

Functional Fungal Endophytes in *Coleus forskohlii* Regulate Labdane Diterpene Biosynthesis for Elevated Forskolin Accumulation in Roots.

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Abstract

Coleus forskohlii is a perennial medicinal shrub cultivated mainly for its forskolin content. The plant has been used since ancient times in ayurvedic traditional medicines for the treatment of hypertension, glaucoma, asthma, congestive heart failures, obesity, and cancer. Use of endophytic microorganisms presents a special interest for the development of value-added bioactive compounds through agriculture. Limited investigations have been undertaken on in planta enhancement of forskolin content using endophytic fungus in sustainable agriculture. Here we report specific roles of three fungal endophytes, *Fusarium redolens* (RF1), *Phialemoniopsis cornearis* (SF1), and *Macrophomina pseudophaseolina* (SF2), functionally acting as plant probiotic fungus, regulating secondary metabolite (forskolin) biosynthesis in *C. forskohlii*. The root endophyte, RF1, and shoot endophytes, SF1 and SF2, were found to enhance forskolin content by 52 to 88% in pot and 60 to 84% in field experiments as compared to uninoculated control plants. The three endophytes also enhanced total biomass owing to plant growth promoting properties. The expression of diterpene synthases (CfTPSs) like CfTPS1, CfTPS2, CfTPS3, and CfTPS4 were significantly upregulated in endophyte-treated *C. forskohlii* plants. Elevated expression of key diterpene synthases (CfTPS2) in the forskolin biosynthesis pathway, exclusively present in the root cork of *C. forskohlii*, was observed following SF2 endophyte treatment. Furthermore, endophyte treatments conferred a variety of antagonistic activity against nematode galls (80%) and plant pathogens like *Fusarium oxysporum*, *Colletotricum gloeosporioides*, and *Sclerotium rolfsii*. RF1 and SF1 fungal endophytes showed positive for IAA production; however, SF1 also indicated phosphate solubilization activity. Overall, the qualitative and quantitative improvement of in planta forskolin enhancement represents an area of high commercial interest, and hence, our work focused on novel insights for the application of three

fungal endophytes for in planta enhancement of forskolin content for *C. forskohlii* cultivation by a sustainable approach.

KEYWORDS: Agriculture; *Coleus forskohlii*; Diterpene synthases; Forskolin; Fungal endophyte

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