ANTIVIRAL DRUGS

Viruses are the ultimate expression of parasitism: they not only take nutrition from the host cell but also direct its metabolic machinery to synthesize new virus particles. Viral chemotherapy, therefore, is difficult, as it would require interference with cellular metabolism in the host. However, virus directed enzymes have been identified in the infected cell and some viruses have few enzymes of their own which may have higher affinities for some antimetabolites or inhibitors than the regular cellular enzymes.

CLASSIFICATION

Anti-Herpes virus

Idoxuridine, Acyclovir, Valacyclovir, Famciclovir, Ganciclovir*, Foscarnet*

Anti-Retrovirus

(a) Nucleoside reverse transcriptase inhibitors (NRTis): Zidovudine ((AZT), Didanosine, Zalcitabine*, Stavudine, Lamivudine, Abaca vir

(b) Nonnucleoside reverse transcriptase inhibitors (NNRTis): Nevirapine, Efavirenz, Delavirdine*

(c) Protease inhibitors: Ritonavir, Indinavir, Nelfinavir, Saquinavir, Amprenavir*, Lopinavir

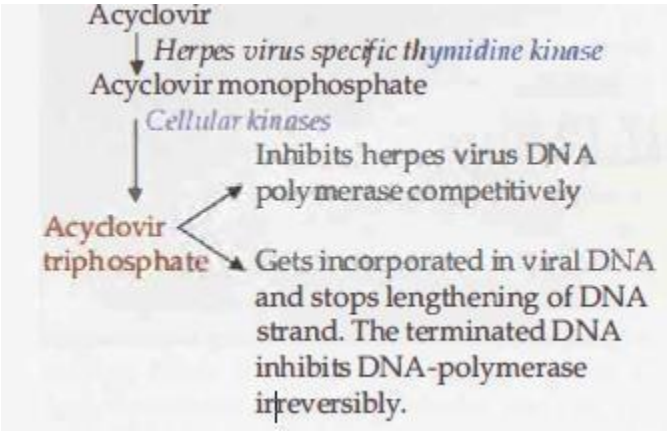
Anti-Influenza virus Amantadine, Rimantadine*

NonselectiVe antiviral drugs Ribavirin, Lamivudine, Adefovir dipivoxil, Interferon a * Not yet marketed in India.

ldoxuridine It is 5-iodo-2-deoxyuridine (IUDR); acts as a thymidine analogue. It was the first pyrimidine antimetabolite to be used as antiviral drug. It competes with thymidine, gets incorporated in DNA so that faulty DNA is formed which breaks down easily. It is effective only against DNA viruses.

Acyclovir

This deoxiguanosine analogue antiviral drug requires a virus specific enzyme for conversion to the active metabolite that inhibits DNA synthesis and viral replication.



Use

1 . Genital Herpes simplex

2. Mucocutaneous H.

3. H. simplex encephalitis (type I virus):

4. H. simplex (type I) keratitis:

5. Herpes zoster

6. Chickenpox:

Adverse effects

Topical: stinging and burning sensation after each application.

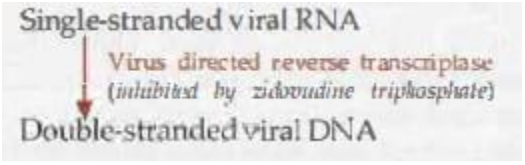
Oral: The drug is well tolerated; headache, nausea, malaise and some CNS effects are reported.

Intravenous: rashes, sweating, emesis and fall in BP occur only in few patients.

Nucleoside reverse transcriptase inhibitors(NRTis)

Zidovudine It is a thymidine analogue (azidothymidine, AZT), the prototype NRTI. After phosphorylation in the host cell-zidovudine triphosphate selectively inhibits viral reverse transcriptase (RNA-dependent DNA polymerase) in preference to cellular DNA polymerase.

On the template of single-stranded RNA genome of HIV a double-stranded DNA copy is produced by viral reverse transcriptase. Finally, viral particles are assembled and matured. Zidovudine thus prevents infection of new cells by HIV, but has no effect on virus directed DNA that has already integrated into the host chromosome



Non-nucleoside reverse transcriptase inhibitors (NNRTis)

Nevirapine (NVP) and Efavirenz (EFV): *These are nucleoside unrelated compounds whichdirectly inhibit HlV reverse transcriptase without the need for intracellular phosphorylation.*

Retroviral protease Inhibitors (Pis)

An aspartic protease enzyme encoded by HIV is involved in the production of structural proteins and enzymes (including reverse transcriptase) of the virus. The large viral polyprotein is broken into various functional components by this enzyme. This protease acts at a late step in HIV replication, i.e. maturation of the new virus particles when the RNA genome acquires the core proteins and enzymes. Five protease inhibitors-Indinavir (IDV), Nelfinavir (NFV), Saquinavir (SQV), Ritonavir (RTV) and Lopinavir.

ANTI-INFLUENZA VIRUS DRUGS

Amantadine

Chemically, it is a tricyclic amine unrelated to any nucleic acid precursor, but inhibits replication of influenza A virus (a myxovirus). It appears to *act at an early step (possibly uncoating) as well as at a late step (viral assembly) in viral replication*