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Anti-human cytomegalovirus (HCMV) activity of sulfonated anthraquinones. D.L. Barnard, T.L. Gage and R.W. Sidwell. Institute for Antiviral Research, Dept. ADVS, Utah State University, Logan, UT, USA.

Previous experiments have shown that a variety of anthrones, anthraquinones and their derivatives had significant anti-HCMV activity in vitro. However, many of these compounds were cytotoxic and difficult to work with because of their low solubilities in water. As a followup to these studies, a number of sulfonated anthraquinone derivatives were evaluated for anti-human cytomegalovirus activity against strain AD-169 in Hs-68 cells in cytopathic effect and plaque reduction studies. Of those compounds evaluated; acid blue 40, acid blue 129, reactive blue 2 and 4, and solway purple showed significant antiviral activity against HCMV. The EC_{50} values ranged from 3-66 μg/ml and the IC_{50} values from 66->1000 μg/ml. The selective indices were from 6 to 24. All of the active compounds were water soluble in contrast to the many inactive anthraquinone derivatives which were less soluble or insoluble. The compounds apparently did not inhibit initial attachment of virus to cells when virus was adsorbed prior to addition of compound. The compounds were virucidal, but at concentrations greater than those achieved for antiviral effects. Structurally, compounds with amino-linked aromatic side chains were more effective inhibitors than those compounds with amino-linked non-aromatic side chains. These results suggest that these compounds may be useful as anti-HCMV drugs.

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Treatment of murine cytomegalovirus (MCMV) infections in cell culture and in immunocompromised mice using antibodies to MCMV alone and in combination with ganciclovir (GCV) or (S)-1-(3-hydroxy-2-phosphonylmethoxypropyl)cytosine (HPMPC). D.F. Smee, S.T. Sugiyama, R.W. Sidwell, and B.B. Barnett. Institute for Antiviral Research, Utah State University, Logan, Utah USA.

Treatment of cytomegalovirus disease with antibodies combined with antiviral agents may be beneficial in immunocompromised individuals. To initially explore the interactions of antibody and drug, cell culture studies were run with hyperimmune rabbit serum (serum neutralization titer of 1:80) with and without GCV or HPMPC. The antibody and drug were added 2 hours after MCMV adsorption so as to not affect the initial infection. The serum at 1:20 to 1:160 dilutions showed synergistic inhibition of virus yield in C127I cells when combined with GCV (0.3 to 5 μM) or HPMPC (0.008 to 0.125 μM). A monoclonal antibody against MCMV, designated D5.F10.B8 (serum neutralization titer of 1:4000), was also developed for the treatment of MCMV disease. The antibody, used in concentrations of 1 to 20 μg/ml when combined with GCV or HPMPC also enhanced inhibition of virus production compared to either substance used alone. The hyperimmune rabbit serum injected undiluted into MCMV-infected severe combined immunodeficient (SCID) mice every three days starting 1 day after virus challenge caused a 4.5 day increase in life span compared to placebo-treated animals. The effects of combinations of GCV plus antibodies in MCMV-infected SCID mice are also being studied. These results indicate antibodies combined with antiviral drugs are effective for the treatment of cytomegalovirus infections in immunocompromised hosts. Supported by PHS Grant 1R01 AI33326-02, NIAID.