

A study on submerged culture production and solvent extraction of cyclosporin A (CyA) by
Tolypocladium inflatum ATCC 34921

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Cyclosporin A (CyA) is cyclic undecapeptide produced as secondary metabolites by various strains of fungi. It is considered as one of the first generation immunosuppressant used as immunotherapy for organ transplantation, autoimmune diseases with tacrolimus. Recently, it has attracted attention as a precursor of γ -hydroxy-N-methyl-L-Leu4-Cyclosporin A (CyA-4-OH) which is effective as a hair loss treatment agent. However, low production rates in submerged culture and high unit costs are still issues to be solved. In this study, *T.inflatum* ATCC 34921, known as one of the most producing CyA, was selected. Glucose consumption, pH, dry cell weight and CyA production were observed in the submerged culture. The effect of various seed culture media (Yeast extract & Malt extract; YM, Potato dextrose broth; PDB, and Semi synthetic media; SSM) was confirmed in order to increase CyA production. Solvent (Ethyl acetate and Butyl acetate) extraction for increasing yield and effective crystallization of CyA was conducted. As a result, the combination of using YM seed culture and ethyl acetate extraction shows the highest production of CyA (96 mg/L).