ANTIVIRAL AND ANTIAIDS AGENTS

Antiviral drugs are a class of medication used specifically for treating viral infections. Viruses are not quite proper living thing, consist of a genome and sometimes a few enzymes stored in a capsule made up of protein and rarely covered with lipid layer. They are the smallest of all self-replicating organisms able to pass through filter that retain the smallest bacteria.

Virus conducts no metabolic process on their own. They invade the host cell, which may be bacteria, animal or plant cell. The virus turns the biochemical system of the host cell to its own purposes completely subverting the infected cell.

Viral diseases include influenza, rabies, poliomyelitis, yellow fever, ornithosis, mumps, measles, ebola human immunodeficiency syndrome, herpes, warts and small pox.

Viral life cycle varies with species, but they all share a general pattern can be sequenced as follows:

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Virus
  ↓
Adsorption
  ↓
Penetration
  ↓
Uncoating
  ↓
Transcription
  ↓ Reverse transcriptase
  ↓
Translation
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Adsorption: Attachment of virus to the host cell.

ii) Penetration: Penetration of virus into the cell.

iii) Uncoating: The genetic material or viral genome (DNA or RNA) passes into the host-cell, leaving the capsid covering outside of the host cell.

iv) Transcription: Production of viral mRNA from the viral genome.

v) Translation: Viral genome enters the cytoplasm or nucleo plasma and direct or utilizes the host nucleic acid machinery for the synthesis of new viral protein and also for the production of more viral genome. The viral protein modifies the host cell and allows the viral genome to replicate by using host and viral enzyme. This is often the stage at which the cell is irreversibly modified and eventually killed.

vi) Assembly of the viral particle: New viral coat protein assembles into capsid and viral genomes.

vii) Release of the mature virus from the cells by budding process or rupture of the cell and repeat of the process, in fresh host cell. Since the host cell machinery is totally utilized for production of new virions, the normal cell function ceases at the time of replication.

General approaches for treating the virus infection by antiviral agents are:

a. Interference of virus attachment to the host.

b. Inhibition of virus associated enzymes.

c. Inhibition of transcription process.

d. Inhibition of translation process.

e. Interference with viral regulatory process.

f. Interference with viral glycosylation, phosphorylation, etc.,

g. Interference with assembly of viral protein.

h. Interference with release of virus from cell surface membrane.
Antiviral drug can be classified as:


v) Interferons

vi) Miscellaneous agents: eg. Foscarnet sodium, Ribavirin.

II. According to the enzyme inhibition, it can also be classified as:


iii) Nucleoside antimitabolite: eg. Ribavirin.


III. According to treatment protocol it is classified as

i) Treatment of respiratory virus infections

ii) Treatment of herpes and cytomegalovirus infections.
   a. Purine nucleotides: eg. Acyclovir, Ganciclovir, Vidarabine
   b. Pyrimidine nucleotides: eg. Trifluridine, Idoxuridine
   c. Phosphorus derivatives: eg. Foscarnet sodium

iii) Treatment of Human Immunodeficiency Virus (HIV) infection
   a. Reverse Transcriptase inhibitor
      i) Purine derivatives: eg. Didanosine
      ii) Pyrimidine derivatives: eg. Zidovudine, Stavudine
   b. Protease inhibitors: eg. Saquinavir, Indinavir, Ritonavir, Nelfinavir, Amprenavir, Lopinavir
Purine Nucleoside and Nucleotide

A. Acyclovir (Acivir, Cyclovir, Zovirax)

\[
\begin{array}{c}
\text{HN} \\
\text{N} \\
\text{CH}_2 \text{OCH}_2 \text{CH}_2 \text{OH} \\
\end{array}
\]

9-[2-(Hydroxyethoxy) methyl] guanine

Use: It is effective against several DNA viruses including HSV-1, HSV-2 and against Varicella Zoster Virus (VZV). An advantage is that uninfected human cell are unaffected by the drug. It is used for short term treatment of shingles and chicken pox caused by VZV.

Ganciclovir (Ganguard, Vitrasert, Cytovene)

It is an analogue of Acyclovir, with an additional hydroxy methyl group on the acyclic side chain.

\[
\begin{array}{c}
\text{HN} \\
\text{N} \\
\text{CH}_2 \text{OH} \\
\text{CH}_2 \text{O} . \text{CH} \cdot \text{CH}_2 \text{OH} \\
\end{array}
\]

9-[(1,3 - Dihydroxy - 2- propoxy)methyl] guanine

Pyrimidine Nucleoside and Nucleotide

Idoxuridine (Toxil)

\[
\begin{array}{c}
\text{HOH}_2 \text{C} \\
\text{HO} \\
\end{array}
\]

5-Iodo-2’- deoxyuridine
Idoxuridine is a nucleoside containing halogenated pyrimidine and is an analogue of thymidine.

Miscellaneous Agents

Ribavirin (Ribavin, Ribamac)

\[
\begin{align*}
\text{HOH}_2\text{C} & \quad \text{N} \\
\text{N} & \quad \text{N} \\
\text{HO OH} & \quad \text{CONH}_2
\end{align*}
\]

1β-D- Ribofuranosyl - 1H - 1,2,4 - triazole - 3- carboxamide

ANTI – HIV AGENTS

Human immuno deficiency virus (HIV) is the cause of acquired immuno deficiency syndrome (AIDS). Both HIV-1 and HIV-2 cause AIDS, but HIV-1 is found world wide. HIV is one of the human T-cell lymphotropic retro virus which infect and kills helper (CD4) T- lymphocytes resulting in the loss of cell mediated immunity and the host will develop opportunistic infections. While there is no permanent cure of AIDS without prevention or elimination of HIV infection, AIDS patients can prolong their life, if early diagnosed and treatment started.

Didanosine (Dinex, Dinosin)

\[
\begin{align*}
\text{O} & \quad \text{HN} \\
\text{N} & \quad \text{N} \\
\text{HOH}_2\text{C} & \quad \text{O}
\end{align*}
\]

2',3'- Dideoxyinosine

Zidovudine (Zidovir, Zilion, Zidine)
HIV protease is an enzyme that is essential for viral growth. The inhibitors act on HIV protease and prevent post-translation processing and budding of immature viral particles from the infected cell.

**Atazanavir (Atazor)**