QSAR MODELLING OF PEPTIDOMIMETIC DERIVATIVES TOWARDS HKU4-CoV 3CL[pro] INHIBITORS AGAINST MERS-CoV

Imad Hammoudan [1,2], Soumaya Matchi [1], Driss Riffi Temsamani[2], Mohamed Bakhouch [3] , Salah Belaidi [4,5] and Samir Chtita [1]*

[1]Laboratory of Physical Chemistry of Materials, Faculty of Sciences Ben M'Sik, Hassan II University of Casablanca, Casablanca P.O. Box 7955, Morocco;

[2]Laboratory of Physical Chemistry, Faculty of Sciences of Tetouan, Universit Abdelmalek Essaadi, Tetouan P.O. Box 2117, Morocco

[3]Laboratory of Bioorganic Chemistry, Department of Chemistry, Faculty of Sciences, Chouaïb Doukkali University, P.O. Box 24, El Jadida M-24000, Morocco;

[4]Group of Computational and Medicinal Chemistry, LMCE Laboratory, University of Biskra, Biskra 7000, Algeria;

[5]Centre de Recherche en Sciences Pharmaceutiques (CRSP), La Nouvelle Ville Ali Mendjeli, Constantine 25000, Algeria

*Correspondence: samir.chtita@univh2c.ma or samirchtita@gmail.com

Abstract:

In this paper, we report the relationship between the anti-MERS-CoV activities of the HKU4 derived peptides for some peptidomimetic compounds and various descriptors using the quantitative structure activity relationships (QSAR) methods. The used descriptors were computed using ChemSketch, Marvin Sketch and ChemOffice software. The principal components analysis (PCA) and the multiple linear regression (MLR) methods were used to propose a model with reliable predictive capacity. The original data set of 41 peptidomimetic derivatives was randomly divided into training and test sets of 34 and 7 compounds, respectively. The predictive ability of the best MLR model was assessed by determination coefficient $R^2 = 0.691$, cross-validation parameter $Q^2_{cv} = 0.528$ and the external validation parameter $R^2_{test} = 0.794$.

Keywords: MERS-CoV; peptidomimetic; QSAR; PCA; MLR

Results and Discussion

Those descriptors remaining after PCA were used as an input for establishing MLR models. The best model obtained using MLR with the best statistical keys is represented by the following equation:[1-2-3]

pIC50 = 1.017 + 0.699 O% + 0.364 PC + 0.065 VDWV+0.037 VDWSA+2.158 NO

R2 = 0.691; R2test = 0.794; R2adj = 0.636; MSE = 0.108; RMSE = 0.328; F = 12.549; Pr < 0.0001

Table. Various values obtained after testing of y-randomization.

Random Models Original		Model	
R	0.380	R	0.831
R2	0.157	R2	0.691
Q2	0.278	Q2	0.528
CRP2	0.614		

Where CRP2 is the coefficient of y-randomization.

Based on all these results obtained by MLR, we can conclude that the built model has a good predictive power.[4-5-6].

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