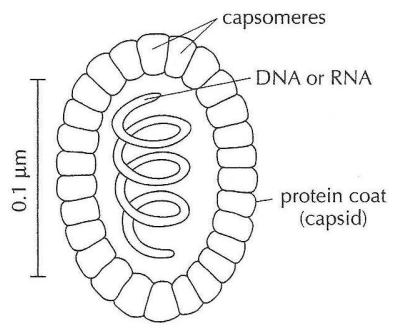
Antivirals



STRUCTURE OF A VIRUS

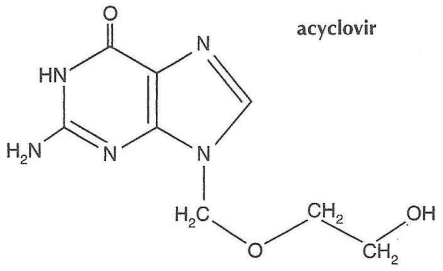
There are many different types of virus with varying shape and structure. All viruses, however, have a central core of DNA or RNA (ribonucleic acid) surrounded by a coat (capsid) of regularly packed protein units (capsomeres), each containing many protein molecules. Unlike bacteria they have no nucleus or cytoplasm and are therefore not cells. They do not feed, excrete, or grow and they can only reproduce inside the cells of living organisms using materials provided by the host cell.

MULTIPLICATION OF VIRUSES

Athough viruses can survive outside the host they can only replicate by penetrating the living host cell and injecting their DNA or RNA into the cell's cytoplasm. The virus then 'takes over' the biochemical machinery inside the cell. This causes the cell to die or become seriously altered and causes the symptoms of the viral infection. The cell is made to produce new DNA or RNA and forms large numbers of new viruses. These are then released and move on to infect other healthy cells.

MODE OF ACTION OF ANTIVIRAL DRUGS

Common viral infections include the common cold, influenza, and childhood diseases, such as mumps and chicken pox. Fortunately the body's own defence mechanism is usually strong enough to overcome infections such as these and drugs are given more to remove the associated pain, fight the fever or to counteract secondary infections. One difficulty in treating viral infections is the speed with which the virus multiplies. By the time the symptoms have appeared the viruses are so numerous that antiviral drugs will have little effect. During the past few years some drugs have been developed to fight specific viral infections. They can work in different ways. Some work by altering the cell's genetic material so that the virus cannot use it to multiply. An example of this is acyclovir, which is applied topically to treat cold sores caused by the herpes virus. Its structure is similar to deoxyguanosine, one of the building blocks of DNA. It tricks the viral enzymes into using it as a building block for the viral DNA and thus prevents the virus from multiplying. However, it is difficult to eliminate the virus completely so the infection may flare up again at a later date.

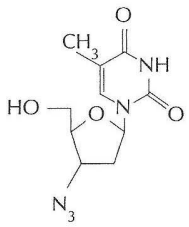


acyclovir

Others work by preventing the new viruses formed from leaving the cell. One such drug is amantadine, which is active against the influenza virus. One of the enzymes used by all influenza viruses to stick to the host cell wall as it leaves is called neuraminidase, and the drug works by inhibiting the active site on this enzyme. One of the problems with developing antiviral drugs is that the viruses themselves are regularly mutating – this is particularly true with the Human Immunodeficiency Virus (HIV).

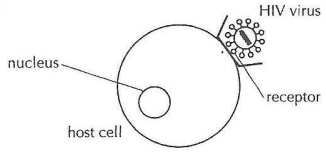
AIDS

AIDS (Acquired Immune Deficiency Syndrome) is caused by a retrovirus – that is, it contains RNA rather than DNA. The virus invades certain types of cells, particularly the white blood cells, which normally activate other cells in the immune system, with the result that the body is unable to fight infection. Once it invades a healthy cell its first task is to make viral-DNA from the RNA template using an enzyme called reverse transcriptase. This is opposite to the process that takes place in normal cells in which RNA is made from a DNA template using transcriptase as the enzyme.

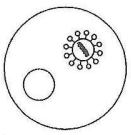


AZT

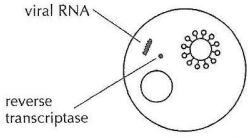
There are various ways in which a drug may be developed to eradicate the HIV virus. One drug that has met with some success is AZT (zidovudine). This combines with the enzyme that the HIV virus uses to build DNA from RNA and clogs up its active site. It is therefore a reverse-transcriptase inhibitor. Since it is only retroviruses that use this enzyme AZT does not affect normal cells.



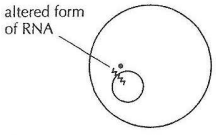
1. Virus binds to a receptor on the host cell.
Possible action of antiviral
Binding site could be altered to prevent virus attaching to host cell.



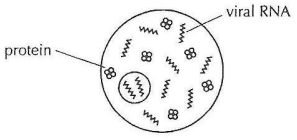
2. Virus enters host cell.
Possible action of antiviral
Cell wall could be altered to prevent virus entering cell.



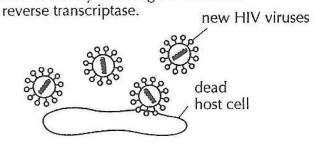
3. Virus loses its protective coat and releases RNA and reverse transcriptase.
Possible action of antiviral
Drugs might be developed which would prevent the virus from losing its protective coat.



4. The reverse transcriptase converts the viral RNA into a form which can enter the nucleus of the host cell so it can integrate with the cell's DNA.
Possible action of antiviral
AZT works by blocking the action of reverse transcriptase.



5. The host cell produces new viral RNA and protein.
Possible action of antiviral
May be able to inhibit the production of new viral RNA and proteins by altering the genetic material of the virus.



6.The new RNA and proteins form new viruses which then leave the host cell. The host cell dies.
Possible action of antiviral
Develop a drug which prevents the new viruses from leaving the cell. This is how amantadine works against the influenza virus.