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5,7,3′,4′,5′-pentamethoxyflavone (PMF) exhibits anti-obesity and neuroprotective effects in an obese zebrafish model

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ABSTRACT

Obesity is a multi-chronic illness characterized by superfluous fat accumulation, contributing to significant metabolic and neurological complications. Current therapeutic approaches have limited efficacy and notable side effects, underscoring an urgent demand for novel, safer alternatives. This study is the first to investigate the anti-obesity potential of 5,7,3′,4′,5′-pentamethoxyflavone (PMF) *in vivo* using a zebrafish model. Our findings demonstrate that PMF administration exerts pronounced anti-obesogenic effects, evidenced by reductions in blood glucose, plasma triglycerides, total cholesterol, hepatic low-density lipoproteins (LDL), and high-density lipoproteins (HDL). Mechanistically, PMF suppressed hepatic adipogenic and lipogenic gene expression while promoting lipid catabolism through activation of peroxisome proliferator-activated receptor-alpha (PPAR-α) and its downstream enzymes, including acyl-CoA oxidase 1 (ACOX1), medium-chain acyl-CoA dehydrogenase (ACADM), and carnitine palmitoyl transferase 1B (CPT-1β). Additionally, PMF markedly mitigated oxidative stress by lowering malondialdehyde (MDA) and nitric oxide (NO) levels, accompanied by increased antioxidant enzyme activities, including superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GSH-Px), and glutathione S-transferase (GST). Notably, PMF effectively prevented obesity by suppressing food intake, down-regulating orexigenic genes, and enhancing anorexigenic signals. Furthermore, PMF exhibited neuroprotective properties by elevating brain-derived neurotrophic factor (BDNF) and its receptor tropomyosin receptor kinase B2 (TrkB2), revealing a novel link between metabolic and neurological regulation. This study provides pioneering, comprehensive *in vivo* evidence supporting PMF as a promising therapeutic candidate with dual beneficial roles in metabolic health and neuroprotection.

1. Introduction

Obesity is an increasingly widespread disorder, affecting all ages and genders across the globe (Afolabi et al., 2020; Cizza, 2022). The Atlas report from the World Obesity Federation (WOF) stated that in 2020 approximately 770 million adults globally were adversely affected by obesity (Lobstein et al., 2022). Obesity is caused by a decrease in energy expenditure and/or increased energy intake for a prolonged period,

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