WHEAT MALT EXTRACT MODULATES BRAIN GENE EXPRESSION: IMPLICATIONS FOR EARLY ALZHEIMER'S DISEASE PREVENTION

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Background: Alzheimer's disease (AD) is a progressive neurodegenerative disorder marked by impaired synaptic plasticity, metabolic imbalance, neuroinflammation, and blood–brain barrier (BBB) dysfunction [1]. Gene expression profiling in vulnerable regions such as the hippocampus and prefrontal cortex (PFC) offers valuable insights into the molecular mechanisms underlying cognitive decline [2]. Previous studies demonstrated that *Limax flavus* agglutinin, a lectin highly selective for α-anomeric sialic acids, can block Aβ-ganglioside interactions and mitigate neurotoxicity [3]. Wheat malt extract (WME), a readily available source of sialic acid-binding lectin wheat germ agglutinin (WGA), may represent a practical dietary intervention capable of modulating neuronal, metabolic, and inflammatory processes relevant to AD.

Materials and methods: Twelve-month-old female APPswe/PS1E9 (APP/PS1) mice and wild-type littermates were treated chronically with WME or tap water. Gene expression was quantified in the hippocampus and PFC using qRT-PCR. The panel included markers of synaptic plasticity (Arc, Egr1, Bdnf), metabolic regulators (Pgc1a, Sirt1, Igf1r, Irs2), synaptic vesicle protein (Syp), pro-inflammatory cytokine (Il1β), and BBB integrity marker (Cldn5).

Results: APP/PS1 mice displayed widespread transcriptional alterations consistent with impaired plasticity and elevated inflammation. Both hippocampus and PFC exhibited reduced Arc, Egr1, Bdnf, and Pgc1a, together with increased Il1β. In the PFC, further downregulation of Sirt1, Igf1r, Irs2, Syp, and Cldn5 were observed. In wild-type mice, WME upregulated Bdnf and Syp, restored Sirt1, Pgc1a, Igf1r, and Irs2, enhanced Cldn5, and reduced Il1β in the PFC. In the hippocampus, WME significantly increased Egr1 and Pgc1a expression and attenuated Il1β elevation, while changes in other gene expression were modest, indicating a differential, region-specific transcriptional responsiveness. In APP/PS1 mice, WME exerted only subtle effects, suggesting that its therapeutic efficacy is likely confined to early or preclinical stages of Alzheimer's disease.

Conclusion: Wheat malt extract, a natural source of wheat germ agglutinin, demonstrated region-specific transcriptional modulation in the brain. In wild-type mice, WME enhanced synaptic plasticity, restored metabolic and BBB-related markers, and reduced neuroinflammatory gene expression, particularly in the prefrontal cortex. In the hippocampus, WME partially improved plasticity-associated factors and attenuated inflammatory changes. However, in APP/PS1 mice, the effects were modest, suggesting that WME's efficacy may be limited once extensive pathology has developed. These findings support the potential of WME as a preventive dietary intervention targeting early molecular abnormalities associated with Alzheimer's disease.

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