Strain Improvement and Synthetic Production Medium Development for Enhanced Production of Monacolin-K and Construction of an Expression Vector with *gpdA* Promotor of *Monascus* sp.

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Monacolin-K is a strong anti-hypercholesterolemic agent produced by *Monascus sp.* via polyketide pathway. High-yielding mutants of monacolin-K were developed through rational screening strategies adopted based on understanding of monacolin-K biosynthetic pathway. Further enhancement in monacolin-K production by these high-yielding producers was achieved not only by introducing a new production medium(K2 medium) developed through statistical Plackett-Burman design, but by investigating their physiological characteristics. Through the experiments for investigating various amino acids as putative precursors for the monacolin-K biosynthesis, it was found that production level of monacolin-K was remarkably increased when optimum amount of cysteine was supplemented into the respective production medium(K2 and BPM medium). We suggested that these phenomena might be related to the special roles of SAM(S-adenosyl methionine), a putative methyl group donor in the biosynthetic pathway of monacolin-K, demonstrating close interrelationship between SAM-synthesizing primary metabolism and monacolin-K synthesizing secondary metabolism. Namely, increase in the intracellular amount of SAM derived from the putative precursor, cysteine which was extracellularly supplemented into the respective production medium might contribute to the significant enhancement in the monacolin-K biosynthetic capability of the highly mutated producers. On the basis of these assumptions derived from the above fermentation results, we decided to construct efficient expression vectors harboring *gpdA* promoter of *Monascus sp.* and SAM synthetase gene(*metK*) cloned from *A. nidulans,* with the hope that increased intracellular level of SAM could lead to further enhancement in the monacolin-K production through overcoming a rate-limiting step associated with monacolin-K biosynthesis.