Mechanism of action

Hydroxychloroquine increases[[39]](https://en.wikipedia.org/wiki/Hydroxychloroquine#cite_note-39) lysosomal pH in [antigen-presenting cells](https://en.wikipedia.org/wiki/Antigen-presenting_cell).[[3]](https://en.wikipedia.org/wiki/Hydroxychloroquine#cite_note-Meyerowitz2020-3) In inflammatory conditions, it blocks [toll-like receptors](https://en.wikipedia.org/wiki/Toll-like_receptor) on [plasmacytoid dendritic cells](https://en.wikipedia.org/wiki/Plasmacytoid_dendritic_cell) (PDCs).[[40]](https://en.wikipedia.org/wiki/Hydroxychloroquine#cite_note-40) [Toll-like receptor 9](https://en.wikipedia.org/wiki/TLR9) (TLR 9), which recognizes DNA-containing immune complexes, leads to the production of [interferon](https://en.wikipedia.org/wiki/Interferon) and causes the [dendritic cells](https://en.wikipedia.org/wiki/Dendritic_cell) to mature and present [antigen](https://en.wikipedia.org/wiki/Antigen) to [T cells](https://en.wikipedia.org/wiki/T_cell). Hydroxychloroquine, by decreasing TLR signaling, reduces the activation of dendritic cells and the inflammatory process.[[*medical citation needed*](https://en.wikipedia.org/wiki/Wikipedia%3AIdentifying_reliable_sources_%28medicine%29)]

In 2003, a novel mechanism was described wherein hydroxychloroquine inhibits stimulation of the [toll-like receptor](https://en.wikipedia.org/wiki/Toll-like_receptor) (TLR) 9 family receptors. TLRs are cellular receptors for microbial products that induce inflammatory responses through activation of the [innate immune system](https://en.wikipedia.org/wiki/Innate_immune_system).[[41]](https://en.wikipedia.org/wiki/Hydroxychloroquine#cite_note-41)

As with other [quinoline](https://en.wikipedia.org/wiki/Quinoline) antimalarial drugs, the antimalarial mechanism of action of [quinine](https://en.wikipedia.org/wiki/Quinine) has not been fully resolved. The most accepted model is based on hydrochloroquinine and involves the inhibition of [hemozoin](https://en.wikipedia.org/wiki/Hemozoin) [biocrystallization](https://en.wikipedia.org/wiki/Biocrystallization), which facilitates the aggregation of cytotoxic [heme](https://en.wikipedia.org/wiki/Heme). Free cytotoxic heme accumulates in the parasites, causing death.[[42]](https://en.wikipedia.org/wiki/Hydroxychloroquine#cite_note-Sullivan-42)

Hydroxychloroquine increases the risk of low blood sugar through several mechanisms. These include decreased clearance of the hormone [insulin](https://en.wikipedia.org/wiki/Insulin) from the blood, increased [insulin sensitivity](https://en.wikipedia.org/wiki/Insulin_sensitivity), and increased release of insulin from the [pancreas](https://en.wikipedia.org/wiki/Pancreas).[[4]](https://en.wikipedia.org/wiki/Hydroxychloroquine#cite_note-Juurlink2020-4)

Hydroxychloroquine has been suggested to be a [zinc](https://en.wikipedia.org/wiki/Zinc) [ionophore](https://en.wikipedia.org/wiki/Ionophore), and may derive an anti-cancer action from increasing [intracellular](https://en.wikipedia.org/wiki/Intracellular) zinc uptake.[[43]](https://en.wikipedia.org/wiki/Hydroxychloroquine#cite_note-43)