# Document details



PLoS ONE Open Access
Volume 14, Issue 1, January 2019, Article number e0210869

## Thioguanine-based DENV-2 NS2B / NS3 protease inhibitors : Virtual screening, synthesis, biological evaluation and molecular modelling (Article)

(Open Access)

Hariono, M.[a,b], Choi, S.B.[a,c], Roslim, R.F.[a], Nawi, M.S.[a,d], Tan, M.L.[e], Kamarulzaman, E.E.[a], Mohamed, N.[a], Yusof, R.[f], Othman, S.[g], Rahman, N.A.[g], Othman, R.[h], Wahab, H.A.[a,i]

[a]School of Pharmaceutical Sciences, Universiti Sains Malaysia, Minden, Pulau Pinang, Malaysia
[b]Faculty of Pharmacy, Sanata Dharma University, Maguwoharjo, Sleman, Yogyakarta, Indonesia
[c]School of Data Sciences, Perdana University, Blok B and d1, MARDI Complex, Jalan MAEPS Perdana, Serdang, Selangor, Malaysia

View additional affiliations

## Abstract

View references (67)

Dengue virus Type 2 (DENV-2) is predominant serotype causing major dengue epidemics. There are a number of studies carried out to find its effective antiviral, however to date, there is still no molecule either from peptide or small molecules released as a drug. The present study aims to identify small molecules inhibitor from National Cancer Institute database through virtual screening. One of the hits, D0713 ($IC_{50}$ = 62 μM) bearing thioguanine scaffold was derivatised into 21 compounds and evaluated for DENV-2 NS2B/NS3 protease inhibitory activity. Compounds 18 and 21 demonstrated the most potent activity with $IC_{50}$ of 0.38 μM and 16 μM, respectively. Molecular dynamics and MM/PBSA free energy of binding calculation were conducted to study the interaction mechanism of these compounds with the protease. The free energy of binding of 18 calculated by MM/PBSA is -16.10 kcal/mol compared to the known inhibitor, panduratin A (-11.27 kcal/mol), which corroborates well with the experimental observation. Results from molecular dynamics simulations also showed that both 18 and 21 bind in the active site and stabilised by the formation of hydrogen bonds with Asn174. 

## SciVal Topic Prominence

Topic: Dengue Virus | Flavivirus | NS2B-NS3 protease

Prominence percentile: 98.481

## Reaxys Database Information

View Compounds

## Funding details

| Funding sponsor | Funding number | Acronym |
|---|---|---|
| Universiti Sains Malaysia | | USM |

Funding text

## Metrics

0 Citations in Scopus

0 Field-Weighted Citation Impact

PlumX Metrics

Usage, Captures, Mentions, Social Media and Citations beyond Scopus.

## Cited by 0 documents

Inform me when this document is cited in Scopus:

Set citation alert ›

Set citation feed ›

## Related documents

Progress and prospects on DENV protease inhibitors
Timiri, A.K. , Sinha, B.N. , Jayaprakash, V.
*(2016) European Journal of Medicinal Chemistry*

C-terminal residue optimization and fragment merging: Discovery of a potent peptide-hybrid inhibitor of dengue protease
Behnam, M.A.M. , Nitsche, C. , Vechi, S.M.
*(2014) ACS Medicinal Chemistry Letters*

Thiazolidinone-peptide hybrids as dengue virus protease inhibitors with antiviral activity in cell culture
Nitsche, C. , Schreier, V.N. , Behnam, M.A.M.
*(2013) Journal of Medicinal Chemistry*

View all related documents based on references

Find more related documents in Scopus based on:

This work is funded under Science Fund Grant No. 02-05-23-SF0019 and Research University Grant for Team (RUT) No.1001/PKIMIA/ 855006. MH thanked Universiti Sains Malaysia for the USM Fellowship Award (2011-2012) and the Malaysian Ministry of Science and Technology Innovation for research assistantship under ScienceFund Grant No. 02-05-23-SF0019 (2014-2015). We thank National Cancer Institute, US for the complementary samples of the 20 NCI hit compounds.

Authors ›

**ISSN:** 19326203
**CODEN:** POLNC
**Source Type:** Journal
**Original language:** English
**DOI:** 10.1371/journal.pone.0210869
**PubMed ID:** 30677071
**Document Type:** Article
**Publisher:** Public Library of Science

## References (67)

View in search results format ›

All | Export | Print | E-mail | Save to PDF | Create bibliography

1 Murray, N.E.A., Quam, M.B., Wilder-Smith, A.
Epidemiology of dengue: Past, present and future prospects (Open Access)

(2013) *Clinical Epidemiology*, 5 (1), pp. 299-309. Cited 353 times.
http://www.dovepress.com/getfile.php?fileID=17199
doi: 10.2147/CLEP.S34440

View at Publisher

2 Brady, O.J., Gething, P.W., Bhatt, S., Messina, J.P., Brownstein, J.S., Hoen, A.G., Moyes, C.L., (...), Hay, S.I.
Refining the Global Spatial Limits of Dengue Virus Transmission by Evidence-Based Consensus (Open Access)

(2012) *PLoS Neglected Tropical Diseases*, 6 (8), art. no. e1760. Cited 452 times.
http://www.plosntds.org/article/fetchObjectAttachment.action?uri=info%3Adoi%2F10.1371%2Fjournal.pntd.0001760&representation=PDF
doi: 10.1371/journal.pntd.0001760

View at Publisher

3 Guzman, M.G., Harris, E.
Dengue

(2015) *The Lancet*, 385 (9966), pp. 453-465. Cited 314 times.
http://www.journals.elsevier.com/the-lancet/
doi: 10.1016/S0140-6736(14)60572-9

View at Publisher

4 Bhatt, S., Gething, P.W., Brady, O.J., Messina, J.P., Farlow, A.W., Moyes, C.L., Drake, J.M., (...), Hay, S.I.
The global distribution and burden of dengue

(2013) *Nature*, 496 (7446), pp. 504-507. Cited 2941 times.
http://www.nature.com.ezproxy.um.edu.my/nature/index.html
doi: 10.1038/nature12060

View at Publisher