Tikrit University
College of Veterinary Medicine

Lect. 4-Virology

Subject name: **Antiviral Drugs**
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Lecturer name: Prof. Dr. Nihad Abdul-Hussain Jafar and Assist.Prof.Dr. Agharid Ali Hussein
Academic Email:
agharidalrasheed@tu.edu.iq
nihadabid73@tu.edu.iq

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Antiviral Drugs

Because viral replication depends on metabolic activities of the host cell, therefore there are little compounds act as antiviral compared with antibacterial or antifungal.

The main steps in viral replication cycle that may be inhibited by antiviral drugs are:

1- Inhibitors of Attachment: inhibition of attachment is the mode of action of antibodies and there is no drugs act by this way, but there is recombinant CD4 molecules (alone or combined with antibodies) can inhibit attachment of HIV with CD4+ T lymphocytes and macrophages under laboratory conditions.

2- Inhibitors of Penetration or Uncoating: Amantadine and rimantadine are amino compounds inhibit infection with RNA viruses by inhibiting uncoating or early transcription of RNA or both of them. At low concentrations can inhibit the assembly. Used as prophylactic drugs against influenza virus or as treatment if used at early stage of infection.

3- Inhibitors of Nucleic acid synthesis: Now most of the antiviral drugs are analogs of nucleotides which interfere with replication of DNA or RNA of the virus. The activity of the drug depends on its specificity to viral enzymes rather than host enzymes. These includes:

a- Idoxuridine and Trifluorothymidine: Idoxuridine is analogs of pyrimidine that blocks nucleic acid synthesis through incorporation into DNA in place of thymidine to produce a non-functional molecule. Used locally in the treatment of herpes infection and do not used systemically because it is converted by phosphorylation and inhibit the DNA replication of the virus and host cells. Trifluorothymidine also are Pyrimidine analogs and used as local treatment of herpes infection which resist treatment with Idoxuridine.

b- Adenine Arabinoside (Vidarabine): is a purine that inhibits DNA polymerase. It is phosphorylated intracellularly to its active form like the preceding two agents, but it has some selective action, in that herpes group viral polymerase are about 15 to 30 times more susceptible than the host cell enzyme. Thus, systemic toxicity is less than with IUdR and Trifluorothymidine, but destruction of blood-forming elements in the bone marrow can occur with high dosages.

c- Acyclovir (acycloguanosine): It is very active against replicating herpes simplex virus. It is first phosphorylated to its monophosphate by virally specified thymidine kinase (but not cellular kinases), limiting the presence of the derivative to virus-infected cells. It is then further phosphorylated by cellular kinases to its triphosphate form, which selectively binds and inhibits viral DNA polymerase. Because of its mode of action, acyclovir has little toxicity for host cells.

Cytomegalovirus does not encode viral thymidine kinase and is thus resistant to this agent.

d- Foscarnet: Is a pyrophosphate analog that directly inhibits DNA polymerase of all herpesviruses, RNA polymerase of influenza viruses, and reverse transcriptase or retroviruses. Unlike acyclovir, it does not require activation by viral specified thymidine kinase and, thus, is highly active against CMV and acyclovir-resistant herpes simplex. It is nephrotoxic and must be administered by continuous intravenous infusion.

e- Zidovudine (azidothymicine): Is a thymidine analog that inhibits HIV replication in vitro. It is phosphorylated in vivo by cellular enzyme to the triphosphate form, which inhibits viral reverse transcriptase and terminates viral DNA elongation. Delay onset of HIV infection but has significant toxicity for bone marrow, producing severe anemia.

f- Didanosine and Zalcitabine: Its mode of action resemble that of Zidovudine and used against HIV.

4- Inhibitors of viral assembly and release: There is no antiviral agent that acts on viral assembly and release is in clinical use. Methisazone acts as a specific inhibitor of poxvirus infections by blocking late viral protein synthesis leading to production of incomplete virus.

5- Interferons.

6- Antibiotics: Rifamycin inhibit poxvirus and oncogenic viruses. In oncogenic viruses it inhibits RNA-dependent DNA polymerase.

Actinomycin D inhibits DNA-dependent RNA polymerase therefore inhibit DNA viruses.