

DESIGN, SYNTHESIS AND POTENT CHEMOTHERAPEUTIC ACTIVITY OF CERTAIN AZOLE NUCLEOSIDES

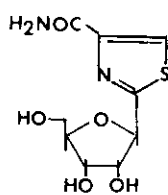
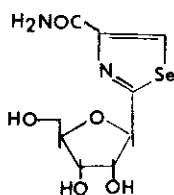
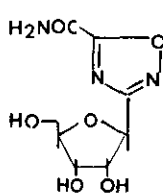
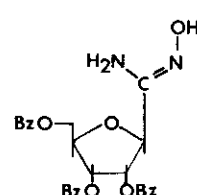
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The azole C-ribonucleosides synthesized in our laboratory have shown a broad spectrum of chemotherapeutic activity. Recently, we have reported the potent antitumor activity of 2- β -D-ribofuranosylthiazole-4-carboxamide (1, tiazofurin) [J. Med. Chem., 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-ribofuranosyl-selenazole-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-allon-amidoxime (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 Nucleotide 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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