

Establishment of cost effective eco-friendly novel extraction methodologies to review the factor-response relationship hidden in the experimental data collected from the extraction process of potent bioactives by soft computing techniques

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Background: Extraction forms the very basic step in natural product drug discovery research. A poorly optimized and planned extraction methodology can jeopardize the entire mission.

Objective: To provide a vivid picture of different chemometric tools and planning for process optimization and method development in extraction of botanicals with emphasis on microwave assisted extraction (MAE) and ultrasound assisted extraction (UAE) of botanicals.

Methodology: Studies involving the applications of chemometric tools in combination with MAE of botanicals in presented here. While attempting to discover the significant extraction factors and then optimizing a response by fine tuning those factors, experimental design or statistical design of experiment (DoE) which is a core area of study in chemometrics has been used for statistical analysis and interpretations.

Result: In this paper a brief explanation of the different aspects and methodologies related to MAE of botanicals that have been subjected to experimental design are reviewed here in particular along with some general chemometric tools and the steps involved in its practice is presented. A detailed study on various factors and responses involved during the optimization is also presented.

Conclusion: This article shall assist to get a better inside into the chemometric strategies of process optimization and method development which shall in turn improve the decision making process in selecting influential extraction parameters.

Discovery of natural product inhibitors of siderophore biosynthesis in *Staphylococcus aureus* and *Bacillus anthracis*

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Siderophores are high-affinity iron sequestering agents produced by microorganisms contributing to the virulence of pathogenic species. Consequently, their metabolic pathway enzymes represent attractive targets for the discovery and development of new antibiotics. Targeted inhibition of the biosynthesis of virulence-associated siderophores staphyloferrin B of *Staphylococcus aureus*^{1,2} and petrobactin of *Bacillus anthracis*^{3,4} hold considerable potential as a treatment for methicillin-resistant *S. aureus* (MRSA) and anthrax infection, respectively. The biosynthetic pathways for both siderophores involve a nonribosomal peptide synthetase independent siderophore (NIS) synthetase, SbnE in staphyloferrin B and AsbA in petrobactin. NISs use similar carboxylate-containing substrates and have a high degree of structural homology, thus discoveries regarding a specific NIS's activity have bearing on other members of this enzyme family. By investigating methods to inhibit the enzymatic activity of SbnE and AsbA, we hope to devise strategies to shut down siderophore biosynthesis and thus, iron acquisition by *S. aureus*, *B. anthracis*, and other dangerous human pathogens. In this study, we employed a malachite green reporter assay⁵ in a high throughput screen for inhibitors of SbnE and AsbA activities in vitro, utilizing a library of 19,055 natural products extracts (NPEs) from cultured marine actinomycetes. This resulted in the identification of 35 extracts for SbnE and 22 extracts for AsbA that were prioritized based on their activities. Scale up and extraction of actinomycete strain 34946-N9I, which provided an extract highly active against both SbnE and AsbA enzymes, yielded at least 2 compounds with IC₅₀ value at 6.0 and 36.2 μ M, recorded against SbnE, respectively. Complete structure elucidation of compounds was conducted using extensive 1D/2D NMR and HRAPCIMS. The most active molecule was also subjected to in vivo assay against *S. aureus* in iron deficient media to observe the IC₅₀ value of 64 μ M.

Biography

Ashootosh Tripathi has completed his PhD at the age of 29 years from Nanyang Technological University, Singapore and continued on to join University of Michigan, USA as post-doctoral research associate. In his yet small scientific career, he has published 8 research papers in high impact journals, 1 book chapter and at least 9 conference papers.