International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 5 Sep-Oct 2022, pp: 120-129 www.ijprajournal.com ISSN: 2456-4494

Quantitative Structure Activity Relationships Study of Antiviral Activity of Some Diterpene Esters

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Submitted: 05-09-2022 Accepted: 13-09-2022

ABSTRACT: The purpose of this work was to establish a quantitative relationship between the anti-viral activities of structurally related diterpene esters and their molecular descriptors. Several types of descriptors, including burden eigenvalues and 2D-autocorelation descriptors, were used to derive a quantitative relationship between biological activity and structural properties. A multiple linear regression analysis shows that a five-parametric model was found to be best for modeling the EC50 biological activity of the present set of compounds. For the best QSAR model, the statistics were R2=0.9317, Q-value = 0.251, F-ratio = 51.844, N = 25 for the present set of compounds. This model was further validated using the leave-one-out (LOO) cross-validation approach.

Key words: QSAR analysis, anti-viral activity, 2D QSAR, LOO, Multivariate analysis.

I. INTRODUCTION

QSAR technique is now widely accepted as a scientifically based strategy for predicting and describing untested compounds' biological activities. It has grown inextricably linked to the pharmaceutical sector, through lead screening and optimization through lead development and computer-aided drug design. From lead identification through optimization to lead development to computer-aided combinatorial chemistry, it has become an inextricably entrenched tool in the pharmaceutical sector. Changes in the biological activity of a series of compounds targeting a similar mechanism of action are associated with variations in their structural, physical, and chemical characteristics, according to QSAR.[1]

Chikungunya fever is caused through an arthropod-borne virus that has been linked to major epidemics and therefore is noted for its mortality rate (inclusive of virus-induced arthralgia, fever, myalgia, and rashes). [2] Chikungunya virus (CHIKV) has expanded from African and the Indian ocean region to Southeast Asia, the Indian Ocean, and, more recently, the Caribbean islands and South and Central America, respect to global migration and the introduction of both the mosquito larvae Aedes aegypti and Aedes albopictus. [3,4] There are no antiviral medicines or vaccines available for treating for prevent CHIKV infection at this time. [5] Recent scientific studies have emphasised problems and recent advancements in the search for novel antiviral therapeutics. [6, 7]

In order to find new inhibitors of CHIKV replication, Euphorbiaceae species were chosen and studied using compounds were isolated refinement, which also yielded to the separation of anti-CHIKV activity diterpenoid esters of the daphnane, jatrophane, and tigliane kinds. [8–12]

Also shown to be strong and specific inhibitors of CHIKV replication in vitro were the structurally similar diterpenoids prostratin and 12-O-tetradecanoylphorbol-13-acetate (TPA). TPA along with other tigliane-, ingenane-, and daphnane-type diterpenes have been shown to anti-HIV characteristics, as well as pro-inflammatory and tumor-promoting properties[13-17]

The current study attempted to model the antiviral activity EC_{50} of a set of 26 diterpene esters derivatives. These derivatives diterpene esters (1-26) from the tigliane (1-23), ingenane (24-25), and daphnane (26) types have a broad range of antiviral activity for chikungunya virus (CHIKV). The model was created by combining a few Burden eigenvalues (SpMin8 Bh(m), SpMin2 Bh(v), SpMin2 Bh(e), SpMax7 Bh(e), SpMax1 Bh(s), SpMin2 Bh(m), and 2D-autocorelation descriptors that are easy to calculate and though successful in predicting biological activity. In fact Burden eigenvalues and 2D-autocorelation parameters have been very successfully used by us in modeling different activities of drug molecules.[18-19]. The antiviral potential of 26 diterpene esters (1-26) from the tigliane (1-23), ingenane (24-25), and daphnane (26) types was antiviral activity against CHIKV. The goal of this research is to use the multivariate regression approach to create QSAR

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 5 Sep-Oct 2022, pp: 120-129 www.ijprajournal.com ISSN: 2456-4494

models and investigate the correlations between actual antiviral activity and estimated chemical descriptors of 26 diterpene esters from the chikungunya virus.

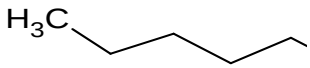
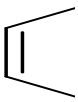
II. BIOLOGICAL ACTIVITY

The antiviral activity of diterpene esters against chikungunya virus is represented in the form of EC_{50} half maximal effective concentration, which is derived straight from the work of Louis-Felix Nothias-Scaglia et.al[20]. and is shown in Table-1.

Table-1 Structure of compounds

1	2
3	4
5	6
8	9
10	11
12	13

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 5 Sep-Oct 2022, pp: 120-129 www.ijprajournal.com ISSN: 2456-4494

14	15 
16 	17
18	19
20	21
22	23
24	25

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 5 Sep-Oct 2022, pp: 120-129 www.ijprajournal.com ISSN: 2456-4494

26	7

III. PRESENTATION OF DATA

In present study, Table-.1 represents the different substitutions on diterpene esters while Table-2 shows the antiviral activity in the form of EC_{50} µM and calculated molecular descriptors and Table-3 represents the correlation matrix between the descriptors and antiviral activity which are used in the present study Table-4 represent the result of regression analysis with statistical descriptors while Table 5 is the cross-validated statistical descriptors for all developed QSAR models Table- 6 represent the calculated and observed antiviral activity with residual from best model. Fig-1 shows the graph plotted between the observed and calculated antiviral activity while the Fig-2 is the graph plotted between the observed and residual to illustrate the systemic erro r.

Table-2- Calculated molecular descriptors for diterpene esters

C.No.	EC_{50}	SpMin8_Bh(m)	SpMin2_Bh(v)	SpMin2_Bh(e)	JGI6	SpMax7_Bh(e)	SpMax1_Bh(s)	SpMin2_Bh(m)
1	4.9	0.716	1.591	1.504	0.029	2.732	7.441	1.544
2	20	0.621	1.592	1.504	0.032	2.672	7.441	1.544
3	2.2	0.697	1.592	1.504	0.029	2.796	7.441	1.544
4	0.99	0.784	1.592	1.504	0.027	2.807	7.441	1.544
5	9.4	0.672	1.592	1.504	0.029	2.707	7.459	1.544
6	1.8	0.691	1.592	1.504	0.029	2.721	7.442	1.544
7	3.2	0.727	1.592	1.504	0.027	2.768	7.442	1.544
8	6	0.884	1.592	1.504	0.026	2.909	7.442	1.544
9	1.5	0.884	1.592	1.504	0.026	2.909	7.442	1.544
10	2.9	0.915	1.592	1.504	0.026	2.955	7.457	1.544
11	2.8	0.915	1.592	1.504	0.026	2.955	7.457	1.544
12	1.1	0.876	1.593	1.504	0.028	2.899	7.442	1.544
13	15	0.849	1.708	1.651	0.029	3.09	7.457	1.655
14	24.6	0.675	1.596	1.506	0.031	2.781	7.459	1.545
15	0.6	1.039	1.693	1.646	0.026	3.204	7.443	1.646
16	1.7	1.08	1.693	1.646	0.027	3.226	7.457	1.646
17	32.6	0.875	1.596	1.506	0.029	3.083	7.462	1.545
18	13.1	0.702	1.605	1.518	0.029	2.742	7.48	1.555
19	0.7	0.924	1.605	1.518	0.026	2.956	7.48	1.555
20	2.7	0.583	1.592	1.504	0.03	2.579	7.457	1.544
21	0.7	0.684	1.595	1.506	0.029	2.694	7.457	1.545
22	50.8	0.894	1.596	1.534	0.028	3.088	7.457	1.546
23	30.1	0.307	1.613	1.549	0.04	2.302	7.426	1.574
24	22.9	0.501	1.636	1.557	0.033	2.688	7.435	1.58
25	1.2	0.904	1.673	1.601	0.027	3.06	7.436	1.605
26	1.8	0.981	1.699	1.651	0.027	3.122	7.441	1.65

SpMin8_Bh(m)=smallest eigenvalue n. 8 of Burden matrix weighted by mass,**SpMin2_Bh(v)**=smallest eigenvalue n. 2 of Burden matrix weighted by van der Waals volume,**SpMin2_Bh(e)**=smallest eigenvalue n. 2 of Burden matrix weighted by Sanderson electronegativity,**JGI6**=mean topological charge in dex of order 6,**SpMax7_Bh(e)**=largest eigenvalue n. 7 of Burden matrix weighted by Sanderson electr onegativity,**SpMax1_Bh(s)**=largest eigenvalue n. 1 of Burden matrix weighted by I-state,**SpMin2_Bh(m)**=smallest eigenvalue n. 2 of Burden matrix weighted by mass

IV. RESULT AND DISCUSSION

QSAR study of a series of diterpene esters (1-26) from the tigliane (1-23), ingenane (24-25), and daphnane (26) types was antiviral activity against CHIKV was performed by using dragon software[22]. In this study, antiviral activity (EC_{50}) as

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 5 Sep-Oct 2022, pp: 120-129 www.ijprajournal.com ISSN: 2456-4494

dependent and various molecular descriptors; Burden eigenvalues and 2D-autocorelation descriptors taken as the independent variable and regression were established using (MLR) multiple linear regression analysis. The models were selected on the basis of its statistical significance for further study. A data set of 26 diterpene esters compounds that the antiviral activities of all 26 compounds gave maximum and minimum value range of antiviral activity against CHIKV. Due to presence of some outliers we have done final regression analysis of 25 selected diterpene esters derivatives as antiviral activity by QSAR method.

In order to understand the experimental inhibitory data of (1-26) diterpene esters against CHIKV antiviral activity on theoretical basis, we established a quantitative structure activity relationship between their antiviral activity and descriptors coding for molecular properties; Burden eigenvalues and 2D-autocorelation descriptors of molecules under consideration using described by Hansch and Free & Wilson.

In order to deduce the correlation of observed antiviral activity in terms of EC_{50} of the reported compounds with different structural parameters a systematic QSAR investigation has been carried out. The biological activity; antiviral is taken as dependent variable to get a linear relationship in the QSAR model. These were correlated with different molecular descriptors like Burden eigenvalues and 2D-autocorelation. The values of the selected descriptors utilised in the regression analysis are shown in Table-2. Using VCC lab's E-dragon software, the above-mentioned parameters were computed for the minimal energy conformers of the compounds in the series.

Table- 3 Correlation matrix

	EC50	SpMin8_Bh(m)	SpMin2_Bh(v)	SpMin2_Bh(e)	JGI6	SpMax7_Bh(e)	SpMax1_Bh(s)	SpMin2_Bh(m)
EC50	1							
SpMin8_Bh(m)	-0.32074	1						
SpMin2_Bh(v)	-0.11558	0.417165	1					
SpMin2_Bh(e)	**-0.05214**	0.41169	**0.991165**	1				
JGI6	0.527448	-0.860737	-0.099339	-0.066998	1			
SpMax7_Bh(e)	-0.11137	**0.945073**	0.574064	0.568537	-0.731536	1		
SpMax1_Bh(s)	0.057586	0.28478	-0.106978	-0.127699	-0.333466	0.246211	1	
SpMin2_Bh(m)	-0.11492	0.402767	**0.99335**	**0.993735**	-0.070098	0.549007	-0.115302	1

Using these above data **Table-3**, a correlation matrix was calculated to find the correlation as well as the collinearity between the descriptors. It is important for further analysis to develop a correlation matrix for the descriptors utilized and their correlation with the antiviral activities. Table -4.6.3 shows that some of the descriptors are mutually correlated. A high interrelationship was observed between SpMin2_Bh(e) and SpMin2_Bh(m**)(r=0.9937)**, SpMin2_Bh(v) and SpMin2_Bh(m) (r=0.99335), SpMin2_Bh(v) and SpMin2_Bh(e) (r=0.991165) as well as the low interrelationship was observed between EC50 and SpMin2_Bh(e) **(r=-0.05214).** The correlation matrix indicated the predominance of molecular descriptors in describing the antiviral activity of synthesized compounds.

The data presented in **Table-3** demonstrated the low co-linearity between the parameters (r<8) indicated that these parameter could be combined to get multiple regression (MLR) models. The analysis of matrix revealed Burden eigenvalues and 2D-autocorelation descriptors for the development of (MLR) models. Validations are a crucial aspect of any QSAR analysis. The statistical quality of the resulting models as depicted in **Table-4** are determined by R^2=regression coefficient, MSE=mean square error of estimations, F-ratio and Q quality factor =R/SE.

Table-4 Regression parameters and quality of correlation

Model No.	parameter	Ai,i=1,2,3….	Intercept	MSE	AR2	R2	F-Ratio	Q-Value
1	JGI6	A1=2277.0194 (±748.6680)	-55.4265	125.488	0.2481	0.2782	9.25	0.047
3	SpMin8_Bh(m) SpMax7_Bh(e)	A1=-150.1702 (±35.3206) A2=109.2380 (±28.8735)	-185.249	100.32	0.3989	0.447	9.296	0.0667
6	JGI6	A1=6618.7338 (±847.2321)	-14.312	49.4216	0.7039	0.7394	20.809	0.1223

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 5 Sep-Oct 2022, pp: 120-129 www.ijprajournal.com ISSN: 2456-4494

	SpMax7_Bh(e) SpMin2_Bh(m)	A2=88.3696 (±14.2562) A3=-267.2519 (±53.1780)						
10	SpMin8_Bh(m) SpMin2_Bh(v) SpMin2_Bh(e) SpMax7_Bh(e)	A1=-197.0866 (±23.7940) A2=-1253.8137 (±225.2900) A3=805.5795 (±167.3314) A4=165.6084 (±21.5871)	478.1823	35.4954	0.7873	0.8214	24.138	0.1521
15	SpMin8_Bh(m) SpMin2_Bh(v) SpMin2_Bh(e) JGI6 SpMax7_Bh(e)	A1=-135.0857 (±30.3888) A2=-958.7726 (±222.7261) A3=546.0353 (±172.7943) A4=2795.3814 (±1003.3333) A5=151.8734 (±19.4113)	310.871	26.8495	0.8391	0.8713	27.081	0.1801
20	SpMin8_Bh(m) SpMin2_Bh(v) SpMin2_Bh(e) JGI6 SpMax7_Bh(e)	A1=-158.6609 (±23.2472) A2=- 1008.5424(±165.6832) A3=574.2008 (±128.3829) A4=2321.2823(±753.0822) A5=165.5307 (±14.7711)	341.621	14.78	0.9137	0.9317	51.844	0.251

After performing regression analysis, we have adopted maximum R2 method and followed stepwise regression analysis. The result have show that for the set of 26 compounds mono parametric regression start giving statistically significant model. The best models are given below.

The statistical equation of the data was performed using NCSS software[23]. To test the quality of regression equations cross validation method is also used. The result of stepwise regression analysis is given below:

The Burden eigenvalues and 2D-autocorelation descriptors data was subjected to regression analysis (**Table-4**) and the best mono parametric model with molecular descriptors is as follows.

Mono parametric models

The regression analysis gave mono-parametric models. Out of which one contain JGI6 was found good result, the models obtained is as follows:

EC_{50} =-55.4265+2277.0194 (±748.6680) JGI6

N=26, MSE=125.4882, R2=0.2782, AR2=0.2481, F-ratio=9.25, Q-Value=0.047

Here N is the number of compounds, MSE is means square error of estimation, R2 is the regression coefficient, AR^2 is adjusted regression coefficient, F-ratio is the Fischer's value and Q-value is the Quality factor[24].

However to have better model we carried out several multi parametric correlation and those which are statistically significant are presented in table 4.6.4.

Bi-parametric model

The data presented in table 4.6.4 show that out of the 3 bi parametric models, the containing SpMin8_Bh(m) and SpMax7_Bh(e) as the correlating parameters gave excellent model. This model is found as:

EC_{50}= -185.2486-150.1702(±35.3206) SpMin8_Bh(m)+109.2380 (±28.8735) SpMax7_Bh(e)

N=26, MSE=100.3195, R^2=0.447, AR^2=0.3989, F-ratio=9.296, Q-value=0.0667

In the model the correlation coefficient between the descriptors and antiviral activity is (r=0.6685) with the variance of 47.7%. So future addition another parameters is required regression diterpene esters derivatives.

Tri-parametric models

As stated earlier step-wise regression give 4 tri-parametric models. Majority of these models were found better than the bi-parametric model discussed above.

EC_{50}= -14.312+6618.7338 (±847.2321) JGI6+ 88.3696 (±14.2562) SpMax7_Bh(e) -267.2519 (±53.1780) SpMin2_Bh(m)

N=26, MSE= 49.42161, R^2= 0.7394, AR^2= 0.7039, F-ratio= 20.809, Q-value= 0.1223

Tetra parametric models

A tetra –parametric model with slightly improved statistics was also obtained. This model contained SpMin8_Bh(m), SpMin2_Bh(v) ,SpMin2_Bh(e) and SpMax7_Bh(e) as the correlating parameters :

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 5 Sep-Oct 2022, pp: 120-129 www.ijprajournal.com ISSN: 2456-4494

EC_{50}= 478.1823-197.0866(±23.7940)SpMin8_Bh(m)-1253.8137(±225.2900)SpMin2_Bh(v)+805.5795(±167.3314)SpMin2_Bh(e)+165.6084(±21.5871)SpMax7_Bh(e)

N=26, MSE= 35.4954, R^2= 0.8214, AR^2= 0.7873, F-ratio= 24.138, Q-value= 0.1521

The developed QSAR models Eq-4 describing the importance of Burden eigenvalues based indices in the case the positive correlation was observed between SpMin2_Bh(e) and SpMax7_Bh(e) and antiviral activity while negative correlation is represent by SpMin8_Bh(m) and SpMin2_Bh(v) variance is about 82.14%. So future addition another parameters is required regression diterpene esters derivatives.

Further in search of most significant correlation, we added one more 2D autocorrelations parameter to above model. We observed six significant penta parametric correlations out of which one involving SpMin8_Bh(m), SpMin2_Bh(v), SpMin2_Bh(e), JGI6 and SpMax7_Bh(e) gave best results. The model is as under:

EC_{50}= 310.871-135.0857(±30.3888)SpMin8_Bh(m)-958.7726(±222.7261)SpMin2_Bh(v)+546.0353(±172.7943)SpMin2_Bh(e)+2795.3814(±1003.3333)JGI6+151.8734(±19.4113)SpMax7_Bh(e)

N=26, MSE=26.8495, R^2=0.8713, AR2=0.8391, F-ratio=27.081, Q-value=0.1801

The QSAR model described by Eq-5, demonstrated the importance of 2D autocorrelations and Burden eigenvalues based indices in describing the antiviral activity against CHIKV. The positive correlation is shown by SpMin2_Bh(e), JGI6, and SpMax7_Bh(e) with antiviral activity reveals that increase in value of molecular descriptors SpMin2_Bh(e), JGI6, and SpMax7_Bh(e) will lead to increase in antiviral activity against CHIKV while negative coefficient is shown by SpMin8_Bh(m) and SpMin2_Bh(v) with antiviral activity reveals that decrease in value of molecular descriptor SpMin8_Bh(m) and SpMin2_Bh(v) will lead in antiviral activity. it is important to note there were one serious outlier in the dataset and after removing it the developed QSAR model is given below.

After deletion compound No. 03

Finally in order to confirm which out of the proposed model is the most appropriated for modeling the antiviral activity.

EC_{50}= 341.621-158.6609(±23.2472)SpMin8_Bh(m)-1008.5424(±165.6832)SpMin2_Bh(v)+574.2008(±128.3829)SpMin2_Bh(e)+2321.2823(±753.0822)JGI6+165.5307(±14.7711)SpMax7_Bh(e)

N=25, MSE=14.7803, R^2=0.9317, AR2=0.9137, F-ratio=51.844, Q-value=0.251

The developed QSAR model Eq-6, demonstrated the importance of all molecular descriptors which are used in the modeling especially SpMin8_Bh(m) and SpMin2_Bh(v) Burden eigenvalues based indices whose coefficient is negative indicates that as their value decreases the antiviral activity increases. The regression coefficient between the descriptors and antiviral activity is R^2= 0.9317, which is quite good with the variance of 93.71% with the smallest MSE.

The developed QSAR model is statistically significant with high correlation coefficient between the descriptors and antiviral activity. Even though the sample size and the 'rule of thumb' allowed us to go for development of five parametric models in multiple linear regression analysis, the high parametric model only. The "rule of thumb" gives information about the number of parameters to be selected for regression analysis in QSAR based on the number of compounds. According to this rule for QSAR model development one should select one parameter for a five compound data set.

We calculated the pogliani's quality factor Q which is Ratio of R and MSE (Square root of means square error) among these Q value maximum value is found for Eq-6 as 0.251. So Eq-6 is the best model for modeling antiviral activity against CHIKV with 2D autocorrelations and Burdeneigenvalues based indices.

We have undertaken a cross validation methodology for deciding the predictive power of the proposed model. It is necessary for a best model to have good statistics but this is not sufficient for good predictive potential.The various cross validation parameters, calculated for the proposed models, are presented on **Table-5** and are discussed below.

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 5 Sep-Oct 2022, pp: 120-129 www.ijprajournal.com ISSN: 2456-4494

Table-5 Cross validation statistical parameters

MODEL NO	NO OF DESCRIPTOR	N	PRESS	SSY	PRESS/SSY	R^2	Adj R^2	R^2_{CV}	PSE	SPRESS
1	1	26	3011.716	1160.801	2.5945	0.2782	0.2481	-1.5945	10.762	11.2021
2	2	26	2307.348	1865.168	1.237	0.447	0.3989	-0.237	9.42	10.0159
3	3	26	1087.275	3085.241	0.3524	0.7394	0.7039	0.6476	6.466	7.03
4	4	26	745.4034	3427.114	0.2175	0.8214	0.7873	0.7825	5.354	5.9578
5	5	26	536.9893	3635.528	0.1477	0.8713	0.8391	0.8523	4.544	5.1816
6	5	25	280.8258	3831.322	0.0732	0.9317	0.9137	0.9268	3.351	3.8445

QSAR should be evaluated according to its ability to predict the activity of molecules, which were not used in the original QSAR table, which contains the data, the dependent activity and the independent variables. Such an evaluation can be done by cross-validation method, which is based on 'leave-n-out 'concept. In each step 'N' molecules are randomly or on turn excluded from the QSAR table. The QSAR equation is then calculated and used to predict the activity of these n molecules. The methodology yields cross-validated parameters, PRESS (predictive residual sum of squares), SSY (sum of the square of the response value), R^2 (regression coefficient), R^2_{cv} (overall predictive ability), R^2_A (adjustable $-R^2$) S_{PRESS} (uncertainty of predictive), and PSE(predictive square error). These parameters obtained for the model discussed above is calculated as given in **Table 5**.

A perusal of Table-5 shows that in each case PRESS<<SSY and also that PRESS/SSY <0.4. This indicates that the proposed models are better than chance and indicate them to be excellent models. The PRESS/SSY value for the model- six, that is, 0.0732 indicates to the best model. The R^2_{cv} values also support these findings. The cross-validated parameters S_{PRESS} is not useful as it similar to the MSE. The other cross-validated parameters viz., PSE is, therefore, used to estimate uncertainty of prediction, the lowest value of PSE for the model-6 establishes it to be the model with best statistics and the best predictive power.

The high R^2_{cv} is indicative of its reliability in predicting the antiviral activity. But, the only way to estimate the true predictive power of a model is to test their ability to predict accurately the biological activities of compounds.

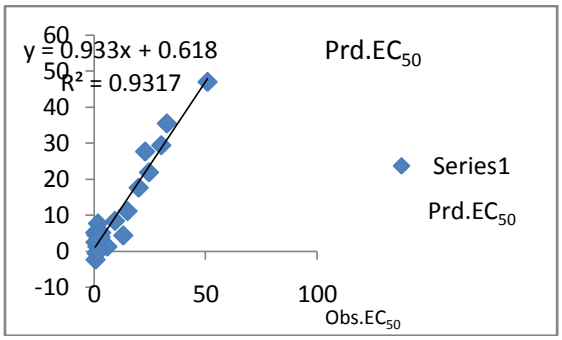
Based on the magnitude of residue a close agreement between the observed and calculated antiviral activity against Chikungunya virus is found. Future, the plot of Predicted EC_{50} values against Observed EC_{50} values also proves the superiority of the model expressed by Eq. No.-5&6 the results of biological studies of diterpene esters (1-26) from the tigliane (1-23), ingenane (24-25), and daphnane (26) types was antiviral activity against CHIKV are summarized in given below **Table.6**.

Table- 6 Residual report (from Eq-5&6)

	Eq-5			Eq-6		
Row	Obs.EC_{50}	Predicted	**Residual**	Obs.EC_{50}	**Predicted**	**Residual**
1	4.9	5.964	-1.064	4.9	6.574	-1.674
2	20	17.112	2.888	20	17.67	2.33
3	2.2	17.292	-15.092	-	-	-
4	0.99	1.619	-0.629	0.99	2.549	-1.559
5	9.4	7.152	2.248	9.4	8.408	0.992
6	1.8	6.712	-4.912	1.8	7.711	-5.911
7	3.2	3.396	-0.196	3.2	5.137	-1.937
8	6	0.806	5.194	6	1.245	4.755
9	1.5	0.806	0.694	1.5	1.245	0.255
10	2.9	3.605	-0.705	2.9	3.941	-1.041
11	2.8	3.605	-0.805	2.8	3.941	-1.141
12	1.1	5	-3.9	1.1	4.493	-3.393
13	15	10.459	4.541	15	11.14	3.86
14	24.6	20.833	3.767	24.6	21.938	2.662
15	0.6	5.372	-4.772	0.6	5.158	-4.558
16	1.7	5.97	-4.27	1.7	4.616	-2.916

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 5 Sep-Oct 2022, pp: 120-129 www.ijprajournal.com ISSN: 2456-4494

17	32.6	34.091	-1.491	32.6	35.554	-2.954
18	13.1	3.595	9.505	13.1	4.37	8.73
19	0.7	-2.279	2.979	0.7	-2.393	3.093
20	2.7	2.53	0.17	2.7	3.662	-0.962
21	0.7	1.772	-1.072	0.7	2.475	-1.775
22	50.8	44.777	6.023	50.8	47.123	3.677
23	30.1	30.136	-0.036	30.1	29.473	0.627
24	22.9	25.302	-2.402	22.9	27.736	-4.836
25	1.2	-0.862	2.062	1.2	-0.606	1.806
26	1.8	0.526	1.274	1.8	-0.072	1.872



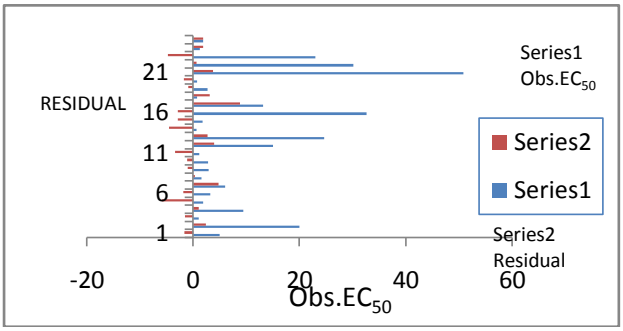


Fig1- Graph between predicted and observed EC_{50} Fig2- plot of the residual values again the experimental

Values of diterpene esters against Chikungunya virus observed EC_{50} values (CHIKV) (From Eq-6)

V. CONCLUSION

On the basis of above discussion following conclusions can be drawn.

1.SpMin8_Bh(m) along with SpMin2_Bh(v),SpMin2_Bh(e),JGI6,SpMax7_Bh(e),SpMax1_Bh(s) and SpMin2_Bh(m) are suitable parameters for modeling the antiviral activity of present set compounds.

2. Coefficients for SpMin2_Bh(e),JGI6 and SpMax7_Bh(e) are positive suggesting that higher values of these parameters will favor the biological activity. Negative coefficient of SpMin8_Bh(m),SpMin2_Bh(v) suggests that it has retarding effect towards EC50 values, hence in future designing of potent compounds its lower value will give better results.

3. The highest value **R^2= 0.9317**are obtained in QSAR models.

Acknowledgements

We are thankful to Dr. V.K. Agrawal professor, Dept. of chemistry, A.P.S.University Rewa for giving their valuable suggestions to complete this study and continuous support and encouragement.

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