. (2020). The role of exosomal microRNAs and oxidative stress in neurodegenerative diseases. *Oxidative medicine and cellular longevity*, 2020(1), 3232869.
5. Singh, A., Kukreti, R., Saso, L., & Kukreti, S. (2019). Oxidative stress: a key modulator in neurodegenerative diseases. *Molecules*, 24(8), 1583.
6. Pohl, F., & Kong Thoo Lin, P. (2018). The potential use of plant natural products and plant extracts with antioxidant properties for the prevention/treatment of neurodegenerative diseases: in vitro, in vivo and clinical trials. *Molecules*, 23(12), 3283.
7. Sharifi-Rad, J., Quispe, C., Castillo, C. M. S., Caroca, R., Lazo-Vélez, M. A., Antonyak, H., ... & Cho, W. C. (2022). [Retracted] ellagic acid: a review on its natural sources, chemical stability, and therapeutic potential. *Oxidative medicine and cellular longevity*, 2022(1), 3848084.
8. Cummings, J. (2023). Alzheimer's disease drug development pipeline. *Alzheimers Dement.*, 25.
9. Sanders, M. E., Merenstein, D. J., Reid, G., Gibson, G. R., & Rastall, R. A. (2019). Probiotics and prebiotics in intestinal health and disease: from biology to the clinic. *Nature reviews Gastroenterology & hepatology*, 16(10), 605-616.
10. Mörkl, S., Butler, M. I., Holl, A., Cryan, J. F., & Dinan, T. G. (2020). Probiotics and the microbiota-gut-brain axis: focus on psychiatry. *Current nutrition reports*, 9(3), 171-182.
11. Marco, M. L., Heeney, D., Binda, S., Cifelli, C. J., Cotter, P. D., Foligné, B., ... & Hutkins, R. (2017). Health benefits of fermented foods: microbiota and beyond. *Current opinion in biotechnology*, 44, 94-102.
12. Sionek, B., & Szydłowska, A. (2025). Probiotics and prebiotics in the aspect of health benefits and the development of novel plant-based functional food. *Applied Sciences*, 15(6), 3137.
13. Dinan, T. G., & Cryan, J. F. (2017). The microbiome-gut-brain axis in health and disease. *Gastroenterology Clinics*, 46(1), 77-89.
14. Marco, M. L., Heeney, D., Binda, S., Cifelli, C. J., Cotter, P. D., Foligné, B., ... & Hutkins, R. (2017). Health benefits of fermented foods: microbiota and beyond. *Current opinion in biotechnology*, 44, 94-102.
15. O'Toole, P. W., Marchesi, J. R., & Hill, C. (2017). Next-generation probiotics: the spectrum from probiotics to live

- biotherapeutics. *Nature microbiology*, 2(5), 17057.
16. Sanders, M. E., Merenstein, D. J., Reid, G., Gibson, G. R., & Rastall, R. A. (2019). Probiotics and prebiotics in intestinal health and disease: from biology to the clinic. *Nature reviews Gastroenterology & hepatology*, 16(10), 605-616.
 17. Markowiak, P., & Śliżewska, K. (2017). Effects of probiotics, prebiotics, and synbiotics on human health. *Nutrients*, 9(9), 1021.
 18. O'callaghan, A., & Van Sinderen, D. (2016). Bifidobacteria and their role as members of the human gut microbiota. *Frontiers in microbiology*, 7, 925.
 19. Kelesidis, T., & Pothoulakis, C. (2012). Efficacy and safety of the probiotic *Saccharomyces boulardii* for the prevention and therapy of gastrointestinal disorders. *Therapeutic advances in gastroenterology*, 5(2), 111-125.
 20. Zmora, N., Zilberman-Schapira, G., Suez, J., Mor, U., Dori-Bachash, M., Bashiardes, S., ... & Elinav, E. (2018). Personalized gut mucosal colonization resistance to empiric probiotics is associated with unique host and microbiome features. *Cell*, 174(6), 1388-1405.
 21. Plaza-Diaz, J., Ruiz-Ojeda, F. J., Gil-Campos, M., & Gil, A. (2019). Mechanisms of action of probiotics. *Advances in nutrition*, 10(suppl_1), S49-S66.
 22. Lehtoranta, L., Latvala, S., & Lehtinen, M. J. (2020). Role of probiotics in stimulating the immune system in viral respiratory tract infections: A narrative review. *Nutrients*, 12(10), 3163.
 23. Dinan, T. G., & Cryan, J. F. (2017). The microbiome-gut-brain axis in health and disease. *Gastroenterology Clinics*, 46(1), 77-89.
 24. Panghal, A., Janghu, S., Virkar, K., Gat, Y., Kumar, V., & Chhikara, N. (2018). Potential non-dairy probiotic products—A healthy approach. *Food bioscience*, 21, 80-89.
 25. Swain, M. R., & Ray, R. C. (2016). Nutritional values and bioactive compounds in lactic acid fermented vegetables and fruits. *Lactic acid fermentation of fruits and vegetables*, 1, 37-52.
 26. Vannette, R. L., & Fukami, T. (2018). Contrasting effects of yeasts and bacteria on floral nectar traits. *Annals of Botany*, 121(7), 1343-1349.
 27. Padhy, G. K. (2021). *Spathodea campanulata* P. Beauv.—A review of its ethnomedicinal, phytochemical, and pharmacological profile. *Journal of Applied Pharmaceutical Science*, 11(12), 017-044.
 28. Lebeer, S., Bron, P. A., Marco, M. L., Van Pijkeren, J. P., Motherway, M. O. C., Hill, C., ... & Klaenhammer, T. (2018). Identification of probiotic effector molecules: present state and future perspectives. *Current opinion in biotechnology*, 49, 217-223.
 29. Strandwitz, P. (2018). Neurotransmitter modulation by the gut microbiota. *Brain research*, 1693, 128-133.
 30. Dalile, B., Van Oudenhove, L., Vervliet, B., & Verbeke, K. (2019). The role of short-chain fatty acids in microbiota–gut–brain communication. *Nature reviews Gastroenterology & hepatology*, 16(8), 461-478.
 31. Plaza-Diaz, J., Ruiz-Ojeda, F. J., Gil-Campos, M., & Gil, A. (2019). Mechanisms of action of probiotics. *Advances in nutrition*, 10(suppl_1), S49-S66.

Copyright & License:



© Authors retain the copyright of this article. This work is published under the Creative Commons Attribution 4.0 International License (CC BY 4.0), permitting unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.