Target Name	Aldose reducatse
Target TTD ID	TTDS00115

Target Species	Human
Chemical Type	Spirosuccinimide type aldose reductase inhibitors
Mode of Action	Inhibitor
QSAR Model 1	$\%\ \text{Inhibition} = 0.718\ \text{PNSA}_1 - 0.528\ V^2_{\text{NCOS}} - 0.342\ \mu_z\ - 0.262\ F^2_{\text{H2O}} + 0.254\ S_z$ $n = 22,\ r = 0.970,\ q^2 = 0.911,\ LOF = 0.187,\ s = 0.276,\ F = 51.822(2.852),\ F_s = 9.881$
QSAR Model 2	$\text{pED}_{50} = 0.780\ \text{Alog}P - 0.409\ V^2_{\text{NCOS}}$ $n = 10,\ r = 0.892,\ q^2 = 0.598,\ LOF = 0.510,\ s = 0.512,\ F = 13.647(4.737),\ F_s = 5.715.$
Molecular Descriptor	Access the following web-servers to compute molecular descriptors: **MoDel** and **e-dragon** n is the number of compounds, r is the regression coefficient, q2 is the cross-validated r2 from the leave one-out procedure, LOF is Friedman's 'lack of fit' score,and where s is the standard deviation of estimation. F is the F value, a measure of statistical significance level of the model, and the F value given in parentheses is that of 95% significance level. Fs is the sequential F value, which is used to compare two regression models with different number of descriptors; AlogP is the primary term; V^2NCOS negatively contributes to the in vivo activity; hydrophobicity is the key factor in QSAR of pED50; VNCOS., the noncommon overlap steric volume; The molecular shape descriptor would reflect the binding conformation of the compound; μ_z, The z-component dipole moment; the polar descriptors such as the difference in charged partial surface area (DPSA1) and the x-component dipole moment (μ_x); μz reflects the polar modulation on the hydrophobic character of the compound binding into the AR active site;FH2O is the aqueous desolvation free energy of the molecule; Sz, the length of the molecule in the z-direction

Reference	Quantitative structure–activity relationship of spirosuccinimide type aldose reductase inhibitors diminishing sorbitol accumulation in vivo. *Bioorganic & Medicinal Chemistry* 14 (2006) 3090–3097

Target Species	Human
Chemical Type	Flavonoid compounds
Mode of Action	Inhibitor
QSAR Model 1	$A = 14.05 - 4.21 \cdot \delta_{4'} + 3.94 \cdot \sum \delta_{2'-4'} - 6.92 \cdot \sum \delta_{a_{3'}} - 1.74 \cdot \sum \delta_{a_3}$ $N = 75 \quad R = 0.790 \quad F = 21.687$
Molecular Descriptor	Access the following web-servers to compute molecular descriptors: **MoDel** and **e-dragon** A is -log(IC50), N is the number of compounds included in the model, R is the correlation coefficient and F is the Fisher ratio. The variables in the equation correspond to quantum chemical descriptors; dn is the net atomic charge on nth carbon atom and Pd is the total electron surface density. RBF, Rotatable bond fraction;nAB, Number of aromatic bonds;nH, Number of hydrogen bonds;Ss, Sum of Kier–Hall electrotopological states;nBO, Number of non-hydrogen bonds;RBN, Number of rotatable bonds;nBnz, Number of benzene-like rings;PW2, Path/walk 2–Randic ´shape index;IDDE, Mean information content of the distance equality;IC4, Information content index (neighbourhood symmetry of 4-order);X4A, Average connectivity index chi-4;VEA1, Eigenvector coefficient sum from adjacency matrix;BELm1, Lowest eigenvalue n.1 of burden matrix/weighted by atomic masses;BELv1, Lowest eigenvalue n.1 of burden matrix/weighted by atomic van der Waals volumes;BELv6, Lowest eigenvalue n.6 of burden matrix/weighted by atomic van der Waals volumes;BELm5, Lowest eigenvalue n.5 of burden matrix/weighted by atomic masses;GGI2, Topological charges index of order 2;GGI3, Topological charges index of order 3;GGI4, Topological charges index of order 4;JGI2, Mean topological charge index of order 2;JGI4, Mean topological charge index of order 4; JGI6, Mean topological charge index of order 6;MATS6m, Moran autocorrelation—lag 6/weighted by atomic masses;GATS1m, Geary autocorrelations—lag 1/weighted by atomic masses;GATS2m, Geary autocorrelations—lag 2/weighted by atomic masses;MATS3e,

	Moran autocorrelations—lag 3/weighted by atomic Sanderson electronegativities;DP03, Molecular profile no 03;DP11, Molecular profile no 11;DP18, Molecular profile no 18;SP10, Shape profile no 10;SP11, Shape profile no 11;SP15, Shape profile no 15;SP16 ,Shape profile no 16;AGDD, Average geometric distance degree;G1, Gravitational index G1;G2, Gravitational index G2 (bond restricted);SPH, Spherosity;SPAN, Span R;MEcc, Molecular eccentricity;RDF095u, Radial distribution function—9.5/unweighted;RDF045m, Radial distribution function—4.5/weighted by atomic masses;RDF045v, Radial distribution function—4.5/weighted by atomic van der Waals volumes;RDF025e, Radial distribution function—2.5/weighted by Sanderson electronegativitiesRDF095e, Radial distribution function—9.5/weighted by Sanderson electronegativities;RDF010p, Radial distribution function—1.0/weighted by atomic polarizabilities; Mor20u, 3D-MoRSE—signal 20/unweighted;Mor07m, 3D-MoRSE—signal 07/weighted by atomic masses;Mor24p, 3D-MoRSE—signal 24/weighted by atomic polarizabilities;Mor20v, 3D-MoRSE—signal 20/weighted by atomic van der Waals volumes;Mor24v, 3D-MoRSE—signal 24/weighted by atomic van der Waals volumes;Mor07e, 3D-MoRSE—signal 07/weighted by Sanderson electronegativities;Mor19e, 3D-MoRSE—signal 19/weighted by Sanderson electronegativities;P1u, First component shape directional WHIM index/unweighted;P1m, First component shape directional WHIM index/weighted by atomic masses;Dp, D total accessibility index/weighted by atomic polarizabilities;L2s, Second component size directional WHIM index/weighted by atomic electrotopological states;Kv, K global shape index/weighted by atomic van der Waals volumes;HATS3m, Leverage-weighted autocorrelation of lag 3/weighted by atomic masses;HATS4m, Leverage-weighted autocorrelation of lag 4/weighted by atomic masses;R3u, R autocorrelation of lag 3/unweighted;H5v, H autocorrelation of lag 5/weighted by atomic van der Waals volumes; RCON, Randic ´-type R matrix connectivity. Equation describes inhibition of AR enzyme
Reference	Quantitative structure–activity relationship to predict differential inhibition of aldose reductase by flavonoid compounds. *Bioorganic & Medicinal Chemistry* 13 (2005) 3269–3277

Target Species	Human
Target Location	Lens, Retina, Heart, Kidney
Chemical	2-, 7- substitutions benzopyrane derivatives

Type	
Mode of Action	Inhibitor
QSAR Model 1	$-\log IC_{50} = 4.8501(\pm1.7) + 12.773(\pm1.4)BELp4 - 4.950(\pm0.7)GGI8 - 12.191(\pm0.9)MATS4e + 0.905(\pm0.2)Mor22e - 16.422(\pm2.1)E1p - 16.844(\pm1.7)R4v$ $N = 55,\ R = 0.9362,\ S = 0.4364,\ FIT = 3.744,\ p < 10^{-4}\ RMSE_{Test\ Set} = 3.9059$ $R_{loo} = 0.914,\ S_{loo} = 0.507,\ R_{I\text{-}30\%\text{-}o} = 0.763,\ S_{I\text{-}30\%\text{-}o} = 0.891$
QSAR Model 2	$-\log IC_{50} = -85.5375(\pm10) - 10.882(\pm1.4)E1u - 15.398(\pm0.9)MATS4e + 55.920(\pm5.35)BELm2 + 7.7606(\pm0.9)HATS6e - 2.6755(\pm0.5)DISPe - 18.253(\pm1.1)R4p$ $N = 55,\ R = 0.9523,\ S = 0.3789,\ FIT = 5.14,\ p < 10^{-5}\ RMSE_{Test\ Set} = 2.9127$ $R_{loo} = 0.934,\ S_{loo} = 0.447,\ R_{I\text{-}30\%\text{-}o} = 0.803,\ S_{I\text{-}30\%\text{-}o} = 0.886$
QSAR Model 3	$-\log IC_{50} = 12.2967(\pm1.5) - 0.1898(\pm0.02)TIC0 - 15.6392(\pm1)MATS4e + 1.7611(\pm0.4)H7e - 10.0425(\pm1.6)E1u + 16.6513(\pm1.9)BELe4 - 14..0207(\pm1.5)R3v$ $N = 55,\ R = 0.9374,\ S = 0.4325,\ FIT = 3.822,\ p < 10^{-4}\ RMSE_{Test\ Set} = 4.1607$ $R_{loo} = 0.917,\ S_{loo} = 0.499,\ R_{I\text{-}30\%\text{-}o} = 0.7739,\ S_{I\text{-}30\%\text{-}o} = 1.106$
Molecular Descriptor	Access the following web-servers to compute molecular descriptors: **MoDel** and **e-dragon** Linear QSAR models for the training set of -logIC50 (N = 55) Model M1: Descriptors used -- LUMO (R=0.616; S=0.931; FIT=0.579); Model M2: Descriptors used -- DISPp, C-027 (R=0.739; S=0.804; FIT=1.059); Model M3: Descriptors used -- Mor32m, H-048, >0.2 (R=0.826; S=0.679; FIT=1.715); Model M4: Descriptors used -- MATS4e, E1u, HATS6e, R4m (R=0.878; S=0.582; FIT=2.379); Model M5: Descriptors used -- GATS4e, DISPe, E1u, HATS5m, R4m (R=0.9; S=0.536; FIT=2.607); Model M6: Descriptors used -- BELp4, GGI8, MATS4e, Mor22e, E1p, R4v (R=0.936; S=0.436; FIT=3.744); Model M7: Descriptors used -- SPP, DISPe, RDF140m, E1p, H4m, Dipole Moment, LUMO (R=0.95; S=0.392; FIT=4.181); Model M6B: Descriptors used -- E1u, MATS4e, BELm2, HATS6e, DISPe, R4p (R=0.952; S=0.379; FIT=5.14); Model M6C: Descriptors used -- TIC0, MATS4e, H7e, E1u, BELe4, R3v (R=0.937; S=0.433; FIT=3.822) Symbols for molecular descriptors involved in different models LUMO: Quantum-chemical descriptor [Lowest unoccupied molecular orbital energy (eV)]; DISPp:

	Geometrical descriptor [d COMMA2 value/weighted by atomic polarizabilities]; C-027: Atom-centred fragments descriptor [C-027 corresponds to: R–CH–X]; Mor32m: 3D-MoRSE descriptor [3D-MoRSE - signal 32/weighted by atomic masses]; H-048: Atom-centred fragments descriptor [H attached to C2(sp3)/C1(sp2)/C0(sp)]; >0.2: Topological descriptor [Number of atoms with charge higher than 0.2]; MATS4e: 2D Autocorrelations descriptor [Moran autocorrelation - lag 4/weighted by atomic Sanderson electronegativities]; E1u: WHIM descriptor [1st component accessibility directional WHIM index/unweighted]; HATS6e: GETAWAY descriptor [Leverage-weighted autocorrelation of lag 6/weighted by atomic Sanderson electronegativities]; R4m: GETAWAY descriptor [R Autocorrelation of lag 4/weighted by atomic masses]; GATS4e: 2D Autocorrelations descriptor [Geary autocorrelation- lag 4/weighted by atomic Sanderson electronegativities]; DISPe: Geometrical descriptor [d COMMA2 value/weighted by atomic Sanderson electronegativities]; HATS5m: GETAWAY descriptor [leverage-weighted autocorrelation of lag 5/weighted by atomic masses]; BELp4: BCUT descriptor [Lowest eigenvalue n. 4 of Burden matrix/weighted by atomic polarizabilities]; GGI8: Topological descriptor [Topological charge index of order 8]; Mor22e: 3D-MoRSE descriptor [3D-MoRSE - signal 22/weighted by atomic Sanderson electronegativities]; E1p: WHIM descriptor [1st component accessibility directional WHIM index/weighted by atomic polarizabilities]; R4v: GETAWAY descriptor [R Autocorrelation of lag 4/weighted by atomic van der Waals volumes]; SPP: Charge descriptor [Subpolarity parameter]; RDF140m: Radial distribution function descriptor [Radial distribution function- 14.0/weighted by atomic masses]; H4m: GETAWAY descriptor [H Autocorrelation of lag 4/weighted by atomic masses]; Dipole moment: Quantum-chemical descriptor [Total molecular dipole moment (Debyes)]; BELm2: BCUT descriptor [lowest eigenvalue n. 2 of Burden matrix/weighted by atomic masses]; R4p: GETAWAY descriptor [R Autocorrelation of lag 4/weighted by atomic polarizabilities]; TIC0: Topological descriptor [total information content index (neighborhood symmetry of 0-order)]; H7e: GETAWAY descriptor [H Autocorrelation of lag 7/weighted by atomic Sanderson electronegativities]; BELe4: BCUT descriptor [lowest eigenvalue n. 4 of Burden matrix/weighted by atomic Sanderson electronegativities]; R3v: GETAWAY descriptor [R Autocorrelation of lag 3/weighted by atomic van der Waals volumes]
Reference	QSAR prediction of inhibition of aldose reductase for flavonoids. *Bioorganic & Medicinal Chemistry* 16 (2008) 7470–7476