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Neuroregenerative Effect of Celery in Cerebrovascular Aging: A Literature Review

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A B S T R A C T

Celery, a common culinary herb, has garnered recent attention for its potential neuroprotective and neuroregenerative properties, particularly in the context of cerebrovascular aging. Preclinical studies suggest that compounds within celery, such as flavonoids and phthalides, may exert antioxidant, anti-inflammatory, and neurotrophic effects. These actions could potentially mitigate age-related cognitive decline, stroke-induced brain damage, and other neurodegenerative conditions. However, the precise mechanisms underlying these effects and their clinical translation in humans remain to be fully elucidated. Further research is warranted to explore the therapeutic potential of celery in promoting brain health and mitigating the effects of cerebrovascular aging.

Keywords: Celery, Neuroprotective, Neuroregenerative, Cerebrovascular Aging

1. INTRODUCTION

Cerebrovascular aging refers to the natural changes that occur in the blood vessels of the brain as part of the aging process. These changes can affect the structure and function of the cerebrovascular system, which plays a crucial role in maintaining brain health by supplying oxygen and nutrients while removing waste products. Cerebrovascular aging is characterized by a progressive decline in cognitive function and an increased susceptibility to stroke, poses a significant public health burden globally. While conventional pharmacological interventions exist, the search for natural, neuroprotective agents has intensified[1,2]. Celery (*Apium graveolens*), a widely consumed vegetable, has recently emerged as a potential candidate for mitigating the detrimental effects of cerebrovascular aging[3]. Preliminary evidence suggests that celery and its bioactive compounds may possess neuroprotective and neuroregenerative properties, offering a promising avenue for developing novel therapeutic strategies to combat age-related cognitive decline and stroke-induced brain damage[4,5]. This review aims to critically evaluate the existing literature on the neuroprotective and neuroregenerative effects of celery in the context of cerebrovascular aging, exploring the underlying mechanisms and potential clinical implications. By synthesizing current knowledge and identifying areas for future research, this review seeks to contribute to a deeper understanding of celery's potential role in promoting brain health and mitigating the consequences of cerebrovascular aging.

2. METHODS

This study is using literature review method. Writer analysed the mechanism that is correlated in celery affecting cerebrovascular aging. Further analysis and data material used for discussion material acquired from journals of previous study of researches and reports that has been published in indexed scientific journal. There are 29 journals that were obtained and screened for this study as main data of discussion in this article. Keywords that are used in this literature searching are celery, cerebrovascular aging, neuroprotective, neuroregenerative.

3. RESULTS AND DISCUSSION

Epidemiology and Pathomechanism of Cerebrovascular Aging

Cerebrovascular aging is a multifaceted biological process characterized by structural, functional, and biochemical changes in the blood vessels of the brain. These changes contribute to an increased risk of neurovascular diseases, including stroke, vascular dementia, and Alzheimer's disease. There are no specifics number that stated statistics of population with cerebrovascular aging. In a 2018 data stated that prevalence of vascular dementia within range of 20%[6], while Alzheimer's disease account for 35.6% population in the whole world[7]. Further study also stated 25-30% of ischaemic stroke injury will leads to vascular cognitive impairment or vascular dementia[8].

Understanding the pathomechanism of cerebrovascular aging involves exploring cellular senescence, vascular remodeling, oxidative stress, inflammation, and endothelial dysfunction. Aging induces profound structural alterations in the cerebrovascular network. Large and small vessels alike undergo stiffening due to increased deposition of extracellular matrix components such as collagen and decreased elastin. These changes lead to reduced vascular compliance and impaired autoregulation of cerebral blood flow[9,10]. In parallel, there is remodeling of the microvasculature, characterized by rarefaction (loss of capillaries) and basement membrane thickening. This results in diminished nutrient and oxygen delivery to neurons and glial cells, promoting neuronal dysfunction and cognitive decline[11].

The endothelium, a critical regulator of vascular homeostasis, becomes dysfunctional with age. Reduced bioavailability of nitric oxide (NO) – a potent vasodilator – is a hallmark of endothelial aging. This reduction arises from decreased expression and activity of endothelial nitric oxide synthase (eNOS) and increased scavenging of NO by reactive oxygen species (ROS). Impaired NO signaling exacerbates vasoconstriction, thrombogenesis, and inflammation, further destabilizing cerebrovascular integrity[12,13].

Oxidative stress plays a pivotal role in cerebrovascular aging. Mitochondrial dysfunction and enzymatic sources such as NADPH oxidase produce excessive ROS, overwhelming the antioxidant defense system. ROS directly damage lipids, proteins, and DNA in vascular cells, promoting cellular senescence and apoptosis. Oxidative stress also upregulates matrix metalloproteinases (MMPs), which degrade the vascular basement membrane and compromise the blood-brain barrier (BBB). The integrity of the BBB declines with age, allowing harmful molecules such as fibrinogen, albumin, and immune cells to enter the brain parenchyma. This disrupts the delicate neural environment and promotes neuroinflammation, synaptic dysfunction, and neuronal loss. BBB breakdown is closely linked to small vessel disease and contributes to the pathogenesis of age-related cognitive decline[12-14].

Aging is associated with a chronic low-grade inflammatory state termed "inflammaging." Elevated levels of pro-inflammatory cytokines (e.g., IL-1β, IL-6, and TNF-α) and chemokines contribute to cerebrovascular damage. These cytokines activate microglia and astrocytes, perpetuating neuroinflammation and impairing the ability of the BBB to regulate immune cell infiltration into the brain parenchyma. Persistent inflammation accelerates vascular aging and neurodegeneration. Vascular cells, including endothelial cells, smooth muscle cells, and pericytes, undergo senescence during aging. Senescent cells exhibit the senescence-associated secretory phenotype (SASP), characterized by the secretion of inflammatory mediators, growth factors, and proteases. The SASP amplifies local inflammation and disrupts vascular homeostasis, impairing angiogenesis and contributing to the formation of leaky, dysfunctional vessels[15-18].

Neurovascular coupling, the mechanism by which neuronal activity regulates local blood flow, deteriorates with age. This dysregulation arises from endothelial dysfunction, loss of pericytes, and altered astrocyte signaling. Impaired neurovascular coupling reduces the brain's ability to meet its metabolic demands, exacerbating neuronal stress and vulnerability to injury[19].

Mechanism of Celery Extract on Cerebrovascular Aging

Celery (*Apium graveolens*), a widely consumed vegetable with significant medicinal properties, has garnered attention for its potential role in promoting cerebrovascular health and mitigating the effects of cerebrovascular aging. This therapeutic potential is attributed to its rich bioactive profile, including flavonoids (e.g., apigenin), phenolic acids, vitamins, and essential minerals. The mechanisms by which celery exerts protective effects on cerebrovascular aging involve antioxidant activity, anti-inflammatory properties, endothelial function improvement, and neurovascular protection[20].

Celery contains potent antioxidants, including flavonoids (e.g., luteolin and apigenin) and vitamin C, which neutralize reactive oxygen species (ROS) and prevent oxidative damage to vascular cells. Apigenin and luteolin inhibit lipid peroxidation and mitochondrial ROS generation, protecting endothelial cells from oxidative stress-induced apoptosis. Celery extract has been shown to upregulate antioxidant enzymes such as superoxide dismutase (SOD) and catalase, enhancing the brain's intrinsic defense mechanisms against oxidative insults[21].

Apigenin suppresses the expression of pro-inflammatory cytokines such as interleukin-1β (IL-1β), interleukin-6 (IL-6), and tumor necrosis factor-alpha (TNF-α). This reduces microglial activation and attenuates vascular inflammation. Apigenin inhibits the nuclear factor-kappa B (NF-κB) signaling pathway, a key regulator of inflammatory responses in endothelial cells and smooth muscle cells[22].

Flavonoids in celery stimulate endothelial nitric oxide synthase (eNOS) activity, restoring NO production and improving vasodilation. Apigenin has been shown to enhance smooth muscle relaxation through its vasodilatory effects, reducing vascular stiffness associated with aging. Phenolic acids in celery inhibit MMP activity, preventing the degradation of vascular basement membranes and reducing vascular permeability. Apigenin modulates collagen synthesis and deposition, reducing vascular stiffness and maintaining vascular elasticity[23,24].

Neurovascular coupling, the mechanism by which cerebral blood flow is adjusted to meet neuronal metabolic demands, declines with age. Celery contributes to the maintenance of neurovascular integrity through two main mechanisms. Flavonoids in celery support the function of astrocytes and pericytes, critical components of the neurovascular unit. Celery extracts mitigate the breakdown of the blood-brain barrier (BBB) by reducing oxidative and inflammatory insults, preserving cerebrovascular homeostasis[25-26].

By mitigating cerebrovascular aging, celery also exerts indirect benefits on cognitive health. Flavonoids in celery promote neurogenesis, protect neurons against oxidative and inflammatory damage, and improve synaptic plasticity. These effects contribute to the prevention of age-related cognitive decline and vascular dementia[27].

Supporting Studies in Celery Extract Effect Toward Cerebrovascular Aging

Several studies has been conducted with animal model induced with various cerebrovascular aging diseases, such as vascular dementia, chronic stroke, and Alzheimer's disease to determine the effect of celery extract. The study by Li et al., investigates the therapeutic effects of Dl-3-n-Butylphthalide (NBP) in chronic cerebral hypoperfusion (CCH), a condition associated with cognitive impairment and white matter damage. The findings reveal that NBP promotes remyelination and reduces inflammation by modulating the AMPK/SIRT1 and STAT3/NF-κB signaling pathways. These pathways play critical roles in energy metabolism, inflammation, and myelin repair. By enhancing AMPK/SIRT1 activity, NBP supports remyelination, while suppressing STAT3/NF-κB reduces neuroinflammation. The study highlights NBP as a promising therapeutic agent for treating CCH and related neurodegenerative conditions[28].

Another study conducted by Tu et al., explores the effects of NBP on neovascularization and neurological recovery in a rat model of intracerebral hemorrhage (ICH). The results demonstrate that NBP significantly enhances angiogenesis and improves neurological outcomes by promoting vascular repair and reducing secondary brain damage. These findings suggest that NBP could be a potential therapeutic agent for improving recovery and restoring function following ICH[29].

4. CONCLUSION

Cerebrovascular aging is one of the most common problems in cerebrovascular health that comes with aging process. Cerebrovascular aging account for problems such as vascular dementia, ischaemia stroke, and Alzheimer's Disease. Current mechanisms that are being understood that could lead to cerebrovascular aging are inflammation, endothelial dysfunction, vasculature remodelling, and oxidative stress. Potential of phytochemicals property found in celery offers possible solution as therapy for diseases related to cerebrovascular aging. Further researches and clinical trials need to be conducted to offers possible application in clinical settings.

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