Target Name	Dihydrofolate reductase (DHFR)
Target TTD ID	TTDS00208

Target Species	Mammals
Chemical Type	Quinazolines
Mode of Action	Inhibitor
QSAR Model 1	$\log 1/C = 0.81\ (\text{MR-6}) - 0.064\ (\text{MR-6})^2 + 0.78\ (\pi\text{-5}) - 0.73\ (I\text{-1}) - 2.14\ (I\text{-2}) - 0.54\ (I\text{-3})$ $- 1.39\ (I\text{-4}) + 0.78\ (I\text{-6}) - 0.20\ (\text{MR-6}{\cdot}I\text{-1}) + 4.92$ $n = 101; r = 0.961; s = 0.441$
Molecular Descriptor	Access the following web-servers to compute molecular descriptors: **MoDel** and **e-dragon** *n* refers to the number of data points, *r* is the correlation coefficient, *s* is the standard deviation, and MR-6 and a-5 refer to the molar refractivity of substituents in position 6 and the hydrophobicity of 5-substituents. The indicator variable I-1 is given a value of 1 for 2-OH or 2-SH, 1-2 takes the value of 1 for 2-H, and *I-3* assumes the value of 1 for 4-OH or SH.
Reference	Quantitative Structure-Activity Relationships of Antimalarial and Dihydrofolate Reductase Inhibition by Quinazolines and 5-Substituted Benzyl-2,4-diaminopyrimidin. Journal of Medicinal Chemistry, 1977, Vol. 20, No. 1, P96-102.

Target Species	Bacteria
Chemical Type	5-Substituted Benzyl-2,4-diaminopyrimidines
Mode of Action	Inhibitor
QSAR Model 1	$\log 1/C = 1.125\ (\pm 0.35)\ (\pi\text{-5}) - 1.103\ (\pm 0.25)\ (\text{MR-5}) - 2.385\ (\pm 0.59)\ (I\text{-1})$ |

	$-4.092\ (\pm 0.82)\ (I\text{-}2) - 2.368\ (\pm 0.37)\ (I\text{-}3) + 8.255\ (\pm 0.27)$ $n = 67; r = 0.926; s = 0.672$
Molecular Descriptor	Access the following web-servers to compute molecular descriptors: **MoDel** and **e-dragon** *n* refers to the number of data points, *r* is the correlation coefficient, *s* is the standard deviation, and MR-6 and a-5 refer to the molar refractivity of substituents in position 6 and the hydrophobicity of 5-substituents. The indicator variable I-1 is given a value of 1 for 2-OH or 2-SH, 1-2 takes the value of 1 for 2-H, and *I-3* assumes the value of 1 for 4-OH or SH.
Reference	Quantitative Structure-Activity Relationships of Antimalarial and Dihydrofolate Reductase Inhibition by Quinazolines and 5-Substituted Benzyl-2,4-diaminopyrimidin. Journal of Medicinal Chemistry, 1977, Vol. 20, No. 1, P96-102.

Target Species	*Plasmodium berghei* in mice
Chemical Type	Quinazolines type I
Mode of Action	Inhibitor
QSAR Model 1	$\log 1/C = 0.877\ (\pm 0.28)\ (\pi\text{-sum} - 0.155\ (\pm 0.05)\ (\pi\text{-sum})^2 - 0.679\ (\pm 0.46)\ (I\text{-}6)$ $+ 0.373\ (\pm 0.32)\ (I\text{-}8) + 1.526\ (\pm 0.29)\ (I\text{-}9) + 1.185\ (\pm 0.40)\ (I\text{-}10) + 3.272\ (\pm 0.40)$ $n = 60; r = 0.906; s = 0.427; \pi_0 = 2.82\ (2.5\text{-}3.2)$
Molecular Descriptor	Access the following web-servers to compute molecular descriptors: **MoDel** and **e-dragon** *n* refers to the number of data points, *r* is the correlation coefficient, *s* is the standard deviation, and MR-6 and a-5 refer to the molar refractivity of substituents in position 6 and the hydrophobicity of 5-substituents. The indicator variable I-1 is given a value of 1 for 2-OH or 2-SH, 1-2 takes the value of 1 for 2-H, and *I-3* assumes the value of 1 for 4-OH or SH. C in log 1/C in this equation is the molar concentration (mol/kg) of orally given drug producing 90% suppression of malaria and a-sum refers to all of the substituents in the *5*, 6, and 8 positions. 1-9 and I-10 are the two most important variables which assume the value of 1 for 25 congeners having the groups 6-N(X)CH_2Ar (*I*-9) and 6-CH_2NHAr (*I*-10).
Reference	Quantitative Structure-Activity Relationships of Antimalarial and Dihydrofolate Reductase Inhibition by Quinazolines and 5-Substituted Benzyl-2,4-diaminopyrimidin. Journal of Medicinal

	Chemistry, 1977, Vol. 20, No. 1, P96-102.

Target Species	Rat
Target Location	Liver
Chemical Type	2,4-diamino-5-(X-benzyl)pyrimidines
Mode of Action	Inhibitor
QSAR Model 1	$\log 1/C = -1.443\ (\pm 0.48)\ \Sigma\sigma^{+} + 5.865\ (\pm 0.38)$ $n = 10; r = 0.926; s = 0.418$
Molecular Descriptor	Access the following web-servers to compute molecular descriptors: **MoDel** and **e-dragon** σ^{+} is Brown's parameter, and σ_R^{+} is Taft's resonance parameter. The σ constant in each equation has been selected with respect to the ortho position of the -CHr bridge. *n* refers to the number of data points, *r* is the correlation coefficient, *s* is the standard deviation, and MR-6 and a-5 refer to the molar refractivity of substituents in position 6 and the hydrophobicity of 5-substituents. The indicator variable I-1 is given a value of 1 for 2-OH or 2-SH, 1-2 takes the value of 1 for 2-H, and *I-3* assumes the value of 1 for 4-OH or SH.
Reference	Quantitative Structure-Activity Relationships of Antimalarial and Dihydrofolate Reductase Inhibition by Quinazolines and 5-Substituted Benzyl-2,4-diaminopyrimidin. Journal of Medicinal Chemistry, 1977, Vol. 20, No. 1, P96-102.

Target Species	Escherichia coli
Chemical Type	Quinazolines
Mode of Action	Inhibitor
QSAR	$\log 1/C = -1.125\ (\pm 0.15)\ \Sigma\sigma_R^{+} + 5.538\ (\pm 0.19)$

Model 1	$n = 10; r = 0.986; s = 0.182$
Molecular Descriptor	Access the following web-servers to compute molecular descriptors: **MoDel** and **e-dragon** σ^+ is Brown's parameter, and σ_R^+ is Taft's resonance parameter. The σ constant in each equation has been selected with respect to the ortho position of the -CHr bridge. *n* refers to the number of data points, *r* is the correlation coefficient, *s* is the standard deviation, and MR-6 and a-5 refer to the molar refractivity of substituents in position 6 and the hydrophobicity of 5-substituents. The indicator variable I-1 is given a value of 1 for 2-OH or 2-SH, 1-2 takes the value of 1 for 2-H, and *I-3* assumes the value of 1 for 4-OH or SH.
Reference	Quantitative Structure-Activity Relationships of Antimalarial and Dihydrofolate Reductase Inhibition by Quinazolines and 5-Substituted Benzyl-2,4-diaminopyrimidin. Journal of Medicinal Chemistry, 1977, Vol. 20, No. 1, P96-102.

Target Species	Escherichia coli
Chemical Type	5-Substituted Benzyl-2,4-diaminopyrimidines
Mode of Action	Inhibitor
QSAR Model 1	$\log 1/C = -1.125\ (\pm 0.15)\ \Sigma \sigma_R^+ + 5.538\ (\pm 0.19)$ $n = 10; r = 0.986; s = 0.182$
Molecular Descriptor	Access the following web-servers to compute molecular descriptors: **MoDel** and **e-dragon** σ^+ is Brown's parameter, and σ_R^+ is Taft's resonance parameter. The σ constant in each equation has been selected with respect to the ortho position of the -CHr bridge. *n* refers to the number of data points, *r* is the correlation coefficient, *s* is the standard deviation, and MR-6 and a-5 refer to the molar refractivity of substituents in position 6 and the hydrophobicity of 5-substituents. The indicator variable I-1 is given a value of 1 for 2-OH or 2-SH, 1-2 takes the value of 1 for 2-H, and *I-3* assumes the value of 1 for 4-OH or SH.
Reference	Quantitative Structure-Activity Relationships of Antimalarial and Dihydrofolate Reductase Inhibition by Quinazolines and 5-Substituted Benzyl-2,4-diaminopyrimidin. Journal of Medicinal Chemistry, 1977, Vol. 20, No. 1, P96-102.

Target Species	Leishmania major
Chemical Type	Triazines
Mode of Action	Inhibitor
Activity Type	Inhibition of Isolated Leishmania major DHFR by Triazines
QSAR Model 1	$\log 1/K_i = 0.31\ (\pm 0.16)\pi'_3 + 5.54\ (\pm 0.39)$ $n = 41 \quad r = 0.538 \quad s = 0.904 \quad F_{1,39} = 15.9$
QSAR Model 2	$\log 1/K_i = 1.04\ (\pm 0.24)\pi'_3 - 1.20\ (\pm 0.35) \log (\beta \cdot 10^{\pi'_3} + 1) + 5.18\ (\pm 0.28)$ $n = 41 \quad r = 0.834 \quad s = 0.606 \quad \pi_0 = 2.51\ (\pm 1.38) \quad F_{1,37} = 24.8 \quad \log \beta = -1.680$
QSAR Model 3	$\log 1/K_i = 0.99\ (\pm 0.17)\pi'_3 - 0.99\ (\pm 0.26) \log (\beta \cdot 10^{\pi'_3} + 1) - 1.19\ (\pm 0.42)I_{OR} + 5.27\ (\pm 0.21)$ $n = 41 \quad r = 0.917 \quad s = 0.445 \quad F_{1,37} = 32.7 \quad \pi_0 \simeq 5.0 \quad \log \beta = -1.790$
QSAR Model 4	$\log 1/K_i = 0.65\ (\pm 0.08)\pi'_3 - 1.22\ (\pm 0.29) \log (\beta \cdot 10^{\pi'_3} + 1) - 1.12\ (\pm 0.29)I_{OR} + 0.58\ (\pm 0.16)MR_Y + 5.05\ (\pm 0.16)$ $n = 41 \quad r = 0.965 \quad s = 0.298 \quad \pi_0 = 4.54 \quad F_{1,35} = 45.2 \quad \log \beta = -4.491$
QSAR Model 5	$\log 1/K_i = 0.64\ (\pm 0.12)\pi'_3 - 1.26\ (\pm 0.46) \log (\beta \cdot 10^{\pi'_3} + 1) + 1.01\ (\pm 0.43)I_{OR} + 0.60\ (\pm 0.21)MR_Y + 4.92\ (\pm 0.22)$ $n = 45 \quad r = 0.922 \quad s = 0.451 \quad \pi_0 = 4.64 \quad \log \beta = -4.635$
Molecular Descriptor	Access the following web-servers to compute molecular descriptors: **MoDel** and **e-dragon** *n* represents the number of data points used to derive the equation, *r* is the correlation coefficient, s is the standard deviation from the regression, *F* is the F statistic for significance of each additional variable, and the values in parentheses are for construction of the 95% confidence intervals; Ki is the Michaelis inhibition constant. The disposable parameter β is obtained by an iterative procedure for the bilinear structure-activity model. The Hydrophobicity variable π, superscribed with a prime (π'), denotes that in lb, for substituents of type $CH_2ZC_6H_4$-Y, where Z = 0, NH, Se, or S, the π value for Y is set equal to zero (i.e. $CH_2ZC_6H_4$-Y = π $CH_2ZC_6H_5$). same parameterization is also applies to groups of the type $ZCH_2ZC_6H_4$-Y, where Z = 0, *S*.

Reference	Quantitative Structure-Activity Relationship of Triazine-Antifolate Inhibition of Leishmania Dihydrofolate Reductase and Cell Growth. *J. Med. Chem.* 1987, 30, 1218-1224

Target Species	Leishmania major
Chemical Type	Triazines
Mode of Action	Inhibitor
Activity Type	Growth Inhibition of Leishmania major Cell Cultures
QSAR Model 1	$\log 1/EC_{50} = 0.29\ (\pm 0.09)\pi_3 + 3.33\ (\pm 0.31)$ $n = 12 \quad r = 0.917 \quad s = 0.251 \quad F_{1,10} = 53$
QSAR Model 2	$\log 1/EC_{50} = 0.21\ (\pm 0.09)\pi_3 + 0.44\ (\pm 0.32) \log 1/K_i + 0.53\ (\pm 2.1)$ $n = 12 \quad r = 0.960 \quad s = 0.186 \quad F_{1,9} = 9.29$
QSAR Model 3	$\log 1/EC_{50} = 0.52\ (\pm 0.06)\pi_3 + 2.64\ (\pm 0.19)$ $n = 10 \quad r = 0.989 \quad s = 0.079$
Molecular Descriptor 3	Access the following web-servers to compute molecular descriptors: **MoDel** and **e-dragon** *n* represents the number of data points used to derive the equation, *r* is the correlation coefficient, s is the standard deviation from the regression, *F* is the F statistic for significance of each additional variable, and the values in parentheses are for construction of the 95% confidence intervals; Ki is the Michaelis inhibition constant. The disposable parameter β is obtained by an iterative procedure for the bilinear structure-activity model. The Hydrophobicity variable π, superscribed with a prime (π'), denotes that in lb, for substituents of type $CH_2ZC_6H_4$-Y, where Z = 0, NH, Se, or S, the π value for Y is set equal to zero (i.e.,π $CH_2ZC_6H_4$-Y = π $CH_2ZC_6H_5$). same parameterization is also applies to groups of the type $ZCH_2ZC_6H_4$-Y, where Z = 0, *S*.
Reference	Quantitative Structure-Activity Relationship of Triazine-Antifolate Inhibition of Leishmania Dihydrofolate Reductase and Cell Growth. *J. Med. Chem.* 1987, 30, 1218-1224

Target Species	Chicken
Target Location	Liver
Chemical Type	3-X-triazines
Mode of Action	Inhibitor
QSAR Model 1	$\log 1/K_i = 1.01\pi'_3 - 1.16 \log (\beta \cdot 10^{\pi'_3} + 1) + 0.86\sigma + 6.33$ $n = 59 \quad r = 0.906 \quad s = 0.267 \quad \pi_0 = 1.89$
Molecular Descriptor	Access the following web-servers to compute molecular descriptors: **MoDel** and **e-dragon** *n* represents the number of data points used to derive the equation, *r* is the correlation coefficient, s is the standard deviation from the regression, *F* is the F statistic for significance of each additional variable, and the values in parentheses are for construction of the 95% confidence intervals; Ki is the Michaelis inhibition constant. The disposable parameter β is obtained by an iterative procedure for the bilinear structure-activity model. The Hydrophobicity variable π, superscribed with a prime (π'), denotes that in lb, for substituents of type $CH_2ZC_6H_4$-Y, where Z = 0, NH, Se, or S, the π value for Y is set equal to zero (i.e.,π $CH_2ZC_6H_4$-Y = π $CH_2ZC_6H_5$). same parameterization is also applies to groups of the type $ZCH_2ZC_6H_4$-Y, where Z = 0, *S*. Π'$_3$, measure of the effect of Hydrophobicity on inhibitor potency.
Reference	Quantitative Structure-Activity Relationship of Triazine-Antifolate Inhibition of Leishmania Dihydrofolate Reductase and Cell Growth. *J. Med. Chem.* 1987, 30, 1218-1224

Target Species	Human
Chemical Type	3-X-triazines
Mode of Action	Inhibitor
QSAR Model 1	$\log 1/K_i = 1.07\pi'_3 - 1.10 \log (\beta \cdot 10^{\pi'_3} + 1) + 0.50I + 0.82\sigma + 6.07$ $n = 60 \quad r = 0.890 \quad s = 0.308 \quad \pi_0 = 1.84$

Molecular Descriptor	Access the following web-servers to compute molecular descriptors: **MoDel** and **e-dragon** *n* represents the number of data points used to derive the equation, *r* is the correlation coefficient, s is the standard deviation from the regression, *F* is the F statistic for significance of each additional variable, and the values in parentheses are for construction of the 95% confidence intervals; Ki is the Michaelis inhibition constant. The disposable parameter β is obtained by an iterative procedure for the bilinear structure-activity model. The Hydrophobicity variable π, superscribed with a prime (π'), denotes that in lb, for substituents of type $CH_2ZC_6H_4$-Y, where Z = 0, NH, Se, or S, the π value for Y is set equal to zero (i.e.,π $CH_2ZC_6H_4$-Y = π $CH_2ZC_6H_5$). same parameterization is also applies to groups of the type $ZCH_2ZC_6H_4$-Y, where Z = 0, *S*. Π'_3, measure of the effect of Hydrophobicity on inhibitor potency.
Reference	Quantitative Structure-Activity Relationship of Triazine-Antifolate Inhibition of Leishmania Dihydrofolate Reductase and Cell Growth. *J. Med. Chem.* 1987, 30, 1218-1224

Target Species	Bovine
Chemical Type	3-X-triazines
Mode of Action	Inhibitor
QSAR Model 1	$\log 1/K_i = 1.10\pi'_3 - 1.23 \log (\beta \cdot 10^{\pi'_3} + 1) + 0.61\sigma + 7.08$ $n = 38 \quad r = 0.914 \quad s = 0.277 \quad \pi_0 = 1.72$
Molecular Descriptor	Access the following web-servers to compute molecular descriptors: **MoDel** and **e-dragon** *n* represents the number of data points used to derive the equation, *r* is the correlation coefficient, s is the standard deviation from the regression, *F* is the F statistic for significance of each additional variable, and the values in parentheses are for construction of the 95% confidence intervals; Ki is the Michaelis inhibition constant. The disposable parameter β is obtained by an iterative procedure for the bilinear structure-activity model. The Hydrophobicity variable π, superscribed with a prime (π'), denotes that in lb, for substituents of type $CH_2ZC_6H_4$-Y, where Z = 0, NH, Se, or S, the π value for Y is set equal to zero (i.e.,π $CH_2ZC_6H_4$-Y = π $CH_2ZC_6H_5$). same parameterization is also applies to groups of the type $ZCH_2ZC_6H_4$-Y, where Z = 0, *S*. Π'_3, measure of the effect of Hydrophobicity on inhibitor potency.
Reference	Quantitative Structure-Activity Relationship of Triazine-Antifolate Inhibition of Leishmania

	Dihydrofolate Reductase and Cell Growth. *J. Med. Chem.* 1987, 30, 1218-1224

Target Species	Rat
Target Location	Liver
Chemical Type	3-X-triazines
Mode of Action	Inhibitor
QSAR Model 1	$\log 1/K_i = 1.12\pi_3 - 1.34 \log (\beta \cdot 10^{\pi_3} + 1) + 6.80$ $n = 18 \quad r = 0.977 \quad s = 0.171 \quad \pi_0 = 1.68$
Molecular Descriptor	Access the following web-servers to compute molecular descriptors: **MoDel** and **e-dragon** *n* represents the number of data points used to derive the equation, *r* is the correlation coefficient, s is the standard deviation from the regression, *F* is the F statistic for significance of each additional variable, and the values in parentheses are for construction of the 95% confidence intervals; Ki is the Michaelis inhibition constant. The disposable parameter β is obtained by an iterative procedure for the bilinear structure-activity model. The Hydrophobicity variable π, superscribed with a prime (π'), denotes that in lb, for substituents of type $CH_2ZC_6H_4$-Y, where Z = 0, NH, Se, or S, the π value for Y is set equal to zero (i.e.,π $CH_2ZC_6H_4$-Y = π $CH_2ZC_6H_5$). same parameterization is also applies to groups of the type $ZCH_2ZC_6H_4$-Y, where Z = 0, *S*. Π'_3, measure of the effect of Hydrophobicity on inhibitor potency.
Reference	Quantitative Structure-Activity Relationship of Triazine-Antifolate Inhibition of Leishmania Dihydrofolate Reductase and Cell Growth. *J. Med. Chem.* 1987, 30, 1218-1224

Target Species	Human
Chemical Type	3-X-triazines
Mode of Action	Inhibitor

Activity Type	Inhibition of L5178Y Leukemia DHFR
QSAR Model 1	$\log 1/K_i = 1.19\pi'_3 - 1.38 \log (\beta \cdot 10^{\pi'_3} + 1) + 0.50I + 0.90\sigma + 6.20$ $n = 38 \quad r = 0.935 \quad s = 0.289 \quad \pi_0 = 1.56$
Molecular Descriptor	Access the following web-servers to compute molecular descriptors: **MoDel** and **e-dragon** *n* represents the number of data points used to derive the equation, *r* is the correlation coefficient, s is the standard deviation from the regression, *F* is the F statistic for significance of each additional variable, and the values in parentheses are for construction of the 95% confidence intervals; Ki is the Michaelis inhibition constant. The disposable parameter β is obtained by an iterative procedure for the bilinear structure-activity model. The Hydrophobicity variable π, superscribed with a prime (π'), denotes that in lb, for substituents of type $CH_2ZC_6H_4$-Y, where Z = 0, NH, Se, or S, the π value for Y is set equal to zero (i.e.,π $CH_2ZC_6H_4$-Y = π $CH_2ZC_6H_5$). same parameterization is also applies to groups of the type $ZCH_2ZC_6H_4$-Y, where Z = 0, *S.* Π'_3, measure of the effect of Hydrophobicity on inhibitor potency.
Reference	Quantitative Structure-Activity Relationship of Triazine-Antifolate Inhibition of Leishmania Dihydrofolate Reductase and Cell Growth. *J. Med. Chem.* 1987, 30, 1218-1224

Target Species	Human
Chemical Type	3-X-triazines
Mode of Action	Inhibitor
Activity Type	Inhibition of L1210 Leukemia DHFR
QSAR Model 1	$\log 1/K_i = 0.98\pi'_3 - 1.14 \log (\beta \cdot 10^{\pi'_3} + 1) + 0.79\sigma + 6.12$ $n = 58 \quad r = 0.900 \quad s = 0.264 \quad \pi_0 = 1.76$
Molecular Descriptor	Access the following web-servers to compute molecular descriptors: **MoDel** and **e-dragon** *n* represents the number of data points used to derive the equation, *r* is the correlation coefficient, s is the standard deviation from the regression, *F* is the F statistic for significance of each

	additional variable, and the values in parentheses are for construction of the 95% confidence intervals; Ki is the Michaelis inhibition constant. The disposable parameter β is obtained by an iterative procedure for the bilinear structure-activity model. The Hydrophobicity variable π, superscribed with a prime (π'), denotes that in lb, for substituents of type $CH_2ZC_6H_4$-Y, where Z = 0, NH, Se, or S, the π value for Y is set equal to zero (i.e. $CH_2ZC_6H_4$-Y = π $CH_2ZC_6H_5$). same parameterization is also applies to groups of the type $ZCH_2ZC_6H_4$-Y, where Z = 0, *S*. Π'_3, measure of the effect of Hydrophobicity on inhibitor potency.
Reference	Quantitative Structure-Activity Relationship of Triazine-Antifolate Inhibition of Leishmania Dihydrofolate Reductase and Cell Growth. *J. Med. Chem.* 1987, 30, 1218-1224

Target Species	Lactobacillus casei
Chemical Type	3-X-triazines
Mode of Action	Inhibitor
QSAR Model 1	$\log 1/K_i = 0.53\pi'_3 - \log(\beta \cdot 10^{\pi'_3} + 1) + 1.49I + 0.70\sigma + 2.93$ $n = 44 \quad r = 0.953 \quad s = 0.319 \quad \pi_0 = 4.31$
Molecular Descriptor	Access the following web-servers to compute molecular descriptors: **MoDel** and **e-dragon** *n* represents the number of data points used to derive the equation, *r* is the correlation coefficient, s is the standard deviation from the regression, *F* is the F statistic for significance of each additional variable, and the values in parentheses are for construction of the 95% confidence intervals; Ki is the Michaelis inhibition constant. The disposable parameter β is obtained by an iterative procedure for the bilinear structure-activity model. The Hydrophobicity variable π, superscribed with a prime (π'), denotes that in lb, for substituents of type $CH_2ZC_6H_4$-Y, where Z = 0, NH, Se, or S, the π value for Y is set equal to zero (i.e. $CH_2ZC_6H_4$-Y = π $CH_2ZC_6H_5$). same parameterization is also applies to groups of the type $ZCH_2ZC_6H_4$-Y, where Z = 0, *S*. Π'_3, measure of the effect of Hydrophobicity on inhibitor potency.
Reference	Quantitative Structure-Activity Relationship of Triazine-Antifolate Inhibition of Leishmania Dihydrofolate Reductase and Cell Growth. *J. Med. Chem.* 1987, 30, 1218-1224

Target	Escherichia coli

Species	
Chemical Type	3-X-triazines
Mode of Action	Inhibitor
QSAR Model 1	$\log 1/K_i = 1.16\pi'_3 - 1.10 \log (\beta \cdot 10^{\pi'_3} + 1) + 1.36\sigma + 0.41I + 5.08$ $n = 31 \quad r = 0.930 \quad s = 0.280$
Molecular Descriptor	Access the following web-servers to compute molecular descriptors: **MoDel** and **e-dragon** *n* represents the number of data points used to derive the equation, *r* is the correlation coefficient, s is the standard deviation from the regression, *F* is the F statistic for significance of each additional variable, and the values in parentheses are for construction of the 95% confidence intervals; Ki is the Michaelis inhibition constant. The disposable parameter β is obtained by an iterative procedure for the bilinear structure-activity model. The Hydrophobicity variable π, superscribed with a prime (π'), denotes that in lb, for substituents of type $CH_2ZC_6H_4$-Y, where Z = 0, NH, Se, or S, the π value for Y is set equal to zero (i.e. $CH_2ZC_6H_4$-Y = π $CH_2ZC_6H_5$). same parameterization is also applies to groups of the type $ZCH_2ZC_6H_4$-Y, where Z = 0, *S*. Π'_3, measure of the effect of Hydrophobicity on inhibitor potency.
Reference	Quantitative Structure-Activity Relationship of Triazine-Antifolate Inhibition of Leishmania Dihydrofolate Reductase and Cell Growth. *J. Med. Chem.* 1987, 30, 1218-1224

Target Species	Human
Chemical Type	Quinazolines
Mode of Action	Inhibitor
Activity Type	Inhibition of DHFR from human leukemic cells
QSAR Model 1	$\log (1/I_{50}) = 10.12 - 2.87(I\text{-}1) + 0.29(I\text{-}2) - 0.38(\text{MR-}6) - 0.29(\pi\text{-R}) - 0.19(\text{MR-R})$ $n = 47; r = 0.956; s = 0.42; F_{5,41} = 86.35$
Molecular	Access the following web-servers to compute molecular descriptors: **MoDel** and **e-dragon**

Descriptor	Inhibition of DHFR in human leukemic cells where *n* refers to the number of data points used in the regression, *r* is the multiple correlation coefficient, and *s* is the standard error of estimation. Hydrophobicity, π,, molar refractivity, MR, and Hammett constant, σ , for the substituents were taken from Leo et al.[14]a and Hansch et al. [15] or estimated following Hansch's approach.[14b] MR values were scaled by 0.1 to make them commensurable with the other parameters. Each indicator variable is given the value 0. 1-1 takes the value of 1 for 4-OH or 4-SH compounds, and 1-2 is given the value of 1 when the substituent in the position 5 is other than hydrogen. 1-3 is equal to 1 for the derivatives with Z = -NHCH,-, and 1-4 assumes the value of 1 for congeners having Z groups other than -CH2NH- or -NHCH2-. 1-5 is taken as 1 when the R group is not an amino acid derivative. If the amino acid is not L-glutamic acid, then 1-6 equals 1, and a value of 1 for 1-7 indicates that R is not in the para but in another position of the phenyl ring. As shown later, some of the indicator variables will be used to express the contribution of certain substituents whose physicochemical parameters showed poor variation and high correlation.
Reference	Multivariate Analysis and Quantitative Structure-Activity Relationships. Inhibition of Dihydrofolate Reductase and Thymidylate Synthetase by Quinazolines. Journal of Medicinal Chemistry, 1979, Vol. 22, No. 5. P483-491.

Target Species	Human
Chemical Type	Quinazolines
Mode of Action	Inhibitor
Activity Type	Inhibition of DHFR from L1210R
QSAR Model 1	$\log (1/I_{50}) = 9.60 + 0.44(I\text{-}2) - 1.06(I\text{-}3) - 0.35(\text{MR-}6) - 0.145(\pi\text{-R})$ $n = 27; r = 0.83; s = 0.33; F_{4,22} = 12.51$
QSAR Model 2	$\log (1/I_{50}) = 9.36 + 0.49(I\text{-}2) - 1.23(I\text{-}3) - 0.296(\text{MR-}6) - 0.115(\pi\text{-R})$ $n = 24; r = 0.904; s = 0.235; F_{4,19} = 21.16$
Molecular Descriptor	Access the following web-servers to compute molecular descriptors: **MoDel** and **e-dragon** Inhibition of DHFR in L1210R where *n* refers to the number of data points used in the regression,

	r is the multiple correlation coefficient, and *s* is the standard error of estimation. Hydrophobicity, π,, molar refractivity, MR, and Hammett constant, σ , for the substituents were taken from Leo et al.[14]a and Hansch et al. [15] or estimated following Hansch's approach.[14b] MR values were scaled by 0.1 to make them commensurable with the other parameters.
Reference	Multivariate Analysis and Quantitative Structure-Activity Relationships. Inhibition of Dihydrofolate Reductase and Thymidylate Synthetase by Quinazolines. Journal of Medicinal Chemistry, 1979, Vol. 22, No. 5. P483-491.

Target Species	Human
Chemical Type	Piritrexim analogues
Mode of Action	Inhibitor
QSAR Model 1	$pIC_{50}(\mu M) = -0.6165(\pm 0.3015)\ {}^{1}\chi^{V} + 1.7096 \times (\pm 0.3251)IP_1 + 3.6080$
QSAR Model 2	$pIC_{50}(\mu M) = 0.0053(\pm\ 8.1955 \times 10^{-4})Sz\ - 2.2762(\pm 0.3233)\ {}^{0}\chi^{V} + 0.5618(\pm 0.3105)IP_2 + 12.0758$
QSAR Model 3	$pIC_{50}(\mu M) = 0.0034(\pm 0.0011)Sz - 1.4013(\pm 0.4499)\,{}^{0}\chi^{V} + 0.9912(\pm 0.3998)IP_1\ + 0.7708(\pm 0.2809)IP_2 + 6.7073$
QSAR Model 4	$pIC_{50}(\mu M) = 0.0018(\pm 0.0014)W + 0.0024(\pm 0.0013)Sz - 1.4787(\pm 0.4440)\,{}^{0}\chi^{V} + 0.9416(\pm 0.3928)IP_1 + 0.6873(\pm 0.2822)IP_2 + 7.3351$
Molecular Descriptor	Access the following web-servers to compute molecular descriptors: **MoDel** and **e-dragon** Wiener (W) is the oldest topological index. It is based on the vertex distances of the respective molecular graph; Szeged (Sz) which is considered as the modification of the Wiener index to cyclic compounds; Molecular connectivity ($^{0}X^{V}$, $^{1}X^{V}$) indices; Indicator parameters (Ip_1, Ip_2) are used in linear multiple regression analysis to account for certain features which cannot be described by continuous variables. The connectivity index $\chi = \chi(G)$ of a graph G is defined by Randic as under: $$\chi = \chi(G) = \sum_{ij} [d_i\ d_j]^{-0.5}$$

	where d_i is the valence of a vertex i, equal to the number of bonds connected to the atom i, in G, representing the graph of a compound. In the case of hetero-systems, the connectivity is given in terms of valence delta values δ_i^V and δ_j^V of atoms i and j and is denoted by χ^V. This version of the connectivity index is called the valence connectivity index.
Reference	QSAR Studies on Biological Activity of Piritrexim Analogues Against *pc* DHFR. *Bioorganic & Medicinal Chemistry* 10 (2002) 2919–2926