Popular abstract: Separation Process Design for the Isolation and Purification of Natural Products

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Natural products are defined as secondary metabolites produced by plants and form a vast pool of compounds with unlimited chemical and functional diversity. Many of these secondary metabolites are high value added chemicals that are frequently used as ingredients in food, cosmetics, pharmaceuticals and other consumer products. Therefore, process technology towards industrial scale production of such high value chemicals from plants has significant value. Natural products can be obtained in pure form via synthetic or semi-synthetic route, but due to their complicated nature these methods have not been developed to the extent of industrial production for majority of natural products. Thus, isolation and purification of such natural products from plants is the most viable way to obtain natural products in pure form.

This PhD project is mainly concerned with the design of separation process to isolate and purify natural products from plants at conceptual level that can serve as a robust foundation for detailed process design. In this work, a methodology consisting of multiple separation techniques is formulated to isolate and purify natural products from plants. Heuristics have been provided for initial selection of separation techniques and operating conditions. The key factor in designing separation processes with multiple unit operations is to determine the synergy between them which in turn demands molecular level understanding of process streams. Therefore, the methodology is fortified with process analytical technology (PAT) framework which consists of tools such as advanced process analyzers (HPLC, NMR, LC-MS, GC-MS, XRPD, Raman spectroscopy etc) combined with chemometric methods. PAT framework is explicitly emphasized as it can help to a great extent in analysis of process streams at molecular level, thereby providing process information crucial for determining synergistic effects between different unit operations.

In this work, the formulated methodology has been used to isolate and purify artemisinin, an antimalarial drug, from dried leaves of the plant *Artemisia annua*. A process flow sheet is generated consisting of maceration, flash column chromatography and crystallization unit operations for extraction, partial purification and final purification of artemisinin, respectively. PAT framework is used extensively to characterize the process streams at molecular level and the generated process information is used to further optimize the process flow sheet. Chemometric methods have been used to extract molecular level information for understanding the process streams in relation to their separation operations.