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Fungal endophytes of *Catharanthus roseus* enhance vindoline content by modulating structural and regulatory genes related to terpenoid indole alkaloid biosynthesis

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Not much is known about the mechanism of endophyte-mediated induction of secondary metabolite production in *Catharanthus roseus*. In the present study two fungal endophytes, *Curvularia* sp. CATDLF5 and *Choanephora infundibulifera* CATDLF6 were isolated from the leaves of the plant that were found to enhance vindoline content by 229–403%. The isolated endophytes did not affect the primary metabolism of the plant as the maximum quantum efficiency of PSII, net CO_2 assimilation, plant biomass and starch content of endophyte-inoculated plants was similar to endophyte-free control plants. Expression of terpenoid indole alkaloid (TIA) pathway genes, geraniol 10-hydroxylase (*G10H*), tryptophan decarboxylase (*TDC*), strictosidine synthase (*STR*), 16-hydoxytabersonine-*O*-methyltransferase (*16OMT*), desacetoxyvindoline-4-hydroxylase (*D4H*), deacetylvindoline-4-*O*-acetyltransferase (*DAT*) were upregulated in endophyte-inoculated plants. Endophyte inoculation upregulated the expression of the gene for transcriptional activator octadecanoid-responsive Catharanthus AP2-domain protein (*ORCA3*) and downregulated the expression of Cys2/His2-type zinc finger protein family transcriptional repressors (*ZCTs*). The gene for the vacuolar class III peroxidase (*PRX1*), responsible for coupling vindoline and catharanthine, was upregulated in endophyte-inoculated plants. These endophytes may enhance vindoline production by modulating the expression of key structural and regulatory genes of vindoline biosynthesis without affecting the primary metabolism of the host plant.

Endophytes are microbes that are found to be present in almost all plants studied[1]. They reside inside the host plant without causing any disease symptoms or harm[2,3]. Most of the endophytes enter the plant through root hairs or the stomata in leaves and then disseminate systemically throughout the plant. Endophytes may be present intercellularly or intracellularly and colonize roots, aerial parts, conduction vessels and seeds[4]. Endophytes may promote host plant growth, improve nutrient supply and protect plants from both biotic and abiotic stresses[5–8]. Endophytic microbes are the potential source of therapeutically important bioactive natural products[9]. Few endophytic fungi produce secondary metabolites similar to their host plant e.g. vinblastine and vincristine[10], taxol[11], azadirachtin[12], podophyllotoxin[13], deoxypodophyllotoxin[14], camptothecin[15] and hypericin[16]. A major limitation

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