Abstract

Synthetic ribonuclease inhibitors have been intensively sought after for various therapeutic purposes. Angiogenin a potent inducer of angiogenesis belongs to the ribonuclease superfamily. Angiogenin has a similar arrangement of ribonucleolytic site residues as ribonuclease A (RNase A), a model protein of this superfamily. In this study, we have investigated the potential of nucleoside-amino acid conjugates, nucleoside-dibasic acid conjugates and backbone modified nucleosides to inhibit RNase A and angiogenin. Agarose gel and precipitation assays showed inhibition of RNase A, which was further confirmed by inhibition kinetics. All the compounds of these three series show competitive inhibition with micromolar inhibition constants. In case of angiogenin they selectively inhibit the ribonucleolytic activity in a competitive fashion with micromolar inhibition constants. Docking studied substantiate the nature of inhibition for RNase A and angiogenin by these inhibitors.

Key words

Ribonuclease A, Angiogenin, Nucleoside-amino acid conjugates, Nucleoside-dibasic acid conjugates, Backbone modified dinucleosides.