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Structure activity and prediction of biological activities of compound (2-methyl-6-phenylethynylpyridine) derivatives relationships rely on electronic and topological descriptors

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ABSTRACT

Here we report the prediction and QSAR of a new series of subtype metabotropic glutamate receptor mGluR5. A series of 21 substituted (MPEP) (2-methyl-6-phenylethynylpyridine) derivatives molecules was submitted to a principal components analysis (PCA),to a descendant multiple regression analyses (MLR) (R^2 = 0,436), to a non-linear regression (RNLM) (R^2 = 0,91) and to a neural network (ANN) (R^2 = 0,94). As a result of quantitative structure-activity relationships, we found that the model proposed in this study is constituted of major descriptors used to describe these molecules. The obtained results suggested that the proposed combination of several calculated parameters could be useful to predict the biological activity of 2-methyl-6-phenylethynylpyridine) derivatives molecules. Density functional theory (DFT) with Becke's three parameter hybrid functional using the LYP correlation functional (B3LYP/6–31G (d)) calculations have been carried out in order to get insights into the structure, chemical reactivity and property information for the series of study compounds. The topological descriptors were computed, respectively, with ACD/ChemSketch and Gaussian 03W programs.

Keywords: *DFT study, QSAR, mGluR5, (MPEP) (2-methyl-6-phenylethynylpyridine).*

INTRODUCTION

The study of structure-activity relationships is a necessary basis for the work of a number of researchers including medicinal chemistry and pharmacologists in charge of preset or selects a new molecule into a drug. This principle applies to anti-infective. There are two advantages to know the structure-activity relationships: optimizing the properties of a molecule of base and assist in the selection of a molecule.

View the approximate number and impressive 'seven million!' Molecules that chemists have synthesized and they determined some properties. Most researchers now have access to the huge database reforming all information and provide, almost instantly, all knowledge already isolated.

Compounds containing 2-methyl-6-phenylethynylpyridine (MPEP) and these derivatives are used in various fields of science and technology and have numerous applications in biology and medicine. The molecule of 2-methyl-6-phenylethynylpyridine (MPEP) is an investigational drug that has been one of the first compounds found to act as a selective antagonist of subtype metabotropic glutamate receptor mGluR5 [1]. After being used as liquid crystals for LCD screens, was developed by the pharmaceutical company Novartis in 1990 and has also been shown to produce antidepressant and anxiolytic effects in animals [2] and reduce the effects of withdrawal morphine. Despite the large number and range of applications that offer this type of compound, the complete analysis of the electronic properties of this compound has not yet been performed. These consist recently been studied by R. Hmamouchi et al. [3-4].

These studies have shown the existence of a structure-activity relationship on the one hand and the synthesis of new organic materials electronic properties of molecules contain aromatic π systems - spelling electrons with a very high absorption maximum (λ_{max}). For this reason, we worked on another series of compounds based on 2-methyl-6-phenylethynylpyridine (MPEP) and these derivatives, but this time the attempt was made to establish a correlation between the activities of these compounds with different physico-chemical parameters (molecular).

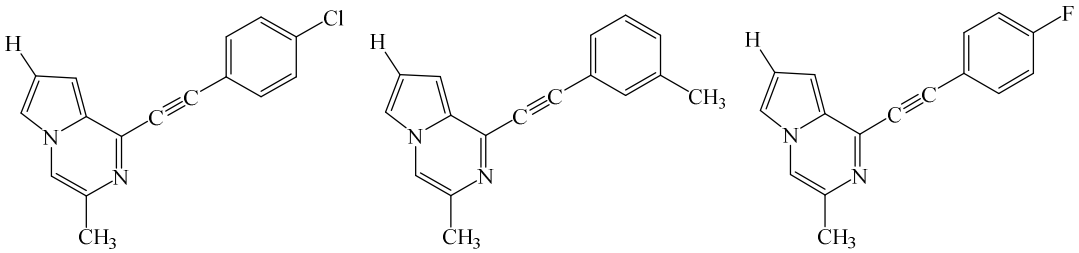
Structure-Property/Activity quantitative relationship (QSPR/QSAR) methods are among the most useful tools in physical chemistry calculation. These methods are based on the axiom that the variance in the properties and activities of physico-chemical compounds is determined by the variance in their molecular structures. Thus, if experimental data are available for some chemicals in a group, we can predict the lack of molecular descriptors calculated for the whole group and adapted mathematical model [5]. The prediction of the overall toxicity using QSAR has been the goal of many workers who used a variety of approaches. This goal is attractive, but has not yet been satisfactorily achieved. There are a number of reasons for the lack of success [6]. Impairment of available toxicity data clearly caught progress. This lack of success was compounded in many studies by a misapprehension of insufficient heterogeneity, or the chemical diversity in the dataset. In this work we have relied on a database 21 contains compounds derived from 2-methyl-6-phenylethynylpyridine (MPEP), we first insert using Gaussian 03 software W 33 of the electronic parameters such as E_{HOMO} (highest occupied molecular orbital energy) E_{LUMO} (lowest unoccupied molecular orbital energy) ΔE (energy gap), μ (dipole moment) and (total energy), E_a (energy of activation) λ_{max} (maximum absorption) and $f_{(SO)}$ of the oscillation factor [7-8],and second using ACD / ChemSketch software we insert molecular parameters such as Weight (PM), Molar Volume (MV (cm^3)), Molecular Weight (MW), Molar Refractivity (MR (cm^3)), Parachor (Pc (cm^3)), Density (D (g/cm^3)), Refractive Index (n), Surface Tension(Y(dyne/cm) and Polarizability (αe (cm^3)).

In this context we used statistical tools for Modeled activity of organic compounds based on 2-methyl-6-phenylethynylpyridine (MPEP), such as principal component analysis (PCA), multiple linear regression (MLR) the non-linear multiple regression (RLNM), the artificial neural networks (ANN) using (XLSTAT 2009) (MATLAB R2009a) as software.

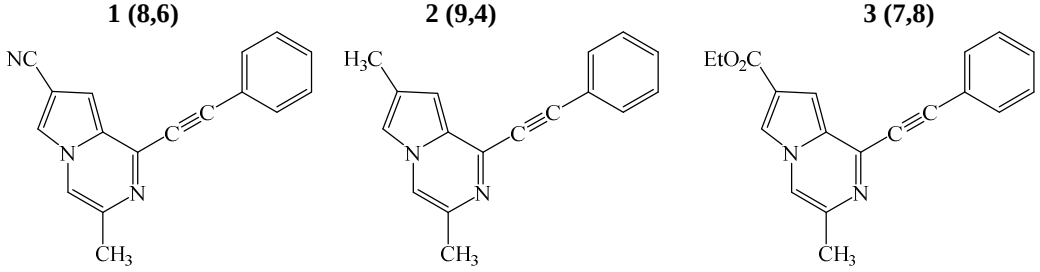
MATERIALS AND METHODS

Chemicals and Toxicological data

Pyrazine derivatives of 21 were studied. Data on their biological activity (pI_{50}) improve the power potential therapeutic application of acceptable mGluR5 antagonists were obtained from the literature [1]. The following figure shows the chemical structures of the test compound.



1 (8,6) **2 (9,4)** **3 (7,8)**



4 (8,9) **5 (7,3)** **6 (8,0)**

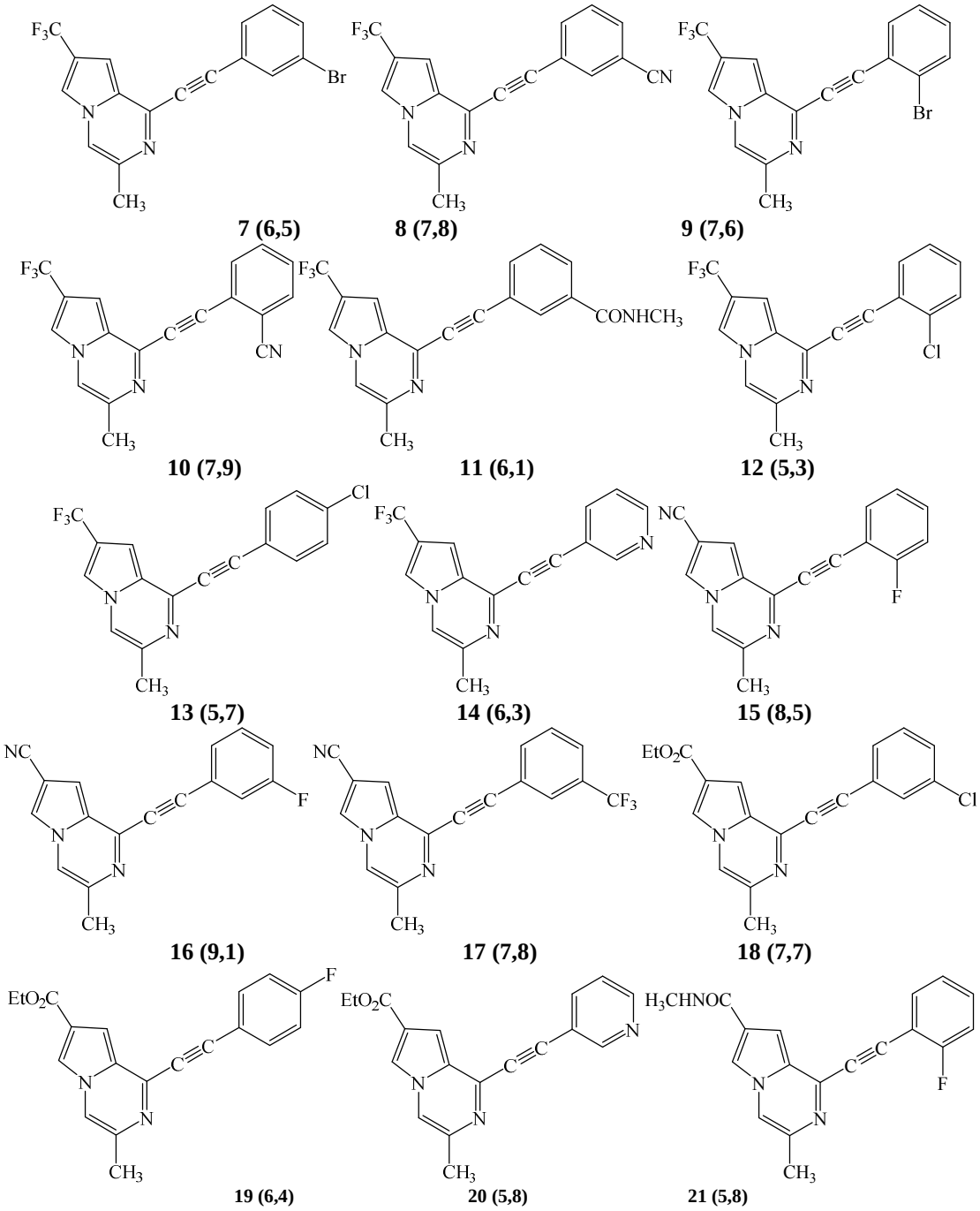


Figure 1:Structures and biological activities N (pI_{50}Obs) of drift pyrazine studied

DFT Calculations

DFT (density functional theory) methods were used in this study. These methods have become very popular in recent years because they can reach similar precision to other methods in less time and less cost from the computational point of view. In agreement with the DFT results, energy of the fundamental state of a polyelectronic system can be expressed through the total electronic density, and in fact, the use of electronic density instead of wave function for calculating the energy constitutes the fundamental base of DFT [9-10] using the B3LYP functional [11-12] and a 6-31G* basis set. The B3LYP, a version of DFT method, uses Becke's three-parameter functional (B3) and includes a mixture of HF with DFT exchange terms associated with the gradient corrected correlation functional of Lee, Yang and Parr (LYP). The geometry of all species under investigation was determined by optimizing all geometrical variables without any symmetry constraints.

Molecular descriptors

Calculation of descriptors using Gaussian 03W:

From the results of the DFT calculations, the quantum chemistry descriptors were obtained for the model building as follows: the total energy (E_T (eV)), the highest occupied molecular orbital energy (E_{HOMO} (eV)), the lowest unoccupied molecular orbital energy (E_{LUMO} (eV)), the energy difference between the LUMO and the HOMO energy (Gap (eV)), the total dipole moment of the molecule (μ (Debye)), maximum absorption (λ_{max}) and f (SO) of the oscillation factor [13].

Calculation of descriptors using ACD/ChemSketch:

Advanced chemistry development's ACD/ChemSketch program was used to calculate Formula Weight (PM), Molar Volume (MV (cm^3)), Molar Refractivity (MR (cm^3)), Parachor (Pc (cm^3)), Density (D (g/cm^3)), Refractive Index (n), Surface Tension (γ(dyne/cm) and Polarizability (α_e (cm^3)) [14].

Statistical analysis

The objective of (quantitative) structure-activity relationship (QSAR) analysis is to derive empirical models that relate the biological activity of compounds to their chemical structure. In this QSAR analysis, quantitative descriptors are used to describe the chemical structure and the analysis results in a mathematical model describing the relationship between the chemical structure and biological activity. To explain the structure-activity relationship, these 16 descriptors are calculated for 48 molecules using the Gaussian03W, Gauss View and Chem Sketch Software[15].The study we conducted consists of:

Principal components analyses

The molecules of pyrazine and derivatives (1 to 21) were studied by statistical methods based on the principal component analysis (PCA) [16-17] using the software XLSTAT 2009 and Mathlab software v 2009a. This is essentially a descriptive statistical method which aims to present, in graphic form, the maximum of information contained in the data table 1. PCA is a statistical technique useful for summarizing all the information encoded in the structures of compounds. It is also very helpful for understanding the distribution of the compounds.

Multiple Linear and Nonlinear Regressions (RLM and RNLM)

The multiple linear and nonlinear regression statistics techniques are used to study the relation between one dependent variable and several independent variables. The multiple linear and nonlinear regression models (MLR and MNLR) are generated using the software XLSTAT, version 2009, to predict pI_{50Obs}.The optimal number of components (N) is employed to do validation MLR and MNLR analysis to get the final model parameters such as correlation coefficient R^2, standard deviation (S) and Fischer test value (F).

Artificial Neural Networks (ANNs)

An artificial neuron network contains a large number of units, neurons that communicate with each other by sending signals through links, called synaptic connections. In general, the system has three types of neuron neurons (Figure 2): the input neurons which receive data; output neurons that send data by the output of the system; hidden neurons whose input signals and output remain in the system.

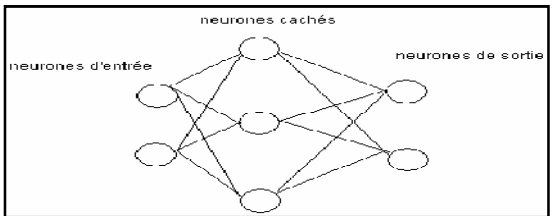


Figure 2: Diagram of a simple neural network

In artificial neural networks mathematical modeling of biological neuron is used, called formal neuron. Each neuron receives (or input signal) input values by neighboring neuron and used to calculate the output signal is spread by other neurons. In accordance with this process we must adjust the weights of the synaptic connections. In the following figure we can see the structure of an artificial neuron. The neuron computes the sum of its inputs, and then this value is passed through the activation function to produce its output.

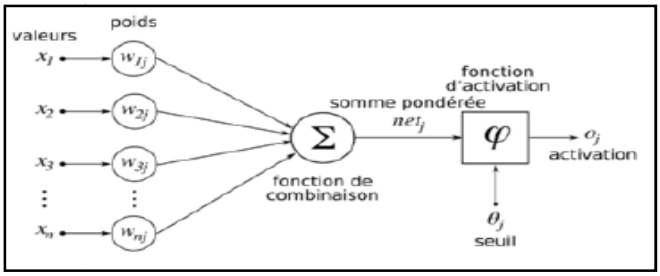


Figure 3: Structure of artificial neural

Several functions can be used as activation functions [18-19], but most used function is the sigmoid function. The sigmoid function itself defined by: $\forall x \in R, g(x) = \frac{1}{1+e^{-X}}$

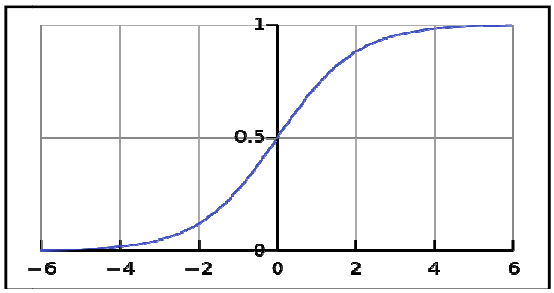


Figure 4: Graph of the sigmoid function

RESULTS

Data base

Toxicological data, chemicals, toxicity, and descriptors obtained by DFT/B3LYP 6-31G optimization, 21 the corresponding pyrazine derivatives are listed in table 1.

Table 1: The values of the sixteen chemical descriptors

N	pI_{50}	PM	MR	MV	Pc	n	Y	D	αe	E_T	E_{HOMO}	E_{LUMO}	ΔE	μ	E_a	λ_{max}	$f_{(SO)}$
1	8,6	236,31	74,45	215,9	571,1	1,61	48,9	1,09	29,51	-726,37	-5,32	-1,68	3,64	1,2	3,19	388,18	0,14
2	9,4	250,34	79,07	231,7	609,3	1,6	47,7	1,08	31,34	-765,69	-6,99	-1,63	5,36	0,77	3,21	386,04	0,15
3	7,8	254,3	74,56	220,5	578,4	1,59	47,3	1,15	29,55	-825,6	-7,33	-1,72	5,61	2,24	3,2	387,4	0,15
4	8,9	261,32	79	226,5	618,5	1,61	55,6	1,15	31,31	-818,61	-6,55	-2,17	4,37	4,27	3,32	373,33	0,24
5	7,3	250,34	79,05	232,8	609,1	1,60	46,8	1,07	31,34	-765,69	-6,97	-1,64	5,34	1,65	3,17	391,61	0,15
6	8	308,37	90,17	268,3	714,7	1,59	50,3	1,14	35,74	-993,57	-7,2	-1,91	5,28	1,93	3,21	386,55	0,17
7	6,5	372,31	84,41	279,4	694,8	1,52	38,2	1,33	33,46	-1400,44	-7,25	-2,22	5,03	1,9	3,22	385,03	0,18
8	7,8	322,3	79,53	252,8	640,2	1,54	41,0	1,27	31,53	-1162,64	-5,8	-2,12	3,67	1,33	3,26	380,87	0,18
9	7,6	383,21	87,14	261,1	683,9	1,58	47,0	1,46	34,54	-3634,51	-7,23	-2,17	5,06	1,44	3,24	383,04	0,19
10	7,9	329,32	83,99	257,7	680,5	1,57	48,6	1,27	33,29	-1155,65	-7,35	-2,37	4,99	3,68	3,17	391,21	0,17
11	6,1	361,36	92,44	284,6	744,6	1,56	46,8	1,26	36,64	-1271,42	-6,38	-2,15	4,23	1,98	3,25	381,19	0,2
12	5,3	338,75	84,25	259,2	669,9	1,56	44,6	1,3	33,4	-1523	-7,37	-2,13	5,24	0,61	3,23	384,32	0,19
13	5,7	338,75	84,25	259,2	669,9	1,56	44,6	1,3	33,4	-1523	-7,52	-2,15	5,37	2,87	3,24	382,34	0,22
14	6,3	305,3	77,22	241,2	628,4	1,55	46,0	1,26	30,61	-1079,44	-6,64	-2,19	4,46	1,54	3,24	383,08	0,17
15	8,5	279,31	79,11	231,0	625,8	1,60	53,8	1,20	31,36	-917,84	-5,92	-2,24	3,68	3,29	3,29	376,8	0,23
16	9,1	279,31	79,11	231,0	625,8	1,60	53,8	1,2	31,36	-917,85	-5,99	-2,3	3,68	3,11	3,28	377,67	0,22
17	7,8	329,32	83,99	257,7	680,5	1,57	48,6	1,27	33,29	-1155,65	-7,25	-2,4	4,85	2,53	3,25	381,11	0,21
18	7,7	342,82	95	279,2	751,9	1,6	52,50	1,22	37,66	-1453,16	-6,95	-2,12	4,83	1,5	3,14	395,29	0,16
19	6,4	326,36	90,29	272,8	722,1	1,58	49,12	1,19	35,79	-1092,8	-7,18	-1,98	5,2	0,33	3,2	387,2	0,17
20	5,8	309,36	87,97	261,2	710,3	1,59	54,60	1,18	34,87	-1009,6	-7,25	-2,13	5,12	1,81	3,14	395,25	0,15
21	5,8	311,35	87,56	258,1	689,9	1,59	51,0	1,2	34,71	-1033,25	-6,89	-1,97	4,91	3,54	3,16	392,63	0,14

Statistical analysis (implementation of the PCA)

The graphical representation of molecules and study the characteristics reports have shown that a large number of chemical and electronic parameters were significant, most of the time one (or more) link between these parameters. It therefore seems worthwhile to try to process the data statistically, using a method of multivariate analysis such as Principal Component Analysis (PCA).

Study of the eigenvalues

Here is the bar chart represents the total inertia

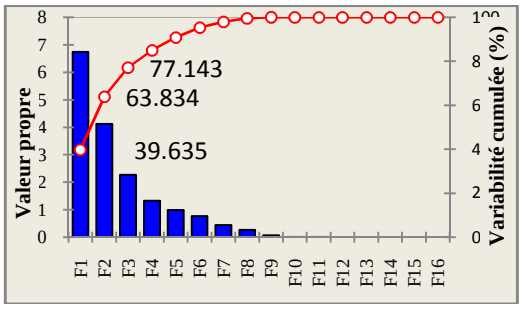


Figure 5: Total inertia diagram

All 16 descriptors (variables) encoding the 21 molecules was subjected to principal component analysis (PCA). 16 main components were obtained (Figure 5). The first three axes F1, F2 and F3, respectively, contributing 39,635%, 24,199% and 13,309% of the total variance; the total information is estimated as a percentage of 77,143%.

Principal component analysis (Training Set Selection)

The selection of the training set is one of the most important steps in the QSAR modeling, since the establishment and optimization of a QSAR model are based on this training set. Predictability and applicability of a QSAR model also depend on the training set selection. In this part, PCA was applied to select a training set from among 21 compounds.

The principal component analysis (PCA) [20-23] was conducted to identify the link between the different variables. Bold values are different from 0 at a significance level of p=0, 05. Correlations between the 16 descriptors are shown in table 2 as a correlation matrix and in figure 6 these descriptors are represented in a correlation circle.

The Pearson correlation coefficients are summarized in the following table 2. The obtained matrix provides information on the negative or positive correlation between variables.

Table 2: Correlation matrix (Pearson (n)) between different obtained descriptors

Var	pI_{50}	PM	MR	MV	Pc	n	Y	D	αe	E_T	E_{HOMO}	E_{LUMO}	ΔE	μ	E_a	λ_{max}	$f_{(SO)}$
pI_{50}	1																
PM	-0,562	1															
MR	-0,449	0,713	1														
MV	-0,588	0,883	**0,906**	1													
Pc	-0,511	0,795	**0,975**	**0,957**	1												
n	0,549	-0,702	-0,183	-0,577	-0,353	1											
Y	0,353	-0,405	0,097	-0,278	0,009	0,812	1										
D	-0,404	0,874	0,338	0,545	0,435	-0,663	-0,423	1									
αe	-0,449	0,713	**1**	**0,906**	**0,975**	-0,183	0,097	0,338	1								
E_T	0,215	-0,702	-0,368	-0,408	-0,353	0,269	0,248	-0,824	-0,368	1							
E_{HOMO}	0,454	-0,418	-0,418	-0,454	-0,425	0,266	0,179	-0,287	-0,417	0,305	1						
E_{LUMO}	0,168	-0,619	-0,292	-0,417	-0,437	0,451	-0,057	-0,691	-0,292	0,315	0,073	1					
ΔE	-0,375	0,178	0,295	0,285	0,25	-0,093	-0,192	0,026	0,295	-0,179	**-0,933**	0,291	1				
μ	0,213	-0,123	-0,136	-0,21	-0,105	0,216	0,431	0,006	-0,136	0,177	0,065	-0,433	-0,219	1			
E_a	0,328	-0,038	-0,355	-0,27	-0,299	-0,067	0	0,214	-0,355	-0,05	0,374	-0,389	-0,499	0,317	1		
λ_{max}	-0,324	0,034	0,356	0,268	0,3	0,076	0,013	-0,219	0,357	0,054	-0,371	0,385	0,495	-0,307	**-1**	1	
$f_{(SO)}$	0,149	0,207	-0,03	0,004	0,029	-0,084	0,149	0,371	-0,03	-0,164	0,127	-0,66	-0,36	0,477	0,86	-0,856	1

Bold values are different from 0 at a level significant for p<0, 05
At a very significant for p<0, 01
At a highly significant to p<0,001

Correlation circle

Now represent those worn by plane 1 and 2 on a circle of correlation variables. Principal component analysis (PCA) was also performed to detect the connection between the different variables.

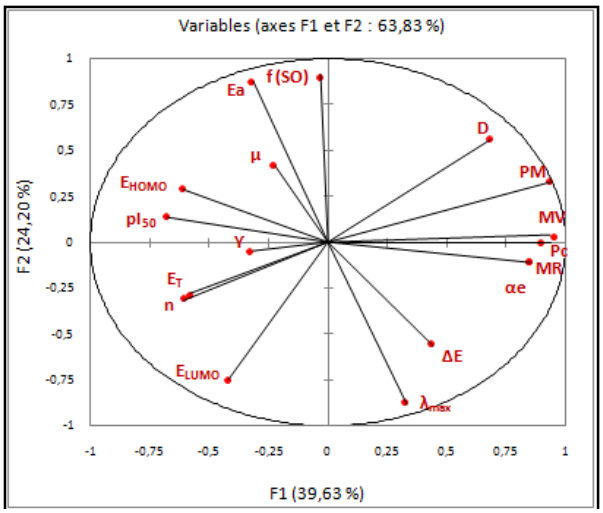


Figure 6: Correlation circle

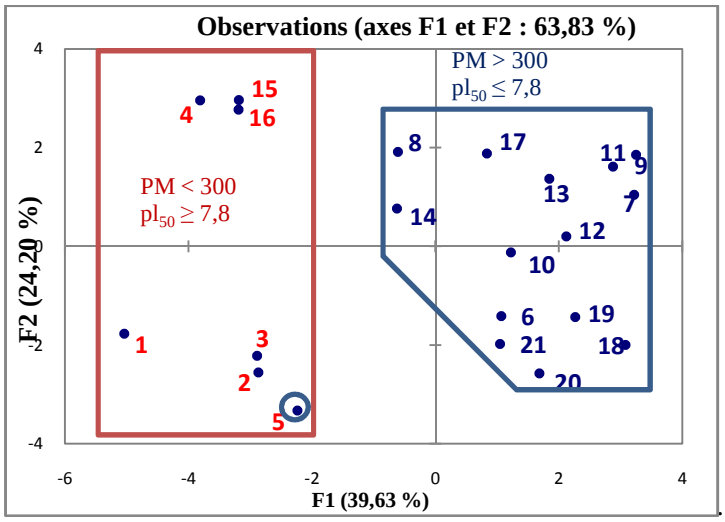


Figure 7: Cartesian diagram according to F1 F2

Multiple linear regressions

A multiple regression analysis was performed for the data table matrices (descriptors/individuals), and toxicity pI_{50} identify as the response variable. The statistical quality of the best models was evaluated on the basis of R^2 (coefficient of determination), RMSE (coefficient indicates the accuracy of the model) and F the Fisher F-statistic.

Multiple linear regression of the variable toxicity (MLR)

Modelling toxicity pI_{50} value of all training compounds (compounds 21 pyrazine derivatives) led to the best value corresponding to the linear combination of the following descriptors: Refractive Index$n$, λ_{max} maximum absorption.

Equation (1):

$$\boldsymbol{pI_{50}\,(cal) = -8,774 + 28,913 \times n - 7,663 \times 10^{-2} \times \lambda_{max}}$$

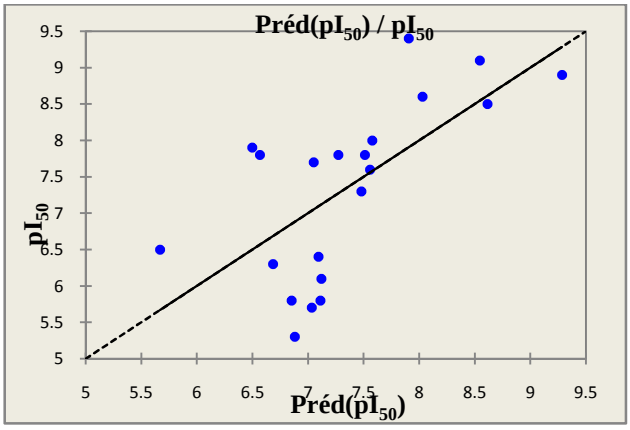


Figure 8: Graphical representation of calculated and observed toxicity by MLR.

For our 21 compounds, the correlation between experimental toxicity and calculated one based on this model is quite significant (Figure 8) as indicated by statistical values:

N = 21 R = 0,660 R^2 = 0,436 F = 6,958 RMSE = 0,971

The Fisher's F test is used. Given the fact that the probability corresponding to the F value is lower than 0.05, it mean that we would be taking a lower than 0.01 % risk in assuming that the null hypothesis is wrong. Therefore, we can conclude with confidence that the model do bring a significant amount of information.

Multiple nonlinear regression of the variable toxicity (MNLR)

We have also used the technique of nonlinear regression model to improve the structure-toxicity in a quantitative way, taking into account several parameters. This is the most common tool for the study of multidimensional data. The resulting equation is:

Equation (2):

$$pI_{50}\,(cal) = 1148,91 - 0,670 \times PM + 119,51 \times MR + 1,25 \times MV - 0,253 \times Pc + 68,68 \times n - 8,012 \times 10^{-2} \times \gamma + 133,937 \times D - 299,765 \times \alpha e - 2{,}793 \times 10^{-3} \times E_T + 1,241 \times E_{HOMO} - 13{,}492 \times E_{LUMO} - 0,102 \times \mu - 231,388 \times E_a - 1,783 \times \lambda_{max} + 14,83 \times f_{(so)}$$

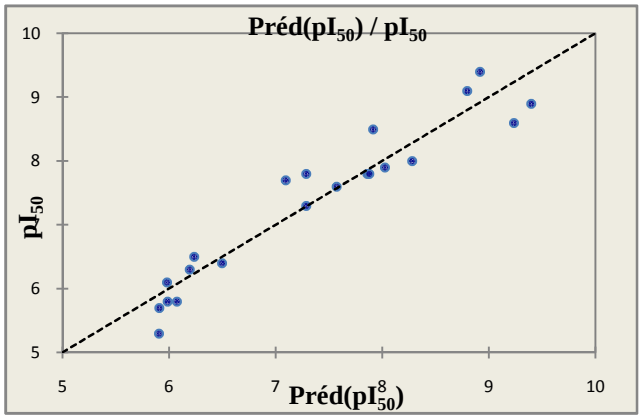


Figure 9: Graphical representation of calculated and observed toxicity by MNLR.

The obtained parameters describing the electronic aspect of the studied molecules are:

N = 21 R = 0,954 R^2 = 0,911 RMSE = 0,818

The toxicity value pI_{50} predicted by this model is somewhat similar to that observed. Figure9 shows a very regular distribution of toxicity values based on the observed values.

The obtained coefficient of correlation in equation (2) is quite interesting (0,911). To optimize the error standard deviation and better finish building our model, we involve in the next part artificial neural networks (ANN). As part

of this conclusion, we can say that the toxicity values obtained from nonlinear regression are highly correlated to that of the observed toxicity comparing to results obtained by MLR method.

Artificial neural networks

Since the laws of behavior of the environment are nonlinear and to model this type of problem, we are interested particularly to a typical neural network model known Multilayer Perceptron (MLP). To create the optimal structure of the neural network, we conducted several learning by varying the network parameters such as the activation function, number of hidden layers, and number of neurons in each layer, the learning function, the number of iteration and learning step [24]. However, we programmed the neural network, using the toolbox of Matlab neural network included in the MATLAB software.

La corrélation entre les valeurs calculées et ANN expérimentales sur la toxicité est très important, comme illustré sur la figure 9 et comme indiqué par les valeurs de R^2 et R.

N = 21 R = 0,967 R^2 = 0, 94 RMSE = 0,096

These values show that the relationship between the estimated values of pI_{50} and their residues established by artificial neural networks are illustrated in figure 10.

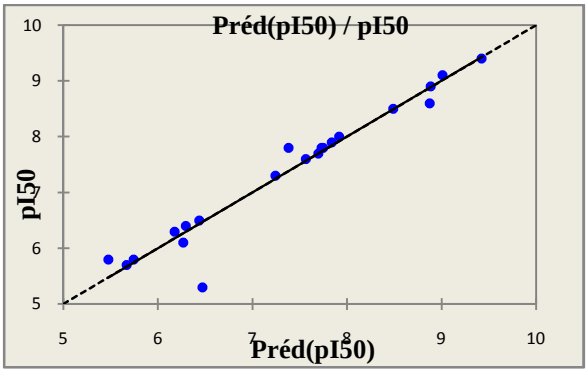


Figure 10: Correlation between the calculated and experimental inhibition pI_{50}

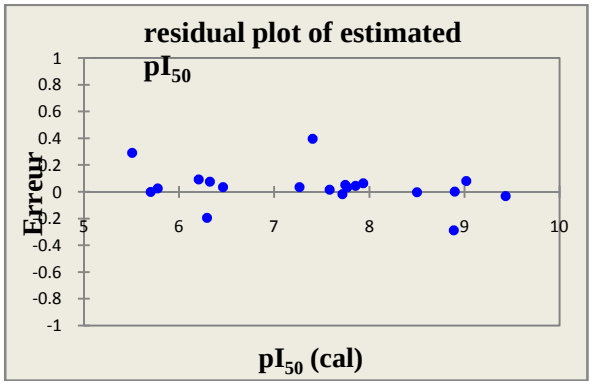


Figure 11: Relationship between the estimated values of pI_{50} and their residues established by artificial neural networks

DISCUSSION

Principal component analysis (Training Set Selection)

*The MR Molar Refractivity is positively correlated with the MV Molar Volume, and Pc Parachor (r=0,906; r=0,975 and p < 0, 05) at a significant level.

*The MVMolar Volume is positively correlated with the PcParachor, and αePolarizability (r=0,957; r=0,906 and p < 0, 05) at a significant level.

*The PcParachor is positively correlated with the αePolarizability, (r=0,975and p < 0, 05) at a significant level.

*The HOMO energy $E_{HOMO}$is negatively correlated with the ΔE the energy gap (r=0,933 and p <0, 05) at a significant level.

*The MRMolar Refractivity is perfectly correlated (r=1), with αePolarizability, both variables are redundant.

*The activation energy E_a is perfectly negatively correlated (r=1), with λ_{max} maximum absorption, both variables are redundant.

Correlation circle

*The principal component analysis revealed from the correlation circle (Figure 6) shows that the F1 axis (39,63 % of the variance) is mainly due to the **MV**, **PM** and **Pc** while the axis F2 (24,20 % of the variance) is located by the other parameters of $\mathbf{f_{(SO)}}$, $\mathbf{E_a}$and$\boldsymbol{\lambda_{max}}$.

*In the projection of the compounds in the plane of the axes F1, F2 (Figure 7), the compounds are distributed in two regions: Region 1 contains compounds having a values of PM < 300 and $pI_{50} \geq 7,8$, region 2 contains compounds having a values of PM > 300 and $pI_{50} \leq 7,8$.

Statistical Analysis

The obtained squared correlation coefficient (R^2) value is 0,946 for this data set of pyrazines. It confirms that the artificial neural network results were the best to build the quantitative structure activity relationship models. In this part, we investigated the best linear QSAR regression equations established in this study. Based on this result, a comparison of the quality of CPA, MLR and ANN models shows that the ANN models have substantially better predictive capability because the ANN approach gives better results than MLR. ANN was able to establish a satisfactory relationship between the molecular descriptors and the activity of the studied compounds.

The accuracy and predictability of the proposed models were illustrated by the comparison of key statistical terms like R or R^2 of different models obtained by using different statistical tools and different descriptors has been shown in table 3.

Table 3: Observed values and calculated values of pI_{50} according to different methods

N°	pI_{50}			
	Obs.	**MLR**	**MNLR**	**ANN**
1	8,60	8,03	9,23	8,89
2	9,40	7,90	8,92	9,43
3	7,80	7,51	7,29	7,75
4	8,90	9,28	9,40	8,90
5	7,30	7,48	7,28	7,26
6	8,00	7,58	8,28	7,94
7	6,50	5,67	6,23	6,46
8	7,80	6,56	7,86	7,77
9	7,60	7,56	7,57	7,58
10	7,90	6,50	8,02	7,86
11	6,10	7,12	5,98	6,29
12	5,30	6,88	5,90	6,50
13	5,70	7,03	5,91	5,70
14	6,30	6,68	6,19	6,21
15	8,50	8,61	7,91	8,50
16	9,10	8,54	8,80	9,02
17	7,80	7,27	7,88	7,40
18	7,70	7,05	7,09	7,72
19	6,40	7,09	6,50	6,32
20	5,80	6,85	6,07	5,51
21	5,80	7,11	5,98	5,77

CONCLUSION

Since the three QSAR models of the variable pI_{50} activity for the antagonists of glutamate receptor mGluR5 prediction and descriptors (16) calculated showed good agreement. It was shown the neural network ANN results have substantially better predictive capability than the MLR and MNLR, yields a regression model with improved predictive power, we have established a relationship between several descriptors and the antagonist activity to the glutamate receptor mGluR5.

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