

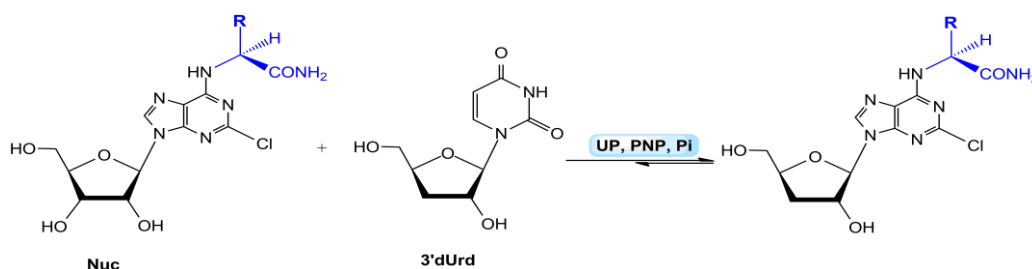
POSTER PRESENTATIONS

STRUCTURAL MODIFICATION OF 2-CHLOROCORDYCEPIN VIA N⁶-AMINO ACID SUBSTITUTION

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Cordycepin (3'-deoxyadenosine) has a wide range of biological activities. However, its therapeutic use is limited by rapid inactivation by the enzyme adenosine deaminase (ADA). The introduction of a halogen (chlorine) into the 2nd position of the purine ring ensures the resistance of such analogues to ADA action and increases their effectiveness. Nevertheless, 2-chlorocordycepin is characterized by high nonspecific cytotoxicity. The introduction of bulky amino acid substituents at the N⁶ position has been proposed as a strategy to reduce this toxicity. Such modifications will change the physicochemical properties of the molecule and affect its interaction with cellular targets. These modifications are expected to neutralize the toxic effect of the chlorine-containing purine nucleus while potentially maintaining metabolic stability with respect to ADA.



N ⁶ -substituent	R
L-Met	CH ₂ CH ₂ SCH ₃
L-Leu	CH ₂ CH(CH ₃) ₂
L-Val	CH(CH ₃) ₂
L-Tyr	CH ₂ C ₆ H ₄ OH
L-Thr	CH(OH)CH ₃
L-Ala	CH ₃
L-S-Me-Cys	CH ₂ SCH ₃

The synthesis of target nucleosides was carried out via enzymatic transglycosylation using bacterial purine nucleoside phosphorylase (PNP) and uridine phosphorylase (UP). 3'-Deoxyuridine was used as the 3-deoxyribose donor. Optimization of the substrate ratios and enzyme concentrations made it possible to achieve high yields of the target N⁶-substituted products, ranging from 68% to 78%. The *in vitro* cytotoxic profiles of all obtained N⁶-amino acid derivatives of 2-chloro-3'-deoxyadenosine were evaluated using the standard MTT assay. Remarkably, none of the synthesized compounds exhibited any significant cytotoxic activity against the tested cell lines (HEK293, HepG2, L929, and MCF-7), even at the maximum tested concentration of 100 μM.

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