

Antiviral Drugs :

I. Virustatics. (((Inhibit viral replication)))

A. Against respiratory viruses :

1. Against influenza virus :

Amantadine (Orally) → Eliminated by renal.

Rimantadine → Eliminated by liver(**mainly**).

Inhibits viral **uncoating**.

- Prevention or for early treatment of influenza A2.
- Useful in Parkinsonism.

Neuraminidase inhibitors : Inhibit **release** of new viral progeny which occurs by budding & may **block** viral entry into host cells.

Oseltamivir (Tamiflu) (Orally) → Prev. & treat. of influenza A or B, or virulent H5N1 virus of avian influenza.

Eliminated by liver & renal.

Zanamivir (Relenza) (Inhalation) → Prev. & treat. of influenza A or B.

2. Against RSV (Respiratory Syncytial Virus) :

Ribavirin (Inhalation) for RSV infection in infants.

Ribavirin (Orally) with interferon-alpha-2b for chronic hepatitis C.

Eliminated by renal.

B. Against herpes viruses :

1) Against herpes simplex & varicella-zoster virus :

Acyclovir $\xrightarrow{\text{Thymidine kinase}}$ Acycloguanosine **monophosphate**

Acycloguanosine **triphosphate** $\leftarrow \text{Host kinase}$

- Inhibition of viral DNA synthesis.
- Premature termination of proviral DNA chain.

(**Topically**) as ointment for herpetic keratitis & as cream for oral & genital herpes simplex infection.

(**Oral**) for primary treat. & prev. recurrence of genital & oral herpes and for herpes zoster. F=20%.

(**IV**) for severe herpes simplex or varicella zoster infection in immuno-suppressed patients & for cases of herpetic encephalitis.

Eliminated by renal.

Valacyclovir(Orally) *F=60%

Converted by **FPHE** into **acyclovir**

Effective as **IV acyclovir**.

Famciclovir & Penciclovir(Orally) :

Famciclovir $\xrightarrow{\text{FPHE}}$ converted to **Penciclovir** \rightarrow Inhibit viral DNA syn.

It is used for herpes zoster.

It is used for genital or oral herpes.

Others : For herpetic keratitis :

Idoxuridine(Eye drops, Ointments)

Vidarabine(3% ointment).

Trifluridine(1% eyedrops)

Inhibition of viral DNA syn. by incorporated into DNA instead of thymidine.

2) Against cytomegala virus (CMV) :

Ganciclovir(IV) \rightarrow converted into triphosphate \rightarrow Useful for CMV retinitis.

It may cause neutropenia, anemia, & thrombocytopenia (due to bone marrow depression).

Foscarnet(IV) \rightarrow Useful for ganciclovir-resistant CMV and for acyclovir-resistant herpes simplex or zoster.

Eliminated by renal.

Cidofovir(IV) \rightarrow **Phosphorylated inside cells** \rightarrow Useful for CMV retinitis.

longer $t_{1/2}$. Given with probenecid to decrease its nephrotoxicity.

C. Against HIV (in AIDS patients) :

1. Nucleoside Reverse Transcriptase Inhibitors [NRTIs] :

Must be converted to **triphosphate** form by host enzymes to become active.

Mechanism : - It inhibits reverse transcriptase (RT) competitively.
- Causes premature termination of proviral DNA chain.

Zidovudine \rightarrow Synthetic analogue of **thymidine**. (Most commonly used).

Eliminated by liver & renal.

CSF level is about 60% of plasma.

Didanosine \rightarrow Synthetic analogue of **adenosine**.

Zalcitabine \rightarrow **Cytidine** analogue \rightarrow Used commonly with **zidovudine**. Long acting.

Stavudine \rightarrow **Thymidine** analogue \rightarrow Short $t_{1/2}$. Reduced by **zidovudine**; so avoid.

Needs intracellular **phosphorylation** to become active.

Excreted by kidney (reduced by **probenecid**).

Lamivudine \rightarrow **cytidine** analogue \rightarrow Long acting & least toxic.

Also useful against hepatitis B virus and can be given with or without interferon-alpha 2b.

- Best additive to **zidovudine** or **stavudine** , Best given in combination.
- Alternative is oral **adefovir** or **tenofovir**.

2. Non-Nucleoside RTIs (NNRTIs) :
Nevirapine, Delaviradine & Efavirenz.

- Don't require intracellular **phosphorylation**.
- Directly inhibit viral RT of HIV.

3. Protease inhibitors (PIs) :
Indinavir(Most commonly used), **Ritonavir, Saquinavir & Nelfinavir.**

- Inhibits protease that converts large viral polyproteins into smaller polyproteins for virions.

Note : Best results in HIV infection treatment are obtained with combination of 4 drugs : 2 NRTIs + 1 NNRTI + 1 protease inhibitor.

4. Fusion inhibitors :
Enfuvirtide(IV) → Binds to surface glycoprotein of HIV, preventing its attachment and penetration into host cells.

5. Others :
Tenofovi → Analogue of **adenosine** → Used in combination therapy.

Also useful against lamivudine-resistant HBV.

Eliminated by renal.

Abcavir(Orally) → **guanosine** analogue.

Metabolized by alcohol DH and GT enzymes in liver.
Slow resistance which needs multiple mutations.

Emtricitabine → **cytidine** analogue → Approved for HIV.

II. Increase immune resistance against viruses :

a. Interferons :



- stimulation of intracellular enzymes in virally infected cells which leads to inhibition of translation of viral mRNA by ribosomes.
- It may also inhibit formation of viral mRNA.

IFN-alpha (2a, 2b) (SC or IM) →



- Are prepared by DNA recombinant biotechnology.
- IFN- α is produced by leukocytes.

- 1) Hepatitis B or C virus infections.
- 2) Severe herpes zoster.
- 3) Kaposi's sarcoma.
- 4) Intra-lesional injection into viral genital warts.

a. Stimulation of intracellular enzymes in virally infected cells which leads to inhibition of translation of viral mRNA by ribosomes; it may also inhibit formation of viral mRNA.

b. Stimulate cellular immune defences against virus , and also against some cancers.

b. Immunoglobulins :

Palivizumab (IM monthly) → Humanized monoclonal antibody against F glycoprotein on surface of RSV.



Usually with ribavirin.

Specific IGs → Against some viruses. e.g. **CMV, rabies, RSV, VZV.**



Provide immediate passive immunity; may prevent infection if used early.

Non-specific gamma globulin → Against heterogenous viral infections. e.g. measles, rubella, varicella.



(Pooled from plasma of convalescent patients).

- It can prevent response to active immunization using specific live virus vaccines: e.g. measles, rubella.
- Main SE is hypersensitivity anaphylactic reactions.

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بالتوفيق للجميع

