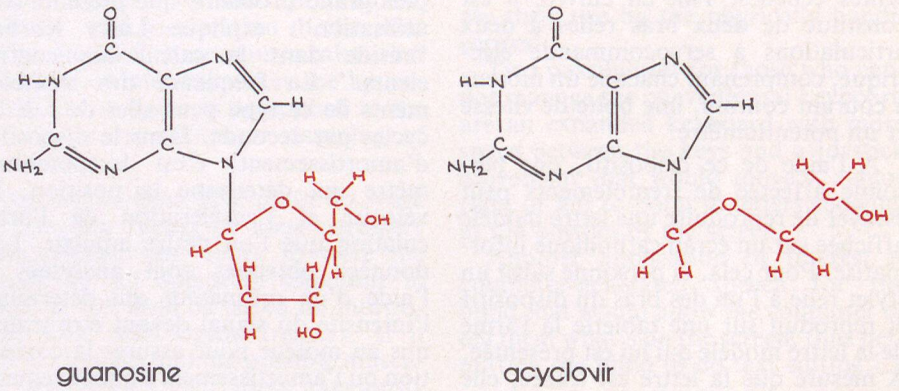
Licenced to heal

The American Food and Drug Administration announced in March that the first antiviral drug ever to be licenced will be used to treat the symptoms of Herpes simplex 2 or genital herpes — a disease from which 20 million Americans now suffer. Scheduled for release in June, the drug's generic name is acyclovir. It isn't a cure, but for some of the victims it will decrease the time and pain involved in the outbreaks. It will also reduce the time during which a person transmits the disease to others. Although the exact nature of acyclovir's action is not yet known, its molecular structure is similar to that of guanosine, a molecule that forms part of the virus's DNA. Because the shapes of the drug and guanosine are similar, acyclovir blocks an enzyme (DNA polymerase) which is necessary for the reproduction of the virus. Of crucial importance, the drug is nontoxic to humans and only extremely small amounts are needed.

This announcement is of interest to NRC's Dr. George Birnbaum and former Research Associate Dr. Miroslaw Cygler, who recently reported the three-dimensional structure of acyclovir (*Biochemical and Biophysical Research Communications*, Vol. 10, No. 3, pp. 968–974, 1981). In cooperation with Dr. Jaroslaw Kusmierek and Dr. David Shugar of the Academy of Sciences, Poland, Birnbaum and Cygler examined acyclovir using a technique known as X-ray diffraction, a method which pinpoints the relative positions of all the atoms in the molecule. When the shape of such a molecule is known, it is then possible to try and correlate it with the activity of that molecule. As a key must fit a lock, the reaction of these molecules with other molecules in the body depends on their shape. This structural knowledge allows chemists to modify the molecule — prune an atom here, add one there — to improve its biological activity.

Acyclovir is the second in a series of compounds, acyclonucleosides, to be studied by X-ray diffraction. Any of these, perhaps with a little modification, might become a useful drug. As the discovery of penicillin precipitated a long line of antibacterial agents, perhaps this first antiviral agent will be just as revolutionary. Although clinical testing will be done by others, Dr. Birnbaum intends to elucidate the molecular structures of other substances in this new class of compounds.□

Margaret Shibley Simmons



(Aili Kurtis)

The shapes of guanosine and acyclovir are so similar that the virus is unable to recognize the difference and incorporates acyclovir into its DNA, thus blocking an enzyme necessary to the reproduction of the virus.

La guanosine et l'acyclovir sont si semblables que le virus est incapable de les différencier. Dans sa confusion, il incorpore dans son ADN de l'acyclovir qui inhibe la production d'une enzyme indispensable à sa reproduction.

(Aili Kurtis)

Dr. George Birnbaum uses X-ray diffraction to pinpoint the positions of each atom in a molecule.

Le Dr George Birnbaum se sert de la diffraction des rayons X pour déterminer l'emplacement de chaque atome à l'intérieur d'une molécule.