| Target Name | 5-HT$_{1A}$ Receptor |
|---|---|
| Target TTD ID | TTDS00098 |

| Target Species | Human |
|---|---|
| Chemical Type | Arylpiperazines |
| Mode of Action | Antagonist |
| QSAR Model 1 | $pK_1 = 23.588\ (\pm 7.988) + 0.012\ (\pm 0.005)S_8\ - 0.885\ (\pm 0.189)\ S_{16}$ $- 1.210\ (\pm 0.632)\ S_{21}\ - 1.730\ (\pm 0.275)I_1 + 1.209\ (\pm 0.404)I_2$ <br><br> $n = 32;\quad R = 0.845;\quad \%EV = 71.40;\quad R_A^2 = 0.659;\ F(5, 26) = 12.988;$ <br> $p < 0.0000;\quad S.E.E. = 0.483$ |
| QSAR Model 2 | $pK_1 = 22.981(\pm 7.525) + 0.012(\pm 0.005)\ S_8 - 0.883 \times (\pm 0.178)\ S_{16}$ $- 1.165\ (\pm 0.595)\ S_{21}\ - 1.692\ (\pm 0.259)I_1 + 1.254\ (\pm 0.381)I_2$ <br><br> $n = 31;\quad DC = 28;\quad R = 0.862;\quad \%EV = 74.30;\quad R_A^2 = 0.692;$ <br> $F(5, 25) = 14.428;\quad p < 0.0000;\ S.E.E. = 0.454$ |
| QSAR Model 3 | $pK_1 = 20.532\ (\pm 5.113) + 5.044\ (\pm 0.911)\ S_8 - 0.973\ (\pm 0.121)\ S_{16}$ $- 1.347\ (\pm 0.404)\ S_{21}\ - 1.598\ (\pm 0.176)\ I_1 + 1.183(\pm 0.258)I_2$ <br><br> $n = 30;\quad DC = 28, 21;\quad R = 0.934;\quad \%EV = 87.30;$ <br> $R_A^2 = 0.846;\quad F(5, 24) = 32.794;\quad p < 0.0000;$ |
| Molecular Descriptor | Access the following web-servers to compute molecular descriptors: **MoDel** and **e-dragon** <br><br> E-state indices of atoms 8, 16, 21—S8, S16 and S21 I1, I2, represent presence of CONHPr group at ortho position and Br at meta position of the phenyl ring respectively. <br><br> n is number of data points, R is correlation coefficient, %EV, $R_A^2$, F, p, S.E.E. are percentage of explained variance, adjusted $R^2$, ratio between the variances of observed and calculated activities, probability factor related to F-ratio and standard error of estimate respectively. <br><br> DC is the deleted compound behaves as outliers may act through a different mechanism of action. The statistical quality of eq 3 was found to be of significant. It explains 87.30% of the variances in the |

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|---|---|
| | activity data. |
| **Reference** | QSAR Study on the Affinity of Some Arylpiperazines towards the 5-HT1A/$\alpha$1-Adrenergic Receptor Using the E-State Index. *Bioorganic & Medicinal Chemistry Letters* 13 (2003) 2837–2842 |

| | |
|---|---|
| **Target Species** | Human |
| **Chemical Type** | Arylpiperazinylthioalkyl derivatives |
| **Mode of Action** | Binder |
| **QSAR Model 1** | $pK_i(5-HT_{1A}) = -4.904 - 8.726(1.076)AAC + 30.091(5.313)SIC3 + 19.993(3.604)GGI9$ $n = 19$, $r = 0.942$, $s = 0.407$, $F = 39.228$, $Q^2_{LOO} = 0.808$, $Q^2_{L3O} = 0.801$, FIT $= 4.203$, LOF $= 0.279$, AIC $= 0.254$, $r^2_{randY}$(s.d.) $= 0.374(0.130)$, $r^2_{Test} = 0.911$, $R^2_p = 0.756$ |
| **Molecular Descriptor** | Access the following web-servers to compute molecular descriptors: **MoDel** and **e-dragon** Descriptor classes and identified descriptors in modelling the 5-HT1A binding activity of arylpiperazinylthioalkyl derivatives. **Descriptor class**: Identified descriptors and their average regression coefficient (incidence) **CONST**: AMW, 1.076(2); Ss, 0.099(1); RBN, 0.432(2); **TOPO**: AAC, 8.723(6); Qindex, 0.502(1); MSD, 55.303(5); JhetZ, 5.452(2); TIE, 0.005(1); PW2, –106.853(2); PW4, –70.574(1); PJI2, 6.012(3); Lop, 2.537(2); IC2, 3.931(1); IC3, 6.115(2); SIC3, 30.091(1); BIC5, 35.263(2); SEigm, 1.297(1); VEA1, –1.352(3); **BCUT**: BEHm4, 21.363(3); BELm3, 14.096(4); **GALVEZ**: GGI9, 20.728(18); GGI10, –12.584(1); **2D-AUTO**: MATS3m, 74.393(1); MATS4m, 94.015(2); MATS6m, 109.735(4); MATS7m, 57.331(2); MATS3v, 13.113(1); MATS1e, 9.480(3); MATS3e, 13.031(1); MATS6e, 7.513(1); MATS7e, 11.500(2); GATS5v, 9.501(1); GATS3e, 4.918(6); GATS5p, 5.272(3); **FUNC**: nCp, 1.082(2); **ACF**: H-047, 0.153(2); H-053, 0.364(4). Highest significant model pertaining to binding activity of 5-HT$_{1A}$ receptor; Identified descriptorsa and their average regression coefficient (incidence). |
| **Reference** | A rationale for the activity profile of arylpiperazinylthioalkyls as 5-HT$_{1A}$-serotonin and $\alpha_1$-adrenergic receptor ligands. *European Journal of Medicinal Chemistry* 45 (2010) 1927–1934 |

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|---|---|
| **Target Species** | Human |

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|---|---|
| **Target Location** | Central Nervous System (CNS) |
| **Chemical Type** | Phenylpiperazinyl-alkyl oxindoles |
| **Mode of Action** | Antagonist |
| **QSAR Model 1** | $\mathrm{pPI} = 7.569(\pm0.332) - 0.182(\pm0.028)R_{20} - 0.128(\pm0.031)R_6 - 0.504(\pm0.157)S_{19} - 0.162(\pm0.235)R_{10} - 5.670(\pm2.610)FEL_{14}$ <br> $n = 26;\ R = 0.900;\ R^2 = 0.810;\ R_A^2 = 0.762;\ F(5,20) = 17.030;\ p < 0.00000;\ S.E.E = 0.144;\ SSY = 2.188;\ PRESS = 0.742;\ R_{CV}^2 = 0.661;$ <br> $SDEP = 0.169;\ S_{PRESS} = 0.193.$ |
| **QSAR Model 2** | $\mathrm{pPI} = 5.678(\pm0.226) - 0.288(\pm0.035)S_{20} + 0.290(\pm0.085)I6\_Cl + 0.574(\pm0.242)Q_{19} + 0.270(\pm0.122)FEH_{21} + 0.242(\pm0.111)S_{22}$ <br> $n = 26;\ R = 0.904;\ R^2 = 0.817;\ R_A^2 = 0.771;\ F(5,20) = 17.859;\ p < 0.00000;\ S.E.E = 0.141;\ SSY = 2.188;\ PRESS = 0.723;\ R_{CV}^2 = 0.670;$ <br> $SDEP = 0.167;\ S_{PRESS} = 0.190.$ |
| **QSAR Model 3** | $\mathrm{pPI} = 7.407(\pm0.282) - 0.167(\pm0.026)R_{20} + 0.311(\pm0.084)I6\_Cl - 0.546(\pm0.150)S_{19} - 0.455(\pm0.208)FEL_8 + 0.258(\pm0.123)FEH_{21}$ <br> $n = 26;\ R = 0.905;\ R^2 = 0.819;\ R_A^2 = 0.774;\ F(5,20) = 18.110;\ p < 0.00000;\ S.E.E = 0.141;\ SSY = 2.188;\ PRESS = 0.716;\ R_{cv}^2 = 0.673;$ <br> $SDEP = 0.166;\ S_{PRESS} = 0.189.$ |
| **QSAR Model 4** | $\mathrm{pPI} = 6.526 - 0.124\,S_{20} - 0.084\,R_{20} + 0.291\,FEH_{21} - 0.458\,FEL_8 + 0.297\,I6\_Cl - 0.377\,S_{19} + 0.224\,S_{22} + 0.381\,Q_{19}$ <br> $n = 26;\ R = 0.929;\ R^2 = 0.863;\ R_A^2 = 0.829;\ F(5,20) = 25.17;\ p < 0.00000;\ S.E.E = 0.300;\ PRESS = 0.620;\ SDEP = 0.154;$ <br> $S_{PRESS} = 0.191;\ R_{cv}^2 = 0.717.$ |
| **Molecular Descriptor** | Access the following web-servers to compute molecular descriptors: **MoDel** and **e-dragon** <br><br> The R-state indices at atom numbers 6, 10 and 20 i.e., (R6, R10 and R20); E-state index of the atom number 19 (S19); Frontier electronic density related to the lowest unoccupied molecular orbital at the atom number 14 (FEL14). <br><br> ETSA index at the atom number 22 (S22); ETSA index at the atom number 20 (S20); Wang–Ford charge of the atom number 19 (Q19); I6_Cl stands for the presence or absence of the chlorine at the atom number 6 of these molecules; The frontier electron density related to the highest occupied molecular orbital of the atom number 21 (FEH21). <br><br> S19, S20 and S22 are E-state indices of atom numbers 19, 20 and 22 respectively; I6_Cl signifies that the presence of chlorine at the atom number 6 |
| **Reference** | Predictive comparative QSAR modelling of (phenylpiperazinyl-alkyl) oxindoles as selective 5-HT$_{1A}$ antagonists by stepwise regression, PCRA, FA-MLR and PLS techniques. *European Journal of Medicinal Chemistry* 45 (2010) 1119–1127 |