Sustainable Strategy for the Selective Recovery of Flavanones from Glycyrrhiza glabra Leaves with Antioxidant and Neuroprotective Properties

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Glycyrrhiza glabra leaves (GGL) represent an underutilized by-product of the licorice supply chain, despite being a promising and sustainable source of bioactive flavanones. In this study, supercritical carbon dioxide fluid extraction (SFE-CO_2) was optimized as an environmentally friendly strategy for the selective recovery of leaf-exudate flavanones, primarily pinocembrin, licoflavanone, and glabranin. A Response Surface Methodology (RSM) approach, combined with UHPLC-UV profiling, was employed to systematically evaluate extraction parameters and identify optimal operating conditions. The best results were achieved at 40°C, 364 bar, 30 minutes, and a CO_2 flow rate of 2 L min^{-1}, maximizing flavanone enrichment while minimizing solvent consumption.
Under these optimized conditions, SFE-CO_2 produced high-purity extracts with a flavanone content of up to 31%, achieving approximately three-fold enrichment compared to conventional exhaustive extraction methods. Moreover, this approach outperformed traditional solvent-based liquid extraction in terms of selectivity, efficiency, and environmental impact. Path2Green assessment further confirmed the sustainability profile of the process, highlighting its potential for industrial scalability and reduced ecological footprint.
The biological activity of the SFE-CO_2 extract was investigated using a yeast model of Parkinson's disease (PD) overexpressing α-synuclein. The extract significantly extended chronological lifespan and reduced intracellular oxidative stress. Pinocembrin, identified as the most abundant flavanone, demonstrated a key role by prolonging yeast lifespan and inhibiting α-synuclein fibril aggregation in vitro. Additionally, its efficacy was validated in a Drosophila melanogaster PD model, where it improved locomotor performance, decreased oxidative protein damage, and enhanced cellular energy metabolism, as evidenced by increased ATP levels and glycogen content.

Overall, these findings support the sustainable valorization of GGL into flavanone-enriched SFE-CO_2 extracts, highlighting their potential application in nutraceutical formulations aimed at promoting healthy aging and mitigating age-related neurodegenerative disorders.