Abstract

There have been significant efforts into improving efficiency, reducing waste and enhancing quality and control in the research and manufacturing of active pharmaceutical ingredients (APIs), natural products, value-added chemicals, and materials, in order to reduce costs while increasing the sustainability of the manufacturing processes.

Recently, applying continuous-flow technologies to the synthesis of valuable compounds has become widespread, particularly in academia. Although the pharmaceutical industry still heavily relies on multipurpose batch or semi-batch reactors, interest is rising towards continuous flow production of synthetic molecules, including highly functionalised and chiral compounds. Furthermore, the industry has typically focused on classical synthetic chemistry and small molecules. However, in recent decades there has been a move towards incorporating bioprocesses and biotechnology for organic synthesis and for the creation of biological agents for therapeutic purposes.

This dissertation focuses on the use of continuous-flow and microfluidics for the improvement of chemical and biochemical processes in the vortex fluidic device (VFD). First, PdNPs were immobilised within cellulose paper using a fast and effective reduction of palladium acetate with hydrogen gas after 90 seconds. The Pd-cellulose catalyst was applied in the VFD for scalable and efficient continuous flow hydrogenation reactions at ambient temperature and pressure. High catalyst stability and re-usability is demonstrated along with the chemoselective and scalable synthesis of industrially important fine chemicals.

The research was extended further to the rapid covalent immobilisation of enzymes through APTES-gluteraldehyde functionalization of cellulose paper. The stable and re-usable

enzyme-cellulose catalyst can be easily and efficiently used in the VFD for continuous-flow biocatalysis with comparable rates to batch. The method was further applied to the continuous-flow synthesis of a valuable chiral terpene, aristolochene, through the immobilisation of aristolochene synthase from *Aspergillus terreus*.

Immobilisation of biomolecules were explored for applications beyond biocatalysis. A bladder cancer biomarker, DJ-1, was immobilised onto nickel affinity resin through a fused histidine-tag, coating the inner surface of the VFD tube, for continuous-flow phage-displayed antibody fragment and peptide selections. Using this system, Fab and peptide binders were isolated for high affinity and specificity for DJ-1, from two highly diverse libraries.

The mechanical energy of the VFD was further explored for accelerating enzymatic catalysis of protenaise K in extracting DNA from formalin-fixed American lobster tissue. Through optimization, the optimal VFD rotational speed was identified for recovery of PCR-amplified DNA; 500+ base pairs were sequenced from the organism, with shorter amplicon lengths more consistently obtained.

Overall the work has established methods for employing catalysis, biocatalysis, immobilisation, and biotechnology in thin-films in the VFD for process enhancement for chemical and biochemical applications.