Artificial intelligence in anti-dengue drug development

ABSTRACT

Dengue fever is a mosquito-borne illness that affects millions of people worldwide. Artificial intelligence (AI) is being employed in the battle against it. AI is being used to analyse dengue immune repertoires, which may yield hitherto unheard-of insights into the complexities of dengue adaptive immunity, help in the development of novel treatments, and influence the creation of vaccines. This AI-driven strategy may contribute to the creation of dengue fever therapies that are more potent.

To the Editor

Aedes aegypti and *A. albopictus* are the carriers of the dengue virus (DENV), which causes dengue illnesses. Dengue is now endemic in more than 100 tropical and subtropical countries in Southeast Asia, Africa, America, and certain regions of Europe. An estimated 390 million dengue infections with 96 million cases exhibiting clinical symptoms, were reported each year, along with 25,000 deaths.[1] There are four antigenically distinct serotypes of the DENV: DENV-1, DENV-2, DENV-3, and DENV-4.[2] However, due to antibody-dependent enhancement (ADE) or original antigenic sin, a subsequent infection with a different DENV serotype may cause a serious disease with complications that lead to dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS).[1] There isn't currently a medication licenced by the FDA to treat dengue; instead, therapy is limited to treating symptoms. Due to strict age restrictions, dengvaxia, the first licenced dengue vaccine, is not thought to be a safe and effective dengue vaccine alternative.[3] Even with improvements in immunisations and traditional therapies, the discovery of new antiviral medications is still essential for controlling and preventing DENV infection.

1. Anti-dengue inhibitors from AI

AI has been used in several research to find possible anti-dengue inhibitors. For example, studies have developed the "Anti-Dengue" algorithm, which uses machine learning and a quantitative structure-activity relationship (QSAR) to identify dengue virus inhibitors.[4] Another paper highlights the promise of AI in drug development and vaccine creation by discussing its application to the analysis of the dengue immune response and the identification of possible therapies.[5] Furthermore, FDA-approved drugs with anti-dengue viral activity were found by a computer screen of the SWEETLEAD database, proving the usefulness of computational screening in locating possible inhibitors.[6] These papers demonstrate how AI may be used to find anti-dengue inhibitors and how this can affect medication repurposing and therapeutic development.

2. Benefits of AI

These benefits demonstrate the potential of AI in enhancing the prevention, control, and management of dengue fever. The benefits of using AI in anti-dengue efforts include:

1. **Prediction and Prevention**: Through the analysis of several factors including climate, population density, and mosquito habitats, AI models can anticipate and avert dengue epidemics.
2. **Vaccine and Therapeutics Development**: AI has the potential to enhance vaccine design and lead to the identification of novel medicines by analysing the dengue immune response.
3. **Disease Monitoring and Forecasting**: AI technology allows for real-time monitoring, early warning, and reaction to dengue outbreaks, assisting in the identification of sensitive areas and the implementation of successful preventative measures.
4. **Public Health Engagement**: With real-time information and encouragement to adopt dengue prevention measures through mobile applications and other digital platforms, AI may support public health participation.

3. Anti-dengue inhibitor from natural products using AI

AI has been used to find natural product compounds with anti-dengue properties. Using AI approach such as virtual screening, researchers have looked into the potential of natural products like phenolic compounds, flavonoids, peptides, alkaloids, and terpenes, as well as medicinal plants and their active phytoconstituents, to control dengue and inhibit viral replication processes.[7,8] This research show how beneficial AI and natural products might be in the continuing fight against dengue fever.

4. Anti-dengue inhibitor from synthesized compounds using AI

Several compounds, including baicalein-derived,[9] heterocyclic molecules,[10] and compounds found by virtual screening of small-molecule libraries,[11] have been synthesised and evaluated for their antiviral effi-

cacy against dengue virus. Additionally, employing docking and structure-activity relationship studies (SARs), imidazole phenazine derivatives have been synthesised and their inhibitory effectiveness as anti-dengue drugs verified.[12]

5. Anti-dengue inhibitor from drug repurposing using AI

AI has been investigated as a potential method for repurposing drugs to combat the dengue virus (DENV). Quinine, N-acetylcysteine, metoclopramide, and indole derivatives are among the putative anti-dengue drugs that have been found in many investigations and may be used to treat DENV. A method for identifying repurposed pharmaceuticals that target DENV has been developed: machine learning-assisted prediction of small molecule antivirals against DENV. FDA-approved substances with anti-DENV viral activity have also been found using a focused computational scan of the SWEETLEAD database. According to this research, medication repurposing with AI may hasten the identification and creation of effective antiviral treatments against DENV.[4,6,13]

6. Anti-dengue inhibitor from protein using AI

Numerous research has investigated the use of AI to develop protein-based anti-dengue medicines. AI was used to analyse dengue immune repertoires. The results might have a significant influence on vaccine and immunotherapeutic design as well as lead to the discovery of novel antibody treatments.[5] Computational approaches have been used in research to predict dengue-human protein interactions, which are important for illness prediction and the development of antiviral drugs.[14]

In conclusion, there is a lot of promise for using AI to discover anti-dengue medications. AI may be used to forecast the specificity of the immune repertoire, find novel antibody therapies, and anticipate the effectiveness of small molecule antivirals against the dengue virus. The development of AI algorithms to anticipate dengue virus inhibitors and the application of AI in computational analyses for the creation of dengue medicines have been highlighted in recent publications. To find new treatments against dengue, future proposals for the development of anti-dengue inhibitors may entail investigating AI-assisted prediction and drug repurposing in greater detail as well as continuing to integrate AI with other scientific fields.

Funding

Data availability

Not applicable.

Uncited references

, .

CRediT authorship contribution statement

Miah Roney: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Validation, Writing – original draft.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgement

References

1. Lee M.F., Wu Y.S., Poh C.L. Molecular mechanisms of antiviral agents against dengue virus. *Viruses.* 2023;15(3):705.
2. García-Ariza L.L., González-Rivillas N., Díaz-Aguirre C.J., Rocha-Roa C., Padilla-Sanabria L., Castaño-Osorio J.C. Antiviral activity of an indole-type compound derived from natural products, identified by virtual screening by interaction on dengue virus NS5 protein. *Viruses.* 2023;15(7):1563.
3. He X., Zheng Y., Tian C., et al. Quassinoids from Eurycoma longifolia with antiviral activities by inhibiting dengue virus replication. *Phytomedicine.* 2023;110:154650.
4. Gautam S., Thakur A., Rajput A., Kumar M. Anti-dengue: a machine learning-assisted prediction of small molecule antivirals against dengue virus and implications in drug repurposing. *Viruses.* 2023;16(1):45.
5. Natali E.N., Babrak L.M., Miho E. Prospective artificial intelligence to dissect the dengue immune response and discover therapeutics. *Front Immunol.* 2021;12:574411.
6. Moshiri J., Constant D.A., Liu B., et al. A targeted computational screen of the SWEETLEAD database reveals FDA-approved compounds with anti-dengue viral activity. *mBio.* 2020;11(6):10–1128.
7. Soares L.B., Silva-Júnior E.F., Moreira K.A., Aquino P.G. Natural products for controlling dengue and its vectors. *Stud Nat Prod Chem.* 2022;72:423–464.
8. Altamish M., Khan M., Baig M.S., et al. Therapeutic potential of medicinal plants against dengue infection: a mechanistic viewpoint. *ACS Omega.* 2022;7(28):24048–24065.
9. Putri G.N., Gudla C.S., Singh M., et al. Expanding the anti-flaviviral arsenal: discovery of a baicalein-derived Compound with potent activity against DENV and ZIKV. *Antivir Res.* 2023;220:105739.
10. Nair V., Chi G., Shu Q., Julander J., Smee D.F. A heterocyclic molecule with significant activity against dengue virus. *Bioorg Med Chem Lett.* 2009;19(5):1425–1427.
11. Zhou Z., Khaliq M., Suk J.E., et al. Antiviral compounds discovered by virtual screening of small– molecule libraries against dengue virus E protein. *ACS Chem Biol.* 2008;3(12):765–775.
12. Khalili N.S.D., Khawory M.H., Salin N.H., et al. Synthesis and biological activity of imidazole phenazine derivatives as potential inhibitors for NS2B-NS3 dengue protease. *Heliyon.* 2024;10(2):e24202.
13. Bajrai L.H., Faizo A.A., Alkhaldy A.A., Dwivedi V.D., Azhar E.I. Repositioning of anti-dengue compounds against SARS-CoV-2 as viral polyprotein processing inhibitor. *PLoS One.* 2022;17(11):e0277328.
14. Jainul Fathima A., Revathy R., Balamurali S., Murugaboopathi G. Prediction of dengue-human protein interaction using artificial neural network for anti-viral drug discovery. *Proceedings of International Conference on Sustainable Computing in Science, Technology and Management (SUSCOM).* Jaipur-India: Amity University Rajasthan; 2019.

Miah Roney

Faculty of Industrial Sciences and Technology, Universiti Malaysia Pahang Al-Sultan Abdullah, Lebuhraya Tun Razak, 26300, Gambang, Kuantan, Pahang Darul Makmur, Malaysia
Centre for Bio-aromatic Research, Universiti Malaysia Pahang Al-Sultan Abdullah, Lebuhraya Tun Razak, 26300, Gambang, Kuantan, Pahang Darul Makmur, Malaysia

E-mail address: saroney35@gmail.com.