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Design and synthesis of anti-viral modified nucleosides based on a new concept to win the battle against emerging viruses

Mary emerging viral infectious diseases, for example, the spreads of AIDS, Flu, West Nile Viruses, SARS, Ebola and so on, are causing major threats to global public health. Viruses adapt themselves to the environmental change by mutation. Mutation causes the emergence of mutants resistant to drugs and or vaccines. Therefore, it has been thought that the treatment of viral infectious diseases is very difficult due to the emergence of resistant mutants. However, I would like to propose a new concept that mutation is the heaven-sent opportunity for the development of anti-viral modified nucleosides for the following reasons. Mutation is that viruses change their genes by taking incorrect (not programmed) nucleosides into them. This indicates that the substrate selectivity of viral nucleic acid polymerases is not strict. On the other hand, human beings do not change their genes by taking incorrect nucleosides. This indicates that the substrate selectivity of human nucleoside polymerases is very strict. Thus, by taking advantage of the different substrate selectivity, it will be possible to develop anti-viral modified nucleosides which are selectively incorporated into viral nucleic acids and inhibit their nucleic acid polymerases. We have been working on the development of anti-viral modified nucleosides based on the concept. The development of EFdA (prevents the emergence of resistant mutants, is supremely high anti-HIV active and low toxic) and CycloSal-EdA [active against Flu-virus, Japanese encephalitis virus (JEV) and Ebola] will be presented. The development of the facile synthetic method of these modified nucleosides will be also discussed.

Biography

Hiroshi Ohrui has received his PhD degree (1971) from The University of Tokyo. He has worked for Dr. J. J. Fox at Sloan Kettering Institute for Cancer Research (1972), for Dr. J. G. Moffatt at Syntex Research (1973) and for The Technical University of Darmstadt (1990). His research interests cover organic synthesis, chemical biology and chiral discrimination.

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