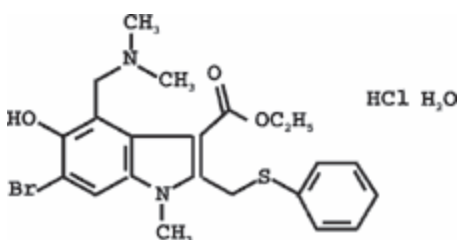


Specific Molecular-Biological Actions of the Antiviral Drug Arbidol

Arbidol is an antiviral drug which is effective against Group A and B influenza strains. The molecular-biological action which distinguishes Arbidol from other drugs is its ability to inhibit viral reproduction in the early stages; the drug acts by changing the regulation of cell metabolism. Arbidol differs from rimantadine in the molecular mechanism of its antiviral action.

Arbidol – 1-methyl-2-phenylthiomethyl-3-carboxy-4-dimethylaminomethyl-5-oxy-6-bromide hydrochloride monohydrate (C₂₂H₂₅BrN₂OS)(HCl)(H₂O) – is an antiviral preparation created by the Center of Chemical/Medicinal Drugs of the Chemical-Pharmaceutical Scientific Research Institute of Russia.



The present work introduces data on the molecular mechanics of Arbidol's antiviral action. As we know, the reproductive mechanism of the influenza virus is unique in that it requires cooperation between viral and cell growth factors.

The LC-MS* method has shown that Arbidol can penetrate in unchanged form both in uninfected and in infected cells and appears in nuclear and cytoplasmic divisions.

The apparent localization of Arbidol in the cell nucleus is linked with the drug's action at one of the stages of the synthesis of cell and viral-specific macromolecules.

The interrupted synthesis of cell macromolecules quickly picks up again when the drug's action is finished. It has been shown that the destruction of DNA synthesis takes place as soon as 15 minutes after introduction of the drug, reaching a maximum 30 minutes after introduction. RNA synthesis is inhibited more slowly, with the effects increasing over a period of 24 hours.

Arbidol does not form a complex with DNA and does not show intercalating properties.

Under the influence of Arbidol, interferon was induced in FEK cell cultures (mouse serum), which is comparable to the activity of the drug in dsRNA RF2.

The method of viral fluorescent staining allowed a comparison study of Arbidol's action to rimantadine in these processes. Under the presence of Arbidol (50 mcg/ml) at pH 5.0, was observed a significant inhibition of RF fluorescence. Under pH 5.0 conditions, the same amount of RF inhibition was produced under the presence of rimantadine 25 mcg/ml.

The addition of Arbidol in concentration 50 mcg/ml under pH 7.4 conditions also caused a decrease in RF. Rimantadine, in concentrations from 25 to 1000 mcg/ml, did not show any inhibition of RF.

This acquired data allows the conclusion to be drawn, that Arbidol inhibits the fusion of the viral lipid membrane with the cell cytoplasmic membrane which happens under the induced low pH level of 5.0, and inhibits the fusion of the viral lipid membrane with endosome membrane which happens inside the cell under the physiological conditions of pH 7.4. In contrast to Arbidol, rimantadine inhibits only the fusion of viral lipid membrane with cytoplasmic cell membrane, but has no effect on the fusion of viral lipid membrane with the endosome membrane.

It is generally accepted that the physiologic conditions in cells under which the influenza virus reproduces require a release of nucleocapsids within the endosome. The available literature and acquired results allow us to propose that the viral-inhibiting effect of Arbidol is tied to the viral reproductive stage where viral lipid membrane fuses with endosome membranes, which takes place at pH 7.4. Therefore, we studied the influence of various concentration of Arbidol on this process. The results show that RF inhibition began at a concentration of Arbidol 5 mcg/ml (8%) and increased with concentrations of Arbidol up to 50 mcg/ml. Under concentrations of more than 50 mcg/ml, RF inhibition did not increase and stayed at 60%. It is important to note that these results corroborate other virological studies, in which minimum inhibitory concentration (MIC) and CPA (cytopathogenic action) in cell culture has been observed under Arbidol concentrations of 5-10 mcg/ml.

Analysis of the foregoing data shows that one of the vulnerable stages of influenza virus reproduction under the effect of Arbidol is the fusion of the viral lipid membrane with the endosome membrane, which takes place inside the cell under the physiological conditions for the release of viral genetic material from surface proteins and the lipid membrane. Unlike amantadine and rimantadine, Arbidol inhibits the release of the nucleocapsid itself from surface proteins, neuraminidase (NA) and the lipid membrane.

It has been shown that Arbidol affects the process of viral lipid membrane fusion with cytoplasmic membrane under pH 5.0, which may be a condition of the drug's entering the lipid membrane and influence on NA conformation changes. Without a doubt, the antiviral preparation's working on the early stages of viral reproduction is the most effective, since the cells have not yet undergone irreversible cytopathologic changes.

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* translator's note: "LC-MS" is the same process that the Russian abbreviates ВЭЖХ. The Russian translates as "highly effective liquid chromatography" and has something to do with spectrometers, as near as I could guess. I couldn't find what LC-MS stands for in English but it seems to be talking about the same process. --Pam