

Design & development of unnatural nucleosides as antiviral & anti-cancer agents

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Unnatural nucleosides are the variants (chemically modified analogs) of five natural nucleosides which constitute the structure of DNA and RNA. Since the first preparation and later, the isolation of unnatural nucleosides from plants; nucleoside chemistry has become a field of extensive medicinal importance. These nucleosides perturb the growth of cancer cells by interfering with replication process and while showing antiviral properties, act on reverse transcriptase. Since the availability of designing tools like QSAR and CADD the two main approaches in design of unnatural nucleosides are the modulation of hydrogen bondings originating from the base and change in the conformation and configuration of ribose sugar counterpart. Currently approved anticancer drugs like gemcitabine and clofarabine (working on polymerase and ribonucleotide reductase) are the fluorinated analogs of the adenosine and cytidine respectively. Similarly, zidovudine (AZT) and zalcitabine (ddC) are the examples of first line of unnatural antiviral drugs acting on reverse transcriptases. Unnatural nucleosides can be categorized into four broad categories namely, base modified, sugar modified, C-Nucleosides and carbocyclics. Design of antiviral drugs, apart from molecular modeling and computer aides also takes its clues from some unnatural nucleosides isolated from natural sources like neplanocins and aristeromycin. This special class of unnatural nucleosides is known as carbocyclic nucleosides, and is currently major source of antiviral drugs for HBV and HCV therapy. The salient feature of carbanucleosides lies in the fact that they don't really have a furanose sugar ring, instead a puckered cyclopentane ring. This gives them two major advantages, making them resistant to enzymatic lyses and at the same time being recognized by receptors of natural nucleosides.

Biography

Ram C. Mishra has completed his Ph.D. in 2005 from Central Drug Research Institute, India and did his postdoctoral studies from Rega Institute for Medical Research, Belgium and Georgia State University, USA. He is currently at the College of Pharmacy of The University of Georgia. He has published more than 25 papers in reputed journals and has six patents. He also reviews grants for Portugese Foundation of Science and Technology.

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