Target Name	Carbonic anhydrase
Target TTD ID	TTDS00304

Target Species	Human
Target Location	Stomach
Chemical Type	Positively charged sulphonamide
Mode of Action	Inhibitor
QSAR Model 1	$\log IC_{50} = 7.66(\pm0.09) \times 10^{-3}P_{xx} + 19.4(\pm1.3)Q_o - 64.3(\pm8.7)S_m^E + 1.87(\pm0.16)E_{L\text{-}H} + 8.56(\pm2.2)Q_p + 12.99(\pm3.17)$ $n = 28, R = 0.964, R_{cv}^2 = 0.866, s = 0.259, F = 57.4, \Lambda = 3.07$
QSAR Model 2	$\log IC_{50} = 1.09(\pm0.17) \times 10^{-3}P_{xx} - 1.76(\pm0.47) \times 10^{-2}P_{yy} + 1.38(\pm0.34) \times 10^{-2}P_{zz} + 27.7(\pm3.5)Q_o + 6.62(\pm1.87)Q_m - 1.92(\pm0.24)E_H - 19.2(\pm3.5)$ $n = 28, R = 0.929, R_{cv}^2 = 0.801, s = 0.37, F = 22.1, \Lambda = 5.4$
QSAR Model 3	$\log IC_{50} = 9.82(\pm1.62) \times 10^{-3}P_{xx} + 0.118(\pm0.040)V_m - 4.13(\pm1.27)\pi_m + 14.1(\pm1.7)Q_o + 13.1(\pm2.9)Q_m + 2.06(\pm0.25)E_{L\text{-}H} - 11.64(\pm0.25)$ $n = 28, R = 0.931, R_{cv}^2 = 0.728, s = 0.36, F = 22.7, \Lambda = 73.9$
QSAR Model 4	$\log IC_{50} = 1.07(\pm0.12) \times 10^{-2}P_{xx} - 1.83(\pm0.33) \times 10^{-2}P_{yy} + 1.25(\pm0.25) \times 10^{-2}P_{zz} + 28.3(\pm2.5)Q_o + 6.42(\pm1.34)Q_m - 1.90(\pm0.17)E_H - 18.6(+2.5)$ $n = 27, R = 0.964, R_{cv}^2 = 0.886, s = 0.26, F = 43.2, \Lambda = 5.4$
Molecular Descriptor	Access the following web-servers to compute molecular descriptors: **MoDel** and **e-dragon** E_H: Energy of highest occupied molecular orbital (HOMO); E_L: Energy of lowest unoccupied

	molecular orbital (LUMO); E_{L-H}: Difference between HOMO and LUMO energies; Ix: Smallest principal moment of inertia; Iy: Intermediate principal moment of inertia; Iz: Largest principal moment of inertia; Lx:Linear dimension corresponding to Ix; Ly: Linear dimension corresponding to Iy; Lz: Linear dimension corresponding to Iz; Qo: Sum of charges of 2,6-carbon atoms on pyridinium ring; Qm: Sum of charges of 3,karbon atoms on pyridinium ring; Qp: Charge of 4-carbon atom of pyridinium ring; Vo: Sum of volumes of substituent on 2,6-positions of pyridinium ring; Vm: Sum of volumes of substituent on 3,5-positions of pyridinium ring; Vp: Volume of substituent on 4-position of pyridinium ring; π_o: Sum of Hansch π's of 2,6 suhstituents; π_m: Sum of Hansch π's of 3,s substituents; π_p: Hansch π of 4-substituent; S_O^E: Sum of electrophilic superdelocalizabilities of 2,6-substituents; S_M^E: Sum of electrophilic superdelocalizabilities of 3,kubstituents; S_P^E: Electrophilic superdelocalizability of 4-substituent; S_h^E: Sum of electrophilic superdelocalizabilities of thiadiazole ring atoms; P_{xx}: Diagonal component of polarizability along Ix; P_{yy}: Diagonal component of polarizability along Iy; P_{zz}: Diagonal component of polarizability along Iz; Pi: $(P_{xx} + P_{yy} + P_{zz})/3$; W: Molecular weight; logP: Calculated octanol-water partition coefficient; IC_{50}: Activity of CA inhibitor Here n is the number of casese, R2 is the square of the conventional multiple correlation ccefficient, R& the square of the crossvalidated correlation coefficient, s the standard error of estimate, F the Fisher variance ratio and A is a measure of the seriousness of collinearity in the equation. The latter is defined as| $$\Lambda = \frac{1}{n}\sum_{i=1}^{n}\frac{1}{\lambda_i}$$ Where n is the number of descriptors and the λ_i are the eigenvalues of the correlation matrix of descriptors.
Reference	Carbonic anhydrase inhibitors. Part 24. A quantitative structure-activity relationship study of positively charged sulfonamide inhibitors. *Eur J Med Chem* (1995) 30, 687-696.

Chemical Type	Sulfonamides from a non-congeneric series
Mode of Action	Inhibitor

QSAR Model 1	$\log k_{on} = 51.2\ Q_N + 1.22\ E_L + 0.373\ A_x - 0.139\ V_w + 0.125\ A_w + 6.33$
QSAR Model 2	$\log K_I = -55.7\ Q_N - 1.64\ E_L + 0.459\ D - 0.572\ A_x - 0.251\ A_y + 0.625 \log P - 8.56$
QSAR Model 3	$\log k_{on} = 51.2\ (\pm 11.1)\ Q_N + 1.22\ (\pm 0.40)\ E_L + 0.373\ (\pm 0.111)\ A_x - 0.138\ (\pm 0.028)\ V_w + 0.125\ (\pm 0.026)\ A_w + 6.33\ (\pm 3.15)$ $R^2 = 0.839,\ Q^2 = 0.669,\ S = 0.705,\ F = 14.5,\ \alpha = 4 \times 10^{-5}$, all $\alpha_i < 0.01$
QSAR Model 4	$\log K_I = -46.5\ (\pm 10.6)\ Q_N - 0.988\ (\pm 0.38)\ E_L - 0.418\ (\pm 0.106)\ A_x + 0.144\ (\pm 0.027)\ V_w - 0.128\ (\pm 0.025)\ A_w - 3.26\ (\pm 2.98)$ $R^2 = 0.857,\ Q^2 = 0.701,\ S = 0.669,\ F = 16.8,\ \alpha = 2 \times 10^{-5},\ \Lambda = 38.0$
Molecular Descriptor	Access the following web-servers to compute molecular descriptors: **MoDel** and **e-dragon** Q_H: Charge on sulfonamide hydrogen, CNDO; Q_S: Charge on sulfonanfide sulfur, CNDO; Q_N: Charge on sulfonamide nitrogen, CNDO; Q_O: Charge on sulfonamide oxygen, CNDO; E_H: Energy of highest occupied molecular orbital, AM 1; E_L: Energy of lowest unoccupied molecular orbital, AM 1. $\prod_{xx}$: Component of polarizability tensor, AM 1; $\prod_{yy}$: Component of polarizability tensor, AM 1; $\prod_{zz}$: Component of polarizability tensor, AM 1. Ax: Length of axis of molecule; Ay: Length of axis of molecule; Az:Length of axis of molecule; Vw: van der Waals volume of molecule, ARVOMOL; Aw: van der Waals area of molecule, ARVOMOL; Log P: Log of octanol-water partition coefficient, CLogP; D: Dipole moment of molecule, AM 1. R^2 is the square of the multiple correlation coefficient, Q^2 is the same quantity based on predicted errors (the leave-one-out technique), S is the standard error of estimate of the equation, F is the Fisher variance ratio, α is the probability (statistical significance) based on this F, and the α_i, values are the individual statistical significance of each of the coefficients of the equation, based on a Student's t-test. The numbers in parentheses are standard errors of estimate for each coefficient in the equation. Diagnostic A is defined as: $$\Lambda = \frac{1}{n}\sum_{i=1}^{n}\frac{1}{\lambda_i}$$

	Where n is the number of descriptors and the λ_i are the eigenvalues of the correlation matrix of descriptors. A value of Λ greater than 5 is taken to indicate that a collinearity problem exists in the equation. The value of 38 suggests that the equation is unreliable. Examination of the eigenvector matrix showed that the problem was entirely due to the very high correlation between Vw and Aw.
Reference	Carbonic anhydrase inhibitors. Part 41. Quantitative structure-activity correlations involving kinetic rate constants of 20 sulfonamide inhibitors from a non-congeneric series. *EurJMed Chem* (1997) 32, 311-319