

# Antivirals

**Antivirals** or **virostatics** are substances that are used to treat viral diseases. Common viral diseases (colds, cold infections, flu) are treated symptomatically - analgesics, antipyretics. Some are vaccinated (flu, hepatitis, childhood infections). Directly, viral infections are rarely treated because the substances are not yet effective enough without a high number of side effects. In immunocompromised patients, antivirals are always given. Antibiotics are given when a viral infection is followed by a bacterial infection.

## Mechanism of action

- Antibodies against virus uptake are on the cell membrane.
- Amantadine prevents the virus from penetrating the cell membrane and releasing its NK.
- Prevention of NK replication using base analogues.
- Interferon blocks the assembly and release of the virus.
- Reverse transcriptase blockers.

## Disadvantages of therapy

- The host cell cannot be affected at the same time.
- In retroviruses, we cannot cure the cell because viral NK is part of the nucleus.
- Often, the infection becomes symptomatic after irreversible cell damage, when it is too late for treatment.

## Substances against herpes and influenza infections

### Acyclovir

It is a **guanine** derivative, it contains an aliphatic residue instead of deoxyribose. It is taken up by infected cells, where it is converted to the monophosphate by a virus-specific thymidine kinase, which is then converted to the active triphosphate by cellular enzymes. It inhibits viral DNA polymerase and, when incorporated into viral DNA, acts as a chain terminator. It has a much higher affinity for viral kinase than for humans (therefore it is effective and safe), mainly against Herpes simplex (local or p.o. administration) and Herpes zoster (p.o. administration).

**Famciclovir**, **valaciclovir** or **adenosine arabinoside**, which acts in the same way, have similar effects to acyclovir, the indication being the same. **Side effects**: decreased kidney function, neurological problems (tremor, confusion), acyclovir-resistant herpes viruses have been identified in immunocompromised patients.

### Amantadine

It is a stable **tricyclic amine** also used to treat Parkinson's disease. It inhibits the replication of influenza A viruses by preventing the release of viral nucleic acid (uncoating) by blocking the ion channel of the virus (M2-protein). It is rarely used for the prophylaxis of influenza A2. It is contraindicated in patients with impaired renal function. **Side effects** of GIT disorders, thinking disorders, nervousness.

## Substances against cytomegalovirus infections

They are **more toxic** than Acyclovir, their use is indicated in immunodeficient patients.

- **Ganciclovir** - DNA polymerase inhibition, aciclovir derivative, higher efficacy, higher toxicity (carcinogenic), only in life-threatening cytomegalovirus infections and immunodeficiency conditions (AIDS, conditions after cytostatics). **Side effects** are hematopoietic depression, neutropenia.
- **Foscarnet** - blocks the binding site for pyrophosphate on viral polymerases and reverse transcriptase, during DNA polymerization pyrophosphate must be cleaved from triphosphorylated nucleosides. It is indicated - i.v. application in severe CMV retinitis in AIDS patients (stabilizes the background image in 80%) and aciclovir-resistant diseases (HSV). It is **nephrotoxic**.

## Retroviral antivirals

It **slows down the course** of HIV infection, prolongs and improves the patient's life.

- **Zidovudine** - has a 30x higher affinity for viral reverse transcriptase than humans, but has many side effects. It can be potentiated in combination with Acyclovir or Interferon. It is used in patients with AIDS or prophylactically in HIV-positive people.
- **Stavudine** - inhibits HIV DNA synthesis in the cell, is used in patients with advanced or progressive HIV infection, can be potentiated in combination with other nucleoside antivirals or protease inhibitors.
- **Direct reverse transcriptase inhibitors** - do not need prior activation, they work immediately. The most effective anti-HIV drugs. **Tenofovir**, **Adefovir** (both Prof. Holý).
- **Non-nucleoside reverse transcriptase inhibitors** - *Nevirapine* - their effect is direct and does not require prior intracellular phosphorylation, they are used only for combination therapy. Exanthemas are a side effect.

Common interactions, cytochrome P450 (ketoconazole, rifampicin).

- **Saquinavir** (*indinavir, nelfinavir, ritonavir*) - are abnormal peptides that inhibit the active site of the protease and thus suppress the maturation of viruses. Cross-resistance. They are administered orally. Side effects include GIT disorders, nausea, diarrhoea, best-tolerated saquinavir. Common interactions (cytochrome P450).

## Other antivirals

- **Zanamivir** - a strong inhibitor of neuraminidases (surface enzyme and antigen of influenza A and B viruses), so viruses cannot exit the cell because the influenza virus replicates in the airway epithelial cells within the first three days of the disease, Zanamivir must be administered by this time.
- **Ribavirin** - a nucleoside antiviral drug showing in vitro activity against a number of DNA and RNA viruses, ideal for the treatment of infections caused by RS virus. However, it works on a wide range of viruses (including togaviruses). It is indicated in combination with interferon  $\alpha$ 2B: therapy for chronic hepatitis C. Side effects are haemolysis, anemia, neutropenia, potential teratogenicity and carcinogenicity.
- **Palivizumab** - a monoclonal antibody against the flu in newborns and children.
- **Interferons** - interferon  $\alpha$ ,  $\beta$  and  $\gamma$  therapies for hepatitis B and C, which cause flu-like symptoms, should be considered in non-cancer patients.
- **Cidofovir** - a cytidine derivative (Prof. Holý), against resistant CMV. It is nephrotoxic - water properly!

## Links

### Related articles

- Herpesviruses
- Cytomegalovirus
- AIDS

### Literature

- HYNIE, Sixtus. *Farmakologie v kostce*. 2. vydání. Praha : Triton, 2001. 520 s. ISBN 80-7254-181-1.