*IOSR Journal of Applied Chemistry (IOSR-JAC)*
*e-ISSN: 2278-5736.Volume 6, Issue 3 (Nov. – Dec. 2013), PP 41-48*
*www.iosrjournals.org*

# QSAR studies of some anilinoquinolines for their antitumor activity as EGFR inhibitors

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***Abstract:*** *Quantitative Structure-Activity Relationship studies has been performed on some anilinoquinolines . A variety of parameters including 2D- autocorelation, RDF, 3D- MoRSE, WHIM and GETAWAY parameters have been chosen for modeling the antitumor activity of these compounds. The multiple regression analysis reveals that the seven –parametric model is the best for modeling the activity of the compounds under present study. This model has been tested by using cross validated parameters. The results are also discussed on the basis of ridge regression.*

**Keywords:** *QSAR, NCSS, EGFR, Ridge regression.*

## I. Introduction

Cancer is now a day's used as a generic term describing a group of about 120 different diseases, which can affect any part of the body and defined as the state characterized by the uncontrolled growth and invasion of normal tissues and spread of cells [1]. According to WHO reports cancer is a leading cause of premature death worldwide, accounting for 7.6 million deaths (around 13% of all deaths) only in 2008. The deaths from cancer worldwide are projected to continue rising, reaching an estimated 13.1 million in 2030 (WHO 2012) [2]. A number of natural and synthetic products have been found to exhibit anticancer activity against tumor cell lines [3-7].

It is worth mentioning that epidermal growth factor receptor (EGFR) is a rational target for antitumor strategies. The EGFR is expressed or highly expressed in a variety of human tumors including non-small cell lung cancer (NSCLC), breast, head and neck, gastric, colorectal, esophageal, prostate, bladder, renal, pancreatic, and ovarian cancers [8]. Particularly, a large number of compounds have been synthesized and evaluated as EGFR inhibitors, with special attention being paid to compounds having a phenyl amino pyrimidine moiety in their structures [9-13]. Evidently Anilinoquinolines are well known EGFR inhibitors as demonstrated in various studies [14-16]. In silico QSAR studies were performed by Pasha et al., [17] on a series of EGFR inhibitory anilinoquinolines . In the study they have reported HQSAR, DFT-based QSAR, ligand – based 3D- QSAR, and receptor- guided HQSAR analysis of 58 anilinoquinoline derivatives using various parameters. In the present study we are also using the same data set of compounds with $pIC_{50}$ activities, but selecting different independent variables.

## II. Computational Details

The structural details of the 58 anilinoquinolines derivatives with EGFR inhibitory activity $pIC_{50}$ have been reported in table 1. The calculated parameters have been summarized in table 2. From the large pool of 2D-autocorrelation parameters, RDF, 3D MoRSE, WHIM and GETAWAY descriptors we have selected a few to carryout multiple regression analysis using variable selection method. For calculating the parameters we have used Dragon software [18] .From all the calculated descriptors, useful descriptors were generated by variable selection of descriptors in multiple regression analysis using NCSS software [19]. The intercorrelatedness among the descriptors and their correlation with the activity values $pIC_{50}$ is presented in Table 3. All the statistically significant models along with their quality have been summarized in table 4. This table also includes the values of Poglianis quality factor Q [20-22], which is the ratio of R and Se (Q = R/Se).

## III. Results and Discussion

The regression analysis of the data set yielded several statistically significant models. However, on the basis of highest $R^2$ value, we propose following statistically significant models to be best for modeling the EGFR inhibitory activity:

**Five variable model (Model no.5 , Table no.4)**

The Five -parametric model having maximum $R^2$ value 0.7779 is as below:

$pIC_{50}$ = -22.2852(±3.3394) G3m -7.6033(±0.8275) MATS1e + 8.2819(±1.6698) MATS3p+
0.0356(±0.0101)RDF095s- 0.4418(±0.1033) RDF110u + 12.9503 (1)

N=58, $R^2$ =0.7779, $R^2_A$= 0.7566, Se= 0.0930, F= 36.429, Q = 9.484

**Six variable model (Model no.6 , Table no.4)**

When H1i is added to the above model a six-parametric model with $R^2 = 0.8177$ is obtained as below:

$pIC_{50}$ = -18.9191(±3.2170) G3m +1.6503(±0.7941)H1i-7.4943(±0.7577) MATS1e + 9.8815(±1.6009) MATS3p+ 0.0477(±0.0099)RDF095s- 0.4949(±0.0958) RDF110u + 5.4334 (2)

N=58, $R^2$ =0.8177, $R^2_A$=0.7963, Se= 0.0851, F= 38.134, Q= 10.626

**Seven variable model (Model no.7 , Table no.4)**

When Mor29u combined with the above six-parametric model a seven- parametric model is yielded with improved $R^2$ value.

$pIC_{50}$ = -20.5758(±2.8191) G3m +3.2238(±0.7024)H1i-7.4577(±0.6576) MATS1e + 11.0537(±1.4168) MATS3p-2.1918(±0.5205)Mor29u+0.0607(±0.0091)RDF095s- 0.7058(±0.0971) RDF110u + 4.8803 (3)

N=58, $R^2$ =0.8654, $R^2_A$= 0.8466, Se= 0.0738, F= 45.943, Q= 12.605

It is evident that the value of $R^2$ is drastically increases from six-parametric model to the seven-parametric model. This means that seven-variable model is statistically better than previous one. Consequently, we observed that the seven-parametric model is the best for modeling the activity.

Further confirmation is obtained by estimating the $pIC_{50}$ activity using model- 7 which is reported in Table 5. The estimated values are in good agreement with observed values. When observed activity values are plotted against estimated values, we obtained a graph which is reported in Fig. 2. The predictive power of the model comes out to be 0.8654.To validate the obtained model cross validation has been done by LOO method, and obtained values are reported in table 6. The highest $R^2_{CV}$ for the model 7 shows that this is the most appropriate model for modeling $pIC_{50}$ value of compounds used in the present study. For any kind of possible defect we have calculated variance inflation factor, tolerance and condition number for various parameters using VIF plot which is given in Table 7. All the parameters show the value within the permissible limit. Therefore, the model is free from any kind of defect. Ridge trace suggests that there is no co- linearity in the model.

## IV. Conclusion

1. 2D –autocorrelation, RDF, 3D MoRSE and GETAWAY parameters are the useful parameters for modeling the EGFR inhibitory activity for the present set of compounds.
2. MATS1e and MATS3p plays a dominating role for prediction of antitumor activity.

## Acknowledgement

The corresponding author is thankful to UGC. This work was financially supported by the UGC MRP.

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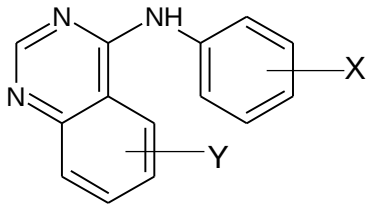


**Fig.1 Basic structure of anilinoquinolines.**

**Table .1 Structural details and $pIC_{50}$ values for the compounds used in present study.**

| Compound no. | X | Y | $pIC_{50}$ |
|---|---|---|---|
| 1 | H | H | 6.46 |
| 2 | 3-F | H | 7.25 |
| 3 | 3-Cl | H | 7.64 |
| 4 | 3-Br | H | 7.57 |
| 5 | 3-I | H | 7.1 |
| 6 | 3-$CF_3$ | H | 6.24 |
| 7 | H | 6-OMe | 7.26 |
| 8 | 3-Br | 6-OMe | 7.52 |
| 9 | H | 6-$NH_2$ | 6.11 |
| 10 | 3-$CF_3$ | 6-$NH_2$ | 6.24 |
| 11 | 3-Br | 6-$NH_2$ | 9.11 |
| 12 | H | 6-$NO_2$ | 5.3 |
| 13 | 3-Br | 6-$NO_2$ | 6.05 |
| 14 | H | 7-OMe | 6.92 |
| 15 | 3-Br | 7-OMe | 8 |
| 16 | H | 7-$NH_2$ | 7 |
| 17 | 3-F | 7-$NH_2$ | 8.7 |
| 18 | 3-Cl | 7-$NH_2$ | 9.6 |
| 19 | 3-Br | 7-$NH_2$ | 10 |
| 20 | 3-I | 7-$NH_2$ | 9.46 |
| 21 | 3-$CF_3$ | 7-$NH_2$ | 8.48 |
| 22 | H | 7-$NO_2$ | 4.92 |
| 23 | 3-F | 7-$NO_2$ | 5.22 |
| 24 | 3-Cl | 7-$NO_2$ | 6.09 |
| 25 | 3-Br | 7-$NO_2$ | 6 |
| 26 | 3-I | 7-$NO_2$ | 6.27 |
| 27 | H | 6,7-di-OMe | 7.54 |
| 28 | 3-F | 6,7-di-OMe | 8.42 |
| 29 | 3-Cl | 6,7-di-OMe | 9.51 |
| 30 | 3-Br | 6,7-di-OMe | 10.6 |
| 31 | 3-I | 6,7-di-OMe | 9.05 |
| 32 | 3-$CF_3$ | 6,7-di-OMe | 9.62 |
| 33 | 3-Br | 6-NHMe | 8.4 |
| 34 | 3-Br | 6-$NMe_2$ | 7.08 |
| 35 | 3-Br | 7-OH | 8.33 |
| 36 | 3-Br | 7-NHMe | 8.16 |
| 37 | 3-Br | 7-NHC2$H_5$ | 7.92 |
| 38 | 3-Br | 7-$NMe_2$ | 7.96 |
| 39 | 3-Br | 6,7-di-$NH_2$ | 9.92 |
| 40 | 3-Br | 6-$NH_2$,7-NHMe | 9.16 |
| 41 | 3-Br | 6-$NH_2$,7-$NMe_2$ | 6.8 |
| 42 | 3-Br | 6-$NH_2$,7-OMe | 8.42 |
| 43 | 3-Br | 6-$NH_2$,7-Cl | 8.19 |
| 44 | 3-Br | 6-$NO_2$,7-$NH_2$ | 7.28 |
| 45 | 3-Br | 6-$NO_2$,7-NHMe | 7.17 |
| 46 | 3-Br | 6-$NO_2$,7-$NMe_2$ | 5.7 |
| 47 | 3-Br | 6-$NO_2$,7-OMe | 7.82 |
| 48 | 3-Br | 6-$NO_2$,7-Cl | 7.6 |
| 49 | 3-Br | 6,7-di-OHa | 9.77 |
| 50 | 3-Br | 6,7-di-$OC_2H_5$ | 11.22 |
| 51 | 3-Br | 6,7-di-$OC_3H_7$ | 9.77 |
| 52 | 3-Br | 6,7-di-$OC_4H_9$ | 6.98 |
| 53 | 3-Br | 5,6-di-OMe | 5.86 |

| | | | |
|---|---|---|---|
| 54 | 3-Br | 5,6,7-tri-OMe | 9.17 |
| 55 | 2-Br | 6,7-di-OMe | 6.89 |
| 56 | 4-Br | 6,7-di-OMe | 9.02 |
| 57 | 3,4-di-Br | 6,7-di-OMe | 10.14 |
| 58 | 3,5-di-Br | 6,7-di-OMe | 6.95 |

**Table 2. Calculated values of 2D autocorrelation, RDF, 3D MoRSE, WHIM, and GETAWAY descriptors for the compounds used in present study.**

| S.No. | MATS1e | MATS3p | RDF110u | RDF095s | Mor29u | G3m | H1i |
|---|---|---|---|---|---|---|---|
| 1 | -0.046 | -0.122 | 0.000 | 0.097 | 0.176 | 0.295 | 2.613 |
| 2 | -0.051 | -0.117 | 0.000 | 0.050 | 0.266 | 0.193 | 2.652 |
| 3 | -0.067 | -0.152 | 0.000 | 12.376 | 0.164 | 0.233 | 2.585 |
| 4 | -0.073 | -0.141 | 0.001 | 6.497 | 0.263 | 0.233 | 2.562 |
| 5 | -0.061 | -0.099 | 0.587 | 5.760 | 0.199 | 0.255 | 2.533 |
| 6 | -0.044 | -0.214 | 0.661 | 37.934 | 0.191 | 0.220 | 2.188 |
| 7 | -0.045 | -0.119 | 0.000 | 0.227 | 0.150 | 0.200 | 2.359 |
| 8 | -0.066 | -0.142 | 0.001 | 6.151 | 0.229 | 0.200 | 2.536 |
| 9 | -0.171 | -0.184 | 0.000 | 0.334 | 0.082 | 0.307 | 2.765 |
| 10 | -0.086 | -0.256 | 0.849 | 35.521 | 0.000 | 0.283 | 2.276 |
| 11 | -0.186 | -0.189 | 0.002 | 6.914 | 0.101 | 0.188 | 2.714 |
| 12 | 0.207 | -0.178 | 0.000 | 0.826 | 0.076 | 0.224 | 2.750 |
| 13 | 0.182 | -0.186 | 0.000 | 5.764 | 0.084 | 0.206 | 2.695 |
| 14 | -0.045 | -0.119 | 0.005 | 2.100 | 0.245 | 0.200 | 2.579 |
| 15 | -0.066 | -0.142 | 0.000 | 9.067 | 0.371 | 0.184 | 2.580 |
| 16 | -0.171 | -0.184 | 0.000 | 1.043 | 0.152 | 0.245 | 2.749 |
| 17 | -0.116 | -0.179 | 0.109 | 1.779 | 0.094 | 0.197 | 2.785 |
| 18 | -0.164 | -0.211 | 0.018 | 12.174 | 0.030 | 0.206 | 2.717 |
| 19 | -0.186 | -0.189 | 0.000 | 7.948 | 0.088 | 0.169 | 2.695 |
| 20 | -0.190 | -0.121 | 0.429 | 7.269 | 0.069 | 0.188 | 2.666 |
| 21 | -0.086 | -0.256 | 1.790 | 25.427 | 0.148 | 0.197 | 2.820 |
| 22 | 0.207 | -0.178 | 0.939 | 3.947 | 0.234 | 0.206 | 2.746 |
| 23 | 0.111 | -0.172 | 0.739 | 0.936 | 0.253 | 0.197 | 2.790 |
| 24 | 0.159 | -0.208 | 0.000 | 3.608 | 0.246 | 0.188 | 2.728 |
| 25 | 0.182 | -0.186 | 0.000 | 9.482 | 0.336 | 0.197 | 2.704 |
| 26 | 0.206 | -0.120 | 0.004 | 4.865 | 0.319 | 0.188 | 2.683 |
| 27 | -0.052 | -0.105 | 0.000 | 2.613 | 0.326 | 0.246 | 2.546 |
| 28 | -0.065 | -0.102 | 0.025 | 1.753 | 0.447 | 0.191 | 2.614 |
| 29 | -0.071 | -0.136 | 0.003 | 11.858 | 0.460 | 0.177 | 2.666 |
| 30 | -0.070 | -0.132 | 0.470 | 15.889 | 0.330 | 0.177 | 2.668 |
| 31 | -0.059 | -0.101 | 0.041 | 6.550 | 0.543 | 0.162 | 2.622 |
| 32 | -0.066 | -0.171 | 2.643 | 73.531 | 0.522 | 0.173 | 2.665 |
| 33 | -0.109 | -0.109 | 0.000 | 8.839 | 0.226 | 0.214 | 2.559 |
| 34 | -0.040 | -0.195 | 0.005 | 16.806 | 0.038 | 0.198 | 2.382 |
| 35 | -0.160 | -0.163 | 0.000 | 8.544 | 0.158 | 0.209 | 2.628 |
| 36 | -0.109 | -0.109 | 0.000 | 16.058 | 0.369 | 0.222 | 2.600 |
| 37 | -0.088 | -0.004 | 2.740 | 16.360 | 0.082 | 0.184 | 2.519 |
| 38 | -0.040 | -0.195 | 0.008 | 16.883 | 0.564 | 0.177 | 2.535 |
| 39 | -0.276 | -0.219 | 0.000 | 10.549 | 0.227 | 0.184 | 2.786 |
| 40 | -0.199 | -0.140 | 0.003 | 11.186 | 0.218 | 0.193 | 2.650 |
| 41 | -0.132 | -0.216 | 0.001 | 16.226 | 0.384 | 0.214 | 2.576 |
| 42 | -0.143 | -0.177 | 0.001 | 11.535 | 0.216 | 0.164 | 2.651 |
| 43 | -0.178 | -0.205 | 0.000 | 7.094 | 0.129 | 0.206 | 2.692 |
| 44 | 0.094 | -0.219 | 0.012 | 11.881 | 0.272 | 0.184 | 2.770 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 45 | 0.131 | -0.137 | 0.001 | 11.248 | 0.050 | 0.179 | 2.634 |
| 46 | 0.163 | -0.215 | 0.001 | 15.532 | 0.250 | 0.187 | 2.557 |
| 47 | 0.113 | -0.175 | 0.064 | 12.855 | 0.166 | 0.180 | 2.645 |
| 48 | 0.141 | -0.204 | 0.000 | 8.518 | 0.049 | 0.169 | 2.672 |
| 49 | -0.216 | -0.182 | 0.000 | 8.698 | 0.173 | 0.197 | 2.676 |
| 50 | -0.043 | 0.128 | 1.364 | 18.212 | 0.090 | 0.169 | 2.543 |
| 51 | -0.024 | 0.068 | 4.719 | 29.548 | -0.171 | 0.177 | 2.548 |
| 52 | -0.010 | 0.071 | 8.684 | 32.772 | -0.415 | 0.182 | 2.524 |
| 53 | -0.070 | -0.126 | 1.904 | 13.297 | 0.605 | 0.205 | 2.709 |
| 54 | -0.075 | -0.112 | 0.346 | 12.074 | 0.378 | 0.165 | 2.775 |
| 55 | -0.070 | -0.090 | 1.679 | 4.607 | 0.273 | 0.191 | 2.405 |
| 56 | -0.070 | -0.132 | 0.285 | 13.644 | 0.392 | 0.184 | 2.733 |
| 57 | -0.086 | 0.020 | 0.828 | 23.506 | 0.452 | 0.177 | 2.639 |
| 58 | -0.086 | -0.174 | 1.367 | 16.717 | 0.499 | 0.198 | 2.723 |

**Table 3. Correlation matrix**

| | pIC50 | MATS1e | MATS3p | RDF110u | RDF095s | Mor29u | G3m | H1i |
|---|---|---|---|---|---|---|---|---|
| pIC50 | 1.000 | | | | | | | |
| MATS1e | -0.602 | 1.000 | | | | | | |
| MATS3p | 0.331 | -0.030 | 1.000 | | | | | |
| RDF110u | 0.035 | 0.022 | 0.571 | 1.000 | | | | |
| RDF095s | 0.244 | -0.079 | 0.095 | 0.521 | 1.000 | | | |
| Mor29u | 0.041 | -0.019 | -0.176 | -0.422 | -0.002 | 1.000 | | |
| G3m | -0.462 | -0.122 | -0.218 | -0.163 | -0.183 | -0.163 | 1.000 | |
| H1i | 0.124 | 0.048 | -0.208 | -0.160 | -0.291 | 0.164 | -0.181 | 1.000 |

**Table 4. Regression parameters and quality of correlations**

| Model No. | Parameters Used | $A_i$=(1……6) | B | Se | $R^2$ | $R^2_A$ | F | Q=R/Se |
|---|---|---|---|---|---|---|---|---|
| 1 | MATS1e | -7.4635(±1.3218) | 7.4706 | 0.1518 | 0.3628 | 0.3514 | 31.883 | 3.968 |
| 2 | G3m<br>MATS1e | -26.3556(±3.8767)<br>-8.2836(±0.9905 | 12.7199 | 0.1129 | 0.6538 | 0.6412 | 51.925 | 7.162 |
| 3 | G3m<br>MATS1e<br>MATS3p | -24.1464(±3.7812)<br>-8.1400(±0.9433)<br>3.9631(±1.5146) | 12.8520 | 0.1074 | 0.6927 | 0.6756 | 40.579 | 7.749 |
| 4 | G3m<br>MATS1e<br>MATS3p<br>RDF110u | -24.5216(±3.6152)<br>-8.0460(±0.9019)<br>6.3734(±1.7418)<br>-0.2308(±0.0929) | 13.4100 | 0.1025 | 0.7248 | 0.7040 | 34.895 | 8.306 |
| 5 | G3m<br>MATS1e<br>MATS3p<br>RDF095s<br>RDF110u | -22.2852(±3.3394)<br>-7.6033(±0.8275)<br>8.2819(±1.6698)<br>0.0356(±0.0101)<br>-0.4418(±0.1033) | 12.9503 | 0.0930 | 0.7779 | 0.7566 | 36.429 | 9.484 |
| 6 | G3m<br>H1i<br>MATS1e<br>MATS3p<br>RDF095s<br>RDF110u | -18.9191(±3.2170)<br>2.6503(±0.7941)<br>-7.4943(±0.7577)<br>9.8815(±1.6009)<br>0.0477(±0.0099)<br>-0.4949(±0.0958) | 5.4334 | 0.0851 | 0.8177 | 0.7963 | 38.134 | 10.626 |
| 7 | G3m<br>H1i<br>MATS1e<br>MATS3p<br>Mor29u<br>RDF095s<br>RDF110u | -20.5758(±2.8191)<br>3.2238(±0.7024)<br>-7.4577(±0.6576)<br>11.0537(±1.4168)<br>-2.1918(±0.5205)<br>0.0607(±0.0091)<br>-0.7058(±0.0971) | 4.8803 | 0.0738 | 0.8654 | 0.8466 | 45.943 | 12.605 |

**Table 5. Observed and Estimated $pIC_{50}$ values using model no 7.(Table 4).**

| Comp. No. | Obs. $pIC_{50}$ | Est. $pIC_{50}$ | Residual |
|---|---|---|---|
| 1 | 6.46 | 5.85 | 0.61 |
| 2 | 7.25 | 7.97 | -0.72 |
| 3 | 7.64 | 7.63 | 0.01 |
| 4 | 7.57 | 7.15 | 0.42 |
| 5 | 7.10 | 6.66 | 0.44 |
| 6 | 6.24 | 6.79 | -0.55 |
| 7 | 7.26 | 7.08 | 0.19 |
| 8 | 7.52 | 7.73 | -0.21 |
| 9 | 6.11 | 6.56 | -0.45 |
| 10 | 6.24 | 5.76 | 0.48 |
| 11 | 9.11 | 9.26 | -0.15 |
| 12 | 5.30 | 5.51 | -0.21 |
| 13 | 6.05 | 6.08 | -0.03 |
| 14 | 6.92 | 7.69 | -0.77 |
| 15 | 8.00 | 8.07 | -0.07 |
| 16 | 7.00 | 7.67 | -0.67 |
| 17 | 8.70 | 8.52 | 0.18 |
| 18 | 9.60 | 8.95 | 0.65 |
| 19 | 10.00 | 9.68 | 0.32 |
| 20 | 9.46 | 9.67 | -0.21 |
| 21 | 8.48 | 7.69 | 0.80 |
| 22 | 4.92 | 5.05 | -0.13 |
| 23 | 5.22 | 6.07 | -0.85 |
| 24 | 6.09 | 6.00 | 0.09 |
| 25 | 6.00 | 5.97 | 0.03 |
| 26 | 6.27 | 6.39 | -0.12 |
| 27 | 7.54 | 6.70 | 0.84 |
| 28 | 8.42 | 7.84 | 0.58 |
| 29 | 9.51 | 8.57 | 0.94 |
| 30 | 10.60 | 8.81 | 1.79 |
| 31 | 9.05 | 8.50 | 0.55 |
| 32 | 9.62 | 9.97 | -0.35 |
| 33 | 8.40 | 8.38 | 0.02 |
| 34 | 7.08 | 7.56 | -0.48 |
| 35 | 8.33 | 8.62 | -0.29 |
| 36 | 8.16 | 8.47 | -0.31 |
| 37 | 7.92 | 8.71 | -0.79 |
| 38 | 7.96 | 7.34 | 0.62 |
| 39 | 9.92 | 9.86 | 0.06 |
| 40 | 9.16 | 9.59 | -0.43 |
| 41 | 6.80 | 7.52 | -0.72 |
| 42 | 8.42 | 9.39 | -0.97 |
| 43 | 8.19 | 8.53 | -0.34 |
| 44 | 7.28 | 7.02 | 0.26 |
| 45 | 7.17 | 7.77 | -0.60 |
| 46 | 5.70 | 6.08 | -0.38 |
| 47 | 7.82 | 7.30 | 0.52 |
| 48 | 7.60 | 7.12 | 0.48 |
| 49 | 9.77 | 9.20 | 0.57 |
| 50 | 11.22 | 11.28 | -0.06 |
| 51 | 9.77 | 9.22 | 0.55 |
| 52 | 6.98 | 6.90 | 0.08 |
| 53 | 5.86 | 6.66 | -0.80 |
| 54 | 9.17 | 9.41 | -0.24 |
| 55 | 6.89 | 6.73 | 0.16 |
| 56 | 9.02 | 8.74 | 0.28 |
| 57 | 10.14 | 10.46 | -0.32 |
| 58 | 6.95 | 7.26 | -0.31 |

**Table 6. Cross validated parameters for the best obtained models.**

| Model No. | Parameters used | PRESS/SSY | $R^2_{cv}$ | $S_{PRESS}$ | PSE |
|---|---|---|---|---|---|
| 1 | MATS1e | 1.7564 | -0.7564 | 1.1855 | 1.1649 |
| 2 | G3m<br>MATS1e | 0.5296 | 0.4704 | 0.8818 | 0.8587 |
| 3 | G3m<br>MATS1e | 0.4436 | 0.5564 | 0.7028 | 0.8089 |

| | | | | | |
|---|---|---|---|---|---|
| | MATS3p | | | | |
| 4 | G3m<br>MATS1e<br>MATS3p<br>RDF110u | 0.3797 | 0.6203 | 0.8008 | 0.7655 |
| 5 | G3m<br>MATS1e<br>MATS3p<br>RDF095s<br>RDF110u | 0.2855 | 0.7145 | 0.7263 | 0.6877 |
| 6 | G3m<br>H1i<br>MATS1e<br>MATS3p<br>RDF095s<br>RDF110u | 0.2229 | 0.7771 | 0.6644 | 0.6230 |
| 7 | G3m<br>H1i<br>MATS1e<br>MATS3p<br>Mor29u<br>RDF095s<br>RDF110u | 0.1555 | 0.8445 | 0.5765 | 0.5353 |

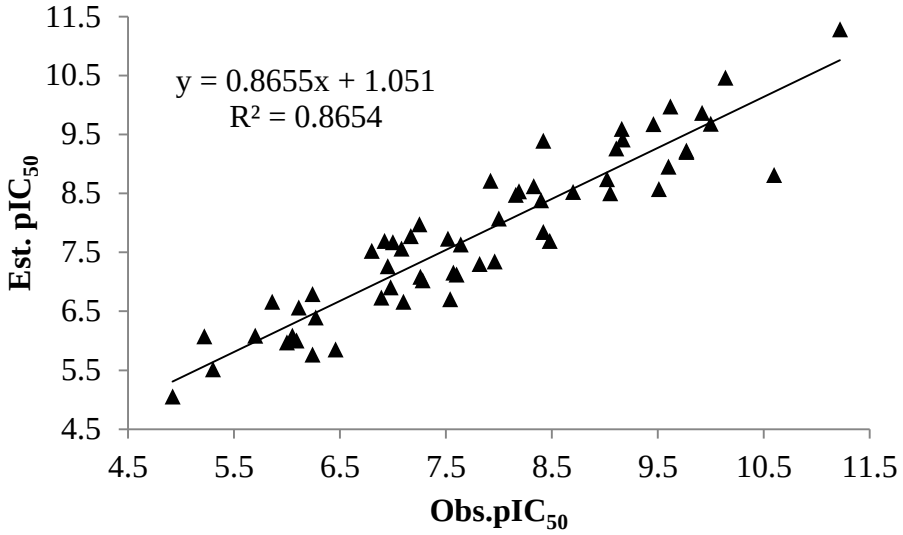


**Figure 2. Correlation between Observed and estimated $pIC_{50}$ activity using model 7(Table 4).**

**Table 7. Ridge analysis for the best seven-parametric model.**

| Model No. | Parameters used | VIF | Tolerence | Eigenvalue | Condition no. |
|---|---|---|---|---|---|
| 7 | MATS1e | 1.0464 | 0.9556 | 2.1416 | 1.00 |
| | MATS3p | 1.9491 | 0.5131 | 1.3253 | 1.62 |
| | RDF110u | 3.1378 | 0.3187 | 1.1028 | 1.94 |
| | RDF095s | 2.0512 | 0.4875 | 0.9363 | 2.29 |
| | Mor29u | 1.4864 | 0.6728 | 0.7875 | 2.72 |
| | G3m | 1.2557 | 0.7964 | 0.5377 | 3.98 |
| | H1i | 1.3308 | 0.7515 | 0.1685 | 12.70 |

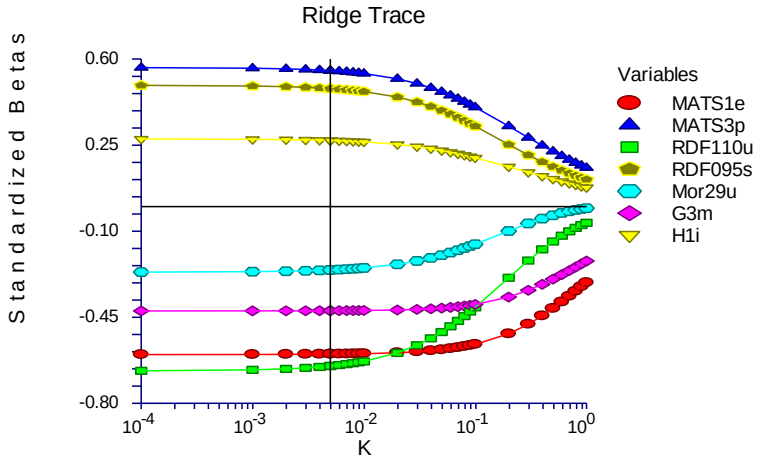


**Fig 3: Ridge trace for seven variable model 7 (Table 4)**

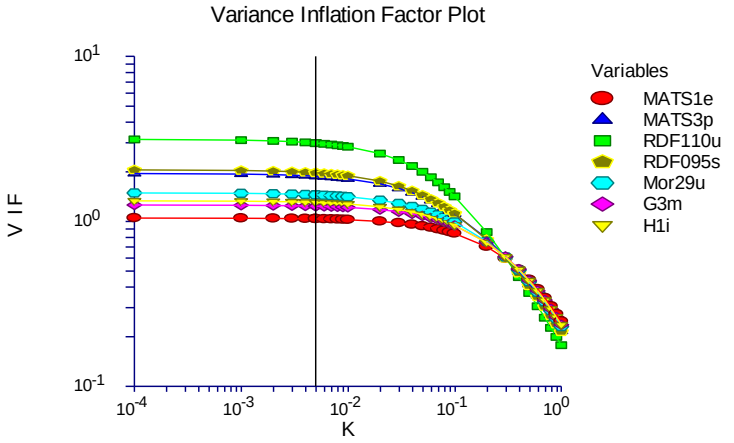


**Fig 4:VIF plot for seven variable model-7(Table 4)**