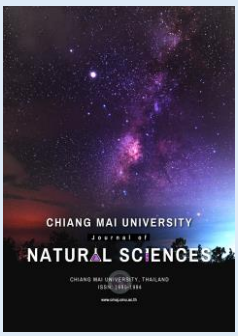


***Editor:***
Wasu Pathom-aree,
Chiang Mai University, Thailand

***Article history:***
Received: April 5, 2020;
Revised: June 17, 2020;
Accepted: August 31, 2020;
Published online: December 3, 2020

***Corresponding author:***
Ihsanul Arief,
E-mail: ihsanul.arief@ugm.mail.ac.id

***Research article***

# QSAR-Based Design of Potent Betulinic Acid Derivatives as HIV Maturation Inhibitors

**Ihsanul Arief[1,2,3,*], Harno Dwi Pranowo[1,2], Mudasir Mudasir[1], and Karna Wijaya[1]**

*1 Department of Chemistry, Faculty of Mathematics and Natural Sciences, Universitas Gadjah Mada, Yogyakarta 55281, Indonesia*
*2 Austria-Indonesia Centre for Computational Chemistry (AIC), Department of Chemistry, Faculty of Mathematics and Natural Sciences, Universitas Gadjah Mada, Yogyakarta 55281, Indonesia*
*3 Akademi Farmasi Yarsi Pontianak, Pontianak 78232, Indonesia*

**Abstract** The maturation process on HIV life-cycles has become one of the targeted steps to inhibit these viruses. This process involves two kinds of proteins, namely HIV-protease and SP1-Gag. Betulinic acid (BA) and its derivatives had been known as potential inhibitors of HIV maturation. As their capability to modeling and also predict the activity of some analog compounds by using the descriptors, quantitative structure-activity relationship (QSAR) has been used to design more potent "new drugs" in recent years. Three-dimensional (3D) descriptors explained the topology of a compound and had proven to have relations to the compound's biological activity. In this study, QSAR models were designed from 29 BA derivatives with HIV maturation inhibition activities. The best model involves 5 descriptors as follows:

$$1/\log EC_{50} = -473.8 + (71.03 \times TDB6u) + (764.7 \times FPSA\text{-}3) + (-0.604 \times RDF140u) + (0.882 \times RDF80e) + (0.262 \times PPSA\text{-}3)$$

$r^2 = 0.792$ SEE = 2.0305 $F_{cal}/F_{tab} = 7.5621$ $r^2_{test} = 0.9798$ $Q^2 = 0.9644$ $r^2_m = 0.9445$

The QSAR model was then used to design and predict some of the new BA derivatives' HIV maturation activities. The best predicted compound had $1/\log EC_{50}$ value of -0.838 and $EC_{50}$ value of 0.064 nM with the chemical name of 4-[(1R,3aR,5aR,5bR,7aS,11aR,11bS,13aS,13bS)-5a,5b,8,8,11b-penta methyl-1-(prop-1-en-2-yl)-3a[({2-[4-(pyrimidin-2-yl)piperazin-1-yl]ethyl} amino)methyl]-icosahydro-1H-cyclo penta[a]chrysen-9-yl]benzoic acid. The synthetic route to the proposed compound also suggested in this report.

**Keywords:** Betulinic acid, Drug design, HIV maturation inhibitor, QSAR

**Funding:** The authors gratefully acknowledge the Austria-Indonesian Centre for Computational Chemistry (AIC) for the facilities and to Indonesian Endowment Fund for Education (LPDP) for its financial support for this research.

**Citation:** Arief, I., Pranowo, H.D., Mudasir, M., and Wijaya, K. 2021. QSAR-based design of potent betulinic acid derivatives as HIV maturation inhibitors. CMUJ. Nat. Sci. 20(1): e2021010