

Selective Inhibition of Myxovirus Replication by a Novel Series of Cholesterol-Naphthalenesulfonic Acid Hybrid Molecules

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We synthesized a novel series of hybrid molecules of cholesterol with naphthalenesulfonic acid and investigated their inhibitory activity against myxoviruses [respiratory syncytial virus (RSV), influenza A and B virus]. Naphthalenesulfonic acids [i.e. 4-amino-1-naphthalenesulfonic acid (1), 4-amino-1,5-naphthalenedisulfonic acid (2), 4-amino-5-hydroxy-2,7-naphthalenedisulfonic acid (3)], cholesterol (4) and cholesteryl chloroformate (5) had no inhibitory effect on myxovirus-induced cytopathicity. However, the hybrid molecules 4-(3-cholesterylcarbamate)-1-naphthalenesulfonic acid (6) and 4-(3-cholesterylcarbamate)-1,5-naphthalenedisulfonic acid (7) proved active against RSV and influenza A virus but not influenza B virus. The antiviral effects of the hybrid compounds 6 and 7 were comparable to those of dextran sulfate. Mixtures of 1 and 5, corresponding to the hybrid molecule 6, and of 2 and 5, corresponding to the hybrid molecule 7, did not show antiviral activity. The mode of action of the cholesterol-linked naphthalenesulfonic acids can be attributed to inhibition of virus-cell fusion (influenza A virus) or inhibition of both virus-cell binding and fusion (RSV).

Inhibition of influenza virus reproduction by combined preparations of medicinal plants

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The main objective of the study was to evaluate the antiviral activity of combined plant preparations with respect to the inhibitory effect of their individual components. "Broncho Pam" is approved for treatment of acute and chronic bronchitis. It was prepared from *Thymus serpyllum* L.(1), *Viscum album* L.(2), *Salvia officinalis* L. (3), *Mentha piperita* L.(4) and *Glycyrrhiza glabra* L.(5). It was shown that the alcohol extract of the preparation inhibited strongly the reproduction of A/H1N1 and A/H3N2 in vitro and in ovo, while the individual components' anti-influenza effect was moderate (1,3) or none at all (2,4,5). SHS-174 was prepared from *Sambucus nigra* L.(1), *Hypericum perforatum* L. (2) and *Saponaria officinalis* L. The preparation inhibited the reproduction of a range of influenza viruses in vitro and reduced the mortality rate of white mice infected with A/H3N2. The antiviral effect was dose-dependent and strain-specific, consistent with a selective inhibition. Two combined preparations (CP-1 and CP-2) were obtained by an original laboratory technology. CP-1 was prepared from *Agrimonia eupatoria* L.(1), *Fragaria vesca* L.(2), *Achillea millefolium* L.(3) and *Gentiana cruciata* L. (4). The separate plants exhibited a limited (1,2) or non-significant (3,4) anti-influenza activity while the combined preparation reduced virus infectivity in vitro and in ovo >99.9%. CP-2 was prepared from *Fragaria vesca* L.(1), *Agrimonia eupatoria* L.(2) and *Polygonum hydropiper* L.(3) The inhibitory effect of the separate plants on the reproduction of influenza viruses A/H1N1, A/H2N2 and A/H3N2 was consistently lower than the antiviral activity of their combination. The more pronounced antiviral activity of the combined plant preparations in comparison with their individual components was attributed to synergistic interactions.