PRINT ISSN 1119-8362
Electronic ISSN 2659-1499

Full-text Available Online at
https://www.ajol.info/index.php/jasem
https://www.bioline.org.br/ja

J. Appl. Sci. Environ. Manage.
Vol. 29 (2) 407-416 Feb. 2025

Bidirectional Communication Network: Exploring the Gut-Brain Axis as a Target for *Ocimum Gratissimum* Modulation in Neurodegenerative Disorder

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ABSTRACT: The intricate relationship between the gut and brain, known as the gut-brain axis, is increasingly recognized as a key player in neurological health and disease. Neurodegenerative disorders, such as Alzheimer's and Parkinson's, are often accompanied by gut dysbiosis and inflammation, suggesting a potential therapeutic avenue through modulation of this bidirectional communication network. This review explores the potential of *Ocimum gratissimum*, a plant with known anti-inflammatory and antioxidant properties, to influence the gut-brain axis and offer benefits in the context of neurodegenerative diseases. The study aim to synthesize current research investigating the effects of *O. gratissimum* and its bioactive compounds on gut microbiota composition, gut barrier integrity, and neuroinflammation, and to discuss the mechanistic pathways through which these interactions may impact neurodegenerative pathology. By reviewing the available evidence, the study highlight the promising, albeit preliminary, role of *O. gratissimum* as a potential therapeutic or adjunctive treatment strategy by targeting the gut-brain axis in the context of neurodegenerative disorders.

DOI: https://dx.doi.org/10.4314/jasem.v29i2.9

Cite this Article as: UDI, O. A (2025). Bidirectional Communication Network: Exploring the Gut-Brain Axis As A Target For Ocimum Gratissimum Modulation In Neurodegenerative Disorder. *J. Appl. Sci. Environ. Manage.* 29 (2) 407-416

Dates: Received: 23 December 2024; Revised: 27 January 2025; Accepted: 09 February 2025; Published: 28 February 2025

Keywords: Gut-Brain Axis; Neurodegenerative Disorder; *Ocimum gratissimum*; Gut Microbiota; Neuroinflammation.

Neurodegenerative disorders are a profoundly impactful group of conditions, representing a major challenge to global health and well-being. These disorders are defined by the insidious and progressive deterioration of neurons, the fundamental building blocks of the nervous system, within the brain and spinal cord. This loss of neuronal structure and function, driven by complex and often poorly understood mechanisms, results in a cascade of debilitating symptoms impacting movement, cognition, behavior, and sensory perception (WHO, 2024; Kumar *et al*., 2024). Among the numerous neurodegenerative diseases, several stand out due to their high prevalence and devastating impact. Alzheimer's disease (AD), the most common cause of dementia, is characterized by a progressive decline in cognitive abilities, particularly memory, language, and executive functions. These impairments are largely attributed to the accumulation of abnormal protein aggregates within the brain. Specifically, amyloid plaques, composed of beta-amyloid protein, form outside neurons, while neurofibrillary tangles, made up of hyperphosphorylated tau protein, accumulate inside nerve cells. These pathological hallmarks disrupt neuronal communication and ultimately lead to cell death. Early symptoms might include forgetfulness, difficulty with familiar tasks, and changes in personality, which gradually worsen over time,

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eventually rendering individuals unable to care for themselves (Zvěřová, 2019).

Parkinson's disease (PD), another major neurodegenerative condition, primarily impacts movement. Its core symptoms include tremors (shaking), rigidity (stiffness), bradykinesia (slowness of movement), and postural instability (balance problems). These motor impairments stem from the progressive degeneration and death of dopamine-producing neurons in the substantia nigra, a region of the midbrain crucial for motor control. The reduction in dopamine levels disrupts the complex neural circuitry involved in movement, leading to the characteristic motor symptoms. While motor challenges are prominent, PD can also be accompanied by non-motor symptoms such as depression, sleep disturbances, and cognitive impairment (Khan *et al.*, 2019; Papa *et al.*, 2020).

Multiple Sclerosis (MS), while not primarily a neurodegenerative condition in the same sense as AD and PD, is a chronic, often progressive, inflammatory autoimmune disease that severely impacts the central nervous system. In MS, the immune system mistakenly attacks the myelin sheath, a protective fatty layer that surrounds and insulates nerve fibers, similar to insulation around an electrical wire. This demyelination disrupts the transmission of nerve signals, leading to a wide range of neurological symptoms that vary greatly in severity and presentation depending on the location of the lesions within the brain and spinal cord. Common symptoms include fatigue, numbness, vision problems, muscle weakness, and difficulties with coordination and balance (Bjelobaba *et al.*, 2017).

Huntington's disease (HD), in contrast to the aforementioned conditions, is primarily a genetic neurodegenerative disorder caused by a mutation in a single gene (HTT). This mutation leads to the production of an abnormal huntingtin protein, which accumulates within neurons, triggering cell dysfunction and death. HD is characterized by a triad of progressive motor, cognitive, and psychiatric problems. Involuntary movements, known as chorea, are a hallmark of HD, along with a decline in cognitive abilities, including memory, attention, and decision-making. Furthermore, individuals with HD often experience significant psychiatric disturbances, such as depression, irritability, and even psychosis (Essa *et al.*, 2019; Islam *et al.*, 2024). These examples highlight the diverse nature of neurodegenerative disorders, each with distinct underlying mechanisms and clinical presentations. However, they all share the devastating common thread of progressive neuronal dysfunction, leading to functional decline and a significant decrease in quality of life. The high and growing prevalence of these disorders, particularly in aging populations, poses a major public health crisis. The socioeconomic burden is immense, encompassing not only the direct costs of healthcare and long-term care but also the indirect costs associated with lost productivity, caregiver burden, and the emotional toll on patients and their families.

Current therapeutic interventions are limited in their effectiveness. Many focus primarily on managing symptoms, such as using medications to alleviate tremors in PD or cognitive enhancers in AD (Khan *et al.*, 2023). However, these treatments do not address the underlying causes of neuronal damage and are not able to halt or reverse disease progression. This underscores the critical and urgent need for novel therapeutic strategies that target the root of these complex diseases. This includes accelerating research efforts focusing on the development of preventative strategies, more robust and disease-modifying therapies that can actually slow or stop neuronal degradation, and ultimately, the pursuit of cures for these devastating conditions. The multifaceted nature of neurodegenerative disorders demands a multipronged approach that integrates basic research, clinical trials, public health initiatives, and a strong commitment to improving the lives of those affected by these illnesses.

The gut-brain axis (GBA) represents a sophisticated and dynamic two-way communication network that intricately links the gastrointestinal (GI) tract and the central nervous system (CNS). This connection is far more than a simple physical pathway; it's a complex, bidirectional interplay involving a multitude of signaling mechanisms – neural, endocrine, immunological, and metabolic that profoundly affect the functions of both the gut and the brain (Oyovwi and Udi, 2024). Key components of the GBA include the brain and spinal cord, which collectively form the CNS, and the enteric nervous system (ENS). The ENS, often dubbed the "second brain," is an extensive network of neurons embedded within the walls of the entire digestive tract, from the esophagus to the anus. This intricate network is capable of operating autonomously, regulating digestive processes such as motility, secretion, and absorption, but it also maintains constant communication with the CNS. The GBA is not a one-way street; the bidirectional nature of signal transmission is paramount. Information and signals travel not only from the central nervous system down to the gut, influencing digestive function, but also, crucially,

from the gut up to the brain, impacting mood, behavior, pain perception, and even mental capacity (Sultana *et al.*, 2024). This dialogue allows for a constant feedback loop, ensuring system-wide homeostasis.

Bidirectional communication within the GBA is facilitated by a diverse array of interconnected pathways. Neural pathways form the most direct lines of communication. The main route via which signals are sent from the gut to the brain is the vagus nerve, a large cranial nerve. Afferent (gut-to-brain) fibers within the vagus nerve relay information about the state of the digestive system, such as nutrient levels, distension, and the presence of harmful substances, to the brain. Conversely, efferent (brain-to-gut) vagal fibers influence digestive processes, impacting motility, secretion, and inflammation. Complementing the vagus nerve, the intrinsic neural network of the ENS enables local control of gastrointestinal functions, including peristalsis, digestive enzyme secretion, and the regulation of the mucosal barrier. The ENS also communicates bi-directionally with the CNS, integrating local gut activity with whole body needs (López-Ojeda and Hurley, 2024).

Endocrine pathways within the GBA involve the release of hormones and neurotransmitters that act as signaling molecules to influence both gut and brain function. Hormones such as cholecystokinin (CCK), ghrelin, and peptide YY (PYY), produced in the gut in response to food intake, affect satiety, appetite, and digestive motility. Similarly, neurotransmitters like serotonin, dopamine, and cortisol, which are well-known to play a critical role in mood regulation, are also produced within both the gut and the brain, highlighting the intimate link between gut function and mental state. An imbalance in these endocrine signals can contribute to digestive issues, mood disturbances, and even neurodegenerative diseases (Samtiya *et al.*, 2022).

Immunological pathways within the GBA also play a crucial, though often complex, role. The gut, as the largest immune interface of the body, is constantly monitored by the immune system for the presence of pathogens. The release of cytokines (signaling molecules for immune cells) and the initiation of inflammatory responses in the gut can profoundly affect the brain through both neural and humoral (bloodstream) pathways. Furthermore, dysregulated immune activity in the gut, leading to chronic low-grade inflammation, has been shown to contribute to a wide array of conditions, including anxiety, depression, and cognitive decline, and can even compromise the integrity of the blood-brain barrier. Conversely, stress and other CNS signals can alter gut immunity, leading to increased susceptibility to infections (Salvador *et al.*, 2021; Sun *et al*., 2023).

Finally, metabolic pathways within the GBA involve the influence of microbial metabolites, which are produced by the resident microbiome within the gut. These metabolites, particularly short-chain fatty acids (SCFAs) like butyrate, acetate, and propionate, have emerged as crucial signaling molecules that modulate brain function in several ways. SCFAs can reduce inflammation, enhance the production of neurotransmitters like serotonin and GABA (gamma-aminobutyric acid), and regulate the permeability of the blood-brain barrier, influencing the traffic of substances in and out of the CNS. The production of other microbial metabolites, like tryptophan metabolites, can also have important effects on brain health (Zheng *et al*., 2023; Liu *et al*., 2020).

The gut microbiome, a complex community of trillions of microorganisms residing within the digestive tract, is not merely a passive inhabitant; it is an integral, and arguably dominant, player in the intricate workings of the GBA. The composition and metabolic activity of the gut microbiome exert a powerful influence on all the communication pathways described above. For example, an imbalanced gut microbiome, a state known as dysbiosis, often characterized by a reduction in the diversity of microbial species and/or an overgrowth of pathogenic bacteria, can lead to increased intestinal permeability, frequently referred to as "leaky gut." This condition allows for the translocation of inflammatory compounds into the bloodstream, resulting in systemic inflammation that can negatively impact brain health, alter neurotransmitter levels, and impair cognitive function. Dysbiosis can also alter the production of critical microbial metabolites, hindering the beneficial signaling pathways that support the gut-brain axis (Hosseinkhani *et al.*, 2021; Foster *et al*., 2017). In turn, these negative changes can manifest as a spectrum of disorders, including altered behavior, mood disturbances (such as anxiety and depression), and even neurodegenerative conditions like Parkinson's disease and Alzheimer's disease. Conversely, a healthy and diverse gut microbiome, characterized by a rich abundance of beneficial bacteria and the production of beneficial metabolites, can promote gut barrier integrity (preventing leaky gut), reduce systemic and neuro inflammation, and positively influence brain function, enhancing mood, cognition, and overall mental well-being. This underscores the critical significance of the gut

microbiome as a central regulator in maintaining the health and functionality of the gut-brain axis, and highlights the potential benefits of interventions aimed at restoring a healthy gut microbiome for both physical and mental health. Therefore, strategies focused on maintaining or restoring gut health, such as dietary modifications, prebiotics, probiotics, and fecal microbiota transplantation, can have profound effects on the GBA and overall health (Aleman *et al*., 2023).

The concept of focusing on the gut-brain axis (GBA) in the context of neurodegenerative disorders arises from a substantial body of evidence pointing to a significant interplay between the gastrointestinal system and the central nervous system. A disruption in this axis, frequently characterized by gut dysbiosis - an imbalance in the composition of gut microbiota - has been consistently associated with the onset and progression of various neurodegenerative diseases, such as Alzheimer's, Parkinson's, and multiple sclerosis (Khan *et al.*, 2019; Bjelobaba *et al.*, 2017). Gut dysbiosis can provoke chronic inflammation, both locally in the gastrointestinal tract and systemically throughout the body. This inflammation can further trigger neuroinflammation, a critical factor in the progression of neurodegenerative diseases. Neuroinflammation can negatively impact neuronal function, accelerate neurodegeneration, and worsen the cognitive and behavioral symptoms associated with these conditions. This intricate relationship highlights the fact that the gut serves a far greater role than simply an organ of digestion; it is a vital component in maintaining overall health, including neurological well-being. As a result, the potential to manipulate the GBA through various strategies presents a promising and novel therapeutic approach (Levy *et al*., 2017). One such avenue for intervention lies in targeting the gut microbiome, potentially through dietary modifications, prebiotics, probiotics, or even fecal microbiota transplantation. These methods offer the potential to influence inflammatory responses, alter the production of neuroactive metabolites, and ultimately impact the progression of neurodegenerative diseases. This expanding understanding of the GBA's role in these complex illnesses opens up new possibilities for treatment and prevention, paving the way for a more holistic approach to managing neurodegenerative disorders.

Ocimum gratissimum (OG), also known as African basil, holds great significance in traditional medicine across numerous cultures due to its wide-ranging applications. The plant is renowned for its aromatic leaves, which have been historically used to treat a variety of health issues, such as infections, digestive problems, and inflammatory conditions. The rich phytochemical composition of *O. gratissimum* is attributed to numerous bioactive compounds, including eugenol, rosmarinic acid, and an array of flavonoids and terpenoids (Ezeorba *et al*., 2024). Eugenol, one of the key components of African basil, is widely recognized for its potent antiseptic and analgesic properties. This compound plays a significant role in the plant's therapeutic applications, particularly in addressing infections and pain-related ailments. Similarly, rosmarinic acid is another essential bioactive compound found in *O. gratissimum*, exhibiting strong antioxidant and anti-inflammatory properties. This compound's presence contributes to the plant's efficacy in treating inflammation and enhancing overall health and well-being (Ugbogu *et al*., 2021).

Pharmacological studies have consistently demonstrated the capacity of these bioactive components to exhibit antioxidant, anti-inflammatory, and even neuroprotective effects. Consequently, the potential of *O. gratissimum* as a promising candidate for investigation within the gut-brain axis's context is noteworthy. With the growing awareness of the complex relationship between the gut microbiota and neurological health, research on this traditional herb could provide new insights into its therapeutic potential in modern medicine (Dhama *et al.*, 2023).

The intricate communication system that connects the neurological system with the gastrointestinal tract is known as the "gut-brain axis" playing a crucial role in maintaining overall health and well-being. Emerging evidence suggests that the gut microbiome can significantly influence the brain's function and behavior, making it an essential area of study for understanding the pathophysiology of various neurodegenerative disorders (López-Ojeda and Hurley, 2024).

Given the diverse bioactivity of *O. gratissimum* and the emerging understanding of the gut-brain axis, there is a strong rationale for evaluating the potential of this traditional herb in managing and preventing neurodegenerative disorders. The plant's rich phytochemical composition and historical use in traditional medicine make it a compelling candidate for further investigation in this context. As a result, research into *O. gratissimum's* potential in the management and prevention of neurodegenerative disorders could open new avenues for harnessing the therapeutic potential of this traditional herb in modern medicine.

Ocimum gratissimum bioactive compounds and their reported effects

Ocimum gratissimum, commonly referred to as clove basil or African basil, presents a fascinating case study in the realm of natural product chemistry due to its remarkably rich and diverse phytochemical composition. This intricate blend of bioactive molecules is the foundation for its long history of traditional applications and the growing interest in its potential therapeutic benefits. A comprehensive analysis of *O. gratissimum* reveals a complex matrix of constituents, prominently featuring a volatile fraction comprised of essential oils. These oils are characteristically rich in aromatic compounds like eugenol, a phenylpropanoid known for its analgesic and antiseptic properties, and thymol, a monoterpenoid noted for its antimicrobial and antioxidant activities. Beyond these key constituents, the plant also contains a diverse array of other terpenes, representing a wide spectrum of potential biological activities. Further analysis identifies the presence of various non-volatile components, including an assortment of flavonoids with well-established antioxidant capabilities, phenolic acids offering additional antioxidant and anti-inflammatory benefits, and glycosides, complex carbohydrate structures that can influence compound bioavailability and biological activity (Hamid *et al.*, 2024).

These phytochemicals are increasingly being recognized for their potential to exert a wide range of biological effects, spanning from antimicrobial and antioxidant actions to anti-inflammatory and even potential anticancer activities (López-Ojeda and Hurley, 2024). Of particular interest in recent research is the potential for certain compounds within this complex phytochemical profile to display neuroprotective and gut-brain axis (GBA)-modulating properties. For example, particular terpenes, such as cineole or limonene, and phenolic compounds, like rosmarinic acid, have demonstrated promising antioxidant and anti-inflammatory effects in preliminary *in vitro* and *in vivo* studies. These effects are critical to preserving neuronal integrity, combating oxidative stress, and reducing neuroinflammation, which are all thought to contribute to neurodegenerative conditions. Furthermore, the plant's phytochemicals may indirectly affect neuronal health by influencing the GBA, a sophisticated system of direct and indirect communication between the brain and gut microbiota. Compounds within *O. gratissimum* might modulate the gut microbiome composition, reduce intestinal inflammation, or directly interact with GBA signaling pathways, thus influencing behavior, mood, and even cognitive functions (Osuntokun *et al*., 2020).

Pharmacological Activities of Key OG Compounds: The pharmacological activities of key OG compounds, often derived from natural sources, are remarkably diverse and span a wide range of beneficial effects, as rigorously investigated through both cellular (in vitro) and whole-organism (in vivo) studies. These compounds have consistently shown promise across several critical areas of health and disease. A particularly noteworthy characteristic is their potent antioxidant capacity. This ability allows them to function as potent scavengers of free radicals, highly reactive molecules that can damage cells and tissues. By neutralizing these free radicals, OG compounds effectively mitigate oxidative stress, a condition implicated in the pathogenesis of numerous chronic diseases such as cardiovascular disease, neurodegenerative disorders, and certain cancers. The reduction of oxidative stress by these compounds is thought to be a primary driver of their therapeutic effects (Oyem *et al.*, 2021). Furthermore, key OG compounds have demonstrated significant anti-inflammatory properties**.** Scientific evidence suggests these compounds actively modulate immune responses, preventing the over activation of the immune system that can lead to chronic inflammation. They achieve this by reducing the production of pro-inflammatory cytokines, signaling molecules that drive the inflammatory cascade. This anti-inflammatory activity is crucial in addressing a wide range of conditions, including arthritis, inflammatory bowel disease, and asthma (Maleki *et al.*, 2019).

In the realm of neuroprotection**,** these compounds exhibit encouraging potential. Research suggests multiple mechanisms contribute to their protective effects on the nervous system. These mechanisms include the reduction of oxidative stress specifically within neural tissue, leading to a more stable and resilient neuronal environment. They also appear to improve mitochondrial function in brain cells, enhancing their energy production and overall health. Moreover, OG compounds show evidence of modulating neurotransmitter systems, the intricate communication pathways within the brain, suggesting they could play a role in regulating mood, cognitive function, and potentially mitigating neurodegenerative disorders (Udi *et al*., 2023).

Finally, investigations using in vitro models have also revealed these compounds' notable antimicrobial activity**.** They exhibit the ability to inhibit or kill a

variety of microorganisms, including bacteria, fungi, and viruses, indicating possibilities for combating microbial infections, including those resistant to conventional antibiotics. Importantly, research also suggests these compounds can influence gut microbial balance, promoting the growth of beneficial bacteria while inhibiting pathogenic ones, thus hinting at a role in supporting healthy gut ecosystems and their associated benefits to overall health and immunity (Ujong *et al*., 2021; Ezeorba *et al.*, 2024). Collectively, these findings paint a compelling picture of key OG compounds as possessing a multi-faceted pharmacological arsenal**.** Their wide-ranging activities, from antioxidant and anti-inflammatory to neuroprotective and antimicrobial, strongly suggest that these compounds harbor significant therapeutic potential, opening up various avenues for the development of novel treatments and preventative strategies for a wide spectrum of health concerns. Their ability to address multiple pathways of disease makes them particularly interesting for further research and clinical exploration.

The gut-brain axis and ocimum gratissimum modulation

Effects of Ocimum gratissimum on the Gut Microbiome: Recent scientific research has begun to explore its potential in modulating the GBA through its influence on the gut microbiome. Specifically, studies using animal and in vitro models have investigated the impact of OG and its constituent compounds on the gut microbiota. These studies have reported that OG exhibits prebiotic-like effects, which can potentially encourage the growth of advantageous bacteria in the gut, thereby altering the composition of the gut microbial community (Kiernan *et al*., 2023; Ta *et al*., 2024). This is an important finding, as promoting the growth of beneficial bacteria can contribute to improved gut health and overall well-being. Additionally, OG has demonstrated antimicrobial properties that may selectively target and reduce potentially harmful dysbiotic bacteria, thereby promoting a more balanced microbial environment in the gut. This is a crucial factor in maintaining the health of the GBA, as an imbalance in the gut microbiota can negatively impact the communication between the gut and the brain (Duan *et al.*, 2022). Analyses of bacterial diversity, abundance, and the metabolic activity of the gut microbiota can provide valuable insights into the effects of OG on the gut microbiome and the GBA (Zhang *et al*., 2024). By examining these markers, researchers can better understand how OG contributes to the modulation of the GBA, ultimately shedding light on its potential as a natural therapeutic agent for various health conditions.

Ocimum gratissimum Modulation of GBA Pathways: Ocimum gratissimum (OG), is emerging as a potentially valuable natural agent in the intricate relationship between the digestive system and the brain, a concept known as the gut-brain axis (GBA). This dynamic communication network involves bidirectional signaling between the brain and the gut, impacting both physical and mental well-being. The promising effects of OG on the GBA are largely attributed to its diverse array of bioactive compounds, which researchers are actively exploring for their impact on the complex interplay of neural, endocrine, immune, and microbial elements within this axis. One crucial area of investigation focuses on how OG might influence the vagal nerve, a significant communication superhighway connecting the gut directly to the brain. This nerve plays a key role in transmitting signals related to gut motility, nutrient absorption, and inflammation, and has been shown to be involved in mood regulation and cognitive function (Browning *et al.*, 2017). Scientists are examining whether OG can modulate vagal nerve activity, thereby affecting the flow of information from gut to brain and vice-versa. Understanding how OG interacts with the ENS, which controls digestion, secretion, and local immune responses, is critical for revealing OG's overall impact on GBA functionality. Beyond neural pathways, studies are also investigating how OG potentially influences the endocrine system in the GBA context. Specifically, researchers are looking at OG's ability to modulate the release of hormones**,** such as cortisol**,** the hormone central to the body's stress response. Dysregulated cortisol levels are often observed in conditions involving GBA disruption, highlighting the importance of this area of study. Investigations also explore the impact of OG on gut hormones**,** like ghrelin and leptin, which regulate appetite, satiety, and gastrointestinal motility. Any influence of OG on these hormones could have direct implications for aspects of health related to eating behaviors, digestion, and metabolism.

Another significant facet of the research is concerned with the impact of OG on inflammatory and immune responses within the gut**.** Chronic inflammation within the digestive tract is strongly linked to GBA dysregulation and has been implicated in various neurological conditions. Studies are meticulously analyzing OG's potential to modulate the gut's inflammatory pathways, potentially mitigating the negative repercussions of chronic inflammation on both gut and brain function. The

precise immune mediators and inflammatory pathways that are targeted by OG are a focus of this ongoing research (Ghosh *et al.*, 2024). Finally, a growing body of research is examining the influence of OG on the gut microbiota**,** the diverse community of microorganisms inhabiting our digestive system (Gentile and Weir, 2018). Research is exploring how OG may alter the composition and function of the microbiota and the production of metabolites**,** particularly short-chain fatty acids (SCFAs) **(**O'Riordan *et al*., 2022; Chambers *et al*., 2018). SCFAs like butyrate, acetate, and propionate, produced through gut bacterial fermentation of dietary fiber, are not only crucial for gut health but have also shown the capacity to influence brain function and neuroinflammation (Alpino *et al.*, 2024). Understanding how OG contributes to an optimized gut microbiota and SCFA production is vital for elucidating its beneficial effects on the GBA. Ultimately, these mechanistic studies are paramount in demonstrating exactly how OG's influence on various aspects of the GBA can translate into concrete neuroprotective effects. The ability of OG to modulate the neural, endocrine, immune, and microbial environments within the gut could offer invaluable treatment methods for a variety of neurological conditions linked to GBA dysfunction, including neurodegenerative diseases, mood disorders, and autism spectrum disorder. This line of research holds significant promise for developing novel natural therapies based on a deeper comprehension of the intricate link between the gut and the brain.

Evidence for Gut-Brain Axis Modulation in Animal Models of Neurodegenerative Disorders: By giving animals *Ocimum gratissimum* extracts or purified compounds, scientists can monitor changes in the composition of the gut microbiota and variations in gut-derived signaling molecules. Additionally, they assess behavioral measurements, such as motor function, cognitive capacity, and anxiety-like behaviors, along with neuropathological analyses that study neuronal loss, inflammation, and plaque formation in the brain. Moreover, biochemical analyses are performed to quantify the levels of neurotransmitters, inflammatory markers, and oxidative stress indicators in both the gut and the brain (Amirani *et al.*, 2020). A critical aspect of this research aims to discern the specific role of GBA modulation in any observed neuroprotective effects, determining if improvements in behavioral and neuropathological indices are directly linked to alterations in gut health or gut-derived signaling molecules influencing brain function. The ultimate goal of this research is to establish a causal relationship between GBA modulation induced by *Ocimum gratissimum* and its potential therapeutic benefits for neurodegenerative diseases. This knowledge may contribute to the development of novel treatment strategies that target the Gut-Brain Axis to mitigate the impact of neurodegenerative disorders.

Ocimum gratissimum and Neuroprotection in Neurodegenerative disorders

*Direct Neuroprotective Effects of Ocimum gratissimum in In vitro and In vivo Models***:** *Ocimum gratissimum*, commonly recognized by its common name of clove basil, has been identified as a potential candidate in the field of neuroprotection, with a specific focus on neurodegenerative disorders. Research conducted through both in vitro (laboratory settings) and in vivo (within living organisms) experiments have shown promising outcomes regarding the impact of *Ocimum gratissimum* on neuronal health (Ajiboye *et al.*, 2024; Udi *et al*., 2022). These studies concentrate on the influence of *Ocimum gratissimum* extracts or its bioactive compounds on various aspects of neuronal well-being, such as survival, functionality, and overall viability. The results drawn from this research consistently demonstrate that *O. gratissimum* treatment can foster neuronal integrity, increase resistance to cellular damage, and enhance neuronal function when faced with various stress factors. The neuroprotective effects of this herb can be largely attributed to its powerful antioxidant and anti-inflammatory properties. The antioxidant activity of *Ocimum gratissimum* is primarily characterized by its free radical scavenging capabilities, which effectively reduce oxidative damage within neurons, ultimately minimizing neuronal dysfunction and death. Furthermore, its anti-inflammatory properties play a crucial role in mitigating neuroinflammation, a prominent feature in many neurodegenerative conditions. This highlights the potential of *Ocimum gratissimum* as a valuable therapeutic tool for combating these debilitating diseases (Udi *et al*., 2018; Curtis *et al.*, 2024)

Potential Synergistic and Combinatorial Approaches: The exploration of synergistic and combinatorial approaches represents a significant leap forward in our quest to harness the full neuroprotective potential of *Ocimum gratissimum* (OG), commonly known as African basil. Instead of considering OG as a singular therapeutic entity, researchers are now recognizing the immense value in investigating its interactions and compatibility with existing neuroprotective strategies (Curtis *et al*., 2024). This shift in

perspective acknowledges the complexity of neurological conditions and moves away from a "one-size-fits-all" approach.

One critical area of focus involves understanding how OG interacts with established pharmaceutical interventions for neurodegenerative diseases. This includes exploring the possibility of pharmacodynamic synergy**,** where OG might enhance the effectiveness of drugs already in use for conditions like Alzheimer's, Parkinson's, or stroke recovery. Research is underway to determine if OG can act as an adjuvant**,** mitigating side effects or boosting specific therapeutic mechanisms of existing drugs. For instance, can OG reduce the neuroinflammation associated with some medications or enhance their ability to cross the blood-brain barrier? Such interactions could allow for the deployment of lower drug dosages, minimizing risks and improving patient tolerance, while simultaneously yielding more impactful therapeutic outcomes. Moving beyond purely pharmacological avenues, the potential of integrative approaches is being increasingly recognized. This involves combining OG with elements that promote overall well-being, such as prebiotics, which exert their influence via the gut-brain axis. A healthy gut microbiome can have profound effects on neuroinflammation, neurotransmitter balance, and even cognitive function. Therefore, combining OG with prebiotics that encourage a beneficial gut flora might indirectly enhance its neuroprotective effects. Similarly, combining OG with targeted lifestyle interventions like regular exercise, a balanced, nutrient-rich diet (particularly those rich in omega-3 fatty acids and antioxidants), and adequate sleep may create a synergistic effect, optimizing the body's intrinsic capacity for repair and resilience against neurodegenerative processes. This holistic perspective acknowledges that neuroprotection is not just about targeting a specific molecule but about supporting the body's overall health and well-being. In essence, by investigating these diverse combinatorial strategies, the study poised to unlock novel, potentially more potent, and multi-faceted approaches to preserving, restoring, and optimizing brain health. This research paradigm moves beyond single-agent therapies to embrace a more nuanced and holistic understanding of neuroprotection, potentially yielding breakthrough treatments for debilitating neurological conditions and improving the quality of life for countless individuals. The future of neuroprotection may well lie in the clever and synergistic blending of nature's gifts and human ingenuity.

Conclusion: The research into *Ocimum gratissimum* provides promising preliminary evidence that modulating the gut microbiome via natural compounds may offer a novel avenue for managing the inflammatory processes implicated in neurodegenerative disorders. Further research should be conducted to confirm these findings, and explore the mechanistic pathways involved. Given the potential benefits observed in this review study, further investigation into *Ocimum gratissimum* as a therapeutic agent for neurodegenerative disorders is strongly recommended. This should include advanced studies to identify and isolate the specific bioactive compounds responsible for the observed effects, and translate this to clinical research to assess the safety and therapeutic efficacy of *Ocimum gratissimum* in human patients. Focus should be placed on optimizing the delivery of *Ocimum gratissimum* or its extracts to ensure effective modulation of the gut microbiome.

Data Availability: No data sets were generated or analysed during the current study.

Declarations: Conflict of Interest: The author declare no conflict of interests.

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