

From Kitchen Waste to Medical Hope:

The ONION PEEL DISCOVERY

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Dengue Hemorrhagic Fever (DHF), a severe and sometimes life-threatening disease spread by *Aedes* mosquitoes, often leads to a sharp drop in platelet counts and triggers intense immune reactions called cytokine storms. There has been no specific cure; a reality that triggers us to explore natural remedies that might help, one of which comes from an unexpected source: yellow onion peels. How do the yellow onion peels work against dengue virus? Let's continue reading.



https://kaltim.tribunnews.com/2024/02/23/apa-itu-penyakit-autoimun-yang-diidap-kartika-putri-ini-penyebab-dan-8-gejala-penyakit-tersebut?page=2

The Challenge of Treating Dengue Hemorrhagic Fever

Dengue Hemorrhagic Fever (DHF) is a severe illness caused by infection with one of four types of dengue virus, all transmitted by *Aedes aegypti* and *Aedes albopictus* mosquitoes. In Indonesia, dengue is an endemic disease that continues to claim lives every year. Data from the Ministry of Health of the Republic of Indonesia show a concerning trend: while cases dropped from over 103,000 in 2020 to around 73,500 in 2021, the number of deaths actually rose from 661 to 705. In 2022, cases spiked again to 95,355, with 853 fatalities reported. In 2023, the Ministry of Health reported 114,720 cases and 894 deaths, a 30 % decrease from 2022's 143,176 cases and 1,236 deaths. However, dengue resurged in 2024: by the 17th week alone there were 88,593 cases and 621 deaths, surpassing the previous year's total. Meanwhile, a mid-year WHO–MoH report indicated a striking ~150,000 cases and 884 deaths by July 2024. More recently, as of early February 2025, there were 6,050 cases and 28 deaths, with an incidence rate of 2.14 per 100,000, across 235 districts in 23 provinces.

One of the most dangerous complications of dengue is a sharp drop in platelet count (a condition called thrombocytopenia) and a surge in inflammatory molecules, known as a cytokine storm. This chain reaction can lead to internal bleeding, shock, and even organ failure. The virus does this by attacking the bone marrow, where platelets are produced, and triggering their destruction through clumping. The resulting inflammation causes fluid to leak from blood vessels, which worsens the condition.

At the molecular level, one of the most promising strategies for fighting dengue is to block the virus's ability to replicate, particularly by targeting its non-structural proteins, like NS3. Despite these insights,

there is still no specific treatment for dengue-induced thrombocytopenia. Current therapies mostly focus on relieving symptoms with painkillers, fever reducers, and in severe cases, platelet transfusions, which is a costly and complex process.

While a vaccine called Qdenga was approved in 2022, concerns remain about its effectiveness and affordability, limiting its widespread use. In the search for more accessible alternatives, scientists have turned to natural compounds. Plants like guava, papaya, and red yeast rice contain quercetin, a flavonoid known to help protect platelets and potentially inhibit the dengue virus. Interestingly, yellow onion peel, often discarded as waste, has been found to contain much higher levels of quercetin, up to 315.6 mg per gram, far exceeding most other sources. Yet, its potential as an anti-dengue agent remains largely unexplored.

Our study was carried out to investigate whether extract from Yellow Onion Peels (YOP) could boost platelet production in living organisms (in vivo) and hinder viral replication in computer simulations (in silico). We also examined the compound's drug-like properties, toxicity profile, and how well it might interact with the dengue virus's NS3 protein, a critical target in viral replication.

Peeking Inside the Peel: Does Onion Skin Really Contain Quercetin?

To find out whether Yellow Onion Peels (YOP) really contain quercetin, we used a simple but effective method called Thin Layer Chromatography (TLC). This technique allows scientists to separate and identify compounds in a mixture by observing how far they travel on a special coated plate when exposed to a solvent.

In our study, the onion peel extract was compared to a pure quercetin sample using a mix of methanol and ethyl acetate (in a 0.2:4.8 ratio) as the solvent.



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https://elements.envato.com/onion-peel-or-skin-on-wood-VVSMRZQ

Both samples produced spots on the TLC plate with nearly identical Rf values, a measure of how far each compound moved. The extract showed an Rf of 0.862, while the quercetin marker showed 0.888. Quercetin's Rf values typically range between 0.309 and 0.975, depending on conditions. Because the Rf values of the extract and the marker were so close, it's a strong indication that the yellow onion peel does indeed contain quercetin, a natural antioxidant known for its potential health benefits, including antiviral and platelet-protective effects.

Testing Onion Peel Compounds Against Dengue Virus: A Computer Simulation

Scientists are increasingly using computer simulations to predict how natural compounds might fight viruses. Our study focused on quercetin, a flavonoid found abundantly in yellow onion peel, to see if it could potentially block a key dengue virus protein called NS3, which is essential for the virus's survival and replication.

Understanding the Compound: Quercetin's Drug-Like Properties

Before considering a compound as a drug candidate, it must meet certain criteria known as Lipinski's Rules, which help predict whether a molecule is likely to be absorbed and used effectively in the body. These rules look at factors like molecular weight, fat solubility (log P), and the number of hydrogen bonds it can form. Using an online tool called SwissADME, we found that quercetin fits well within these guidelines:

- Molecular weight: 302.24 g/mol (below the 500 Da limit)
- Hydrogen bond acceptors: 7
- Hydrogen bond donors: 5
- Log P value: 1.23 (indicating good solubility)

This means quercetin has promising characteristics as a drug candidate.

Is Quercetin Safe? Evaluating Toxicity

Toxicity was predicted using ADMETlab, a platform

that estimates how harmful a compound might be. The key measure is LD_{50}, the dose at which a compound would be lethal to half of a test population. Quercetin showed an LD_{50} of about 699 mg/kg, placing it in the low toxicity category, which suggests it's relatively safe for further development.

The Target: Stability of the Dengue NS3 Protein

The NS3 protein structure was obtained from the Protein Data Bank (PDB code: 2JLR). To ensure the protein model was reliable for docking studies, its stability was assessed with a Ramachandran plot, a tool that checks the quality of protein structures. The results were excellent, with 0% of non-glycine amino acids falling into disallowed regions, confirming the protein's suitability for interaction studies.

Predicting Activity: How Likely Is Quercetin to Work?

Using the PASS Online tool, we predicted quercetin's biological activity. The Pa value (probability of activity) was 0.262. This means quercetin shows some computational potential as an antiviral agent, but laboratory confirmation is still needed to prove its effectiveness.

Molecular Docking: How Quercetin Binds to the Virus?

To simulate how quercetin fits into the NS3 protein, we performed molecular docking using Biovia Discovery Studio (Fig 1). We prepared the protein by removing water molecules and natural ligands, then added hydrogen atoms to complete its structure; these steps are necessary for accurate simulation of interactions. These docking studies help visualize how well quercetin might block the dengue virus's key enzyme, potentially stopping the virus from replicating. This combination of computational analyses provides valuable early insights into the potential of natural compounds like quercetin from yellow onion peels as antiviral agents, paving the way for future laboratory and clinical studies.

Testing the Yellow Onion Peel Compounds, Platelet Enhancement: An Animal Testing

In this study, we worked with 28 healthy male mice (*Mus musculus*), each weighing around 30 g and aged between 7 to 12 weeks (Animal Ethical Clearance No. 00022/04/LPPT/VII/2023 issued on 13 July 2023 by the Integrated Research and Testing Laboratory, Universitas Gadjah Mada). The Yellow Onion Peels (YOP) used in our study was identified as *Allium cepa* L. and was clearly stated in a certificate No. 0391/5.Tb./VII/2023 issued on 28 July 2023 by the Plant Systematics Laboratory of the Faculty of Biology, Universitas Gadjah Mada.
We split the mice into six groups. Some were left untreated as a control (positive and negative), while others got different kinds of treatments, including medication called Psidii which is made from the extract of guava leaf (standardized herbal medicine) and the extract of Yellow Onion Peels (YOP). The YOP extract were given in three different amounts, i.e., small (250 mg), medium (500 mg), and large (1000 mg). While the Psidii were given at 500 mg.

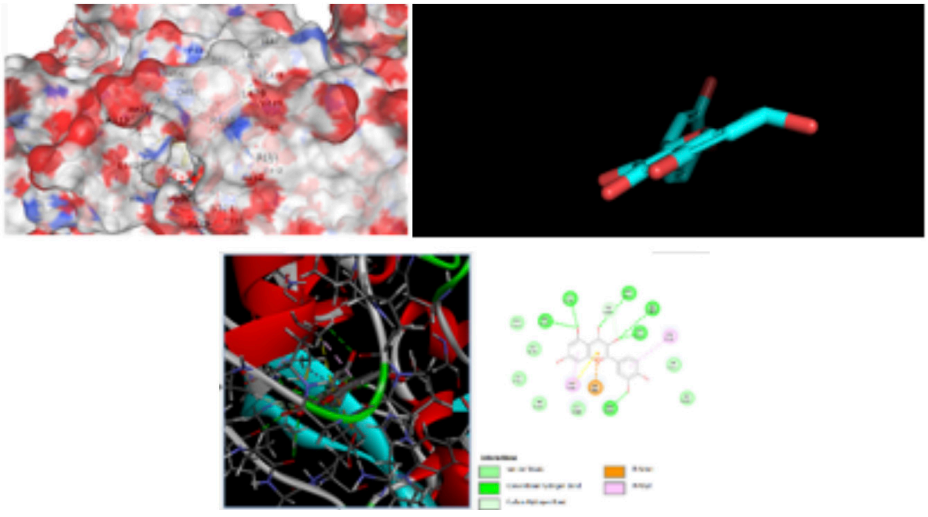


Figure 1 Docking results and visualization between 2JLR protein and quercetin
Source: In silico study at Animal Physiology Laboratory, Faculty of Biology, Universitas Gadjah Mada, 2023.

Before the experiment really started, the mice were given a week to get used to their new environment, a comfortable cage with soft wood husks on the bottom, good air flow, and just the room temperature in range 24 - 26 ^{o}C. The mice were fed about 3 g of food each day and had unlimited access to distilled water.

To mimic what happens in people with dengue fever, where blood platelets (the cells that help stop bleeding) drop to dangerous levels, we gave heparin to the five groups (except positive control). Heparin is a drug that lowers platelet counts. We tested the mice's blood three times: before any treatments, after getting heparin, and after giving them the plant extracts. The blood was taken carefully from behind the eye (a standard procedure in laboratory mice). The mice were given anesthesia so they wouldn't feel any pain. Each sample was checked using a machine that counts blood cells.

The most exciting result? The extract of YOP at 500 mg worked the best at raising platelet levels. Even though the statistics didn't show a big difference between all the groups, there was a clear pattern: YOP, which contains a natural compound called quercetin, seemed more helpful in boosting platelets than Psidii, a standardized herbal medicine.




https://elements.envato.com/two-female-scientists-conducting-in-depth-laborato-YN26JKT

So while more research is needed, this study gives hope that Yellow Onion Peels (YOP) could someday be useful in helping people with low platelet counts, like those with dengue fever.

Future Directions: Exploring New Treatments for Dengue Hemorrhagic Fever

This study offers promising insights for scientists working to develop new treatments for DHF. It highlights the potential of YOP extract, not only to help increase platelet counts but also to block the dengue virus from multiplying. Moving forward, further research is needed to deepen our understanding. We plan to explore how YOP affects inflammatory gene expression, which plays a key role in the body's response to dengue infection. We also aim to develop and test different formulations of the extract to find the most effective and practical way to deliver the extract as medicine. By advancing this line of research, we hope to contribute valuable knowledge to health and pharmacology fields and, ultimately, offer safer, more affordable options for those affected by dengue worldwide.

Conclusion

Yellow onion peels extract (YOP) shows promising potential as a natural option to support platelet recovery in dengue and related conditions.

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