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| **Target Name** | COX-2 |
| **Target TTD ID** | TTDS00041 |

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| **Target Species** | Human |
| **Chemical Type** | Diaryl furanones |
| **Mode of Action** | Inhibitor |
| **QSAR Model 1** | $pIC50_{COX\text{-}2} = 1.281(Std\_dim2) + 1.719(Kier\ A3) - 0.042(SlogP\_vsa1) - 0.076$<br>$N = 31;\ r = 0.870;\ r^2 = 0.757;$ adjusted $r^2 = 0.730; S = 0.432; F_{3,27} = 28.084; F_{\alpha = 5\%\ 3,27} = 2.96.$ |
| **QSAR Model 2** | $pIC50_{COX\text{-}2} = 0.921(Std\_dim2) + 1.919(Kier\ A3) - 0.037(SlogP\_vsa1) - 0.238$<br>$N = 30;\ r = 0.922;\ r^2 = 0.849;$ adjusted $r^2 = 0.832; S = 0.339;\ q^2 = 0.80;\ F_{3,26} = 48.807;\ F_{\alpha = 5\%\ 3,26} = 2.98;\ S\ dep = 0.35.$ |
| **QSAR Model 3** | $pIC50_{COX\text{-}2} = 0.819(\log P) + 3.556$<br>$N = 30;\ r = 0.764;\ r^2 = 0.584;$ adjusted $r^2 = 0.569; S = 0.542; F_{1,28} = 39.341; F_{\alpha = 5\%\ 1,28} = 4.20.$ |
| **Molecular Descriptor 3** | Access the following web-servers to compute molecular descriptors: **MoDel** and **e-dragon**<br>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 |

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|---|---|
| **Target Species** | Human |
| **Chemical Type** | 1,3-diaryl-4,5,6,7-tetrahydro-2H-isoindole derivatives |
| **Mode of Action** | Inhibitor |
| **QSAR Model 1** | $pIC_{50} = -0.000617 \times \text{Apol} + 16.269758$<br>$n = 25,\ r = 0.870,\ r^2 = 0.757,\ F_{1,23\ \text{cal}} = 32.673,\ F_{\alpha\ 5\%\ 1,23\ \text{tab}} = 4.284,\ \text{std} = 0.581$ |
| **QSAR Model 2** | $pIC_{50} = -0.000664 \times \text{Apol} + 0.449673 \times \text{HBD} + 16.405326$<br>$n = 25,\ r = 0.904,\ r^2 = 0.817,\ F_{2,22\ \text{cal}} = 29.819,\ F_{\alpha\ 5\%\ 2,22\ \text{tab}} = 3.45,\ \text{std} = 0.516$ |
| **QSAR Model 3** | $pIC_{50} = -0.000606 \times \text{Apol} - 0.327658 \times \text{HOMO} + 13.056474$<br>$n = 25,\ r = 0.873,\ r^2 = 0.761,\ F_{2,22\ \text{cal}} = 21.276,\ F_{\alpha\ 5\%\ 2,22\ \text{tab}} = 3.45,\ \text{std} = 0.590$ |
| **QSAR Model 4** | $pIC_{50} = -0.000703 \times \text{Apol} - 0.063167 \times F_{H_2O} + 16.543090$<br>$n = 25,\ r = 0.897,\ r^2 = 0.804,\ F_{2,22\ \text{cal}} = 27.334,\ F_{\alpha\ 5\%\ 2,22\ \text{tab}} = 3.45,\ \text{std} = 0.535$ |
| **QSAR Model 5** | $pIC_{50} = -0.000629 \times \text{Apol} - 1.443421 \times \text{Sxyf} + 17.278286$<br>$n = 25,\ r = 0.871,\ r^2 = 0.758,\ F_{2,22\ \text{cal}} = 20.872,\ F_{\alpha\ 5\%\ 2,22\ \text{tab}} = 3.45,\ \text{std} = 0.594$ |
| **QSAR Model 6** | $pIC_{50} = -0.000642 \times \text{Apol} - 1.990139 \times \text{Sxzf} + 17.990429$<br>$n = 25,\ r = 0.874,\ r^2 = 0.764,\ F_{2,22\ \text{cal}} = 21.530,\ F_{\alpha\ 5\%\ 2,22\ \text{tab}} = 3.45,\ \text{std} = 0.587$ |
| **QSAR Model 7** | $pIC_{50} = 6.687 \times (\text{TOT}/1481) + 0.790 \times (\text{InterVDWEnergy}) - 11.0154 \times (\text{TOT}/1710) + 4.321 \times (\text{TOT}/1263) + 10.411 \times (\text{TOT}/1709) + 12.254$<br>$n = 25, \text{LOF} = 0.123, r = 0.940, r^2 = 0.883,\ r^2_{\text{adj}} = 0.859, F\text{-test} = 36.311,\ \text{PRESS} = 6.464, \text{LSE} = 0.139$ |
| **Molecular Descriptor** | Access the following web-servers to compute molecular descriptors: **MoDel** and **e-dragon**<br>The Apol descriptor computes the sum of the atomic polarizabilities. HBD is a structural descriptor that counts the number of hydrogen-bonding donor groups in the current molecule. HOMO (highest occupied molecular orbital) is the highest energy level in the molecule that contains electrons. LUMO (lowest unoccupied molecular orbital) is the lowest energy level in the molecule that contains no electrons. Both these energies are important in governing molecular reactivity.<br>$F_{H2O}$ is the aqueous desolvation free energy in kcal $mol^{-1}$ derived from a hydration shell model developed by Hopfinger This is a physicochemical property associated with linear free energy (LFE) models that measure |

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| | absolute hydrophilicityof the molecule. LFE computations are based solely on the connectivity of the atoms in a molecule and are not conformationally dependent. This property is useful as molecular descriptor in QSAR. QSAR calculates $F_{H2O}$ for each molecule by searching the molecule for recognizable substituent groups and their bonding patterns and summing the substituent constants' contributions for each group that is present in the molecule.<br><br>Sxyf and Sxzf are geometric descriptors that help to characterize the shape of the molecules. Sxyf and Sxzf are fraction of areas of molecular shadow in the XY and ZX planes, respectively, over area of enclosing rectangle. The descriptors are calculated by projecting the molecular surface on mutually perpendicular planes, XY and XZ.<br><br>The descriptors TOT/1481, TOT/1710, etc. are added energy of both electrostatic and van der Waals interaction energies at points 1481, 1710, etc. Descriptor InterVDWEnergy is non-bond van der Waals energy between molecule and receptor.<br><br>The statistical measures, $r^2$, LSE and F, determine the estimation power of model for the same data from which it has been determined and evaluate it only internally. Cross-validated parameters, LOF, $r^2_{adj}$ and PRESS, determine the prediction power for the data not included in deriving the model and evaluate the model externally to avoid chance of correlation completely. |
| **Reference** | QSAR analysis of 1,3-diaryl-4,5,6,7-tetrahydro-2H-isoindole derivatives as selective COX-2 inhibitors. *European Journal of Medicinal Chemistry* 43 (2008) 1559e1569 |

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|---|---|
| **Target Species** | Human |
| **Chemical Type** | 2,6-di-*tert*-Butylphenol derivatives |
| **Mode of Action** | Inhibitor |
| **QSAR Model 1** | $pIC_{50}(COX) = 0.43(\pm 0.09)ClogP + 3.13(\pm 0.47)$<br><br>$n = 14 \;\; r^2 = 0.645 \;\; Q^2 = 0.566 \;\; s = 0.586 \;\; F = 21.78$ |
| **QSAR Model 2** | $pIC_{50}(COX) = -1.11(\pm 0.29)Qt + 0.37(\pm 0.07)ClogP + 3.02(\pm 0.32)$ |

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| | $n = 14\ \ r^2 = 0.845\ \ Q^2 = 0.767\ \ s = 0.405\ \ F = 29.81$ |
| **Molecular Descriptor** | Access the following web-servers to compute molecular descriptors: **MoDel** and **e-dragon**<br>Hydrophobicity, the ClogP parameter. |
| **Reference** | QSAR Study of Dual Cyclooxygenase and 5-Lipoxygenase Inhibitors 2,6-di-tert-Butylphenol Derivatives. *Bioorganic & Medicinal Chemistry* 11 (2003) 4207–4216 |

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|---|---|
| **Target Species** | Human |
| **Chemical Type** | Terphenyl methyl sulfones |
| **Mode of Action** | Binder |
| **QSAR Model 1** | $pC_2 = 0.414(\pm 0.181)I_{W1} + 0.861(\pm 0.285)I_{W2} - 0.584(\pm 0.145)N'_{OMe} + 1.385(\pm 0.239)I_{9,10\text{-}F2} + 6.673(\pm 0.206)$<br>$n = 38,\ Q^2 = 0.842,\ R^2_a = 0.874,\ R^2 = 0.888, R = 0.942,\ F = 65.3(df4, 33),\ s = 0.231,$ AVRES $= 0.178,$ SDEP $= 0.256,$ $S_{PRESS} = 0.274,$ PRESS $= 2.485,$ $Pres_{av} = 0.208$ |
| **QSAR Model 2** | $pC_2 = -0.799(\pm 0.362)S_{19} + 0.464(\pm 0.340)I_{W2} - 0.592(\pm 0.147)N'_{OMe} + 1.316(\pm 0.257)I_{9,10\text{-}F2} + 4.075(\pm 1.314)$<br>$n = 38,\ Q^2 = 0.837,\ R^2_a = 0.871,\ R^2 = 0.885,\ R = 0.941,\ F = 63.5(df4, 33),\ s = 0.234,$ AVRES $= 0.182,$ SDEP $= 0.260,$ $S_{PRESS} = 0.279,$ PRESS $= 2.561,$ $Pres_{av} = 0.214$ |
| **QSAR Model 3** | $pC_2 = -1.212(\pm 0.626)S_{19-20} + 0.532(\pm 0.347)I_{W2} - 0.625(\pm 0.156)N'_{OMe} + 1.321(\pm 0.273)I_{9,10\text{-}F2} - 11.346(\pm 9.444)$<br>$n = 38,\ Q^2 = 0.820,\ R^2_a = 0.859,\ R^2 = 0.874, R = 0.935,\ F = 57.2(df4, 33),\ s = 0.245,$ AVRES $= 0.191,$ SDEP $= 0.273,$ $S_{PRESS} = 0.293,$ PRESS $= 2.828,$ $Pres_{av} = 0.224$ |
| **Molecular Descriptor** | Access the following web-servers to compute molecular descriptors: **MoDel** and **e-dragon**<br>$I'_{OMe-Me}$: 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; |

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| | $I_{9,10\text{-}F2}$: Indicator variable having value 1 in presence of fluoro substitution on $C_9$ and $C_{10}$, value 0 otherwise;<br>$I_{OMe}$ : Indicator variable having value 1 to denote presence of methoxy group at R2, value 0 otherwise;<br>$I_{Me}$ : Indicator variable having value 1 to denote presence of methyl group at R2, value 0 otherwise;<br>$N'_{OMe}$: Number of methoxy group at the phenyl ring (R positions) in presence of fluoro substitution on $C_9$ and $C_{10}$;<br>$I_{W1}$ : 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;<br>$I_{W2}$ : 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;<br>$S_X$ : 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. |

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|---|---|
| **Target Species** | Human |
| **Chemical Type** | Sulfonamides |
| **Mode of Action** | Binder |
| **QSAR Model 1** | $pC_2 = 0.414(\pm0.181)I_{W1} + 0.861(\pm0.285)I_{W2} - 0.584(\pm0.145)N'_{OMe} + 1.385(\pm0.239)I_{9,10\text{-}F2} + 6.673(\pm0.206)$<br>$n = 38,\ Q^2 = 0.842,\ R^2_a = 0.874,\ R^2 = 0.888, R = 0.942,\ F = 65.3(df4, 33),\ s = 0.231,$ AVRES $= 0.178,$ SDEP $= 0.256,\ S_{PRESS} = 0.274,$ PRESS $= 2.485,\ Pres_{av} = 0.208$ |
| **QSAR Model 2** | $pC_2 = -0.799(\pm0.362)S_{19} + 0.464(\pm0.340)I_{W2} - 0.592(\pm0.147)N'_{OMe} + 1.316(\pm0.257)I_{9,10\text{-}F2} + 4.075(\pm1.314)$<br>$n = 38,\ Q^2 = 0.837,\ R^2_a = 0.871,\ R^2 = 0.885,\ R = 0.941,\ F = 63.5(df4, 33),\ s = 0.234,$ AVRES $= 0.182,$ SDEP $= 0.260,\ S_{PRESS} = 0.279,$ PRESS $= 2.561,\ Pres_{av} = 0.214$ |

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| **QSAR Model 3** | $pC_2 = -1.212(\pm 0.626)S_{19-20} + 0.532(\pm 0.347)I_{W2} - 0.625(\pm 0.156)N'_{OMe} + 1.321(\pm 0.273)I_{9,10\text{-}F2} - 11.346(\pm 9.444)$<br>$n = 38,\ Q^2 = 0.820,\ R^2_a = 0.859,\ R^2 = 0.874, R = 0.935,\ F = 57.2(df4, 33),\ s = 0.245,$ AVRES $= 0.191,$ SDEP $= 0.273,\ S_{PRESS} = 0.293,$ PRESS $= 2.828,\ Pres_{av} = 0.224$ |
| **Molecular Descriptor** | Access the following web-servers to compute molecular descriptors: **MoDel** and **e-dragon**<br>$I'_{OMe-Me}$: 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;<br>$I_{9,10\text{-}F2}$: Indicator variable having value 1 in presence of fluoro substitution on $C_9$ and $C_{10}$, value 0 otherwise;<br>$I_{OMe}$ : Indicator variable having value 1 to denote presence of methoxy group at R2, value 0 otherwise;<br>$I_{Me}$ : Indicator variable having value 1 to denote presence of methyl group at R2, value 0 otherwise;<br>$N'_{OMe}$: Number of methoxy group at the phenyl ring (R positions) in presence of fluoro substitution on $C_9$ and $C_{10}$;<br>$I_{W1}$ : 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;<br>$I_{W2}$ : 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;<br>$S_X$ : 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. |

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|---|---|
| **Target Species** | Human |
| **Chemical Type** | 2-acetoxyphenyl alkyl sulfides |
| **Mode of Action** | Inhibitor |

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| **QSAR Model 1** | $pC_2 = 0.043(\pm 0.20) + 2.265(\pm 1.401)\text{CLOGP} - 0.247(\pm 0.204)(\text{CLOGP})^2 - 1.138(\pm 0.587)I_1 + 0.377(\pm 0.354)I_2$<br>$n = 22$. $r = 0.93$. $s = 0.34$. $F = 25.35$. Chance $< 0.001$, $Q^2 = 0.76$, $S_{\text{PRESS}} = 0.43$, and $S_{\text{DEP}} = 0.38$ |
| **QSAR Model 2** | $pC_2 = 2.600(\pm 0.979) + 0.390(\pm 0.097)\text{SI2} + 2.739(\pm 2.063)\text{DE} - 0.708(\pm 0.517)I_1 + 0.475(\pm 0.326)I_2$<br>$n = 22$, $r = 0.93$, $s = 0.32$, $F = 28.22$, Chance $< 0.001$, $Q^2 = 0.79$, $S_{\text{PRESS}} = 0.41$, and $S_{\text{DEP}} = 0.36$ |
| **QSAR Model 3** | $pC_2 = -23.951(\pm 5.878) + 75.897(\pm 19.313)\text{X2A} - 1.561(\pm 0.721)\text{O-058} + 1.685(\pm 0.886)\text{BEHm4}$<br>$n = 22$, $r = 0.93$, $s = 0.31$, $F = 39.13$, Chance $< 0.001$, $Q^2 = 0.693$, $S_{\text{PRESS}} = 0.364$, and $S_{\text{DEP}} = 0.353$ |
| **Molecular Descriptor** | Access the following web-servers to compute molecular descriptors: **MoDel** and **e-dragon**<br>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. |

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| **Target Species** | Human |

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| **Chemical Type** | Resveratrol analogues |
| **Mode of Action** | Inhibitor |
| **QSAR Model 1** | $\log(1/\mathrm{IC}_{50})_{\text{COX-2}} = 0.044(\pm 0.0056)\mathrm{TPSA} - 1.827(\pm 0.392)$<br>$n = 12,\ r = 0.93,\ F = 60.4$ |
| **Molecular Descriptor** | Access the following web-servers to compute molecular descriptors: **MoDel** and **e-dragon**<br>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 |

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|---|---|
| **Target Species** | Human |
| **Chemical Type** | 2,3-diaryl benzopyran analogues |
| **Mode of Action** | Inhibitor |
| **QSAR Model 1** | $p\mathrm{IC}_{50} = 0.336(\pm 0.138)a\_nS - 0.047(\pm 0.010)S\log P\_VSA1$<br>$- 0.013(\pm 0.003)\mathrm{vdw\_vol} + 12.258(\pm 1.624)$<br>$n = 26,\ r = 0.826,\ r^2 = 0.683,\ s = 0.269,\ F_{3,22} = 15.79,\ q^2 = 0.5765,\ \mathrm{Spress} = 0.311,$<br>$\mathrm{SDEP} = 0.286,\ p = 0.000$ |
| **QSAR Model 2** | $p\mathrm{IC}_{50} = -8.372(\pm 2.850)E\_\mathrm{oop} - 0.250(\pm 0.071)\mathrm{chi0\_C}$<br>$- 0.049(\pm 0.008)S\log P\_VSA1 + 10.010(\pm 1.210)$<br>$n = 26,\ r = 0.857,\ r^2 = 0.735,\ s = 0.246,\ F_{3,22} = 20.30,\ q^2 = 0.6649,\ \mathrm{Spress} = 0.277,$<br>$\mathrm{SDEP} = 0.255,\ p = 0.000$ |

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| **Molecular Descriptor** | Access the following web-servers to compute molecular descriptors: **MoDel** and **e-dragon**<br><br>S log P_VSA1 is a subdivided surface area descriptor based on approximate accessible van der Waals surface area calculated for each atom. a_nS is a function of count of sulphur atoms. vdw_vol is the van der Waals volume. E_oop is the out of plane potential energy, an internal3D descriptor. chi0_C (topological descriptor) is the carbon connectivity index of order 0. Aro denotes an aromatic ring probe, Don denotes an H-bond donor, and Acc denotes an H-bond acceptor, Cat denotes the cations, Ani denotes the anions, and Hyd denotes hydrophobic areas. |
| **Reference** | Quantitative structure–activity relationship analysis of a series of 2,3-diaryl benzopyran analogues as novel selective cyclooxygenase-2 inhibitors. *Bioorganic & MedicinalChemis try Letters* 14 (2004) 4005–4011 |

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|---|---|
| **Target Species** | Human |
| **Chemical Type** | Diaryl furanones |
| **Mode of Action** | Inhibitor |
| **QSAR Model 1** | $pIC50_{COX\text{-}2} = 1.281(Std\_dim2) + 1.719(Kier\ A3) - 0.042(SlogP\_vsa1) - 0.076$<br><br>$N = 31$; $r = 0.870$; $r^2 = 0.757$; adjusted $r^2 = 0.730$; $S = 0.432$; $F_{3,27} = 28.084$; $F_{\alpha = 5\%\ 3,27} = 2.96$. |
| **QSAR Model 2** | $pIC50_{COX\text{-}2} = 0.921(Std\_dim2) + 1.919(Kier\ A3) - 0.037(SlogP\_vsa1) - 0.238$<br><br>$N = 30$; $r = 0.922$; $r^2 = 0.849$; adjusted $r^2 = 0.832$; $S = 0.339$; $q^2 = 0.80$;<br>$F_{3,26} = 48.807$; $F_{\alpha = 5\%\ 3,26} = 2.98$; $S$ dep $= 0.35$. |
| **QSAR Model 3** | $pIC50_{COX\text{-}2} = 0.819(Log\ P) + 3.556$<br><br>$N = 30$; $r = 0.764$; $r^2 = 0.584$; adjusted $r^2 = 0.569$; $S = 0.542$; $F_{1,28} = 39.341$;<br>$F_{\alpha = 5\%\ 1,28} = 4.20$ |
| **Molecular Descriptor** | Access the following web-servers to compute molecular descriptors: **MoDel** and **e-dragon**<br><br>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 |

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| | 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.<br><br>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. |

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|---|---|
| **Target Species** | Human |
| **Chemical Type** | 2,3-Diaryl Benzopyrans/Pyrans |
| **Mode of Action** | Inhibitor |
| **QSAR Model 1** | $pIC_{50} = 0.443(\pm 0.046)\text{LogP} - 0.115(\pm 0.024)\text{Dipole-Z} - 1.086\ (\pm 0.282)\ E_{LUMO} + 0.462\ (\pm 0.427)$<br><br>$n = 28,\ r = 0.919,\ r^2 = 0.844,\ s = 0.214,\ F_{(3,24)} = 43.42,\ S_{PRESS} = 0.2515,\ Q^2 = 0.786,$ $SDEP = 0.2328,\ DW = 1.718.,\ p = 0.000,\ \text{chance} < 0.01.$ |
| **Molecular Descriptor** | Access the following web-servers to compute molecular descriptors: **MoDel** and **e-dragon**<br><br>LogP, the calculated partition coefficient is a measure of hydrophobicity of compounds. The dipole moment descriptor, Z component is a 3D electronic descriptor that indicates the strength and orientation behavior of the molecule in an electrostatic field. Descriptor $E_{LUMO}$ is an electronic parameter and measures the electrophilicity of the molecules.When a molecule acts as a Lewis acid (an electron pair acceptor) in bond formation, incoming electrons are received in its LUMO. Molecules with low-lying LUMO are more able to accept electron than those with high energy LUMO. |
| **Reference** | QSAR Analysis of 2,3-Diaryl Benzopyrans/Pyrans as Selective COX-2 Inhibitors Based on Semiempirical AM1 Calculations. *QSAR Comb. Sci*. 2004, 23 |

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|---|---|
| **Target Species** | Human |
| **Chemical Type** | 2-(4-methanesulfonylphenyl)pyran-4-ones |
| **Mode of Action** | Inhibitor |
| **QSAR Model 1** | $\mathrm{pIC}_{50(\text{COX-2 MPM})} = 0.639(\pm 0.100)\log P + 1.438(\pm 0.238)$<br>$n = 18,\quad r = 0.848,\quad r^2 = 0.720,\quad s = 0.283,\quad F_{1,16} = 41.07,\quad q^2 = 0.6040,$<br>$p = 0.000,\quad DW = 2.655.$ |
| **QSAR Model 2** | $\mathrm{pIC}_{50(\text{COX-2 MPM})} = 0.487(\pm 0.094)MR \quad - 1.860(\pm 0.926)$<br>$n = 18,\quad r = 0.791,\quad r^2 = 0.625,\quad s = 0.327,\quad F_{1,16} = 26.67,\quad q^2 = 0.5497,$<br>$p = 0.000,\quad DW = 2.896.$ |
| **QSAR Model 3** | $\mathrm{pIC}_{50(\text{COX-2 MPM})} = 0.499(\pm 0.074)MR \quad - 1.928(\pm 0.729)$<br>$n = 17,\quad r = 0.866,\quad r^2 = 0.750,\quad s = 0.257,\quad F_{1,15} = 45.03,\quad q^2 = 0.6984,$<br>$p = 0.000,\ DW = 2.685.$ |
| **QSAR Model 4** | $\mathrm{pIC}_{50(\text{COX-2 MPM})} = 1.285(\pm 0.239)I_{\mathrm{BP}} \quad + 2.762(\pm 0.080)$<br>$n = 18,\quad r = 0.803,\quad r^2 = 0.644,\quad s = 0.318,\quad F_{1,16} = 28.97,\quad q^2 = 0.5907,$<br>$p = 0.000,\quad DW = 2.469.$ |
| **QSAR Model 5** | $\mathrm{pIC}_{50(\text{COX-2 MPM})} = 0.423(\pm 0.130)\log P + 0.627(\pm 0.277)I_{\mathrm{BP}} + 1.864(\pm 0.284)$<br>$n = 18,\quad r = 0.889,\quad r^2 = 0.791,\quad s = 0.252,\quad F_{2,15} = 28.41,\quad q^2 = 0.7497,$<br>$p = 0.000,\quad DW = 2.796.$ |
| **Molecular Descriptor** | Access the following web-servers to compute molecular descriptors: **MoDel** and **e-dragon**<br>B1 is a measure of width of the first atom of substituents. $I_{2F}$ is an indicator variable given a value of 1 for 2 |

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| | fluoro substituents and 0 for others. MR = $(n^2-1)/(n^2+2)$MW/d, where n is the index of refraction, MW represents molecular weight of the compound and d is the density. IBP assumes a value of 1 when biphenyl substitution occurs at the 3- position of the pyran-4-one structure and 0 for others. ICl, (used in order to account for binary structural variation at the fifth position of pyran-4-one ring among the congeners) |
| **Reference** | QSAR studies on structurally similar 2-(4-methanesulfonylphenyl)pyran-4-ones as selective COX-2 inhibitors:a Hansch approach. *Bioorganic & Medicinal Chemistry Letters* 15 (2005) 313–320 |

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| **Target Species** | Human |
| **Chemical Type** | 1,5-diaryl pyrazoles |
| **Mode of Action** | Inhibitor |
| **QSAR Model 1** | $$pIC_{50(COX\text{-}2)} = -17.143(\pm 2.216)\text{std\_dim3} + 26.818(\pm 2.536)$$ $$n = 14,\ r = 0.913,\ r^2 = 0.833,\ r^2_{Adj} = 0.819,\ s = 0.360,\ F = 59.86,$$ $$p = 0.000,\ q^2 = 0.7464,\ DW = 1.792 \quad \text{outlier} : A = S,\quad B = CH_2,$$ $$R_1 = 7F,\ R_2 = CN,\ Y = NH_2$$ |
| **QSAR Model 2** | $$pIC_{50(COX\text{-}2)} = -0.164(\pm 0.037)\text{b\_single} - 56.975(\pm 5.812)\text{glob} + 19.550(\pm 1.564)$$ $$n = 14,\ r = 0.948,\ r^2 = 0.898,\ r^2_{Adj} = 0.880,\quad s = 0.294,\ F = 48.55,$$ $$p = 0.000,\ q^2 = 0.8399,\ DW = 2.802 \quad \text{outlier} : A = S,\ B = CH_2,$$ $$R_1 = 7F,\ R_2 = CN,\quad Y = NH_2$$ |
| **QSAR Model 3** | $$pIC_{50(COX\text{-}1)} = 3.829(\pm 0.558)C^7 + 5.117(\pm 0.111)$$ |

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| | $n = 10,\ r = 0.925,\ \ r^2 = 0.855,\ r^2_{\text{Adi}} = 0.837,\ s = 0.268,\ F = 47.15,$ $p = 0.000,\ q^2 = 0.7949,\ \ \text{DW} = 2.661\ \ \text{outliers}: \text{A} = \text{S},\ \text{B} = \text{CH}_2,$ $\text{R}_1 = \text{H},\ \text{R}_2 = \text{CF}_3,\ \text{Y} = \text{NH}_2;\ \text{A} = \text{S},\ \text{B} = \text{CH}_2,\ \text{R}_1 = 7\text{OCH}_3,$ $8\text{F},\ \text{R}_2 = \text{CF}_3,\ \ \text{Y} = \text{NH}_2$ |
| **QSAR Model 4** | $\text{pIC}_{50(\text{COX-1})} = 1.325(\pm 0.227)\text{a\_nS} - 45.911(\pm 8.187)\text{Balaban } J + 74.503(\pm 12.551)$ $n = 10,\ r = 0.934,\ r^2 = 0.872,\ r^2_{\text{Adj}} = 0.836,\ s = 0.267,\ F = 23.87,$ $p = 0.001,\ q^2 = 0.7491,\ \text{DW} = 2.211\ \ \text{outliers}: \text{A} = \text{CH}_2,\ \text{B} = \text{S},$ $\text{R}_1 = \text{H},\ \text{R}_2 = \text{CF}_3,\ \text{Y} = \text{NH}_2;\ \ \text{A} = \text{S},\ \ \text{B} = \text{CH}_2,\ \text{R}_1 = 7\text{F},$ $\text{R}_2 = \text{CN},\ \text{Y} = \text{NH}_2$ |
| **Molecular Descriptor** | Access the following web-servers to compute molecular descriptors: **MoDel** and **e-dragon**<br>2D adjacency and distance matrix descriptors: Balaban J; diameter; Petitjean; radius; VDistEq VDistMa; WeinerPath; WeinerPol.<br>2D atom counts and bond counts: a_aro; a_count; a_heavy; a_nH; a_nC; a_nN; a_nO; a_nS; b_single; b_double; b_triple; b_heavy; VAdjMa.<br>3D surface area, volume and shape descriptors: ASA; dens; glob; pmi; pmiX; pmiYl; pmiZ; rgyr; std_dim1; std_dim2; Std_dim3; vol; VSA |
| **Reference** | QSAR analyses of conformationally restricted 1,5-diaryl pyrazoles as selective COX-2 inhibitors:application of connection table representation of ligands. *Bioorganic & Medicinal Chemistry Letters* 15(2005 ) 2097–2102 |

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| **Target Species** | Human |
| **Chemical Type** | Meclofenamic acid analogues |
| **Mode of Action** | Inhibitor |

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| **QSAR Model 1** | $pIC_{50(COX\text{-}2)} = 0.651(\pm 0.098)\text{kierflex} - 0.365(\pm 0.082)\text{chi1\_C} + 9.020(\pm 2.003)\text{glob} + 21.682(\pm 4.514)\text{petitjean} - 6.748(\pm 2.280),$ $n = 21,\ r = 0.891,\ r^2 = 0.794,\ \text{SE} = 0.406,\ F = 15.465.$ |
| **QSAR Model 2** | $pIC_{50(COX\text{-}2)} = 0.613(\pm 0.130)\text{kierflex} + 9.017(\pm 2.578)\text{glob} + 17.680(\pm 5.568)\text{petitjean} + 12.220(\pm 5.076)\text{PEOE\_VSA\_FPPOS} - 7.115(\pm 2.691),$ $n = 21,\ r = 0.814,\ r^2 = 0.662,\ \text{SE} = 0.521,\ F = 7.827.$ |
| **QSAR Model 3** | $pIC_{50(COX\text{-}1)} = 0.057(\pm 0.018)\text{PEOE\_VSA} + 2 - 0.892(\pm 0.140)\text{E\_ang} + 0.001(\pm 0.0002)\text{pmiZ} + 24.741(\pm 4.148)\text{PEOE\_VSA\_FPPOS} + 4.677(\pm 0.471),$ $n = 21,\ r = 0.899,\ r^2 = 0.810,\ \text{SE} = 0.459,\ F = 17.032.$ |
| **QSAR Model 4** | $pIC_{50(COX\text{-}2)} = 4.188(\pm 0.876) + 0.364(\pm 0.149)\text{kierflex},$ $n = 21,\ r = 0.489,\ r^2 = 0.239,\ \text{variance} = 0.515,\ \text{SE} = 0.717,\ F = 5.963.$ |
| **QSAR Model 5** | $pIC_{50(COX\text{-}1)} = 4.917(\pm 1.174) + 0.076(\pm 0.200)\text{kierflex},$ $n = 21,\ r = 0.089,\ r^2 = 0.008,\ \text{variance} = 0.925,\ \text{SE} = 0.962,\ F = 0.146.$ |
| **Molecular Descriptor** | Access the following web-servers to compute molecular descriptors: **MoDel** and **e-dragon**<br><br>Kier molecular flexibility index is given by (KierA1) (KierA2)/n. Molecular flexibility (kierflex), a topological 2D parameter, indicates the influence of the molecule's shape on COX-2 activity. chil_C is calculated as the sum of 1/sqrt (didj) over all bonds between carbon atoms i and j where i < j. Petitjean, a negatively contributing distance and adjacency matrix descriptor is defined as (diameter_ radius)/diameter. Globularity (a 3D molecular descriptor) is the inverse condition number (smallest eigenvalue divided by the largest eigenvalue) of the covariance matrix of atomic coordinates.<br><br>Fractional positive polar van der Waals surface area (PEOE_VSA_FPPOS). The vi are calculated using a connection table approximation, which is a partial charge descriptor that utilizes the PEOE method. a_don is the number of hydrogen bond donor atoms (not counting the basic atoms but counting the atoms that are both hydrogen bond donors and acceptors, such as -OH). vsa_don represents the approximation to the sum of van der Waals surface areas of pure hydrogen bond donors (not counting the basic atoms and atoms that are both hydrogen bond donors and acceptors, such as -OH). Fractional positive polar van der Waals surface area (PEOE_VSA_FPPOS) |

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| **Reference** | QSAR analysis of meclofenamic acid analogues as selective COX-2 inhibitors. *Bioorganic & Medicinal Chemistry Letters* 16 (2006) 461–468 |

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| **Target Species** | Human |
| **Chemical Type** | 2,3,5-Substituted tetrahydrofurans |
| **Mode of Action** | Inhibitor |
| **QSAR Model 1** | $C = -1.01\text{TPSA} + 15.30\chi^0 - 4.78\psi^0 - 71.29$<br>$r^2_{CV} = 0.28,\ r^2 = 0.55.$ |
| **QSAR Model 2** | $C = -11.78 \log P - 1.37\ \text{TPSA} + 13.93\chi^0 - 3.28\psi^0 - 12.47$<br>$r^2_{CV} = 0.43,\ r^2 = 0.61.$ |
| **Molecular Descriptor** | Access the following web-servers to compute molecular descriptors: **MoDel** and **e-dragon**<br>Partition coefficient (log P); total polar surface area (TPSA); $\chi^0$ = connectivity index ($0^{th}$ order); $\psi^0$ = valence connectivity index ($0^{th}$ order). |
| **Reference** | 2,3,5-Substituted tetrahydrofurans: COX-2 inhibitory activities of 5-hydroxymethyl-/carboxyl-2,3-diaryl-tetrahydro-furan-3-ols. *European Journal of Medicinal Chemistry* 43 (2008) 2792-2799 |

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| **Target Species** | Human |
| **Chemical Type** | Commercially available inhibitors |
| **Mode of Action** | Inhibitor |
| **QSAR** | $pIC_{50} = 20.295 + 2.612\ (\text{HOMO}) + 0.006\ (\text{Volume})$ |

| Model 1 | |
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| **Molecular Descriptor** | Access the following web-servers to compute molecular descriptors: **MoDel** and **e-dragon**<br>HOMO is a measure of the nucleophilicity of the molecule. Molecule with high HOMO energy is ready to donate its electrons and thus is more reactive than molecule with low value. |
| **Reference** | Quantitative Structure-Activity Relationships for Commercially Available Inhibitors of COX-2. *Medicinal Chemistry*, 2008, 4, 110-115 |

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| **Target Species** | Human |
| **Chemical Type** | Benzylideneamino scaffolds |
| **Mode of Action** | Inhibitor |
| **QSAR Model 1** | $pIC50_{(COX\text{-}2)} = -0.099(\pm0.059)\ \log P - 0.172(\pm0.90)\ I_{ma} - 0.622(\pm0.170)\ I_{mOH} + 0.736(\pm0.146)$ m-HD + 5.595(±0.101)<br>n= 31, r = 0.736, $r^2_{Adj} = 0.471$, s = 0.141, $F_{(4,26)} = 7.668$, p = 0.000, DW=2.007. |
| **QSAR Model 2** | $pIC50_{(COX\text{-}2)} = -0.191(\pm0.030)\ \log P - 0.064(\pm0.031)\ I_{mono} - 0.104(\pm0.033)\ I_{OCH3} + 5.836(\pm0.058)$<br>n= 26, r = 0.825, $r^2_{Adj} = 0.636$, s = 0.066, $F_{(3,22)} = 15.588$, p = 0.000, q2 = 0.555,<br>Spress = 0.078, SDEP = 0.072, DW=2.187. |
| **Molecular Descriptor** | Access the following web-servers to compute molecular descriptors: **MoDel** and **e-dragon**<br>Hydrophobicity ($\pi$), molar refractivity (MR), Hammett electronic ($\sigma$), 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 |

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| **Target** | Human |

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| **Species** | |
| **Chemical Type** | Phenyliminomethyl scaffolds |
| **Mode of Action** | Inhibitor |
| **QSAR Model 1** | $pIC50_{(COX-2)} = -0.099(\pm0.059)\ \log P - 0.172(\pm0.90)\ I_{ma} - 0.622(\pm0.170)\ I_{mOH} + 0.736(\pm0.146)$ m-HD + 5.595(±0.101)<br>n= 31, r = 0.736, $r^2_{Adj}$ = 0.471, s = 0.141, $F_{(4,26)}$ = 7.668, p = 0.000, DW=2.007. |
| **QSAR Model 2** | $pIC50_{(COX-2)} = -0.191(\pm0.030)\ \log P$ -0.064(±0.031) $I_{mono}$ - 0.104(±0.033) $I_{OCH3}$ + 5.836(±0.058)<br>n= 26, r = 0.825, $r^2_{Adj}$ = 0.636, s = 0.066, $F_{(3,22)}$ = 15.588, p = 0.000, q2 = 0.555, Spress = 0.078, SDEP = 0.072, DW=2.187. |
| **Molecular Descriptor** | Access the following web-servers to compute molecular descriptors: **MoDel** and **e-dragon**<br>Hydrophobicity ($\pi$), molar refractivity (MR), Hammett electronic ($\sigma$), 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 |

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| **Target Species** | Human |
| **Chemical Type** | Benzenesulfonamide derivatives |
| **Mode of Action** | Inhibitor |

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| **QSAR Model 1** | $pIC_{50}(COX\text{-}2) = 6.433 + 5.496(0.961)BEHm2 - 23.901(8.962)MATS2m + 0.471(0.076)C\text{-}009$<br>$n = 31,\ r = 0.842,\ s = 0.183,\ F = 22.011,\ Q^2_{LOO} = 0.627,$<br>$Q^2_{L5O} = 0.626,\quad r^2_{randY}(sd) = 0.306(0.117)\quad FIT = 1.651,$<br>$LOF = 0.045,\ AIC = 0.044,\ r^2_{Test} = 0.693$ |
| **QSAR Model 2** | $pIC_{50}(COX\text{-}2) = 8.755 + 5.929(0.814)BEHm2 - 28.157(7.596)MATS2m + 0.544(0.067)C\text{-}009$<br>$n = 30,\ r = 0.897,\ s = 0.153,\ F = 35.592,\ Q^2_{LOO} = 0.755$<br>$Q^2_{L5O} = 0.765,\ r^2_{randY}(sd) = 0.283(0.125)$<br>$FIT = 2.738,\ LOF = 0.032,\ AIC = 0.031,\ r^2_{Test} = 0.658$ |
| **Molecular Descriptor** | Access the following web-servers to compute molecular descriptors: **MoDel** and **e-dragon**<br>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 |