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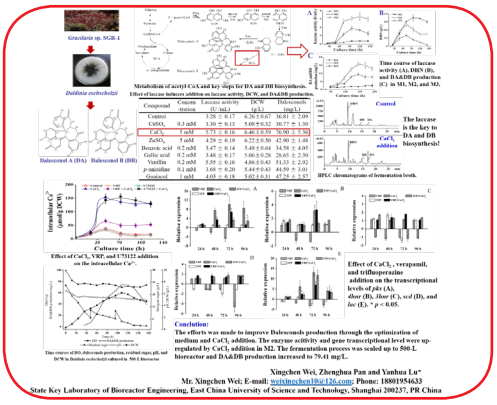
Study on the fermentation process of dalesconols A and dalesconols B by marine-derived fungus

Xingchen Wei, Zhenghua Pan and Yanhua Lu
East China University of Science and Technology, China

Dalesconols A (DA) and Dalesconols B (DB) are two skeletally unprecedented polyketides isolated from the marine-derived fungus Daldinia eschscholzii IFB-TL01. They are of significant immunosuppressive activity comparable to that of cyclosporine A (CsA), which is a clinically used immune-compromising compound. However, their further pharmaceutical researches have been severely restricted by the low production from submerged fermentation. Allowing for the urgent need in looking for new immunosuppressant, it is quite necessary to improve DA and DB production from the fermentation process. In this work, the effects of different media on fungus growth, Dalesconols biosynthesis and metabolites were firstly tested and compared. Additionally, the detection as well as analysis of four organic acids, intermediates DHN and the laccase activity analysis experimentally confirmed that laccase was the key role on Dalesconols biosynthesis. Based on the biosynthetic pathway of Dalesconols, DA and DB production was supposed to be elevated by the regulation of secondary metabolism in D. eschscholzii. Ca2+ induction was employed to up-regulate of laccase activity and further enhanced Dalesconols production (76.90 mg/L), which was 122.8% higher than that in the control. Ca2+ channel and calmodulin inhibitors were applied to investigate the involvement of calcium/calmodulin signaling in regulating Dalesconols production. The transcriptional levels of Dalesconols biosynthetic genes were up-regulated after CaCl2 addition and down-regulated after inhibitors were added. The results demonstrated that Ca2+ addition induces Dalesconols biosynthesis through up-regulation of Dalesconols biosynthesis genes via regulation of calcium/calmodulin signaling. Then, the fermentation process will scale up to 500-L bioreactor and Dalesconols production reached 79.41 mg/L. The information obtained in this work would be helpful to the large-scale production of DA and DB and other marine-derived secondary metabolites.



Biography

Xingchen Wei is a PhD student in State Key Laboratory of Bioreactor Engineering, East China University of Science and Technology, China. He devotes himself to study on the marine microbial fermentation process, especially marine-derived fungus. His main research involves gene transcription levels, protein expression levels, enzyme kinetics, cell metabolic level and reactor level.

weixingchen10@126.com

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