ISSN:1226-7244 (Print)
ISSN:2288-243X (Online)
논문번호 17-03-23
136
j.inst.Korean.electr.electron.eng.Vol.21,No.3,309~319,September 2017
http://dx.doi.org/10.7471/ikeee.2017.21.3.309

The effective model of the human Acetyl-CoA Carboxylase inhibition by aromatic-structure inhibitors

Nguyen Truong Cong Minh*, Bui Tho Thanh*★, Le Xuan Truong**, Nguyen Thi Bang Suong**, Le Thi Xuan Thao**

Abstract

The research investigates the inhibition of fatty acid biosynthesis of the human Acetyl-CoA Carboxylase enzyme by the aromatic-structure inhibitors (also known as ligands) containing variables of substituents, contributing an important role in the treatment of fatty-acid metabolic syndrome expressed by the group of cardiovascular risk factors increasing the incidence of coronary heart disease and type-2 diabetes. The effective interoperability between ligand and enzyme is characterized by a 50% concentration of enzyme inhibitor (IC_{50}) which was determined by experiment, and the factor of geometry structure of the ligands which are modeled by quantum mechanical methods using HyperChem 8.0.10 and Gaussian 09W softwares, combining with the calculation of quantum chemical and chemico-physical structural parameters using HyperChem 8.0.10 and Padel Descriptor 2.21 softwares. The result data are processed with the combination of classical statistical methods and modern bioinformatics methods using the statistical softwares of Department of Pharmaceutical Technology – Jadavpur University – India and R v3.3.1 software in order to accomplish a model of the quantitative structure – activity relationship between aromatic-structure ligands inhibiting fatty acid biosynthesis of the human Acetyl-CoA Carboxylase.

Key words: Acetyl-CoA, QSAR, Quantum chemical calculation, Bioinformatics, Artificial Neural Network, Fuzzy

---

* Dept. of Physical Chemistry, Faculty of Chemistry, HCMUS

** Dept. of Biochemistry, Faculty of Medicine, HCM-UMP

★ Corresponding author

E-mail: congminh.ngtruong@gmail.com, Tel: (+84-8) 3856 6154

※ Acknowledgment

This research was supported by Ho Chi Minh city University of Science through the 10th Scientific Conference on 11th November 2016

Manuscript received Jun. 13, 2017; revised Aug. 16, 2017 ; accepted Aug. 30, 2017

This is an Open-Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (http://creativecommons.org/licenses/by-nc/3.0) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited. *Logic*

I. Introduction

Metabolic syndrome (MS) is a series of cardiovascular risk factors including abdominal fat, glucose intolerance, triglycerid increment and hypertension related to an increment in crude fat content in the human body [1]. This leads to be exposure to higher chance of having a stroke, type 2 diabetes and cardiac death. According to NHANES (The National Health and Nutrition Examination Survey), during the past decade, the proportion of men and women age between 12 and 19 having MS has increased by more than 50%. In addition, there are approximately more than 200 million adolescents all over the world who have suffered from MS today. In supporting treatment of fatty-acid metabolic disorder at the molecular level, the inhibition of Acetyl-CoA Carboxylase activity plays an important role in constraining the synthetic biology reaction rate of fatty acids and promoting their oxidation process in the human body [2].

In mammals, ACC exists with the two isoforms which catalyse the transformation of Acetyl-CoA into Malonyl-CoA. The first isoform (ACC1) is mainly expressed in lipogenic tissues: liver, adipose, and lactating mammary gland and has a crucial role in regulating the synthetic biology reaction rate of fatty acids. The second isoform (ACC2) is highly expressed in mitochondrial membrane, heart and muscle which supports the oxidation process of fatty acids [3]-[4]-[5].

Researchers have developed different inhibitors that inhibit the two kinds of ACC isoforms, including inhibiting the formation of malonyl-CoA by ACC1 and the inhibition of ACC2 activity, which promotes the oxidation process of fatty acids. However, the selection of which inhibitor achieves the highest inhibitory effect has not been elucidated. Our research is derived from the increasing incidence of metabolic syndrome in the world, with the purpose of investigating and clarifying factors affecting ACC inhibitory efficacy, including the two isomers ACC1 and ACC2. In addition, the research promises to contribute orientation, supporting the treatment of fatty acid metabolism in the future.

In our previous articles which are published in the Journal of Medical Research of the Medicine and Pharmacy University and the Journal of Science and Technology of the National University at Ho Chi Minh City, we applied the computational methods in chemistry, including modeling and optimizing structures of various ligand molecules by using the Semi-Empirical calculation (PM3) and the Density Function Theory (DFT), and combined with a variety of classical statistical and modern bioinformatics methods such as linear multivariable

regression, genetic algorithm, artificial neural network and fuzzy logic to perform Quantitative Structural and Activity Relationships (QSAR) of multiple organic compounds with medicinal properties against pathogens, typically Chlorokojic acid derivatives having antifungal activity against Trichophyton mentagrophytes. In addition, we proposed the new compounds which were predicted to have the highest pharmaceutical activity without being investigated by experiment before.

Inheriting the experienced previous research methods, in this paper, we optimize 65 SMILES structures of aromatic inhibitors, which have been studied experimentally in determination of the half maximal inhibitory concentration (IC_{50}) and cited from the open source database of the University of California – San Diego [6] based on quantum mechanical methods: PM3 and DFT using HyperChem 8.0.10 and Gaussian 09W, combining with the calculation of quantum chemical and chemico-physical structural parameters using HyperChem 8.0.10 and Padel Descriptor 2.21 softwares [7] respectively. The result data are processed with the combination of classical statistical methods: linear regression and modern bioinformatics methods as Genetic Algorithm (GA), Artificial Neural Network (ANN), and Fuzzy logic using the statistical softwares of Department of Pharmaceutical Technology – Jadavpur University – India and R v3.3.1 in order to accomplish a QSAR model [8] between aromatic-structure ligands inhibiting fatty acid biosynthesis of the human ACC.

II. Softwares and Methods

2.1 Modeling, optimizing and calculating descriptors

Gaussian 09w and Hyperchem 8.0.10 are utilized to model and optimize the structures based on the two quantum mechanical methods: PM3 and DFT at the B3LYP/6-31G(d,p) level. The calculation of 17 quantum chemical descriptors: Approx Surface Area, Grid Surface Area, Volume, Hydration Energy, LogP, Refractivity, Polarizability, Mass, Lumo, Homo, Gap(Homo-Lumo), Total Energy, Binding Energy, Heat of Formation, Electron Energy, Nuclear Energy, and Total dipole [9]-[10] is proceeded. With PaDel Descriptor 2.21, we calculate 16018 chemico-physical descriptors of the optimized structures including 2D and 3D descriptors.

2.2 Initial data processing and refinement of descriptors

In this research, the best group of 10 descriptors are selected initially with calculation of the correlation coefficients (R) and the mean absolute error (MAE) in statistical significance (P<0.05) by the Genetic Algorithm – Linear Regression (GA-LR)

analysis, as shown in Fig. 1. , utilizing the open source statistical software of Department of Pharmaceutical Technology - Jadavpur University - India [11]-[12].

2.3 ANN

R v3.3.1 [13] is utilized to build the 10-1-1 ANN model (10 inputs as selected descriptors - 1 hidden layer - 1 output as log(IC_{50})) based on backpropagation algorithm using logistic function to calculate the weights for each descriptor which is pre-selected by the GA-LR method, thereby screening the 10 most influential descriptors on the IC_{50} as shown in Fig. 2-3.

2.4 Fuzzy logic

The 65 compounds data with the 10 selected descriptors by one-hidden-layer ANN is divided randomly into 85% of the data as the training set and 15% of the data as the test set to build ANN models automatically using an looping structure, in R with the stop conditions: Correlation coefficient (R) of the test set ≥ 0.90, Sum Squared Errors (SSE) < 9, Mean Squared Errors (MSE) of the test set ≤ 0.15. In addition, MSE of the 65 compounds data (MSE_{total}), MSE of the training set (MSE_{train}), MSE of the test set (MSE_{test}), R^2 of the 65 compounds data (R^2_{total}), R^2 of the training set (R^2_{train}), and R^2 of the test set (R^2_{test}) are calculated.

Setting up the fuzzy logic models [14], corresponding to the descriptors screened from the ANN models which have more than one hidden layer and are satisfied with the above stop conditions, results in the Hybrid Neural Fuzzy Inference System (HYFIS), as shown in Fig. 4-5. , including the parameters: 13 Gaussian membership functions, DIENES_RESHER implicit function, Hamacher t-norm operator, center of gravity defuzzification method, 15 iterations for the case of ACC1 which has the four greatest impact descriptors including GATS2c, JGI5, ETA_EtaP and CIC5, as shown in Table 1. , 20 iterations for the case of ACC2 which has the four greatest impact descriptors including GATS6s, GATS1e, MATS3s and GATS3s, as shown in Table 2.

III. RESULTS

3.1 The overview of refined descriptors

3.1.1 GATS2c

GATS2c is a Geary autocorrelation descriptor [15] which is based on an autocorrelation function using Geary Coefficient at lag 2, defined as Equation 1. :

$$c(d) = \frac{\frac{1}{2\Delta} \cdot \sum_{i=1}^{A} \sum_{j=1}^{A} \delta_{ij} \cdot (w_i - w_j)^2}{\frac{1}{A-1} \cdot \sum_{i=1}^{A} (w_i - \overline{w})^2}$$

Equation 1.

Where w_i is the atom charge of the ith atom and A is the atom number. 3.1.2 JGI5

JGI5 is a topological charge index [15] proposed to evaluate the charge transfer between a pair of atoms, and therefore, the global charge transfer in the molecule. An unsymmetric charge term matrix CT is derived from the matrix M. Its terms are calculated as Equation 2. :

$$CT_{ij} = \delta(i) \text{ if } i=j$$

$$CT_{ij} = m_{ij} - m_{ji} \text{ if } i \neq j$$

Equation 2.

Where m_{ij} are the elements of the M matrix, $\delta(i)$ is the vertex degree of the ith atom. The charge terms CT_{ij} are graph invariants that are related to the charge transfer between the pair of considered vertices. For each path of length k, a topological charge index G_k is defined as Equation 3. :

$$G_k = \frac{1}{2} \cdot \sum_i \sum_j \left| CT_{ij} \right| \cdot \delta(k, d_{ij})$$

Equation 3.

Where δ(k, dij) indicates the Kronecker delta: 1 if dij = k, zero otherwise.

3.1.3 ETA_EtaP

ETA_EtaP is an Extended Topochemical Atom (ETA) descriptor [16]-[17]. Definitions of some basic parameters used in the ETA scheme are given in Equation 4. :

$$\eta = \sum_{i<j} \left[\frac{\gamma_i \gamma_j}{r_{ij}^2} \right]^{0.5} \quad \gamma_i = \frac{\alpha_i}{\beta_i} \quad \alpha = \frac{Z - Z^v}{Z^v} \frac{1}{PN - 1}$$

$$\beta = \sum x\sigma + \sum y\pi + \delta$$

Equation 4.

Where α is the core count of a non-hydrogen vertex. Z and Z^v represent atomic number and valence electron number respectively while PN stands for period number. Hydrogen atom being considered as the reference, α for hydrogen is taken as zero value. β is the valence electron mobile (VEM) count, and δ is a correction factor of value 0.5 per atom with lone pair of electrons capable of resonance with an aromatic ring. For calculation of the VEM count, contribution of a sigma bond (x) between two atoms of similar electronegativity (≤ 0.3) is considered to be 0.5, and for a sigma bond between two atoms of different electronegativity (> 0.3) it is considered to be 0.75. Again, in case of pi bonds, contributions (y) are considered depending on the type of double bond: (i) for pi bond between two atoms of similar electronegativity (≤ 0.3), y is taken to be 1; (ii) for pi bond between two atoms of different electronegativity (> 0.3) or for conjugated (nonaromatic) pi system, y is considered to be 1.5; (iii) for aromatic pi system, y is taken as 2. γ_i is the VEM vertex count of the i^{th} vertex in a molecular graph. α_i stands for α value for the i^{th}

vertex and β_i stands for VEM count considering all bonds connected to the atom and lone pair of electrons (if any). η is the composite index both bonded and non-bonded interactions have been considered. The parameter r_{ij} stands for the topological distance between i^{th} atom and j^{th} atom.

3.1.4 CIC5

The rth order Neighbourhood Information Content IC_r, is calculated as defined by Shannon ' s entropy [15]. CIC_r is the Complementary Information Content descriptor measuring the deviation of IC_r, from its maximum value, which corresponds to the vertex partition into equivalence classes containing one element each as shown in Equation 5. :

$$CIC_r = \log_2 A - IC_r$$
$$IC_r = -\sum_{g=1}^{G} \frac{A_g}{A} \cdot \log_2 \frac{A_g}{A} = -\sum_{g=1}^{G} p_g \cdot \log_2 p_g$$

Equation 5.

Where g runs over the G equivalence classes, A_g, is the cardinality of the gth equivalence class, A is the total number of atoms, and p_g is the probability of randomly selecting a vertex of the gth class. It represents a measure of structural complexity per vertex.

3.1.5 GATS6s

GATS6s is a Geary autocorrelation descriptor [15] which is based on an autocorrelation function using Geary Coefficient at lag 6, defined as Equation 6. :

$$c(d) = \frac{\frac{1}{2\Delta} \cdot \sum_{i=1}^{A} \sum_{j=1}^{A} \delta_{ij} \cdot (w_i - w_j)^2}{\frac{1}{A-1} \cdot \sum_{i=1}^{A} (w_i - \overline{w})^2}$$

Equation 6.

Where w_i is the intrinsic state of the ith atom and A is the atom number. The intrinsic state of the ith atom is calculated by Equation 7. :

$$I_i = \frac{(2/L_i)^2 \cdot \delta_i^v + 1}{\delta_i}$$

Equation 7.

Where L_i is the principal quantum number (2 for C, N, 0, F atoms, 3 for Si, S, Cl ...), δ^v_i is the number of valence electrons (valence vertex degree) and δ_i is the number of sigma electrons (vertex degree) of the ith atom in the H-depleted molecular graph.

3.1.6 GATS1e

GATS1e is a Geary autocorrelation descriptor [15] which is based on an autocorrelation function using Geary Coefficient at lag 1, defined as Equation 8. :

$$c(d) = \frac{\frac{1}{2\Delta} \cdot \sum_{i=1}^{A} \sum_{j=1}^{A} \delta_{ij} \cdot (w_i - w_j)^2}{\frac{1}{A-1} \cdot \sum_{i=1}^{A} (w_i - \overline{w})^2}$$

Equation 8.

Where w_i is the Sanderson electronegativity of the ith atom and A is the atom number. The Sanderson electronegativity of the ith atom is proportional to the ratio of the atomic number to theatom volume [18]. 3.1.7 MATS3s

MATS3s is a Moran autocorrelation descriptor [15] which is based on an autocorrelation function using Moran Coefficient at lag 3, defined as Equation 9. :

$$I(d) = \frac{\frac{1}{\Delta} \cdot \sum_{i=1}^{A} \sum_{j=1}^{A} \delta_{ij} \cdot (w_i - \overline{w}) \cdot (w_j - \overline{w})}{\frac{1}{A} \cdot \sum_{i=1}^{A} (w_i - \overline{w})^2}$$

Equation 9.

Where w_i is the intrinsic state of the ith atom and A is the atom number.

3.1.8 GATS3s

GATS3s is a Geary autocorrelation descriptor [15] which is based on an autocorrelation function using Geary Coefficient at lag 3.

3.2 ANN – Fuzzy logic

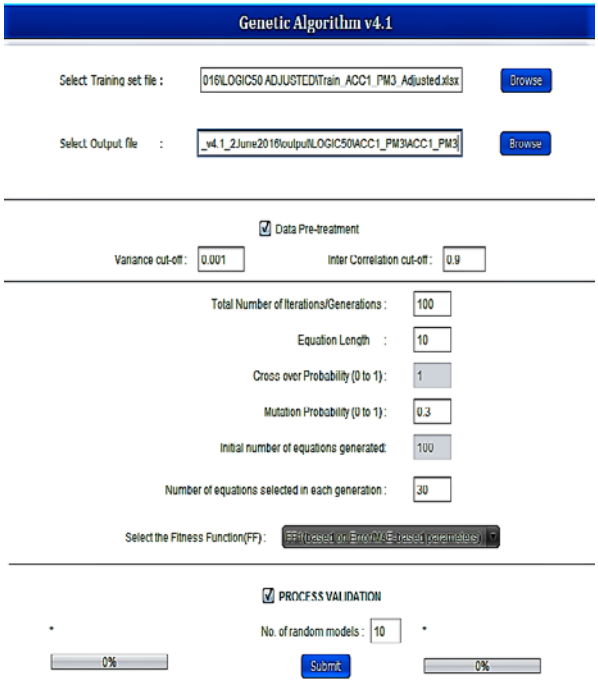

Fig. 1. GA-LR method

Table 1. HYFIS for the case of ACC1 – PM3 optimization

Index	Log(IC_{50}) Obs.	Log(IC_{50}) Cal.	Index	Log(IC_{50}) Obs.	Log(IC_{50}) Cal.
1	1.8	1.8	34	1.0	1.1
2	2.4	2.2	35	3.4	3.6
3	1.8	1.8	36	1.9	1.8
4	2.2	2.2	37	2.7	2.6
5	2.3	2.2	38	4.0	3.6
6	1.6	1.5	39	0.8	0.7
7	3.8	4.0	40	1.0	1.0
8	2.1	2.3	41	4.1	3.7
9	2.0	2.3	42	1.2	1.2
10	1.2	1.2	43	1.3	1.3
11	1.0	1.4	44	3.3	3.3
12	2.3	3.6	45	3.1	3.1
13	1.5	2.0	46	2.5	2.4
14	3.6	3.6	47	3.1	2.8
15	1.9	1.5	48	1.8	1.8
16	2.6	2.7	49	1.9	2.2
17	3.5	2.3	50	2.0	1.8
18	1.5	1.5	51	3.5	3.5
19	2.6	2.7	52	3.6	2.6
20	2.8	3.1	53	3.4	3.3
21	2.0	2.0	54	1.8	2.4
22	3.0	3.5	55	4.0	3.9
23	3.8	4.0	56*	3.1	3.1
24	1.7	1.8	57*	3.1	3.1
25	1.7	1.8	58*	3.3	3.1
26	3.9	4.0	59*	3.5	3.1
27	2.2	2.1	60*	3.0	2.4
28	3.0	3.1	61*	2.7	2.8
29	1.3	2.3	62*	1.1	1.2
30	3.1	3.1	63*	0.7	1.3
31	3.8	3.5	64*	3.0	3.1
32	1.8	2.0	65*	2.3	1.6
33	3.6	3.6			

(Index*: the test set)

MSE_{total} = 0.14; MSE_{train} = 0.14; MSE_{test} = 0.15;

R^2_{total} = 84.1%; R^2_{train} = 84.6%; R^2_{test} = 82.9%

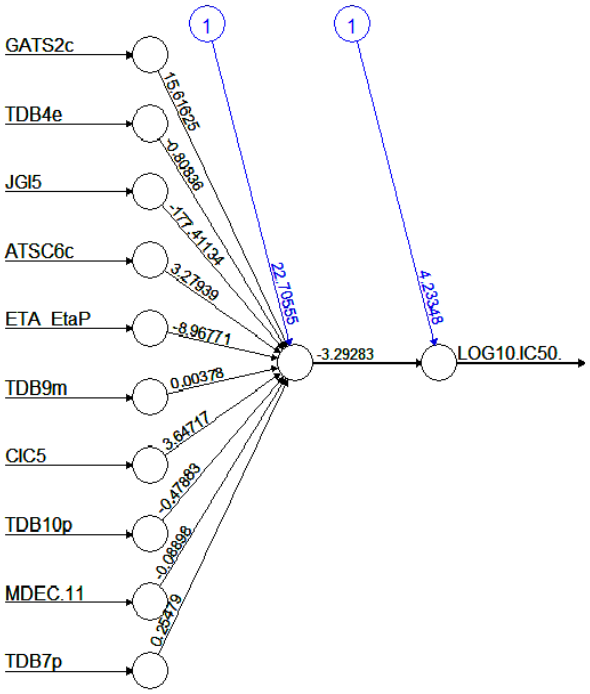

Fig. 2. The 10-1-1 ANN model with the best 10 selected descriptors for the case of ACC1 - PM3 optimization

Table 2. HYFIS for the case of ACC2 - DFT optimization

Index	Log(IC_{50}) Obs.	Log(IC_{50}) Cal.	Index	Log(IC_{50}) Obs.	Log(IC_{50}) Cal.
1	1.9	1.9	34	2.8	3.0
2	1.9	2.0	35	1.6	1.6
3	2.9	3.2	36	3.6	3.5
4	1.5	1.4	37	0.8	1.0
5	2.5	2.7	38	1.8	2.0
6	2.3	2.4	39	1.8	1.9
7	2.8	2.7	40	3.1	3.2
8	4.3	4.2	41	2.6	2.7
9	-0.5	-0.7	42	1.7	1.9
10	1.2	1.4	43	0.8	1.0
11	2.2	2.4	44	2.9	2.7
12	1.1	1.3	45	1.5	1.4
13	2.0	2.2	46	1.2	1.7
14	1.9	1.9	47	2.8	2.7
15	3.1	2.8	48	1.6	1.4
16	2.9	2.7	49	3.2	2.2
17	2.2	2.0	50	2.4	1.5
18	2.9	3.2	51	1.6	2.2
19	2.2	1.9	52	1.9	1.9
20	-0.5	-0.2	53	2.2	2.4
21	3.3	3.2	54	2.8	2.7
22	2.1	1.7	55	3.4	3.2
23	2.7	2.5	56*	2.8	3.5
24	1.4	1.4	57*	3.1	3.1
25	1.3	1.8	58*	1.8	1.9
26	2.4	2.3	59*	3.0	3.2
27	-0.7	-0.7	60*	1.5	1.9
28	3.4	3.5	61*	2.7	2.3
29	2.3	2.4	62*	3.5	3.2
30	1.5	1.4	63*	1.2	1.8
31	1.5	1.4	64*	1.0	1.1
32	3.2	3.1	65*	1.6	1.6
33	2.3	2.3			

(Index*: the test set)

MSE_{total} = 0.09; MSE_{train} = 0.08; MSE_{test} = 0.14;

R^2_{total} = 90.8%; R^2_{train} = 92.1%; R^2_{test} = 83.2%

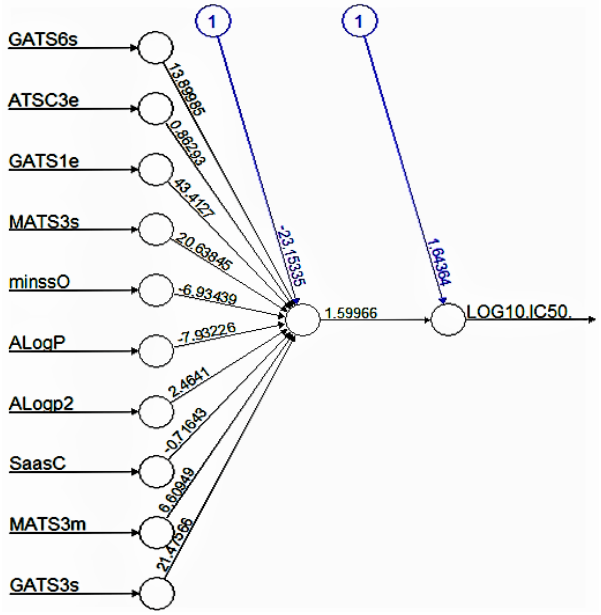

Fig. 3. The 10-1-1 ANN model with the best 10 selected descriptors for the case of ACC2 - DFT Optimization

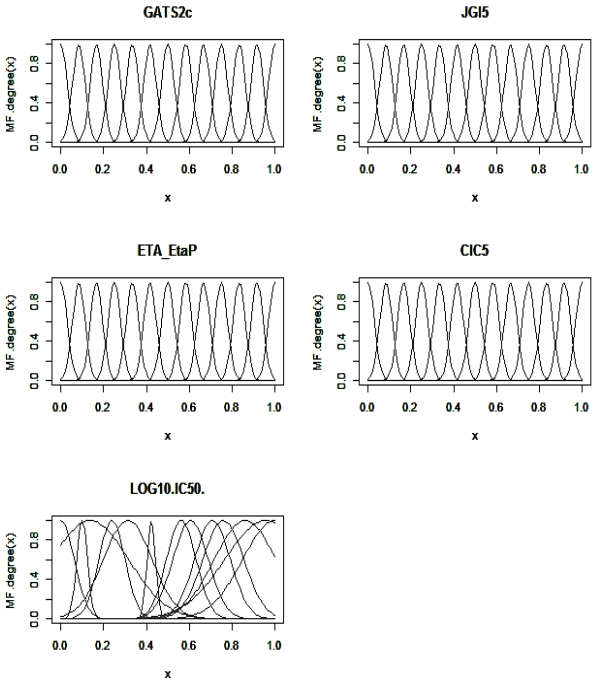

Fig. 4. Membership functions of HYFIS for the case of ACC1 - PM3 optimization

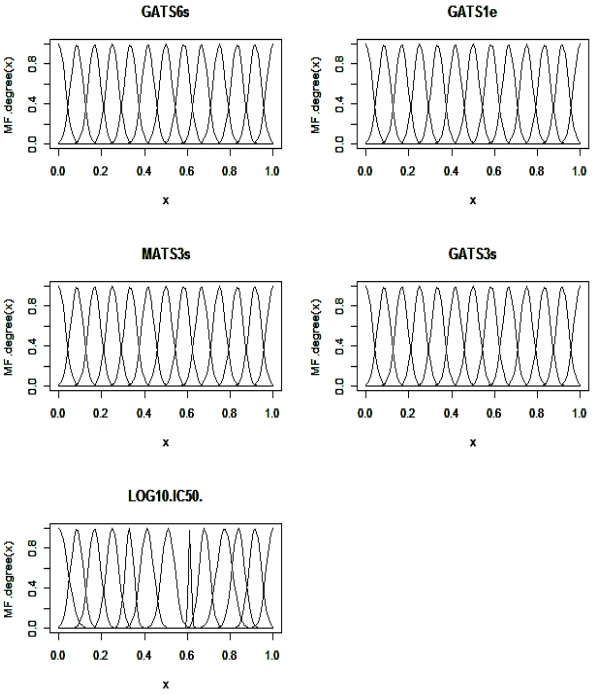

Fig. 5. Membership functions of HYFIS for the case of ACC2 - DFT optimization

IV. Conclusions

The ACC inhibitory activity of the aromatic compounds has the high correlation with the descriptors calculated by Padel Descriptor 2.21. The results are the two models set up by the fuzzy logic method in R software combined with pre-selecting descriptors using GA-LR followed by ANN.

In the case of ACC1, the HYFIS model of the compounds optimized by the PM3 method shows that the four descriptors including GATS2c, JGI5, ETA_EtaP, and CIC5 correlate closely with log IC_{50} (R^2 = 84.1%).

In the case of ACC2, the HYFIS model of the compounds optimized by the DFT method shows that the four descriptors including

GATS6s, GATS1e, MATS3s, and GATS3s correlate closely with log IC_{50} (R^2 = 90.8%).

References

[1] T. Q. Than, "Metabolic syndrome", *Journal of Cardiology Information,* vol.21, no.9, pp. 1-5, 2004.

[2] *L. X. Truong*, *Clinical biochemistry*, *1st ed.* Medical Publishers - HoChiMinh City Branch, 2015.

[3] Salih J. Wakil and Lutfi A. Abu-Elheiga, "Fatty acid metabolism: target for metabolic syndrome", *Journal of Lipid Research,* vol.50, pp. 138-143, 2009.
DOI : 10.1194/jlr.R800079-JLR200

[4] Timothy H. Tran and Yu-Shan Hsiao, "Structure and function of a single-chain, multi-domain long-chain acyl-CoA carboxylase", *Nature,* vol.518, pp. 120-124, 2015.
DOI : 10.1038/nature13912

[5] Tong L, "Acetyl-coenzyme A carboxylase : crucial metabolic enzyme and attractive target for drug discovery", *Cellular and Molecular Life Sciences*, vol.62, pp. 1784-1803, 2005.
DOI : https://doi.org/10.1007/s00018-005-5121-4

[6] Tiquing Liu, "The Binding Database", http://bindingdb.org/ (URL).

[7] Chun Wei, "PaDEL-Descriptor", http://yapcwsoft.com/dd/padeldescriptor/ (URL).

[8] *Kunal Roy*, *Quantitative Structure-Activity Relationships in Drug Design - Predictive Toxicology and Risk Assessment*, *3rd. ed.* Scopus, 2015.

[9] MakoLab, "Hypercube, Inc.", http://hyper.com/ (URL).

[10] *Warren J. Hehre*, *A Guide to Molecular Mechanics and Quantum Chemical Calculations*, *2nd ed.* Wavefunction, 2003.

[11] Ambure and Aher, "NanoBRIDGES software : Open access tools to perform QSAR and nano-QSAR modeling", *Chemometrics and Intelligent Laboratory Systems*, vol.147, pp. 1-13, 2015.
DOI : https://doi.org/10.1016/j.chemolab.2015.07.007

[12] *Melanie Mitchell*, *Introduction to Genetic Algorithms*, *5th ed.* The MIT Press, 1999.

[13] R Core Team, "R : A language and environment for statistical computing", http://www.R-project.org/ (URL).

[14] J. Kim and N. Kasabov, "HyFIS: adaptive neuro-fuzzy inference systems and their application to nonlinear dynamical systems", *Neural Networks,* vol.12, pp. 1301-1319, 1999.
DOI : https://doi.org/10.1016/S0893-6080(99)00067-2

[15] *R. Todeschini and V. Consonni*, *Handbook of Molecular Descriptors*, *1st ed.* Wiley-VCH, 2000.

[16] K. Roy and G. Ghosh, "Introduction of Extended Topochemical Atom (ETA) Indices in the Valence Electron Mobile (VEM) Environment as Tools for QSAR/QSPR

Studies", *Internet Electronic Journal of Molecular Design,* vol.2, pp. 599-620, 2003.
[17] K. Roy and G. Ghosh, "QSTR with Extended Topochemical Atom Indices. 10. Modeling of Toxicity of Organic Chemicals to Humans Using Different Chemometric Tools", *Chem Biol Drug Des,* vol.72, pp. 383-394, 2008.
DOI: 10.1111/j.1747-0285.2008.00712.x
[18] R.T. Sanderson, "Electronegativity and Bond Energy", *J. Am. Chem. Soc.,* vol.105, pp. 2259-2261, 1981.
DOI : 10.1021/ja00346a026

BIOGRAPHY

Nguyen Truong Cong Minh

2007 : BS degree in Physical Chemistry, HCMUS.
2015 : MS degree in Physical Chemistry, HCMUS.
2015~2018 : PhD student in Physical Chemistry, HCMUS.

2009~2017 : Laboratory technician, Dept. of Biochemistry of HCM-UMP and University Medical Center HCMC.

Bui Tho Thanh

1977 : BS degree in Chemistry, Saigon Combined University.
1984~1988 : MS degree and PhD degree in Chemistry, University of Paris-Sud (Paris 11).

1995~2017 : A. Prof. in Physical Chemistry, HCMUS.

Le Xuan Truong

1981 : General practitioner, HCM-UMP.
1997 : MS degree in Medicine, HCM-UMP.
2011 : PhD degree in Medicine, HCM-UMP.
2015 : Certificate as A. Professor, HCM-UMP.

2011~2017 : Chief of Biochemistry Department, HCM-UMP.

Nguyen Thi Bang Suong

1998 : General practitioner, HUE-UMP.
2003 : MS degree in Biochemistry, Hanoi Medical University.
2009 : PhD degree in Biochemistry, Hanoi Medical University.

2014~2017 : Head of Medical Laboratory, University Medical Center HCMC.

Le Thi Xuan Thao

2008 : BS degree in Public Health, HCM-UMP.
2016 : MS degree in Science of Public Health, HCM-UMP.
2010~2017 : Laboratory technician, Dept. of Biochemistry, HCM-UMP.