International Conference on
Bioprocess-2013
Fermentation Technology, Bioprocess and Cell Culture
October 28-30, 2013 Kansas City, USA

Polymer Based Fermentation of New Anti-inflammatory compounds, from a Myxobacterial strain

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Abstract

Myxobacteria do not biosynthesize a single natural product belonging to a structural type, but often an array of closely-related metabolites. At least 30 different epothilone variants have been reported from extracts of the epothilone producing Sorangium strain. Additionally, myxobacteria often produce numerous, structurally distinct secondary metabolites simultaneously. Nevertheless a majority of such new scaffolds synthesized by myxobacteria are in very dilute amount, which restricts their detectability and isolation. A way to overcome this limitation is by use of adsorbing resins in fermentation media which allows concentration of such active and rare metabolites. However use of such resins at fermentor level creates some practical difficulties. During our in-house isolation and screening strategy of myxobacteria for getting novel anti-inflammatory compounds, we optimized use of AMBERLITE™ XAD™1180N resin (a non-ionic, hydrophobic, macroreticular crosslinked polymeric adsorbent) during fermentation at shake-flask's levels. The resin was eluted using methanol. The metabolites in the eluates were screened and characterised. By using this polymer based fermentation process two novel anti-inflammatory compounds were discovered from the in-house myxobacteria strain PM0670013-(MTCC 5570). The two compounds were with molecular formula C13H21NO4 and C13H28N2O2; their respective molecular weights as 255.15 and 244.36 daltons. Both displayed significant activity against pro-inflammatory cytokines such as Tumor Necrosis Factor - _ (TNF-_) and Interleukins such as IL-6. Aerobic fermentation scale-up (20 L) for this strain was optimized so as to produce the same two metabolites in significant amounts in absence of the resin. The spin off in the bioprocess to produce the same novel scaffolds will be presented.

Biography

At Piramal Enterprises Ltd, Dr.Girish Mahajan-(Ph.D) is spearheading a team of Scientists involved in exploring Actinomycetes and Myxobacteria from extreme resources to acquire novel bioactive leads. His core expertise is in discovery & developing the microbial derived drugs by unique ways of fermentation of wild strain isolates. He has inherited enriched experience from Uni-Lever, Hoechst, Johnson & Johnson. He is a contributive member, mentor of ASM & AMI, member of board of studies of reputed universities in India. He has published 54 international papers, 10 patents & guided 25 postgraduates. Couple of his compounds are in preclinical development. He has received several national awards and recently; "OPPI Scientist Award-2012" by Organisation of Pharmaceutical Producers of India.