RTI Author Awards Series

Antiviral Activity of C-5 Substituted Tubercidin Analogs

Bergstrom, D.E., Brattesani, A.J., Ogawa, M.K., **Reddy**, **P.A.**, Schweickert, M.J., Balzarini, J., De Clercq, E. (1984). Antiviral activity of C-5 substituted tubercidin analogs. *Journal of Medicinal Chemistry*, 27 (3):285-292.

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DNA/RNA component analogs are a class of antiviral products used in the prevention of viral replication in infected cells. The most commonly used in this class are acyclovir and AZT. Once they are activated, they work as antimetabolites by being similar enough to nucleotides to be incorporated into growing strands of DNA, but they act as chain terminators and stop DNA polymerase.

Tubercidin, an adenosine analog, is an antibiotic isolated from the bacterium Streptomyces tubercidicus. Tubercidin is highly cytotoxic and interferes with numerous cellular processes such as de novo purine synthesis, methylation of tRNA, and protein and nucleic acid syntheses. However, C-5 substituted derivatives of tubercidin are more selective because of their incorporation into RNA and appear to be good antiviral agents. As potential drugs, one factor that favors the utility of these compounds is their stability to deamination by adenosine deaminase and to glycosidic bond cleavage by purine nucleoside phosphorylases, the two major pathways by which bioactive purine nucleoside analogs are deactivated. This paper describes the result of our antiviral tests with the C-5 substituted tubercidin derivatives in cell cultures infected with Coxasackie virus B4, herpes simplex virus type 1 or 2, parainfluenza virus type 3, poliovirus type1, reovirus type 1, Sindbis virus, vaccinia virus, and vesicular stomatitis virus.

In conclusion, the primary objective of this paper has been to point out the potential significance of C-5 substituted tubercidin analogs: They can be built to be significantly less toxic than the nucleoside tubercidin and other similar antibiotics such as toyocamycin and sangivamycin, and yet still retain activity against both RNA and DNA viruses.

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