Target Name	α1-Adrenoceptor
Target TTD ID	TTDS00027

Target Species	Human
Chemical Type	3-Arylpiperazinylalkylpyrrolo[3,2-d]pyrimidine-2,4-dione derivatives
Mode of Action	Ligand
QSAR Model 1	$\mathrm{Aff} = 21.0309 + 0.715137\ \mathrm{HOMO} - 1.53546\ \mathrm{S\_ssCH2} + 0.089448\ \mathrm{MR} - 0.00095\ \mathrm{PMI\text{-}mag}$ $r^2 = 0.920222$, CV $r^2 = 0.734$, LOF = 0.200777
QSAR Model 2	$\mathrm{Aff} = 30.9349 - 1.42254\ \mathrm{S\_ssCH2} - 0.00085\ \mathrm{PMI\text{-}mag} + 0.978227\ \mathrm{HOMO}$ $r^2 = 0.843812$, LOF = 0.221106
QSAR Model 3	$\mathrm{Aff} = 14.9317 - 1.28305\ \mathrm{S\_ssCH2} - 0.001135\ \mathrm{PMI\text{-}mag} + 0.590941\ \mathrm{S\_dO} + 0.88154\ \mathrm{HOMO}$ $r^2 = 0.881520$, LOF = 0.298178
QSAR Model 4	$\mathrm{Aff} = -1.42385 + 0.218582\ \mathrm{MR} - 0.000713\ \mathrm{PMI\text{-}mag} - 1.41618\ \mathrm{S\_ssCH2} + 13.7639\ \mathrm{Jurs\text{-}RPCG}$ $r^2 = 0.881415$, LOF = 0.298444
QSAR Model 5	$\mathrm{Aff} = 35.7893 - 0.001058\ \mathrm{PMI\text{-}mag} + 1.20452\ \mathrm{HOMO} - 1.71175\ \mathrm{S\_ssCH2} + 0.430969\ \mathrm{Jurs\text{-}RPCS}$ $r^2 = 0.877877$, LOF = 0.307347
QSAR Model 6	$\mathrm{Aff} = 29.5356 - 0.033243\ \mathrm{S\_sCl} - 1.4278\ \mathrm{S\_ssCH2} - 0.000758\ \mathrm{PMI\text{-}mag} + 0.880362\ \mathrm{HOMO}$ $r^2 = 0.870094$, LOF = 0.326934
QSAR Model 7	$\mathrm{Aff} = 18.8665 + 1.10796\ \mathrm{Jurs\text{-}RNCS} - 1.43661\ \mathrm{S\_ssCH2} + 0.093934\ \mathrm{MR} - 0.000938\ \mathrm{PMI\text{-}mag} + 0.664025\ \mathrm{HOMO}$ $r^2 = 0.941940$, LOF = 0.328768
QSAR	$\mathrm{Aff} = 30.219 - 0.000863\ \mathrm{PMI\text{-}mag} + 0.938424\ \mathrm{HOMO} - 1.40417\ \mathrm{S\_ssCH2} + 0.037602\ \mathrm{S\_ssO}$

Model 8	$r^2 = 0.869239$, LOF = 0.329087
Molecular Descriptor	Access the following web-servers to compute molecular descriptors: **MoDel** and **e-dragon** MR, Thermodynamic Molar refractivity; Density, Spatial Molecular density;PMI-mag, Spatial Principal moment of inertia; Dipole-mag, Electronic Dipole moment; HOMO, Electronic Highest occupied molecular orbital energy; LUMO, Electronic Lowest unoccupied molecular orbital energy; Sr, Electronic Superdelocalizability; Jurs-RPCG, Spatial Relative positive charge; Jurs-RNCG, Spatial Relative negative charge; Jurs-RPCS, Spatial Relative positive charge surface area; Jurs-RNCS, Spatial Relative negative charge surface area; Jurs-RPSA, Spatial Relative polar surface area; S_sCH3, Electrotopological Sum for a methyl group; S_ssCH2, Electrotopological Sum for a methylene group; S_dssC, Electrotopological Sum for a carbon atom with a double bond and two single bonds (i.e., a carbonyl carbon); S_aasC, Electrotopological Sum for a carbon atom with a single bond and two aromatic bonds (i.e., a carbon of the pyrrole ring); S_ssNH, Electrotopological Sum for a nitrogen atom linked to a hydrogen and involved in two additional single bonds;(i.e., the NH group of the pyrimidinedione system); S_aaNH, Electrotopological Sum for a nitrogen atom linked to a hydrogen and involved in two additional aromatic bonds (i.e., the NH group of the pyrrole ring); S_dO, Electrotopological Sum for an oxygen atom bound through a double bond (i.e., a carbonyl oxygen); S_ssO, Electrotopological Sum for an oxygen atom bound through two single bonds (i.e., the oxygen of a methoxy group); S_sCl, Electrotopological Sum for a chlorine atom; Aff represents log(1/*K*i) where *K*i is the affinity of compounds toward R1-ARs, expressed in nM. *r*2, CV *r*2, and LOF are the correlation coefficient, the cross-validated correlation coefficient, and the lack-of-fit values, respectively.
Reference	Synthesis of 3-Arylpiperazinylalkylpyrrolo[3,2-d]pyrimidine-2,4-dione Derivatives as Novel, Potent, and Selective α1-Adrenoceptor Ligands. *J. Med. Chem*. 2005, 48, 2420-2431

Target Species	Human
Chemical Type	Arylpiperazines
Mode of Action	Antagonist

QSAR Model 1	$pK_2 = 31.556\ (\pm 10.768) + 5.221(\pm 1.707)\ S_{10} - 1.382\ (\pm 0.238)\ S_{16} - 2.197\ (\pm 0.832)\ S_{21} - 1.560\ (\pm 0.367)\ I_1$ $n = 32;\quad R = 0.807;\quad \%EV = 65.18;\quad R_A^2 = 0.600;\quad F(4, 27) = 12.634;\quad p < 0.0000;\quad S.E.E. = 0.646$
QSAR Model 2	$pK_2 = 26.139\ (8.839) + 4.719\ (\pm 1.389)\ S_{10} - 1.689\ (\pm 0.209)\ S_{16} - 1.705\ (\pm 0.686)\ S_{21} - 1.649\ (\pm 0.298)\ I_1 + 1.709\ (\pm 0.440)\ I_2$ $n = 32;\quad R = 0.883;\quad \%EV = 77.97;\quad R_A^2 = 0.737;\quad F(5, 26) = 18.399;\quad p < 0.0000;\quad S.E.E. = 0.523$
QSAR Model 3	$pK_2 = 26.956\ (\pm 8.098) + 3.841(\pm 1.321)\ S_{10} - 1.915\ (\pm 0.212)\ S_{16} - 1.671\ (\pm 0.628)\ S_{21} - 1.907\ (\pm 0.292) I_1 + 1.871\ (\pm 0.408) I_2 - 0.756\ (\pm 0.308)\ I_3$ $n = 32;\quad R = 0.907;\quad \%EV = 82.25;\quad R_A^2 = 0.780;\quad F(6, 25) = 19.304;\quad p < 0.0000;\quad S.E.E. = 0.479$
Molecular Descriptor	Access the following web-servers to compute molecular descriptors: **MoDel** and **e-dragon** S10 (E-state index of atom 10). 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. 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. 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 activity data.
Reference	QSAR Study on the Affinity of Some Arylpiperazines towards the 5-HT1A/α1-Adrenergic Receptor Using the E-State Index. *Bioorganic & Medicinal Chemistry Letters* 13 (2003) 2837–2842

Target Species	Human
Chemical Type	Arylpiperazinylthioalkyl derivatives
Mode of	Binder

Action	
QSAR Model 1	$pK_i(\alpha_1) = 0.717 + 14.496(2.028)GGI9 + 1.915(0.378)GATS3e + 0.132(0.017)H-047$ $n = 18,\ r = 0.942,\ s = 0.207,\ F = 36.520,\ Q^2_{LOO} = 0.798,$ $Q^2_{L3O} = 0.731,\ FIT = 4.058,$ $LOF = 0.075,\ AIC = 0.068,\ r^2_{randY}(s.d.) = 0.366(0.154),$ $r^2_{Test} = 0.749,\ R^2_p = 0.766$
Molecular Descriptor	Access the following web-servers to compute molecular descriptors: **MoDel** and **e-dragon** Descriptor classes and identified descriptors in modeling the α1-binding activity of arylpiperazinylthioalkyl derivatives. **Descriptor class**: Identified descriptors and their average regression coefficient (incidence) **CONST**: AMW, 0.400(1); nDB, 0.360(1); nBnz, 0.421(1); **TOPO**: AAC, 2.287(2); ZM2V, 0.008(1); PJI2, 3.427(4); IVDE, 2.973(3); IC3, 3.081(1); piPC03, 0.016(1); **BCUT**: BEHm4, 11.776(1); BELm4, 3.791(1); BEHv8, 6.231(3); **GALVEZ**: GGI6, 3.692(1); GGI8, –4.563(1); GGI9, 12.974(6); GGI10, –15.802(1); JGI1, –11.673(2); **2D-AUTO**: ATS6m, 0.059(1); MATS3m, 42.727(3); MATS4m, 60.897(1); MATS3v, 7.851(3); MATS6v, 5.357(2); MATS1e, 2.862(1); MATS2e, 3.951(3); MATS6e, 4.000(1); MATS7e, 5.209(8); MATS6p, 5.051(2); GATS3e, 1.915(1); GATS4p, 4.962(1); GATS5p, 1.872(1); GATS6p, 4.538(2); **ACF**: C-026, 0.341(1); C-034, 0.209(2); H-047, 0.107(6); H-053, 0.291(2). Binding data pertaining to α_1-adrenergic receptor.
Reference	A rationale for the activity profile of arylpiperazinylthioalkyls as 5-HT_{1A}-serotonin and α_1-adrenergic receptor ligands. *European Journal of Medicinal Chemistry* 45 (2010) 1927–1934