ABSTRACT

The present study deals with the enhanced productivity of β-lactum antibiotic cephalosporin C from the fungus *A. chrysogenum* by optimization of parameters and use of various integrated techniques. Sixteen different strains of *A. chrysogenum* were isolated from different soil samples collected from Mayo and Services Hospitals, Lahore. ISL-5 proved to be a better isolate with the CPC activity of 1.74±0.07 IU/g/min after primary screening. Solid state fermentation was carried out using linseed meal as a substrate. The selected isolate was proceeded for the optimization of various parameters viz. substrate level and moisture content. Strain improvement was done by induced mutagenesis of wild-type *A. chrysogenum* ISL-5. Mutagenesis was done by irritations (UV) and chemical mutagenesis (EMS). As a result of UV mutagenesis, UV-t2 was found to be a superior isolate with CPC productivity of 4.65±0.27 IU/g/min. Moreover, chemical mutagenesis was accomplished with 0.5 mM concentration of EMS for an interval of 25 min. The final mutant derivative (EMS-t5) was able to produce 16.87±0.5 IU/g/min of CPC. Resistance development in EMS-cys5 was performed using 0.25 µM of L-cysteine HCl. Various physical and nutritional parameters were optimized for enhancing CPC biosynthesis. It was found that optimized conditions i.e., substrate level of 25 g, MC-4 (pH 5.5) as a diluent, temperature 30°C and incubation time 48 h, stimulated the CPC activity to 25.61±0.96 IU/g/min by EMS-cys5 which is highly significant. The CPC production was further stimulated by optimization of nutritional parameters viz., Tween 80 (0.5%), ammonium nitrate (0.3%) and inclusion of various additive such as glycerol (0.2%), methionine (0.4%), and sesame oil (0.15%). Later, cell immobilization was used for the entrapment of fungal cells intending to produce a stable CPC by mutant variant EMS-cys5. During entrapment, several parameters were optimized particularly sodium alginate concentration (2.5%), holding time (80 min) and syringe size (24 G×$1^{1/4}$"). The final immobilized mutant cell yielded 103.2±2.66 IU/g/min of CPC under optimized parameters. It was concluded that the immobilized mutant strain not only exhibited higher CPC yield but was also able to synthesize a stable antibiotic and thus, could be commercially an attraction for the antibiotic producing community.