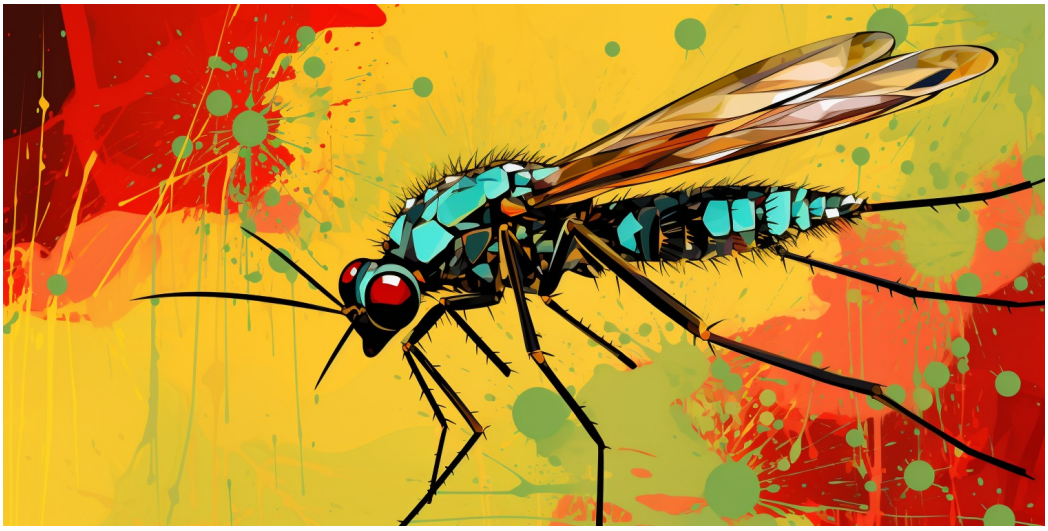

# [Research Note] Dengue – Therapeutic Efforts in Mexico

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## Abstract

In this communication, we present the research efforts regarding dengue treatments that are being carried out in Mexico, a country that suffers from the dengue pandemic. This is why they have begun to implement some treatment measures, hoping to limit the said pandemic.

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Mexico is one of the countries with the highest prevalence of dengue in the Americas, so there has been a need to resort to empirical herbalism based on popular beliefs. This includes the use of cane juice, grapes, and coconut water, which are rich in polyphenol flavonoids (mainly resveratrol, quercetin, and fisetin) with antiviral, anti-inflammatory, and anticytokine properties. The usefulness of these substances in dengue virus infection has been documented. [1][2]

Furthermore, other actions have been implemented against the vector, such as the sterile mosquito technique and the use

of wolbachia. Both techniques aim to reduce the fertility rate of mosquitoes to decrease their population. Preliminary results show a statistically significant reduction in treatment versus control areas. The reduction rate was 90.9% one month after the start of the suppression phase, 47.7% two months later (when the number of males released was reduced by 50%, coinciding with local abundance), 61.4% four months later (when the initial number of released males was restored), 88.4% five months later, and 89.4% six months after the start of the suppression phase. This study was carried out in Yucatán over a period of 24 weeks. [3]

In a more scientific and objective way, CINVESTAV researchers have studied various common drugs with known anti-inflammatory and antiviral properties. These drugs act on structural proteins NS3 and NS4, thereby reducing viral replication. One of the first drugs worth highlighting is Metformin. Diabetic patients under treatment with this drug did not, in most cases, develop severe dengue. An investigation showed that Metformin significantly reduced the levels of the NS3 protein and inhibited the formation of dengue replicative complexes. At this point, viral replicative complexes depend on cholesterol and other lipid species to form. Therefore, another pharmacological group came into the scene, with lipid-lowering agents being the main focus. Ezetimibe is a drug that reduces cholesterol absorption by inhibiting endocytosis through the Niemann-Pick C1-Like 1 (NPC1L1) receptor, expressed on the membrane of enterocytes and hepatocytes. During dengue infection, there is an increase in the amount of NPC1L1 on the surface of Huh-7 cells, which correlates with an increase in cholesterol levels. Blocking NPC1L1 with ezetimibe decreases total cellular cholesterol, the percentage of infected cells, viral yield, viral RNA, and protein synthesis without affecting dengue virus binding and/or entry into Huh-7 cells. Furthermore, ezetimibe inhibited dengue virus replicative complex formation and lipid droplet accumulation. All these results indicate that ezetimibe is an excellent drug for inhibiting dengue virus infection and confirm that cholesterol is a key target for inhibiting viral infection. In this regard, statins have also been studied in vitro (highlighting lovastatin and atorvastatin) and have shown an excellent antiviral effect on dengue virus by inhibiting the mevalonate and/or fatty acid pathway. Some of these effects also apply to other flaviviruses such as the Zika virus. [4][5][6][7]

These research efforts are in vitro. We consider it is time to carry them out in vivo in search of therapeutic options to control dengue.

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