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Endophytes of *Withania somnifera* modulate *in planta* content and the site of withanolide biosynthesis

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Abstract

Tissue specific biosynthesis of secondary metabolites is a distinguished feature of medicinal plants. *Withania somnifera*, source of pharmaceutically important withanolides biosynthesizes withaferin-A in leaves and withanolide-A in roots. To increase the *in planta* withanolides production, a sustainable approach needs to be explored. Here, we isolated endophytes from different parts of *W. somnifera* plants and their promising role in *in planta* withanolide biosynthesis was established in both *in-vivo* grown as well in *in-vitro* raised composite *W. somnifera* plants. Overall, the fungal endophytes improved photosynthesis, plant growth and biomass, and the root-associated bacterial endophytes enhanced the withanolide content in both *in-vivo* and *in-vitro* grown plants by modulating the expression of withanolide biosynthesis genes in leaves and roots. Surprisingly, a few indole-3-acetic acid (IAA)-producing and nitrogen-fixing root-associated endophytes could induce the biosynthesis of withaferin-A in roots by inducing *in planta* IAA-production and upregulating the expression of withanolide biosynthesis genes especially MEP-pathway genes (*DXS* and *DXR*) in roots as well.