Immobilized enzyme reactors based on nucleoside phosphorylases and 2′-deoxyribosyltransferase for the in-flow synthesis of pharmaceutically relevant nucleoside analogues

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Abstract

In this work, a mono- and a bi-enzymatic analytical immobilized enzyme reactors (IMERs) were developed as prototypes for biosynthetic purposes and their performances in the in-flow synthesis of nucleoside analogues of pharmaceutical interest were evaluated. Two biocatalytic routes based on nucleoside 2′-deoxyribosyltransferase from Lactobacillus reuteri (LrNDT) and uridine phosphorylase from Clostridium perfrigens (CpUP)/purine nucleoside phosphorylase from Aeromonas hydrophila (AhPNP) were investigated in the synthesis of 2′-deoxy, 2′,3′-dideoxy and arabinonucleoside derivatives. LrNDT-IMER catalyzed the synthesis of 5-fluoro-2′-deoxyuridine and 5-iodo-2′-deoxyuridine in 65–59% conversion yield, while CpUP/AhPNP-IMER provided the best results for the preparation of arabinosyladenine (60% conversion yield).

Both IMERs proved to be promising alternatives to chemical routes for the synthesis of nucleoside analogues. The developed in-flow system represents a powerful tool for the fast production on analytical scale of nucleosides for preliminary biological tests.

Keywords

Biocatalysis; Immobilized enzyme reactors; Nucleoside analogues; Nucleoside 2′-deoxyribosyltransferases; Nucleoside phosphorylases