Target Name	CCR5 receptor
Target TTD ID	TTDS00326

Target Species	Human
Chemical Type	Substituted 1-(3,3-diphenylpropyl)-piperidinyl amides
Mode of Action	Binder
QSAR Model 1	$\mathrm{pIC_{50}} = -0.863(\pm0.820)\sigma_{\mathrm{R2\_m}} + 1.230(\pm0.355)\sigma_{\mathrm{R2\_p}} + 0.737(\pm0.614)\sigma_{\mathrm{R3\_p}} + 1.179(\pm0.469)\mathrm{mr}_{\mathrm{R3\_p}} - 0.356(\pm0.142)\mathrm{mr}^2_{\mathrm{R3\_p}} + 0.791(\pm0.371)I_{\mathrm{NHCH2}} - 1.279(\pm0.670)I_{\mathrm{BRANCH}} - 1.206(\pm0.666)I_{\mathrm{R4\_4S}} + 2.986(\pm0.185)$ $n = 79,\ R^2_a = 0.719,\ R^2 = 0.747,\ R = 0.865,\ F = 25.9(\mathrm{df}8, 70),\ s = 0.455,\ \mathrm{SDEP} = 0.487,$ $S_{\mathrm{PRESS}} = 0.517,\ Q^2 = 0.674,\ \mathrm{PRESS} = 18.706$
QSAR Model 2	$\mathrm{pIC_{50}} = 3.709(\pm2.315)\log P_{\mathrm{calcd}} - 0.332(\pm0.204) \times [\log P_{\mathrm{calcd}}]^2 - 1.752(\pm1.389)\sigma^2_{\mathrm{R2\_m}} + 1.238(\pm0.331)\sigma_{\mathrm{R2\_p}} + 0.813(\pm0.573)\sigma_{\mathrm{R3\_p}} + 1.391(\pm0.483)\mathrm{mr}_{\mathrm{R3\_p}} - 0.415(\pm0.144)\mathrm{mr}^2_{\mathrm{R3\_p}} + 0.764(\pm0.349)I_{\mathrm{NHCH2}} - 1.346(\pm0.625)I_{\mathrm{BRANCH}} - 1.229(\pm0.623)I_{\mathrm{R4\_4S}} - 7.287(\pm6.615)$ $n = 79,\ R^2_a = 0.757,\ R^2 = 0.788,\ R = 0.888,\ F = 25.3(\mathrm{df}10, 68),\ s = 0.423,\ \mathrm{SDEP} = 0.468,$ $S_{\mathrm{PRESS}} = 0.505,\ Q^2 = 0.698,\ \mathrm{PRESS} = 17.344$
QSAR Model 3	$\mathrm{pIC_{50}} = 4.794(\pm2.367)\log P_{\mathrm{calcd}} - 0.430(\pm0.210) \times [\log P_{\mathrm{calcd}}]^2 + 1.013(\pm0.361)\sigma_{\mathrm{R2\_p}} + 0.579(\pm0.397)L_{\mathrm{R2\_p}} - 0.050(\pm0.046)L^2_{\mathrm{R2\_p}} + 0.840(\pm0.547)\sigma_{\mathrm{R3\_p}} + 1.416(\pm0.459)\mathrm{mr}_{\mathrm{R3\_p}} - 0.423(\pm0.138)\mathrm{mr}^2_{\mathrm{R3\_p}} + 0.878(\pm0.329)I_{\mathrm{NHCH2}} - 1.058(\pm0.609)I_{\mathrm{BRANCH}} - 1.250(\pm0.595)I_{\mathrm{R4\_4S}} - 11.609(\pm6.770)$ $n = 79,\ R^2_a = 0.779,\ R^2 = 0.810,\ R = 0.900,\ F = 25.9(\mathrm{df}11, 67),\ s = 0.403,\ \mathrm{SDEP} = 0.462,$ $S_{\mathrm{PRESS}} = 0.501,\ Q^2 = 0.706,\ \mathrm{PRESS} = 16.845$

QSAR Model 4	$$\mathrm{pIC_{50}} = -2.008\sigma^2_{\mathrm{R2\_m}} + 0.461\sigma_{\mathrm{R2\_p}} + 0.786\sigma^2_{\mathrm{R2\_p}} - 0.201\pi_{\mathrm{R2\_p}} - 0.071\mathrm{mr}^2_{\mathrm{R3\_p}} + 0.890\sigma_{\mathrm{R3\_p}} + 0.163B5_{\mathrm{R3\_p}} + 0.032B5^2_{\mathrm{R3\_p}} - 0.007L^2_{\mathrm{R3\_p}} + 0.666I_{\mathrm{NHCH2}} - 1.237I_{\mathrm{BRANCH}} - 0.504I_{\mathrm{R2\_2S}} - 1.448I_{\mathrm{R4\_4S}} + 3.006$$ $$n = 79,\ R^2_a = 0.757,\ R^2 = 0.797,\ R = 0.893,\ F = 98.5, \mathrm{SDEP} = 0.437,\ S_{\mathrm{PRESS}} = 0.448,\ Q^2 = 0.737,\ \mathrm{PRESS} = 15.068$$
QSAR Model 5	$$\mathrm{pIC_{50}} = -0.156(\pm0.086)fs1 + 0.158(\pm0.086)fs2 + 0.141(\pm0.086)fs3 + 0.559(\pm0.086)fs4 - 0.157(\pm0.086)fs5 - 0.154(\pm0.086)fs6 + 0.170(\pm0.086)fs8 - 0.157(\pm0.086)fs9 + 0.234(\pm0.086)fs10 - 0.207(\pm0.086)fs12 + 0.132(\pm0.086)fs14 - 0.121(\pm0.086)fs18 + 3.651(\pm0.086)$$ $$n = 79,\ R^2_a = 0.804,\ R^2 = 0.834,\ R = 0.913,\ F = 27.6(\mathrm{df}\,12, 66),\ s = 0.380, \mathrm{SDEP} = 0.408,\ S_{\mathrm{PRESS}} = 0.447,\ Q^2 = 0.770, \mathrm{PRESS} = 13.174$$
Molecular Descriptor	Access the following web-servers to compute molecular descriptors: **MoDel** and **e-dragon** I_{CH2}: Indicator variable having value 1 if methylene group is present at X position, value 0 otherwise. I_{NH}: Indicator variable having value 1 if NH group is present at X position, value 0 otherwise I_{NHCH}: Indicator variable having value 1 if NH–CH_2 group is present at X position, value 0 otherwise I_{BRANCH}: Indicator variable having value 1 if branching is present at X position, value 0 otherwise I_{ETHYL}: Indicator variable having value 1 if ethyl group is present at R^1-position, value 0 otherwise I_{ALLYL}: Indicator variable having value 1 if allyl group is present at R^1-position, value 0 otherwise $I_{C\text{-}PRO}$: Indicator variable having value 1 if c-propyl group is present at R^1-position, value 0 otherwise I_{R2_2S}: Indicator variable having value 1 if any substituent is present at 2nd position at R^2, 0 otherwise I_{R4_3S}: Indicator variable having value 1 if any substituent is present at 3rd position at R^4, 0 otherwise I_{R4_4S} : Indicator variable having value 1 if any substituent is present at 4th position at R^4, 0 otherwise Lipophilicity (π), electronic (Hammett σ), and steric (molar refractivity mr and STERIMOL L, B1, and B5). Hydrophobic whole molecular descriptor (partition coefficient $\log P_{calcd}$). Molar refractivity of R^3 substituents (mr_{R3_p}). The STERIMOL parameter (L) of the para-substituents at R3-position. Lipophilic substituent constant (π_{R2_p}) of the para-substituents at the R^2-position. Molar refractivity (mr), length (L) and width (B5) of para-substituents at R^3. Molar refractivity (mr), length (L) and width (B5) of para-substituents at R^2. Lipophilicity (π), electronic (Hammett σ) parameters, and width (B5) of para-substituents at R^2. The

	electronic (Hammett σ) parameters of the para-substituents at R^3. NHCH2 substituents at X, para-substituents at R^4-position.
Reference	Comparative QSAR modeling of CCR5 receptor binding affinity of substituted 1-(3,3-diphenylpropyl)-piperidinyl amides and ureas. *Bioorganic & Medicinal Chemistry Letters* 16 (2006) 4467–4474

Target Species	Human
Chemical Type	Substituted 1-(3,3-diphenylpropyl)-piperidinyl ureas
Mode of Action	Binder
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QSAR Model 4	$$\mathrm{pIC_{50}} = -2.008\sigma^2_{\mathrm{R2\_m}} + 0.461\sigma_{\mathrm{R2\_p}} + 0.786\sigma^2_{\mathrm{R2\_p}} - 0.201\pi_{\mathrm{R2\_p}} - 0.071\mathrm{mr}^2_{\mathrm{R3\_p}} + 0.890\sigma_{\mathrm{R3\_p}} + 0.163B5_{\mathrm{R3\_p}} + 0.032B5^2_{\mathrm{R3\_p}} - 0.007L^2_{\mathrm{R3\_p}} + 0.666I_{\mathrm{NHCH2}} - 1.237I_{\mathrm{BRANCH}} - 0.504I_{\mathrm{R2\_2S}} - 1.448I_{\mathrm{R4\_4S}} + 3.006$$ $$n = 79,\ R^2_a = 0.757,\ R^2 = 0.797,\ R = 0.893,\ F = 98.5, \mathrm{SDEP} = 0.437,\ S_{\mathrm{PRESS}} = 0.448,\ Q^2 = 0.737,\ \mathrm{PRESS} = 15.068$$
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	electronic (Hammett σ) parameters of the para-substituents at R^3. NHCH2 substituents at X, para-substituents at R^4-position.
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