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Antiviral drugs

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Virology, Stephen N.J. Korsman, Gert U. van Zyl, ... Wolfgang Preiser 2012

Jawetz Melnick & Adelbergs Medical Microbiology, Stefan Riedel (Author), Stephen Morse (Author), Timothy Mietzner (Author), Steve Miller.

Viruses, Pandemics, and Immunity, By Arup K. Chakraborty and Andrey S. Shaw

Antiviral Drugs

Antiviral drugs are a class of medication used for treating viral infections. Most antivirals target specific viruses, while a broad-spectrum antiviral is effective against a wide range of viruses. Unlike most antibiotics, antiviral drugs do not destroy their target pathogen; instead they inhibit its development.

The Number of antiviral drugs is very small because:

1- The viruses are obligate intracellular parasite so its difficulty to induce selective toxicity against viruses.
2- Drugs are relatively ineffective because many cycles of the viral replication occur during incubation period when the health of the patient in well.
3- Some of viruses are latent in the cells e.g. Herpes virus.
4- The emergency of drugs resistant by the viral mutant.

When do we need antiviral drugs?

1- Against viruses to which vaccine are not available
2- To reduce of morbidity and economic loss due to viral infection.
3- To treat number of immune suppression patient.

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

1- Attachment of the virus to host cell and uncoating of the viral genome.

a- Using agents which mimic the virus-associated protein (VAP) and bind to the cellular receptors.

b- Using agents which mimic the cellular receptor and bind to the VAP.

2- Reverse transcription of the certain viral genome.

One way of doing this is to develop nucleotide or nucleoside analogues that look like the building blocks of RNA or DNA, but deactivate the enzymes that synthesize the RNA or DNA once the analogue is incorporated. This approach is more commonly associated with the inhibition of reverse transcriptase (RNA to DNA) than with "normal" transcriptase (DNA to RNA).

3-Assembly maturation and release of progeny virus particles.

Mechanism of action

A- Inhibition of early Events Drugs

B- Inhibition viral nucleic acid synthesis

A-Inhibition of early Events Drugs includes:

Amantadine (synthetic amine Inhibit influenza A viral uncoating) and **Rimantadine** (Is derivative of amantadine have action against A and B influenza virus with fewer side effect)

B-Inhibition viral nucleic acid synthesis

a. suger nitrogen base (Nucleoside analogs)
b. nucleotide analogs
c. Nucleoside Reverse transcriptase inhibitor
d. Protease inhibitors

a.suger nitrogen base (Nucleoside analogs)

Mainly used against herpes and HIV

Mode of action

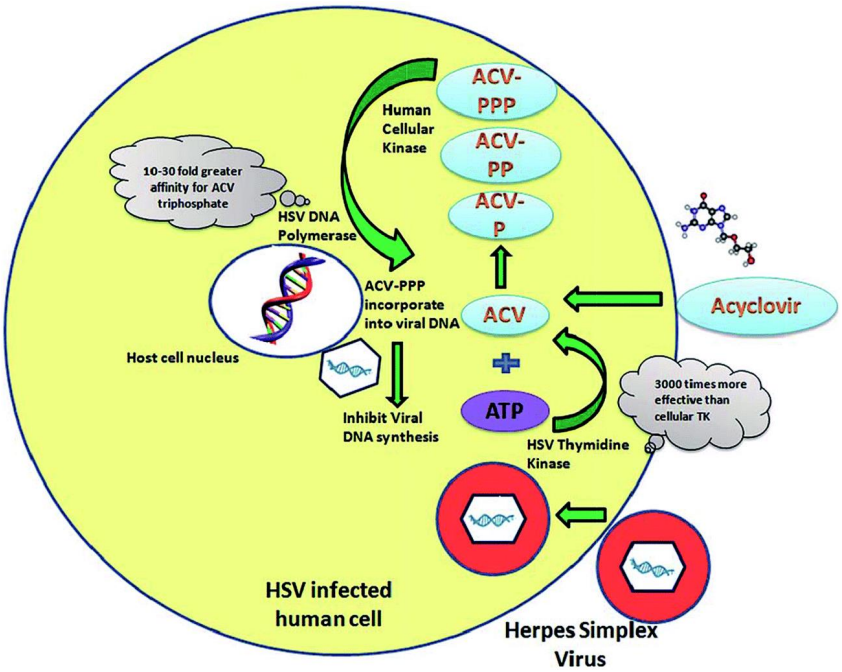
Inhibition of enzyme of metabolic pathway of purine and pyrimidine and polymerases which is important for nucleic acid replication, also viral encode was inhibited.

Nucleoside analogs include

Acyclovir (Acycloquanosin) used against HSV-1, HSV-2, and varicella zoster.

Mode of action

Inhibits the action of the viral DNA polymerase (Acyclovir is converted to its triphosphate form, acyclovir triphosphate (ACV-TP), which competitively inhibits viral DNA polymerase, incorporates into and terminates the growing viral DNA chain, and inactivates the viral DNA polymerase).



Ganciclovir

Name as Methyl quinine derivatives and Act against cytomegal virus. Mode of action is Inhibition of viral DNA polymerase by the same mechanism of Acyclovir.

Idoxuridine

Used against Topical keratoconjunctivitis due to HSV. Its halogenated pyrimidine so incorporated into viral and cellular DNA after phosphorylation by cellular kinase leading to Mismatching bearing of quinine.

Vidarabine

They effect against Varicella zoster, HSV, CMV, and HBV. **Mode of action** is the purine analog blocks viral DNA synthesis then inhibit action of viral DNA polymerase.

Trifluridin

Used against Topical herpes keratitis and Vaccinia and Its act against synthesis of viral mRNA.

b.nucleotide analogs

Cidofavire

They are used against CMV and HSV.

Mode of action: Inhibit proviral DNA polymerase so terminate growing DNA chain.

c.Nucleoside Reverse transcriptase inhibitor

Nevirapin

They used against HIV.

Mode of action: bind directly to RT enzyme .

d.Protease inhibitors

Indinavire, Ritonavire, and Saquinavire. They used against HIV.

Mode of action: They inhibit protease required at late stage of replication to cleavage structural protein to form mature viruses.

Immune system simulation

Rather than attacking viruses directly, a second category of tactics for fighting viruses involves encouraging the body's immune system to attack them. Some antivirals of this sort do not focus on a specific pathogen, instead stimulating the immune system to attack a range of pathogens.

One of the best-known of this class of drugs are interferons, which inhibit viral synthesis in infected cells. One form of human interferon named "interferon alpha" is well-established as part of the standard treatment for hepatitis B and C.

Antiviral resistance

The mechanisms for antiviral resistance development depend on the type of virus in question. RNA viruses such as hepatitis C and influenza A have high error rates during genome replication because RNA polymerases lack proofreading activity.

RNA viruses also have small genome sizes that are typically less than 30 kb, which allow them to sustain a high frequency of mutations. DNA viruses, such as herpesvirus, hijack host cell replication machinery, which gives them proofreading capabilities during replication. DNA viruses are therefore less error. In both cases, the likelihood of mutations is exacerbated by the speed with which viruses reproduce, which provides more opportunities for mutations to occur in successive replications.

The most commonly used method for treating resistant viruses is combination therapy, which uses multiple antivirals in one treatment regimen. This is thought to decrease the likelihood that one mutation could cause antiviral resistance, as the antivirals in the cocktail target different stages of the viral life cycle.