Neuroprotective Role of Fenchol in Modulating the B-CSF Barrier in Neurodegenerative Diseases

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Current underlying mechanisms to treat neurodegenerative diseases (ND) are limited due to an incomplete understanding. Tight junctions (TJ) and efflux pumps on the BBB restrict drug permeability, causing a major limitation in current treatments which prevents therapeutic agents from reaching neurons. However, the blood-cerebrospinal fluid barrier (B-CSFB) is a potential alternative route for the clearance of toxins associated with ND since it's more accessible with fewer efflux pumps on membranes. A permeability increase in B-CSFB in ND patients causes inflammatory toxins, such as lipopolysaccharides (LPS) to enter the brain, contributing to neurodegeneration. This study aimed to determine whether fenchol improves the integrity of the B-CSFB after LPS challenge through the regulation of i) TJs, ii) inflammatory cytokines, and iii) cell viability. LPS significantly decreased the expression of TJ proteins, Ocln ($p<0.01$), and ZO-1 ($p<0.001$). While fenchol didn't prevent TJ downregulation ($p>0.05$), butyrate treatment improved TJ expression in LPS-treated cells ($p<0.01$). LPS didn't cause a notable change in IL-6 or IL-1ß expression ($p>0.05$). This suggests it may not play a role in inflammation in NDs. In comparison to the control group, fenchol reduced inflammatory gene expression. suggesting a role in preventing inflammatory conditions ($p>0.05$). 24 hours after LPS treatment, cell viability decreased ($p<0.01$). However, butyrate protected cells against LPS-induced cell death ($p<0.0001$), whereas fenchol exacerbated this effect, suggesting butyrate and fenchol as a combination therapy may have synergistic effects. This project is the first to establish fenchol's potential as a natural-based treatment, expediting approval pathways for plant-derived neuroprotective agents.

Awards Won: