Elucidating Pharmacophore of Novel NS3 Inhibitor for Dengue via Proteochemometric Modeling and Molecular Dynamics Simulation

By: Dr. Zafirah Liyana Abdullah

The global incidence of infectious diseases presents a substantial threat to human health. Among these infections, dengue virus (DENV) has become the most notable and the most rapidly spreading mosquito-borne viral disease1. According to the World Health Organization (WHO), the number of incidences has increased 30-fold from the past 50 years, as well as the geographical expansion of the disease to new countries2. Therefore, the research titled "Elucidating Pharmacophore of Novel NS3 Inhibitor for Dengue via Proteochemometric Modeling and Molecular Dynamics Simulation" is proposed to make contributions to the development of antivirals for dengue infection, a mosquito-borne viral disease that affects millions of people worldwide.

The study aims to identify inhibitors targeting the NS3 protein, an essential enzyme in the replication of the dengue virus. The NS3 protein plays a pivotal role in the viral life cycle, making it an attractive target for antiviral drug development3. Despite the cumulative research effort throughout the years, there is still a lack of effective inhibitors that can specifically and efficiently block NS3 activity. This is where the project comes into play, where computational approaches are used to address the gap in knowledge.

In this study, protochemometric modeling (PCM) will be employed to identify the main pharmacophores, which are molecular features that are essential for biological activity and are critical for inhibiting the NS3 enzyme. PCM modeling is an approach that allows the analysis of protein-ligand interactions on a large scale, helping researchers to predict how different compounds might interact with the NS3 protein. By integrating molecular dynamic (MD) simulations, the dynamic behavior of these interactions in real-time can be observed, providing deeper insights into the mechanisms of inhibition specifically that target the active site of the NS3 protein. Thus, this computational approach is expected to lead to the identification of novel NS3 inhibitors that can be further developed into effective antiviral therapies for dengue. These findings will not only contribute to dengue research but could also have broader applications in the development of treatments for other viral diseases.

References

Tian, Y. S., Zhou, Y., Takagi, T., Kameoka, M. & Kawashita, N. Dengue Virus and its inhibitors: A brief review. Chem. Pharm. Bull. (Tokyo) 66, 191–206 (2018)

World Health Organization. Dengue and severe dengue. https://www.who.int/news-room/fact-sheets/detail/dengue-and-severe-dengue (2023).

Norshidah, H., Leow, C.H., Ezleen, K.E., Wahab H.A., Vignesh, R., Rasul, A., Lai NS. Assessing the potential of NS2B/NS3 protease inhibitors biomarker in curbing dengue virus infections: In silico vs. In vitro approach. Front Cell Infect Microbiol. 2023 Feb 14;13:1061937. doi: 10.3389/fcimb.2023.1061937. PMID: 36864886; PMCID: PMC9971573.

Project Leader

Dr. Zafirah Liyana Abdullah
Faculty of Pharmacy, UiTM

Team Members

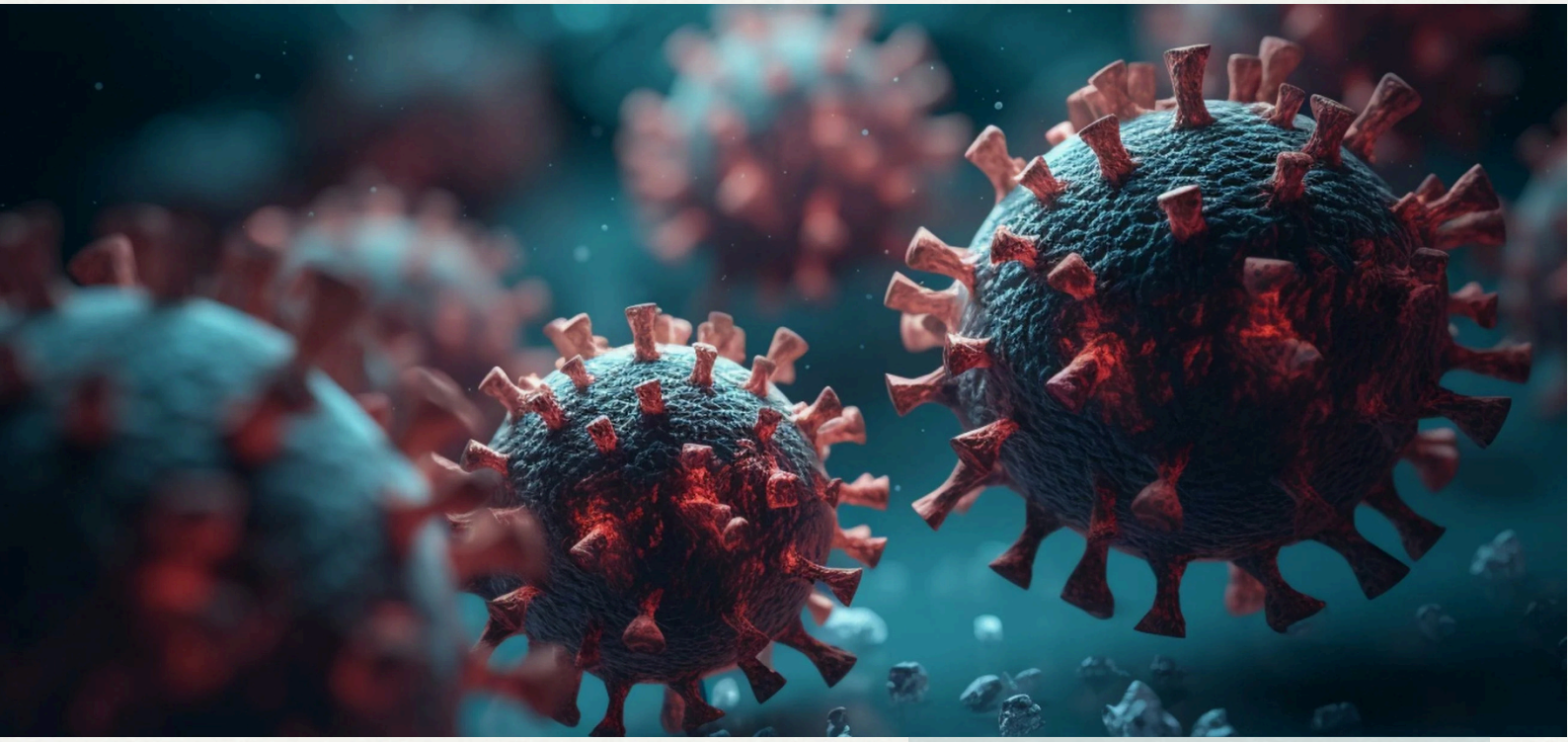
Assoc. Prof. Dr. Fazlin Mohd Fauzi
Faculty of Pharmacy, UiTM

Dr. Siti Azma Jusoh
Faculty of Pharmacy, UiTM

ISSUE 10/2024 OCTOBER 2024

PRESCRIPTION

LATEST NEWS AND UPDATES FROM THE FACULTY OF PHARMACY



PRESCRIPTION

Faculty of Pharmacy,
Universiti Teknologi MARA,
Kampus Puncak Alam,
42300 Bandar Puncak Alam, Selangor.

@pharmacyuitm

@pharmacy_uitm

Faculty of Pharmacy UiTM

https://pharmacy.uitm.edu.my/

+603-3258 4645

korporatff@uitm.edu.my