

High Throughput Screening for the Strain Development in Immunosuppressant Mycophenolic Acid Fermentation

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Abstract

Mycophenolic acid(MPA) blocking the synthesis of xanthosine monophosphate is a nonnucleoside inhibitor of inosine monophosphate dehydrogenase. Therefore mycophenolic acid is a drug currently used for immunosuppressive agent such as in transplantation of heart, kidney and liver. In addition, mycophenolic acid be able to used as antiviral, anti bacterial, antifungal, anti autoimmune diseases and anticancer agent with broad range.

In this study, assay methods were established such bioassay and thin layer chromatography and HPLC analysis for the development of producing strain and mycophenolic acid production. Specially, agar piece culture technique using agar diffusion method was designed for high throughput bioassay on the large bioassay dish. The high throughput bioassay was optimized for the isolation of greater number of strain and quantitative analysis of more distinct yield with convenience and speed. UV irradiation time for 99% lethality was 63 sec, NTG treatment time for 90% lethality was 35min and heat shock time at 55°C for 95% lethality was 30min in the case of spores of *Penicillium brevi-compacticum*. Isolated strains inoculated on agar pieces were cultured at 23°C for 4 days. *Candida albicans* was used as best test organism of various test microorganisms at 30°C overnight. Isolated strains through bioassay were secondly tested in flask culture and then finally tested in 7-L jar fermenter. 5 best strains were able to isolated through developed high throughput screening and about four times of mycophenolic acid yield was improved in MPA fermentation.