We need antiviral drugs for the following reasons:

1. The number of antiviral drugs is very small because the viruses are obligate intracellular parasites. It's difficult to induce selective toxicity against viruses.

2. Drugs are relatively ineffective because many cycles of viral replication occur during the incubation period when the health of the patient is well.

3. Some viruses are latent in the cells, e.g., Herpes virus.

4. The emergency of drugs resistant by the viral mutant is a concern.

5. Against viruses to which vaccine are not available.

6. To reduce morbidity and economic loss due to viral infection.

7. To treat increased number of immune suppression patients.

Antiviral drugs may be target of the following stages in viral replication:

- Attachment of the virus to host cell and uncoating of the viral genome
- Reverse transcription of the certain viral genome
- Translation of viral protein
- Assembly maturation and release of progeny virus particles

The viruses are obligate intracellular parasites, making it difficult to induce selective toxicity against them.
**Mechanism of action**

**Inhibition of early Events**

- Drugs include:
  - **Amantidin**: Synthetic amine (1)
  - **Rimantidin**: Is derivative of amantidin (2)

Inhibit influenza A viral uncoating

- So use as:
  - Prophylactically
  - Therapeutically

Mainly used against herpes and HIV

**Inhibition viral nucleic acid synthesis**

- A sugar nitrogen base (Nucleoside analogs) (N-a)

- Nucleotide analog

- **Nitrogen**
- **Sugar**
- **Phosphate group**

Mode of action

- attach to phosphate group.
- they have ability to persist in cell.

**Some of analogie 5 may be incorporated into nucleic acid**

- So

**Inhibit cellular enzyme as well as viral encoded enzyme**

- Inhibition of enzyme of metabolic pathway of Purina and pyrimidin
- Inhibition of polymerases which is important for nucleic acid replication
- Block further synthesis of NA
Nucleoside analogs include

1. Acyclovir

1. Name as Acyclovir or zovirax

2. Active against Acyclovir

HSV-1

HSV-2

HSV-2

HSV-1

varicella

zoster

little effect

DNA viruses

host cell

3. Mode of action

Acyclovir HSV thymidine kinase

Acyclovir monophosphate

Cellular kinase

Acyclovir triphosphate (ACV-TP)

Incorporated into growing herpes DNA chain

Inhibition the action of the viral DNA polymerase

Explanation

Infected of cells with HSV or HIV

Viral thymidin kinase is formed by the viruses inside the cell

Which action

The cyclovir converted it to ACV-TP

Then the action of cellular kinase

ACV-TP

4. Acyclovir usage

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Acyclovir

Use topically as

- No effect against recurrent herpetic lesion
- Treatment eye herpetic lesion
- Prophylactic

Effect against

- Replicating viruses
- But not against latent infection in ganglia

Oral administered of ACV prevent reactivation of latent herpes virus infection

Effect against

- Herpetic lesion in immune compromised patient
- HSV-1 encephalitis by I.V
**Ganciclovir**

- **Mode of action**
  - Inhibition of viral DNA polymerase by the same mechanism of Acyclovir
  - But CMV not have thymidin kinase
  - So directly acting upon by cellular kinase
  - Inhibition viral DNA polymerase

**Idoxuridine**

- **Name**
  - IDU, IUDR

- **Mode of action**
  - Its halogenated pyrimidine
  - Incorporated into viral and cellular DNA after phosphorylation by cellular kinase
  - Mis matching bairing of quinine

**Act against cytomegal virus**

**Name as Methyl quinine derivatives**

**Not use systemic because it affect also against cellular DNA**

**So too toxic when use systemically**

**Usage or clinical useful**

**Topical TR. of keratoconjunctivitis due to HSV**
Vidarabin

- Medical useful
- Name as Adenine arabinoside
- Effect against Varicella zoster, HSV, CMV
- Vaccinia, Hepatitis B V
- Mvented 1976 use to topical treatment

Trifluridin

- Name as Triflurothymidin
- Effect against Flsal,2, Vaccinia
- Its Fluorinated pyramiding nucleoside
- Topical Px for herpes keratitis

Ribavirin

- Medical use
- Effective against I.V for Lassa fever
- Its synthetis neocleoside related S. quanosine
- Its act against synthesis of viral mRNA

Aerosot TR. of Resp. syngytial virus (RSV) and influenza virus

Medical useful

Effect against

Name as

Adenine

arabinoside

Mode of action

Its purin analogue

Block viral DNA synthesis

Inhibit action of viral DNA polymerase

Vaccinia

Flsal,2

Topical Px for herpes keratitis

HSV

CMV
**Zidovudine**

**Name as**
- Its thymidine analogue use against Retro viruses because its Reverse transcriptase inhibitor

**Mode of action**
- **Zidovudin**
- Phosphorylation by cellular kinase
- **Zidovudin Triphosphat**
- Incorporation into viral DNA proviral
- So inhibit the action of viral reverse transcriptase
- Chain terminal

**Invention**
- 1987
- First anti virus drug for TR. of HIV orally

**Medical use**
- Act against
  - HIV
  - Hepatitis B-virus
Didanosin
Name as Dideoxyinosin (ddI)
Invented in 1991
Inhibit HIV reverse transcriptase and blocking synthesis of proviral DNA

Zaicilabine
Invented 1992
Act against HIV

Stavudin
Name as duT
Act against HIV

Lamivudin
Invented in 1995
Act against HIV

Stavudin
Invented in 1995
Act against HIV

Hepatitis B

Cidofavire
Mode of action
Inhibite proviral DNA polymerase
So terminate growing DNA chain

Nucleoside Reverse transcriptase inhibitor

Nevirapin
Act against HIV
Mode of action
Bind directly to RT enzyme
Invented in 1996

Protease inhibitors

Indinavire
HIV 1996

Ritonavire
HIV 1996

Saquinavire
HIV 1995

Types

They inhibit protease required at late stage of Replication to cleavage structural protein to form mature viruses
Other types of antiviral agent

- Foscarnet
  - Name as phosphonophormic acid
  - Its organic analog of inorganic pyrophosphate

- Methisazone
  - It inhibits protein synthesis of pox viruses by blocking translation of late mRNA

Viral DNA polymerase
- Act against RT
- Action against HSV, CMV, EBV, HBV, Retro v.

Interferon (IFN)
- They are host-coded protein produced by all vertebrate species
- Inducer of interferon synthesis
  - IFN Alpha
    - Produced by leukocyte induced by viruses DS (RNA)
  - IFN-Beta
    - Produced by fibroblast induced by viruses DS (DNA)
  - IFN-gamma
    - Produced by lymphocyte
    - Induced by mitogen

RNA viruses stronger than DNA viruses
- DS RNA
- Bacterial endotoxin and mitogen
Characters of IFN

- Its host species specific
- Not viral species specific in human or any other species
- Play primary important role in defence of the host against viral infections

1. Viral infection induce production of interferon from the host cell
2. Interferon bind to uninfected cells and stimulate these cell to produce of anzyme or protein (antiviral protein)
3. These antiviral protein blocking translation of mRNA to viral protein

Uninfected cell

Viral mRNA

Antiviral protein

IFN molecules

Host

Virus

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These antiviral proteins are

- Protein kinase (ds RNA dependent)
  - phosphorylation of inactivation of cellular inhibition factor
  - Inhibition of protein synthesis

- Oligonucleotide synthetase
  - Z-A synthetase
  - Activation of cellular endonuclease
  - Degradation of viral mRNA

- Cellular endo kinase
  - Production of specific viral protein
  - Block activation of protein kinase

Some of viruses counteract interferons by

- Neutralize of IFN-gam receptor
- Activation cellular inhibitor of protein kinase
  - e.g.
  - Influenza n.
  - Polio v.

Examples:
- Adeno
- Herpes