

Variation in the metabolites and α -glucosidase inhibitory activity of *Cosmos caudatus* at different growth stages

ABSTRACT

Background: *Cosmos caudatus* is an annual plant known for its medicinal value in treating several health conditions, such as high blood pressure, arthritis, and diabetes mellitus. The α -glucosidase inhibitory activity and total phenolic content of the leaf aqueous ethanolic extracts of the plant at different growth stages (6, 8, 10, 12 and 14 weeks) were determined in an effort to ascertain the best time to harvest the plant for maximum medicinal quality with respect to its glucose-lowering effects. **Methods:** The aqueous ethanolic leaf extracts of *C. caudatus* were characterized by NMR and LC-MS/MS. The total phenolic content and α -glucosidase inhibitory activity were evaluated by the Folin-Ciocalteu method and α -glucosidase inhibitory assay, respectively. The statistical significance of the results was evaluated using one-way ANOVA with Duncan's post hoc test, and correlation among the different activities was performed by Pearson's correlation test. NMR spectroscopy along with multivariate data analysis was used to identify the metabolites correlated with total phenolic content and α -glucosidase inhibitory activity of the *C. caudatus* leaf extracts. **Results:** It was found that the α -glucosidase inhibitory activity and total phenolic content of the optimized ethanol:water (80:20) leaf extract of the plant increased significantly as the plant matured, reaching a maximum at the 10th week. The IC₅₀ value for α -glucosidase inhibitory activity (39.18 $\mu\text{g mL}^{-1}$) at the 10th week showed greater potency than the positive standard, quercetin (110.50 $\mu\text{g mL}^{-1}$). Through an ¹H NMR-based metabolomics approach, the 10-week-old samples were shown to be correlated with a high total phenolic content and α -glucosidase inhibitory activity. From the partial least squares biplot, rutin and flavonoid glycosides, consisting of quercetin 3-O-arabinofuranoside, quercetin 3-O-rhamnoside, quercetin 3-O-glucoside, and quercetin 3-O-xyloside, were identified as the major bioactive metabolites. The metabolites were identified by NMR spectroscopy (J-resolve, HSQC and HMBC experiments) and further supported by dereplication via LC-MS/MS. **Conclusion:** For high phytomedicinal quality, the 10th week is recommended as the best time to harvest *C. caudatus* leaves with respect to its glucose lowering potential.

Keyword: *Cosmos caudatus*; α -Glucosidase inhibition; Total phenolic content; Harvesting age; Quercetin derivatives; NMR-based metabolomics