

## Abstract

# In silico and in vitro models investigating anti-dengue potential of flavonoids from *Carica papaya* leaf juice<sup>†</sup>

Bee Ping Teh<sup>1,2</sup>, Nur Hana Binti Md Jelas<sup>1</sup>, Mohd Ridzuan Bin Mohd Abd Razak<sup>1,#</sup>, Saharuddin Bin Mohamad<sup>2,3,#</sup>

<sup>1</sup> Herbal Medicine Research Centre, Institute for Medical Research, National Institutes of Health, Ministry of Health Malaysia, 40170 Shah Alam, Selangor Darul Ehsan, Malaysia; tehbp@moh.gov.my, adlinafzan@moh.gov.my

<sup>2</sup> Institute of Biological Sciences, Faculty of Science, Universiti Malaya, 50603 Kuala Lumpur, Malaysia; tehbp@moh.gov.my, saharuddin@um.edu.my

<sup>3</sup> Centre of Research in Systems Biology, Structural Bioinformatics and Human Digital Imaging (CRYSTAL), Universiti Malaya, 50603 Kuala Lumpur, Malaysia; saharuddin@um.edu.my

\* Correspondence: Bee Ping Teh (tehbp@moh.gov.my), Saharuddin Bin Mohamad (saharuddin@um.edu.my)

# Author contributed equally to the paper

† Presented at 9th International Electronic Conference on Medicinal Chemistry, e-conference, 1–30 November 2023.

**Abstract:** Despite the complexity of research, high cost and time constraint, dengue research is undergoing a vast transformation with remarkable findings, include investigating the potential of plant-based compounds. A research investigated the potential of two flavonoids (clitorin and manghaslin) detected in *Carica papaya* leaf juice against dengue virus serotype-2 was conducted. This research used in silico model (docking simulation) in exploring the interaction of the two flavonoids on functional activity of two non-structural proteins involving in dengue viral ribonucleic acid (RNA) replication, i.e. NS2B/NS3 protease (NS2B/NS3) and NS5-RNA-dependent RNA polymerase (NS5-RdRp). The same flavonoids were then tested on in vitro model (plaque assay) to assess their antiviral effect through number of plaque forming units per mL. The docking simulation revealed the two flavonoids potentially bind onto the two targeted dengue proteins that are important for dengue viral replication but manghaslin is predicted to have stronger binding interaction with both NS2B/NS3 protease and NS5-RdRp than clitorin. Both flavonoids inhibited the plaque formation. Other than in vivo research, the findings from this study also propose clitorin and manghaslin as a potential inhibitor of NS5-RdRp and NS2B/NS3 protease, which could be further investigated to exploit their drug likeness properties such as adsorption, distribution, metabolism and excretion.

**Keywords:** *Carica papaya*; leaf, juice; flavonoid; clitorin; manghaslin; dengue; protease; polymerase

**Citation:** Lastname, F.; Lastname, F.; Lastname, F. Title. *Med. Sci. Forum* 2023, 2, x.

<https://doi.org/10.3390/xxxxx>

Academic Editor: Firstname Lastname

Published: date

**Publisher's Note:** MDPI stays neutral with regard to jurisdictional claims in published maps and institutional affiliations.



**Copyright:** © 2023 by the authors. Submitted for possible open access publication under the terms and conditions of the Creative Commons Attribution (CC BY) license (<https://creativecommons.org/licenses/by/4.0/>).

**Author Contributions:** Conceptualisation, B.P.T., M.R.B.M.A.R. and S.B.M.; Methodology, B.P.T., M.R.B.M.A.R. and S.B.M.; Data curation, B.P.T. and M.R.B.M.A.R.; Writing—original draft preparation, B.P.T.; Writing—review and editing, B.P.T., N.H.B.M.J., M.R.B.M.A.R. and S.B.M.; Project administration, M.R.B.M.A.R. and S.B.M.; Visualisation, B.P.T., M.R.B.M.A.R. and S.B.M.; Resources, B.P.T., M.R.B.M.A.R. and S.B.M.; Supervision, M.R.B.M.A.R. and S.M. All authors have read and agreed to the published version of the manuscript.

**Funding:** This study is funded by the Ministry of Health Malaysia and with approval from the National Institutes of Health, Malaysia (NMRR-18-2906-44574).

**Institutional Review Board Statement:** Not applicable

---

<b>Informed Consent Statement:</b> Not applicable	1
<b>Data Availability Statement:</b> Please refer to suggested Data Availability Statements in section “MDPI Research Data Policies” at <a href="https://www.mdpi.com/ethics">https://www.mdpi.com/ethics</a> .	2 3
<b>Acknowledgments:</b> We would like to thank the Director General of Health Malaysia for his permission to publish this manuscript.	4 5
<b>Conflicts of Interest:</b> No conflict of interest with regard to the review, authorship and publication of this manuscript. The funders had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript, or in the decision to publish the results.	6 7 8 9