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Biotransformation Process for the Enhanced Production of the Pharmaceutical Agents Sakuranetin and Genkwanin: Poised to be Potent Therapeuctic Drugs

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Abstract : Sakuranetin, an antifungal agent and genkwanin, an anti-inflammatory agent, are flavonoids with several potential pharmaceutical applications. To produce such valuable flavonoids in large quantity, an Escherichia coli cell factory has been created. E. coli harboring O-methyltransferase (SaOMT2) derived from Streptomyces avermitilis was employed for regiospecific methylation of naringenin and apigenin. In order to increase the production via biotransformation, metK gene was overexpressed and the conditions were optimized. The maximum yield of sakuranetin and genkwanin under optimized conditions was 197 µM and 170 µM respectively when 200 µM of naringenin and apigenin were supplemented in the separate cultures. Furthermore, sakuranetin was purified in large scale and used as a substrate for in vitro glycosylation by YjiC to produce glucose and galactose derivatives of sakuranetin for improved solubility. We also found that unlike naringenin, sakuranetin effectively inhibits α-melanocyte stimulating hormone (α-MSH)-stimulated melanogenesis in B16F10 melanoma cells. In addition, genkwanin more potently inhibited angiogenesis than apigenin. Based on our findings, we speculate that these compounds warrant further investigation in vivo as potential new therapeutic anti-carcinogenic, anti-melanogenic and anti-angiogenic agents.

Keywords : anti-carcinogenic, anti-melanogenic, glycosylation, methylation
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