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Bromelain-digested casein peptide pool mitigates stress-induced neural and behavioral deficits in rats

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ABSTRACT

This study aimed to evaluate the therapeutic effects of a bromelain-digested casein peptide pool (BDCPP) on behavioral, biochemical, molecular, and histological changes induced by chronic stress in male rats. BDCPP is a non-toxic compound against erythrocyes, U87 MG, and HepG2 cells. Wistar rats were subjected to a chronic stress protocol and treated orally with BDCPP. Behavioral assessments included the elevated plus maze (EPM), Light/Dark (L/D), forced swim test (FST), Morris water maze (MWM), and T-Maze. Biochemical assays measured corticosterone, malondialdehyde (MDA), superoxide dismutase (SOD), and total antioxidant capacity (TAC) levels. Western blotting was performed to assess the expression of hippocampal brain-derived neurotrophic factor (BDNF) and insulin-like growth factor 1 (IGF-1). Using Golgi-Cox staining, histological evaluations focused on dendritic morphology in the hippocampus (CA3 region) and basolateral amygdala (BLA). BDCPP administration improved anxiety and depression-like behaviors, normalized corticosterone levels, enhanced antioxidant capacity, and increased the expression of BDNF and IGF-1 in the hippocampus. BDCPP attenuated stress-induced dendritic retraction in CA3 pyramidal neurons and mitigated hypertrophy in BLA neurons. BDCPP exerts beneficial effects against chronic stress-induced behavioral and neurobiological impairments, particularly by modulating the plasticity of the hippocampus and amygdala. These findings highlight its potential as a functional food-based intervention for stress-related disorders.

1. Introduction

Stress is a physiological and psychological condition in which internal or external factors disrupt the body's homeostasis [1,2]. Chronic stress has profound effects on the central nervous system, contributing to disorders such as depression, anxiety, motor dysfunction, and cognitive impairment [3]. The primary biological systems mediating the stress response are the sympathetic nervous system and the hypothalamic-pituitary-adrenal (HPA) axis. Activation of the sympathetic nervous system rapidly increases catecholamine levels (e.g., epinephrine, norepinephrine), while the HPA axis elevates glucocorticoids, such as corticosterone in rodents and cortisol in humans [4]. Prolonged elevation of corticosterone can lead to the adverse effects of chronic stress, including structural and functional changes in key brain regions such as the hippocampus, amygdala, prefrontal cortex (PFC), and hypothalamus [5,6]. Chronic stress has been shown to reduce hippocampal volume [7], increase dendritic spine density in the basolateral amygdala (BLA) [8], and decrease levels of neurotrophic factors, including brain-derived neurotrophic factor (BDNF), which supports neuronal growth and survival, and insulin-like growth factor-1 (IGF-1), which is critical for neurogenesis, synaptogenesis, cell proliferation, and the maintenance of overall neuronal function [9,10]. Additionally, stress-induced inflammation contributed by increased malondialdehyde (MDA) levels and reduced antioxidant enzyme activity, including glutathione (GSH)

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