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Unlocking Developmental Stage-Specific Therapeutic Profiles of *Moringa oleifera* Leaves through Integrated Metabolomics

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Moringa oleifera (*M. oleifera*) is a widely cultivated medicinal plant valued for its rich phytochemical profile. While its leaves are commonly used in traditional and modern formulations, the impact of developmental stages on their bioactivity remains underexplored. This study provides an integrated metabolomic–bioactivity analysis of *M. oleifera* leaves across growth stages, offering new insights for stage-specific therapeutic applications. Leaves harvested at 30, 45, and 60 days in Kuala Terengganu, Malaysia were extracted with ethanol and assessed for phenolic and flavonoid content, antioxidant activities (DPPH, FRAP), and acetylcholinesterase (AChE) inhibition. Untargeted UHPLC-MS/MS profiling was performed, with multivariate analyses (PCA, PLS-DA) to characterize stage-specific metabolomes and correlate metabolites with bioactivity. Marked age-dependent variations were observed. Day-60 leaves showed the highest phenolic and flavonoid contents with strong antioxidant capacity, while day-30 leaves exhibited superior AChE inhibition. A total of 27 metabolites were annotated, predominantly flavonoids (59%), followed by phenolic acids (19%), glucosinolates (7%), and minor coumarins, folates, and alkaloid-like compounds. Multivariate clustering distinguished leaf stages, with day-60 extracts enriched in quercetin rutinoside, chlorogenic acid, kaempferol derivatives, and procyanidin B2. Correlation models linked quercetin derivatives, chlorogenic acid, and procyanidin B2 to antioxidant activity, whereas coumarin and folic acid were associated with AChE inhibition. *M. oleifera* leaves display dynamic, stage-dependent metabolomic and functional signatures. Day-60 leaves represent a potent antioxidant reservoir, while day-30 leaves exhibit neuroprotective potential through AChE inhibition. These findings highlight the importance of developmental stages in optimizing therapeutic value and support precision harvesting for nutraceuticals targeting oxidative stress and neurodegenerative disorders such as Alzheimer's disease.

Keywords: *Moringa oleifera*, Bioactive, Stage-dependent, Metabolomics

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