KP03

Comparative QSAR of cyclic urea inhibitors with HIV-1 protease

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In this work, we analyzed quantitatively the interaction between cyclic urea inhibitors and HIV-1 protease in their complex structures. Molecular dynamics and molecular orbital calculations (LocalSCF; AM1) for their complexes were carried out for two data sets. Data set I consists of "mixed series" with a moderate structural diversity, and Data set II consists of "congeneric series" with the common skeletal structure. We formulated a regression equation for Data set I with the interaction energy and the change of accessible surface area. For Data set II, we obtained a more significant equation with the polarized atomic charge of the carbonyl oxygen atom in the urea moiety than the variable σ used in the traditional QSAR. This result is consistent with the interaction between this oxygen and Ile50/50' in the protein. It is suggested that the results in this study could be a bridge between the molecular calculation/simulation and traditional QSAR.