

Antiviral Drugs



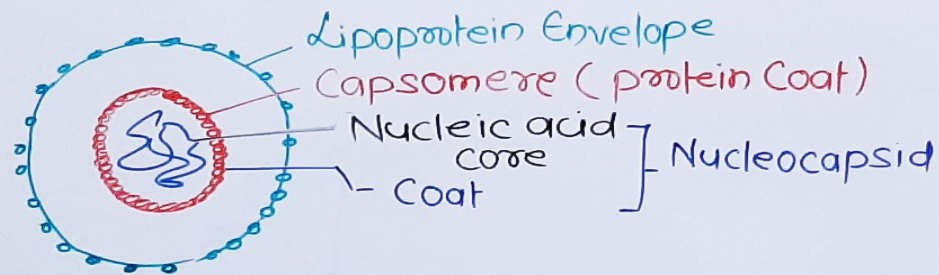
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Videos

ANTI VIRAL DRUGS

VIRUSES :- are the obligate intracellular parasites that depends on metabolic processes of host cells for their replication. VIRUSES either DNA or RNA



1 DNA VIRUSES -

- # Poxviruses - Small pox
- # Herpesviruses (Vercella Zoster, H. Simplex, CMV)
- # Adenoviruses - RTI & Conjunctivitis
- # Papova viruse - Papilloma (warts & Verruca)

2. RNA VIRUSES -

- # Orthomyxo viruses - Influenza (Type A, B & C)
- # Paramyxo viruses - Mumps, measles, RTI
- # Rhabdo viruses - Rabies
- # Toga viruses - Rubella
- # Arbo viruses - Yellow fever, Rift Valley fever
- # Hepatitis viruses - Hepatitis
- # Arena viruses - Lassa fever
- # Retro viruses - HIV (AIDS), T-cell leukaemia
- # CORONA VIRUSES - SARS-CoV (2003), HCoV NL63 (2004), HKU1 (2005), MERS Cov (2012), SARS-Cov-2 (2019)
- # COVID-19

① Antiherpes → Idoxuridine, Trifluridine, Acyclovir, Valacyclovir, Famciclovir, Ganciclovir, Cidofovir, Foscarnate

② Antiinfluenza - Amantadine, Rimantadine, Oseltamivir, Zanamivir, Peramivir

③ Antihepatitis -

Ⓐ For Hep B - Lamivudine, Entecavir, Tenofovir, Adefovir, Telbivudin

Ⓑ For Hep C - Ribavirin, Sofosbuvir, Interferon α , Simeprevir, Daclatasvir, Ledipasvir,

Anti Retroviruses Drugs

① NRTIs - Zidovudin (AZT), Stavudine, Lamivudin, Didanosin, Abacavir, Tenofovir

② NNRTIs - Nevirapin, Efavirenz, Delavirdine

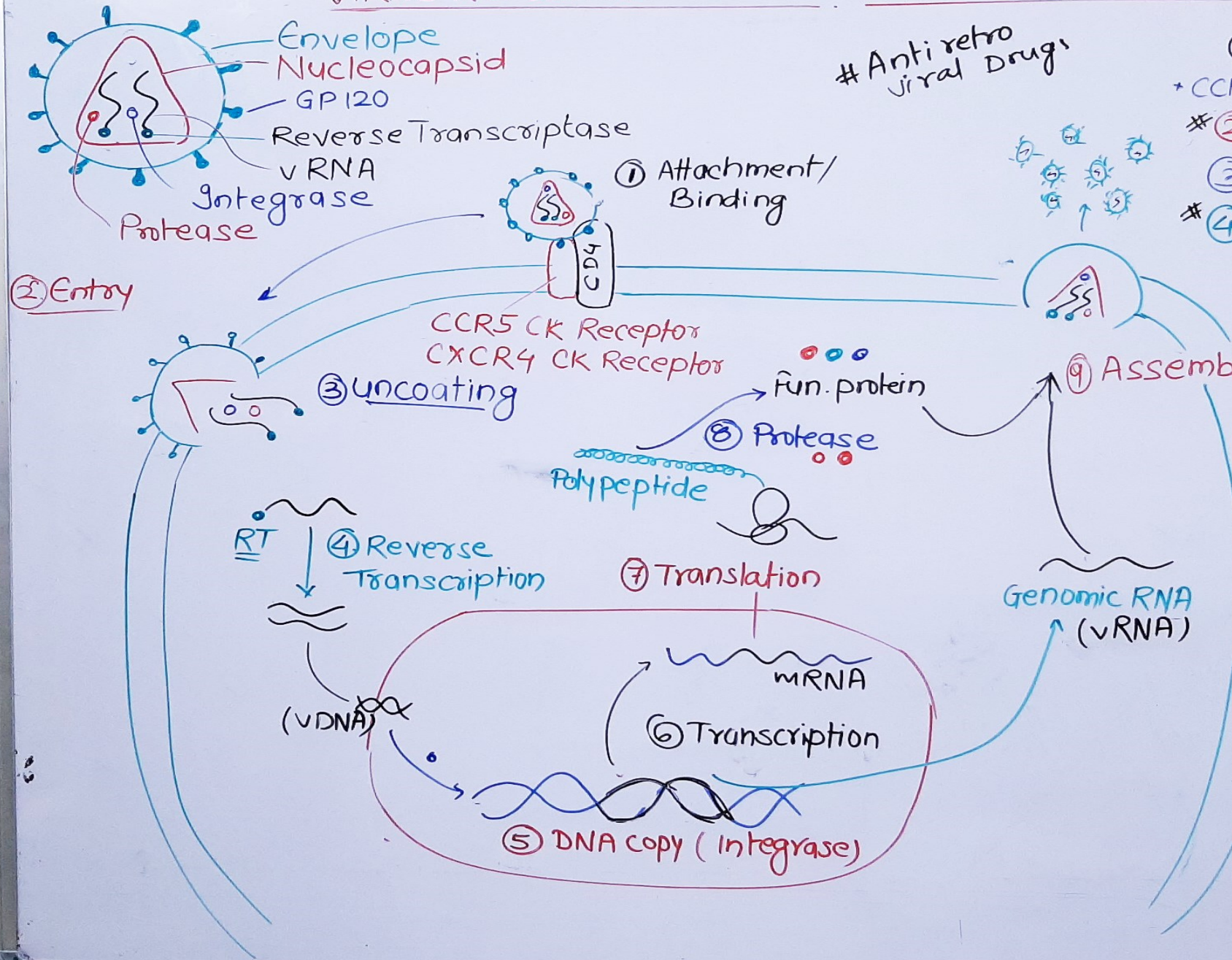
③ Protease Inhibitors (PIs) - Ritonavir, Indinavir, Nelfinavir, Saquinavir, Lopinavir

④ Entry Inhibitor - Enfuvirtide

⑤ CCR-5 Receptor Inhibitor - Maraviroc

⑥ Integrase Inhibitor - Raltegravir, Dolutegravir

VIRAL REPLICATION & SITE OF ACTION OF ANTI VIRAL DRUGS



Anti retro viral Drugs

- ① Immunoglobulins - HBIG, HRIG
- * CCR5 R. blocker - Maraviroc
- # ② Enfuvirtide (T-20)
- ③ Amantadine, Rimantadine
- # ④ RTIs → NRTIs (Zidovudine) - NNRTIs (Nevirapine)

⑤ Raltegravir

⑦ InFA, Methisazone

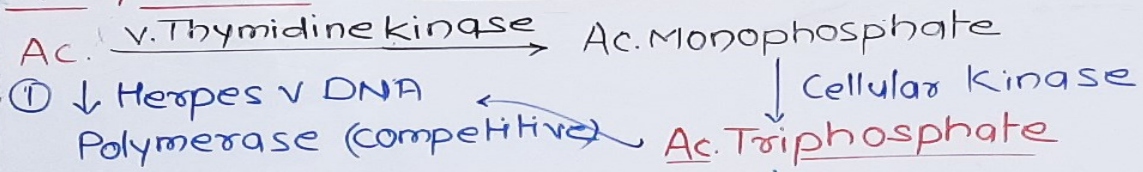
⑧ Protease Inhibitor
 # HIV-1 → Ritonavir (NAVIR)
 HepC → Simeprevir (PREVIR)

⑨ Amantadine, Rifampicin

DNA Synthesis Inhibitor
 ↳ Acyclovir, Idoxuridine
 • HSV-1 - Oral, ocular, face
 HSV-2 - Genital

vRNA polymerase Inhibitor
 Foscarnate

ACYCLOVIR → Deoxyguanosine Analogue



② Incorporated into vDNA & stops lengthening of strand & terminated DNA inhibits DNA polymerase irreversibly.

- # Acyclovir selectively taken up by infected cell, and has lower toxicity for host cell (C. Index - 100 fold)
- # Activity → HSV-1 > HSV-2 > VZV = EBV
- # No active against - CMV, GPAT

RESISTANCE - HSV & VZV, due to mutatioⁿ on viral thymidine kinase Enz & ↓ affinity for Acyclovir

PKINETICS: - # 20% Bioavailability, # Widely distributed cross the BBB, P^o excreted through urine (GF & TS) unchanged form. # t_{1/2} = 2-3h

- Dose should be reduce in renal impairment
- # Topical Applicatioⁿ has negligible systemic absorptⁿ but penetrates cornea well

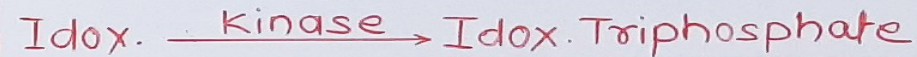
USES - # Genital Herpes (HSV-2) - P^o & Recurrent disease

- # Mucocutaneous (HSV-1) - Lips & Gums
- # HSV2-Encephalitis,
- # HSV1-Keratitis
- # chickenpox, # Herpes Zoster

ADR - ① Topical - Stinging & Burning Sensation
② oral - nausea, Malaise, headach, CNS effects
③ I.V. → ↓ BP, ↓ GFR, tremors, lethargy, convulsion

"IDOXURIDINE" - 5-iodo-2-deoxyuridine

- # Act as a Thymidine Analogue
- # It was 1st pyrimide antiviral antimetabolite



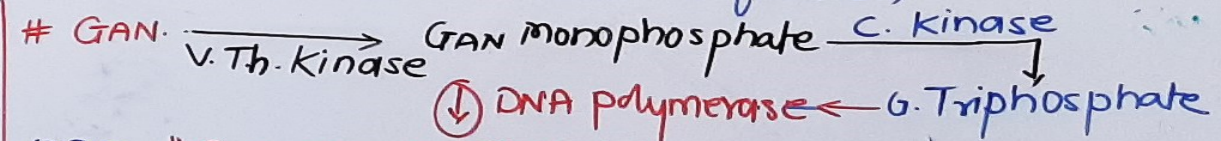
↓
Compete with the Thymidine & produce Faulty DNA → ↓ DNA Synthesis

- # Also affects the host cells DNA

USE - 0.5% eye ointment - Keratoconjunctivitis

"GANCICLOVIR" - Acyclovir Analogue

- # It is also used in CMV infection



ADR - "Bone Marrow Toxicity"

KINETIC - < 10% BA, So Valganciclovir prodng used

- # Excreted through urine, t_{1/2} = 2-4h
- t_{1/2} > 24h in CMV infected cell

USE - Against CMV infection in immunocompromised patient (AIDS)

ANTI INFLUENZA DRUGS

- Influenza Virus (RNA Virus) - Type A, B, & C
- # Majority of Human infection & Epidemic - Type A
 - # Subtypes of Influenza A is characterized by its hemagglutinin (H) and Neuraminidase (N), surface glycoproteins - have produce epidemics & pandemics
 - # H5N1 (bird flu, 1997) - Epidemic in east Asia
 - # H1N1 (Swine Flu, 2009) - Pandemic & Epidemic

"Amantadine" - Tricyclic Amine (1960s)

- MOA - # It inhibits the viral M_2 protein (ion channel) and prevents the Uncoating of viral genome.
- # Also inhibit Assembling of viral particle
 - # Active against "Influenza A"
 - # Not active against - Influenza B & H5N1 (A)
 - # Also having Antiparkinson Activity

Resistance - Mutatⁿ on M_2 viral protein, NO cross resistance

ADR - # Ivedo Reticularis, # GI distress, # Dizziness, # Ataxia # Slurred speech

CI = pregnancy (Teratogenic effect)

Dose - 100 mg BD for 5 days - Rarely used

Rimantadine - Methyl-derivative of Amantadine
- Similar Action & use (Type A)
= have longer $t_{1/2}$

"OSELTAMIVIR" - "Sialic acid Analogue"

- # Broad spectrum - In: A, H5N1, & H1N1 & Influenza B
- MOA - Ester prod^g $\xrightarrow[\text{Intestine}]{\text{HOH}}$ Os $\xrightarrow[\text{Liver}]{\text{Esterase}}$ Os-Carboxylate
- # Inhibits Influenza virus "Neuraminidase" (responsible for releasing of progeny virions from inf cells)
- PKinetic \rightarrow 80% BA, Metabolite are excreted through urine, $t_{1/2}$ - 6-10h.
- * Dose Reductⁿ require in renal insufficiency
- * Not used in Infant due to lack of metabolic Enz

Resistance - Seasonal influenza, H5N1

ADR - Nausea, Gastric irritatⁿ, Abdominal Pain, headach, weakness, skin reaction

ZANAMIVIR

- # Active Against Influenzae A & B, H5N1, H1N1
- # Inhibit - Neuraminidase
- # Given by inhalation (due to low oral BA)
- # Reserved for Osetamivir-Resistant strain
- # ADR - Bronchospasm, Headach, Dizziness

"PERAMIVIR" -

- # New single iv. dose for Influenza A & B, H5N1 & H1N1 approved by USFDA - 2014

ANTI HEPATITIS VIRUS DRUGS

1. Hepatitis-B (HBV) - DNA virus - **Suppressive**
2. Hepatitis-C (HCV) - RNA virus - **Curative**

Anti HBV - Lamivudine, Entecavir, Adefovir, Tenofovir, Telbivudine,

Entecavir → "Guanosine Analogue", most active and 1st line drug for chronic Hep-B. * Anti HIV
↳ En. $\xrightarrow{\text{Phosphorylat}^n}$ En. **Triphosphate** → X HBV DNA polymerase
X - HIV RT

Adefovir - "Monophosphate Analogue of AMP"
↳ Active against HBV & other DNA & RNA viruses
↳ Ad. → Ad. **diphosphate** → X HBV DNA polymerase
↳ Indicate for Chronic Hep-B (HIV patient)

Tenofovir disoproxil Fumarate - AMP Analogue
↳ Active against HBV & HIV
↳ Ten. → Ten. **diphosphate** - X HBV DNA polymerase
- X HIV R. Transcriptase
↳ Adefovir & Tenofovir - Nephrotoxic (ARF)

Telbivudine - Newer Anti HBV, Thymidine Analogue
↳ Tel. → Tel. **Triphosphate** - X HBV DNA polymerase

All → Inhibit the HBV DNA polymerase & Terminate the DNA chain after phosphorylation by cellular Kinase Enzyme

ANTI HCV - Ribavirin, Interferon- α , Sofosbuvir, Simeprevir, Daclatasvir, ledipasvir, Velpatasvir
↳ The aim is to attain "Sustained viral Response (SVR)" means undetectable HCV-RNA in blood for 6 months after completion of therapy.

↳ Conventional - Oral Ribavirin + Injected PegINF α
Ribavirin - (Purine Analogue), Broad Spectrum Antiviral drug → HCV, Influenza A & B, Respiratory Syncytial virus & other DNA & double stranded RNA virus
Rib → Rib. mono & triphosphate - X GTP Synthesis
- X viral RNA Synthesis

ADR - Teratogenic, BMS, Haemolytic Anaemia

INF- α → (Cytokines produced by host cell)
↳ It binds with the cell surface receptor and → X viral penetratⁿ, X v. mRNA syn., X Assembly
↳ Use - HBV, HCV, AIDS related Kaposi's Sarcoma, Herpes viral infectⁿ.
↳ ADR - Neurotoxicity, BMS, Thyroid dysfunctⁿ, ↓ BP, Arrhythmia

Simeprevir - HCV protease inhibitor

Sofosbuvir - X Nonstructural protein 5B (NS5B)
- X (HCV RNA polymerase)

Daclatasvir, Ledipasvir, Velpatasvir - X NS5A
- X RNA replication

Dal & Val - HCV - Genotype 1-6
* Lad - HCV Genotype 1, 4, 5, 6

LDV + SOF
VEL + SOF