# DESIGN, SYNTHESIS AND POTENT CHEMOTHERAPEUTIC ACTIVITY OF CERTAIN AZOLE NUCLEOSIDES

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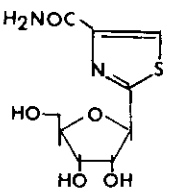
The azole C-ribonucleosides synthesized in our laboratory have shown a broad spectrum of chemotherapeutic activity. Recently, we have reported the potent antitumor activity of 2-β-D-ribofuranosylthiazole-4-carboxamide (1, tiazofurin) [J. Med. Chem., 25, 107 (1982)]. Since then additional in vivo antitumor data related to tiazofurin has been obtained. The 4-carboxamidine, 5'-phosphate and 3',5'-cyclic phosphate analogs of tiazofurin have now been synthesized for biological evaluation. The selenium analog of tiazofurin, 2-β-D-ribofuranosylselenazole-4-carboxamide (2) has recently been synthesized [J. Med. Chem., 26, 445 (1983)]. In addition to its reported potent antitumor activity, 2 has also been found to exhibit broad spectrum antiviral activity in vitro against both RNA and DNA viruses. A new heterocyclic ring analog of tiazofurin, 3-β-D-ribofuranosyl-1,2,4-oxadiazole-5-carboxamide (3), has recently been synthesized in our laboratory by condensation of 2,5-anhydro-3,4,6-tri-O-benzoyl-D-allonamidoxime (4) with methyl oxalylchloride followed by ammonolysis. The detailed synthetic studies, structure activity relationships and the potent chemotherapeutic activity exhibited by this class of novel C-ribonucleosides (see table) will be presented.

| Azole Nucleoside | Substituent | Biological Activity (*Under Evaluation) | | |
|---|---|---|---|---|
| | | Antiviral | Antitumor | Enzyme Inhibition |
| Thiazole | 4-Carboxamide | Significant | Potent | Guanine Nculeotide IMP Dehydrogenase |
| Thiazole | 4-Carboxamidine | * | Moderate | Purine Phosphorylase |
| Thiazole | 5'-Phosphate | Significant | Significant | Guanine Nucleotide |
| Thiazole | 3',5'-Cyclic Phosphate | * | Moderate | * |
| Selenazole | 4-Carboxamide | Potent | Potent | Guanine Nucleotide |
| Selenazole | 5'-Phosphate | * | Significant | Guanine Nucleotide |
| Oxadiazole | 4-Carboxamide | * | * | * |

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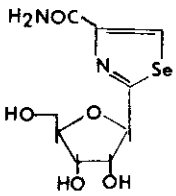


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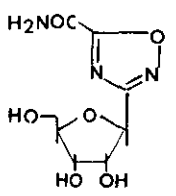


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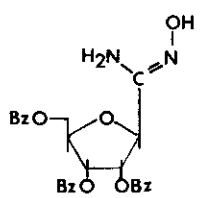


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