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QSAR Study and Determination of More Potent Peptidic HIV-1-Protease Inhibitors

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Abstract

QSAR study of three sets of peptidic HIV-protease inhibitors has been studied. The descriptor used for study is log P. For QSAR modeling, log P has been calculated using the atom-typing scheme of Ghose and Crippen associated with CAChe. From the structure activity relationship discussion it is clear that log P is an important parameter for QSAR study. Compounds-16, 18, 19, 20, 21, 22, 24, 25, 27, 29 and 30 have high inhibitory activity greater than 9.2 but their log P value is more than 5.0 hence these compounds do not follow minimal hydrophobicity principle and show poor pharmacokinetics. While, compounds-07, 09, 11, 13, 23 and 28 have inhibitory activity ranging from 8.11 to 9.51 and their log P value is less than 5.0, hence these compounds follow minimal hydrophobicity principle and show good pharmacokinetics. Finally QSAR modeling has been made using log P as a descriptor. The QSAR model $A_{Predicted}$ *= 0.620278 log P + 5.53898 has reliable predictive power as it has rCV^2 = 0.566415 and r^2 = 0.59635. On the basis of this QSAR model one can propose theoretical formalism of new peptidic HIV-protease inhibitors that show better pharmacokinetics, including higher oral bioavailability and slow excretion.*

Keywords: QSAR, Protease inhibitor, Log P, Pharmacokinetics

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