Target Name	COX-1
Target TTD ID	TTDS00040

Target Species	Human
Chemical Type	Diaryl furanones
Mode of Action	Inhibitor
QSAR Model 1	$pIC50_{COX\text{-}1} = -0.029(Peoe\_vsa{+}2) - 0.013(E\_sol) + 0.044(vsa\_other) + 4.228$ $N = 18;\ r = 0.788;\ r^2 = 0.641;$ adjusted $r^2 = 0.621;\ S = 0.306;\ F_{3,14} = 7.660;\ F_{\alpha\ =\ 5\%\ 3,14} = 3.34;\ q^2 = 0.401;$ S dep=0.33.
QSAR Model 2	$pIC50_{COX\text{-}1} = 0.122(Std\_dim2) + 0.302(Kier\ A3) + 0.016(SlogP\_vsa1) + 2.699$ $N = 18;\ r = 0.410;\ r^2 = 0.168;$ adjusted $r^2 = 0.00;\ S = 0.453;\ F_{3,14} = 0.943;\ F_{\alpha\ =\ 5\%\ 3,14} = 3.34.$
QSAR Model 3	$pIC50_{COX\text{-}1} = 0.114(Log\ P) + 4.584$ $N = 18;\ r = 0.146;\ r^2 = 0.021;$ adjusted $r^2 = 0.00;\ S = 0.463;\ F_{1,16} = 0.350.$
Molecular Descriptor	Access the following web-servers to compute molecular descriptors: **MoDel** and **e-dragon** vsa_other is a pharmacophore feature descriptor; E_sol the solvation energy descriptor and Peoe_vsa+2 the partial charge descriptor; Vsa_other is the van derWaal's surface area of all atoms other than donor, acceptor, polar (both donor and acceptor), positive (base), negative (acid) and hydrophobic which shows that increase in van der Waal's surface area of other atoms increases inhibitory activity. Peoe_vsa+2 is the partial charge descriptor; an electronic parameter showing that compound shows electronic interaction with COX-1 enzyme. The partial charges are calculated by Gasteiger method, in which charge is transferred between bonded atoms until equilibrium. Std_dim2 is three dimensional surface area, volume and shape descriptor, which depends upon structure connectivity and conformation. It is calculated as the square root of the second largest eigenvalue of the covariance matrix of the atomic coordinates and is equivalent to the standard deviation along a principal component axis. Kier A3 is Kier and Hall Connectivity and Kappa Shape

	Index, which compares the molecular graph with minimal and maximal molecular graphs, and is intended to capture different aspects of molecular shape.
Reference	Quantitative structure activity relationship studies of diaryl furanones as selective COX-2 inhibitors. *European Journal of Medicinal Chemistry* 39 (2004) 383–388

Target Species	Human
Chemical Type	Terphenyl methyl sulfones
Mode of Action	Binder
QSAR Model 1	$pC_1 = 1.365(\pm0.794)S_5 - 0.974(\pm0.274)I'_{OMe-Me} + 0.870(\pm0.300)I_{9,10\text{-}F2} + 2.532(\pm1.362)$ $n = 18,\ Q^2 = 0.675,\ R^2_a = 0.777,\ R^2 = 0.816, R = 0.903,\ F = 20.7(df3, 14),\ s = 0.200,$ AVRES $= 0.141,$ SDEP $= 0.234,\ S_{PRESS} = 0.265,$ PRESS $= 0.985,\ Pres_{av} = 0.184$
QSAR Model 2	$pC_1 = 0.485(\pm0.303)S_{4+5} - 0.975(\pm0.286)I'_{OMe-Me} + 0.759(\pm0.280)I_{9,10\text{-}F2} + 3.327(\pm1.015)$ $n = 18,\ Q^2 = 0.654,\ R^2_a = 0.761,\ R^2 = 0.803,\ R = 0.896,\ F = 19.1(df3, 14),\ s = 0.207,$ AVRES $= 0.145,$ SDEP $= 0.242,\ S_{PRESS} = 0.274,$ PRESS $= 1.050,\ Pres_{av} = 0.189$
Molecular Descriptor	I'_{OMe-Me}: Indicator variable having value 1 to denote presence of methoxy or methyl group at R_2 in presence of fluoro substitution on C_9 and C_{10}, value 0 otherwise; $I_{9,10\text{-}F2}$: Indicator variable having value 1 in presence of fluoro substitution on C_9 and C_{10}, value 0 otherwise; I_{OMe} : Indicator variable having value 1 to denote presence of methoxy group at R2, value 0 otherwise; I_{Me} : Indicator variable having value 1 to denote presence of methyl group at R2, value 0 otherwise; N'_{OMe}: Number of methoxy group at the phenyl ring (R positions) in presence of fluoro substitution on C_9 and C_{10}; I_{W1} : Indicator variable having value 1 to denote presence of amino group at W in presence of fluoro substitution on C_9 and C_{10}, value 0 otherwise; I_{W2} : Indicator variable having value 1 to denote presence of amino group at W in absence of fluoro

	substitution on C_9 and C_{10}, value 0 otherwise; S_X : E-state value of atom X.
Reference	Exploring QSAR with E-state index: selectivity requirements for COX-2 versus COX-1 binding of terphenyl methyl sulfones and sulfonamides. *Bioorganic & Medicinal Chemistry Letters* 14 (2004) 4665–4670.

Target Species	Human
Chemical Type	Sulfonamides
Mode of Action	Binder
QSAR Model 1	$pC_1 = 1.365(\pm 0.794)S_5 - 0.974(\pm 0.274)I'_{\text{OMe–Me}} + 0.870(\pm 0.300)I_{9,10\text{-F2}} + 2.532(\pm 1.362)$ $n = 18,\ Q^2 = 0.675,\ R^2_a = 0.777,\ R^2 = 0.816, R = 0.903,\ F = 20.7(\text{df}3, 14),\ s = 0.200,$ $\text{AVRES} = 0.141,\ \text{SDEP} = 0.234,\ S_{\text{PRESS}} = 0.265, \text{PRESS} = 0.985,\ \text{Pres}_{\text{av}} = 0.184$
QSAR Model 2	$pC_1 = 0.485(\pm 0.303)S_{4+5} - 0.975(\pm 0.286)I'_{\text{OMe–Me}} + 0.759(\pm 0.280)I_{9,10\text{-F2}} + 3.327(\pm 1.015)$ $n = 18,\ Q^2 = 0.654,\ R^2_a = 0.761,\ R^2 = 0.803,\ R = 0.896,\ F = 19.1(\text{df}3, 14),\ s = 0.207,$ $\text{AVRES} = 0.145,\ \text{SDEP} = 0.242,\ S_{\text{PRESS}} = 0.274, \text{PRESS} = 1.050,\ \text{Pres}_{\text{av}} = 0.189$
Molecular Descriptor	$I'_{\text{OMe–Me}}$: Indicator variable having value 1 to denote presence of methoxy or methyl group at R_2 in presence of fluoro substitution on C_9 and C_{10}, value 0 otherwise; $I_{9,10\text{-F2}}$: Indicator variable having value 1 in presence of fluoro substitution on C_9 and C_{10}, value 0 otherwise; I_{OMe} : Indicator variable having value 1 to denote presence of methoxy group at R2, value 0 otherwise; I_{Me} : Indicator variable having value 1 to denote presence of methyl group at R2, value 0 otherwise; N'_{OMe}: Number of methoxy group at the phenyl ring (R positions) in presence of fluoro substitution on C_9 and C_{10}; I_{W1} : Indicator variable having value 1 to denote presence of amino group at W in presence of fluoro

	substitution on C_9 and C_{10}, value 0 otherwise; I_{W2} : Indicator variable having value 1 to denote presence of amino group at W in absence of fluoro substitution on C_9 and C_{10}, value 0 otherwise; S_X : E-state value of atom X.
Reference	Exploring QSAR with E-state index: selectivity requirements for COX-2 versus COX-1 binding of terphenyl methyl sulfones and sulfonamides. *Bioorganic & Medicinal Chemistry Letters* 14 (2004) 4665–4670.

Target Species	Human
Chemical Type	2-acetoxyphenyl alkyl sulfides
Mode of Action	Inhibitor
QSAR Model 1	$pC_1 = 1.050(\pm 0.951) + 1.624(\pm 1.150)\text{CLOGP} - 0.171(\pm 0.160)(\text{CLOGP})^2$ $n = 20$, $r = 0.83$, $s = 0.31$, $F = 19.22$, Chance < 0.001, $Q^2 = 0.59$, $S_{\text{PRESS}} = 0.36$, and $S_{\text{DEP}} = 0.33$
QSAR Model 2	$pC_1 = 3.775(\pm 1.019) + 0.278(\pm 0.098)\text{SI2} + 3.679(\pm 2.275)\text{DE}$ $n = 20$, $r = 0.83$, $s = 0.32$, $F = 18.48$, Chance < 0.001, $Q^2 = 0.54$, $S_{\text{PRESS}} = 0.38$, and $S_{\text{DEP}} = 0.35$
QSAR Model 3	$pC_1 = 9.466(\pm 5.197) + 2.573(\pm 0.632)\text{BELe6} - 62.753(\pm 33.604)\text{GATS3m} - 1.961(\pm 1.691)\text{Ui}$ $n = 20$, $r = 0.91$, $s = 0.24$, $F = 26.80$, Chance < 0.001, $Q^2 = 0.74$, $S_{\text{PRESS}} = 0.30$, and $S_{\text{DEP}} = 0.27$
Molecular Descriptor	CLOGP: Calculated logarithm of partition coefficient (lipophilicity); SI2: a topological index that quantifies shape of the chemical sample (shape index); DE: Dielectric energy is a portion of the total energy of a molecule embedded in a dielectric (energy); I_1: Indicator variable having value 1 if aromatic ring is present at S-alkyl chain, value 0 otherwise; I_2: Indicator variable having value 1 if

	triple bond is present at S-alkyl chain, value 0 otherwise; X2A: Average connectivity index chi-2 (topological); O-058: O = (atom-centered fragments); BEHm4: Highest eigenvalue no. 4 of burden matrix/weighted by atomic masses (BCUT); BELe6: Lowest eigenvalue no. 6 of burden matrix/weighted by atomic Sanderson electronegativities (BCUT); Ui: Unsaturation index (empirical descriptors); GATS3m: Geary autocorrelation-lag 3/weighted by atomic masses (2D autocorrelation).
Reference	Inhibitory mode of 2-acetoxyphenyl alkyl sulfides against COX-1 and COX-2: QSAR analyses. *Bioorganic & Medicinal Chemistry Letters* 16 (2006) 5280–5284.

Target Species	Human
Chemical Type	Resveratrol analogues
Mode of Action	Inhibitor
QSAR Model 1	$\log(1/\mathrm{IC}_{50})_{\text{COX-1}} = -0.586(\pm 0.216)\mathrm{MR} + 4.449(\pm 1.706)$ $n = 12,\ r = 0.65,\ F = 7.34$
Molecular Descriptor	Physicochemical descriptors (logP, lipophilicity index; TPSA, topological surface area; MR, molar refractivity; APOL, atom polarizability
Reference	Resveratrol analogues as selective cyclooxygenase-2 inhibitors: synthesis and structure–activity relationship. *Bioorganic & Medicinal Chemistry* 12 (2004) 5571–5578

Target Species	Human
Chemical Type	Diaryl furanones
Mode of Action	Inhibitor
QSAR	$\mathrm{pIC50}_{\text{COX-1}} = -0.029(\mathrm{Peoe\_vsa+2}) - 0.013(\mathrm{E\_sol}) + 0.044(\mathrm{vsa\_other}) + 4.228$

Model 1	$N = 18$; $r = 0.788$; $r^2 = 0.641$; adjusted $r^2 = 0.621$; $S = 0.306$; $F_{3,14} = 7.660$; $F_{\alpha = 5\%\ 3,14} = 3.34$; $q^2 = 0.401$; S dep=0.33.
QSAR Model 2	$pIC50_{COX\text{-}1} = 0.122(Std\_dim2) + 0.302(Kier\ A3) + 0.016(SlogP\_vsa1) + 2.699$ $N = 18$; $r = 0.410$; $r^2 = 0.168$; adjusted $r^2 = 0.00$; $S = 0.453$; $F_{3,14} = 0.943$; $F_{\alpha = 5\%\ 3,14} = 3.34$.
QSAR Model 3	$pIC50_{COX\text{-}1} = 0.114(Log\ P) + 4.584$ $N = 18$; $r = 0.146$; $r^2 = 0.021$; adjusted $r^2 = 0.00$; $S = 0.463$; $F_{1,16} = 0.350$.
Molecular Descriptor	N = number of samples, r = coefficient of correlation, F-test for quality of fit, t-test for test of significance, and s = standard deviation, S dep = standard error of prediction. Std_dim2 is three dimensional surface area, volume and shape descriptor, which depends upon structure connectivity and conformation. Kier A3 is Kier and Hall Connectivity and Kappa Shape Index, which compares the molecular graph with minimal and maximal molecular graphs, and is intended to capture different aspects of molecular shape. Log P as the octanol/water partition coefficient including implicit hydrogens and is calculated from a linear atom type model. Vsa_other is the van derWaal's surface area of all atoms other than donor, acceptor, polar (both donor and acceptor), positive (base), negative (acid) and hydrophobic. Peoe_vsa+2 is the partial charge descriptor
Reference	Quantitative structure activity relationship studies of diaryl furanones as selective COX-2 inhibitors. *European Journal of Medicinal Chemistry* 39 (2004) 899–904.

Target Species	Human
Chemical Type	Benzylideneamino scaffolds
Mode of Action	Inhibitor
QSAR Model 1	$pIC50_{(COX\text{-}1)} = 0.323(\pm0.058)\ I_{pm} + 0.506(\pm0.086)\ I_{mOH} - 0.185(\pm0.057)\ I_{OCH3} - 0.452(\pm0.054)\ I_{(-N=C-)} + 4.265(\pm0.044)$

	n= 31, r = 0.916, r^2_{Adj} = 0.814, s = 0.134, $F_{(4, 26)}$ = 33.866, p = 0.000, q2 = 0.764, Spress = 0.162, SDEP = 0.148, DW=2.089.
QSAR Model 2	$pIC50_{(COX\text{-}1)} = 0.368(\pm0.052)\ I_{pm} + 0.511(\pm0.074)\ I_{mOH} + 4.268(\pm0.038) - 0.240(\pm0.052)\ I_{OCH3} - 0.470(\pm0.047)\ I_{(-N=C-)}$ n= 30, r = 0.941, r^2_{Adj} = 0.867, s = 0.115, $F_{(4,25)}$ = 48.064, p = 0.000, q2 = 0.827, Spress = 0.141, SDEP = 0.129, DW=2.042.
Molecular Descriptor	Hydrophobicity (π), molar refractivity (MR), Hammett electronic (σ), electronic field effect (F), resonance effect (R); $I_{(-N=C-)}$ suggest that N=C- as central core(X) in the aryl sulphonamides
Reference	QSAR Investigations on Benzylideneamino and Phenyliminomethyl Scaffolds for Selective COX-2 Inhibition: A Hansch Approach. *Medicinal Chemistry*, 2009, 5, 440-445

Target Species	Human
Chemical Type	Phenyliminomethyl scaffolds
Mode of Action	Inhibitor
QSAR Model 1	$pIC50_{(COX\text{-}1)} = 0.323(\pm0.058)\ I_{pm} + 0.506(\pm0.086)\ I_{mOH} - 0.185(\pm0.057)\ I_{OCH3} - 0.452(\pm0.054)\ I_{(-N=C-)} + 4.265(\pm0.044)$ n= 31, r = 0.916, r^2_{Adj} = 0.814, s = 0.134, $F_{(4, 26)}$ = 33.866, p = 0.000, q2 = 0.764, Spress = 0.162, SDEP = 0.148, DW=2.089.
QSAR Model 2	$pIC50_{(COX\text{-}1)} = 0.368(\pm0.052)\ I_{pm} + 0.511(\pm0.074)\ I_{mOH} + 4.268(\pm0.038) - 0.240(\pm0.052)\ I_{OCH3} - 0.470(\pm0.047)\ I_{(-N=C-)}$ n= 30, r = 0.941, r^2_{Adj} = 0.867, s = 0.115, $F_{(4,25)}$ = 48.064, p = 0.000, q2 = 0.827, Spress = 0.141, SDEP = 0.129, DW=2.042.
Molecular Descriptor	Hydrophobicity (π), molar refractivity (MR), Hammett electronic (σ), electronic field effect (F), resonance effect (R); $I_{(-N=C-)}$ suggest that N=C- as central core(X) in the aryl sulphonamides

Reference	QSAR Investigations on Benzylideneamino and Phenyliminomethyl Scaffolds for Selective COX-2 Inhibition: A Hansch Approach. *Medicinal Chemistry*, 2009, 5, 440-445

Target Species	Human
Chemical Type	Benzenesulfonamide derivatives
Mode of Action	Inhibitor
QSAR Model 1	$$pIC_{50}(COX\text{-}1) = 19.425 - 16.478(3.826)MATS5m + 2.373(0.523)MATS6v + 2.003(0.437)GATS6p + 0.513(0.080)Hy$$ $$n = 30,\ r = 0.877,\ s = 0.198,\ F = 20.844,\ Q^2_{LOO} = 0.666$$ $$Q^2_{L5O} = 0.711,\ r^2_{randY}(sd) = 0.336(0.121)$$ $$FIT = 1.812,\ LOF = 0.061,\ AIC = 0.055,\ r^2_{Test} = 0.584$$
Molecular Descriptor	MW: molecular weight; TOPO: HNar, Narumi harmonic topological index; X3A: average connectivity index chi-3; X1Av: average valence connectivity index chi-1; PW3,PW4: path/walk-3 and -4 Randic shape index; IVDE: mean information content valence degree equality; LP1: LovaszePelikan index (leading eigenvalue); ICk: information content index of k-order neighborhood symmetry; SIC5: structural information content of 5-order neighborhood symmetry; TIE: E-state topological parameter; BCUT: BEHm2, and BELm2, highest and lowest eigenvalue n.2 of Burden matrix, respectively, weighted by atomic masses; BEHv1 and BEHv2: highest eigenvalue n.1 and n.2, respectively, of Burden matrix weighted by atomic polarizabilities; BELv1 and BELp1: lowest eigenvalue n.1 of Burden matrix weighted by atomic van der Waals volumes and polarizabilities, respectively; BEHe1, BEHp1: highest eigenvalue n.1 of Burden matrix weighted by atomic Sanderson electronegativities and polarizabilities, respectively; 2D-AUTO: MATSnk, and GATSnk, Moran and Geary autocorrelation of lag n weighted by molecular property (k) such as atomic masses, van der Waals volumes, polarizabilities and Sanderson electronegativities; FUNC: nCconjR, number of exo-conjugated carbon C(sp2); nHDon: number of donor atoms for H-bonds (with N and O); ACF: C-009, CHRX2; EMP: Hy, hydrophilic factor; PROP: PSA, fragment based polar surface area.
Reference	A rationale for the activity profile of benzenesulfonamide derivatives as cyclooxygenase (COX)

	inhibitors. *European Journal of Medicinal Chemistry* 45 (2010) 2389-2395