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Rohitukine, a chromone alkaloid and a precursor of flavopiridol, is produced by endophytic fungi isolated from *Dysoxylum binectariferum* Hook.f and *Amoora rohituka* (Roxb).Wight & Arn

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Abstract

Rohitukine, a chromone alkaloid, has gained considerable international attention in recent years because of its novel semi-synthetic derivative, flavopiridol and P-276-00. Both these molecules are in advanced stages of clinical development and trial for cancer treatment. Recently, flavopiridol was approved as an orphan drug for treatment of chronic lymphocytic leukemia cancer. The natural occurrence of rohitukine is restricted to only four plant species, *Amoora rohituka* and *Dysoxylum binectariferum* (both from the Meliaceae family) and from *Schumanniophyton magnificum* and *Schumanniophyton problematicum* (both from the Rubiaceae family). Recently, an endophytic fungi isolated from *D. binectariferum* was reported to produce rohitukine in culture. In this study, we report the production of rohitukine and its subsequent attenuation by endophytic fungi, *Fusarium oxysporum* (MTCC-11383), *Fusarium oxysporum* (MTCC-11384) and *Fusarium solani* (MTCC-11385), all isolated from *D. binectariferum* and *Gibberella fujikuroi* (MTCC-11382) isolated from *Amoora rohituka*. The fungal rohitukine which was analyzed by HPLC, LC–MS and LC–MS/MS was identical to reference rohitukine and that produced by the plant. The rohitukine content in the mycelial samples ranged from 192.78 μg to 359.55 μg 100 g^{-1} of dry weight of and in broth it ranged from 14.10 to 71.90 μg 100 ml^{-1}. In all the fungal cultures, the production declined from first to fourth sub-culture. Studies are underway to unravel the mechanism by which the fungi produce the host metabolite in culture.

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Keywords

Dysoxylum binectariferum; *Amoora rohituka*; Rohitukine; Flavopiridol; Endophytic fungi