NEUROPROTECTIVE EFFECTS OF ETHANOLIC EXTRACTS FROM *SOLANUM MACROCARPON* IN A ZEBRAFISH MODEL OF SCOPOLAMINE-INDUCED ALZHEIMER'S DISEASE-RELATED DEMENTIA

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Introduction. Alzheimer's disease (AD) is a progressive neurodegenerative disorder characterized by cognitive decline and oxidative stress. Natural bioactive compounds with antioxidant and neuroprotective properties have gained interest as potential therapeutic agents. *Solanum macrocarpon*, known for its antimicrobial, antioxidant, and anti-inflammatory effects, may offer neuroprotective benefits. This study investigates the effects of its ethanolic extract (SMEE) in a zebrafish model of scopolamine (Scop)-induced cognitive impairment, emphasizing its impact on oxidative stress, cholinergic modulation, and behavioral parameters.

Materials and Methods. Zebrafish were exposed to SMEE at concentrations of 1, 3, and 6 mg/L for 23 days before immersion in scopolamine (100 μM) to induce cognitive deficits. Behavioral tests, including the Novel Tank Diving Test (NTT), Novel Approach Test, Y-Maze, and Novel Object Recognition (NOR), were performed to assess memory and anxiety-related behaviors. Acetylcholinesterase (AChE) activity and oxidative stress markers were quantified using spectrophotometric methods. To elucidate the neuroprotective mechanisms, antioxidant enzyme activities (superoxide dismutase - SOD, catalase - CAT, and glutathione peroxidase - GPX) were measured, along with markers of oxidative damage such as protein carbonylation and lipid peroxidation (malondialdehyde - MDA). Pearson correlation analyses were conducted to assess relationships between behavioral parameters, enzymatic activities, and oxidative stress markers. In addition, HPLC analysis identified chlorogenic acid and rutin as major polyphenolic components in SMEE, followed by an in silico pharmacokinetic evaluation (ADMET) to assess their absorption, metabolism, and toxicity profiles.

Results. SMEE administration significantly improved spatial and recognition memory, reducing anxiety-like behavior in zebrafish exposed to Scop. The extract also counteracted oxidative stress by enhancing the activity of antioxidant enzymes (SOD, CAT, GPX) and reducing protein oxidation and lipid peroxidation (MDA levels). Pearson correlation analysis showed significant negative correlations between MDA levels and behavioral performance, as well as SOD, CAT, and GPX activities, indicating a direct link between oxidative stress reduction and cognitive improvement. HPLC analysis confirmed the presence of chlorogenic acid and rutin, which exhibited strong antioxidant properties. ADMET analysis suggested that these compounds have lower intestinal absorption but a favorable neuroprotective profile.

Conclusions. The findings indicate that *Solanum macrocarpon* ethanolic extract has potential therapeutic benefits in mitigating cognitive decline and oxidative stress, supporting its use as a natural neuroprotective agent in Alzheimer's disease. Further studies are warranted to elucidate its precise mechanisms and clinical relevance.

Keywords. *Solanum macrocarpon*, zebrafish, cognitive impairment, oxidative stress, acetylcholinesterase, scopolamine, Alzheimer's disease, HPLC, antioxidant enzymes, neuroprotection.