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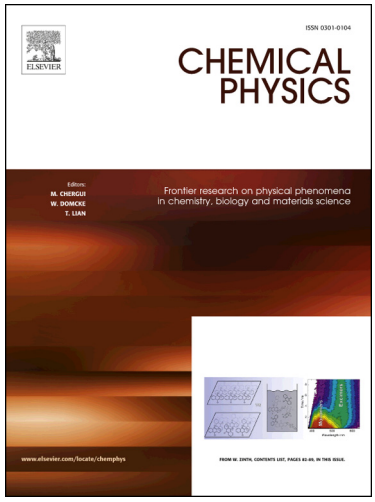

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Binding affinity of the L-742,001 inhibitor to the endonuclease domain of A/H1N1/PA influenza virus variants: Molecular simulation approaches

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(**Abstract**) The steered molecular dynamics (SMD), molecular mechanics Poisson-Boltzmann surface area (MM-PBSA) and free energy perturbation (FEP) methods were used to determine the binding affinity of the L-742,001 inhibitor to the endonuclease domain of the A/H1N1/PA influenza viruses (including wild type (WT) and three mutations I79L, E119D and F105S for both pH1N1 PA and PR8 PA viruses). Calculated results showed that the L-742,001 inhibitor not only binds to the PR8 PAs (1934 A influenza virus) better than to the pH1N1 PAs (2009 A influenza virus) but also more strongly interacts with the WT endonuclease domain than with three mutant variants for both pH1N1 PA and PR8 PA viruses. The binding affinities obtained by the SMD, MM-PBSA and FEP methods attain high correlation with available experimental data. Here the FEP method appears to provide a more accurate determination of the binding affinity than the SMD and MM-PBSA counterparts.