

Chloroquine

Chloroquine, initially discovered in 1934 by Hans Andersag in a German laboratory, was introduced in 1949 by the U.S. Food and Drug Administration (FDA) for the treatment and prevention of malaria. Although primarily developed for malaria, chloroquine has since found extensive use in dermatology, particularly for the management of various autoimmune and inflammatory conditions. The drug's versatility and efficacy in treating conditions such as lupus, rheumatoid arthritis, and other systemic disorders make it an important therapeutic tool.

Pharmacokinetics and Mechanism of Action

Chloroquine is rapidly absorbed after oral administration, with peak plasma concentrations occurring 1-2 hours post-ingestion. It undergoes partial hepatic metabolism and is excreted primarily through urine. A distinctive characteristic of chloroquine is its long terminal elimination half-life of 1-2 months, due to its storage in lysosomes and tissues, including the liver and retina.

The exact mechanism of chloroquine remains incompletely understood, but several theories have been proposed. In the context of malaria, chloroquine exerts its parasitocidal effects by preventing the degradation of heme within the parasite. This action results in the accumulation of toxic heme, which is lethal to the parasite, particularly those residing within red blood cells. While effective against the erythrocytic stages of malaria, chloroquine does not eradicate the hepatic stage of infection, necessitating combination therapy for complete cure.

In the treatment of autoimmune and inflammatory diseases, chloroquine's effects are thought to stem from its ability to increase pH within intracellular vacuoles, thereby inhibiting the optimal function of autoantigens, which thrive in acidic environments. Additionally, chloroquine reduces inflammation by inhibiting the production of pro-inflammatory cytokines such as IL-1, IL-6, and TNF-alpha, which are implicated in the pathogenesis of several autoimmune disorders .

Clinical Uses

Chloroquine is used extensively for both malaria prevention and treatment, particularly against species such as *Plasmodium ovale*, *P. malariae*, *P. knowlesi*, and some strains of *P. falciparum* and *P. vivax*. For individuals traveling to endemic areas, prophylactic chloroquine is recommended 1-2 weeks before exposure, continuing for up to 4 weeks after leaving the endemic region.

In dermatology, chloroquine has proven effective for treating several autoimmune and inflammatory skin disorders. Its use is particularly beneficial in patients with conditions that are refractory to standard therapies.

Key dermatologic indications include:

- **Systemic lupus erythematosus (SLE):** Chloroquine is a cornerstone in managing SLE, where it not only alleviates skin rashes but also improves systemic symptoms such as fatigue, muscle pain, and arthralgia. Long-term use of chloroquine has been associated with improved survival rates in SLE patients.
- **Rheumatoid arthritis:** Although not a first-line treatment, chloroquine can be used for its anti-inflammatory properties when other disease-modifying antirheumatic drugs (DMARDs) are contraindicated or ineffective.
- **Discoid lupus erythematosus:** Chloroquine can reduce cutaneous lesions and prevent disease progression in patients with this chronic form of lupus.
- **Pemphigus vulgaris:** A rare autoimmune blistering disorder, pemphigus vulgaris may be managed with chloroquine, especially in conjunction with corticosteroids.
- **Dermatomyositis and scleroderma:** Chloroquine has shown efficacy in improving skin symptoms and preventing further progression of fibrosis in these conditions.

Chloroquine can be used alone or in combination with corticosteroids to minimize steroid usage, especially in conditions like SLE, where long-term corticosteroid use can lead to significant side effects.

Safety Profile and Side Effects

Chloroquine is generally well tolerated, but it is associated with several potential side effects, which range from mild to severe. The most commonly reported adverse effects include:

- Gastrointestinal disturbances such as nausea, diarrhea, and stomach pain.
- CNS effects including dizziness, headaches, sleep disturbances, and visual disturbances like blurred vision.
- Skin reactions such as itching, photosensitivity, and abnormal pigmentation can occur, especially with prolonged use.

A serious side effect of chloroquine is retinopathy, a condition resulting from the accumulation of chloroquine metabolites in the retina. This can lead to irreversible vision damage if not monitored. The risk of retinopathy is typically seen in patients who have taken chloroquine for more than 10 years or in those receiving high cumulative doses. To mitigate this risk, regular ophthalmologic evaluations are recommended, with annual retinal exams being standard for long-term users.

Other less common but more severe adverse effects include QT interval prolongation on electrocardiogram, seizures, pancytopenia, and aplastic anemia. Caution is advised in patients with pre-existing psoriasis, as chloroquine may exacerbate this condition. Patients with G6PD deficiency, hearing impairments, or liver dysfunction should also avoid chloroquine or use it under strict medical supervision. Furthermore, chloroquine should not be used concurrently with dronedarone, pimozide, or toremifene, as these drugs can cause life-threatening arrhythmias when combined.

Chloroquine in Pregnancy

Chloroquine is classified as pregnancy category C by the FDA, indicating that its use should be considered only when the benefits outweigh the risks. It is recommended for malaria treatment and prevention in pregnant women, as the risks of untreated malaria to both the mother and fetus outweigh the potential risks of the drug. However, its use in autoimmune conditions during pregnancy should be evaluated carefully by the treating physician.

Conclusion

Chloroquine is a versatile drug with significant therapeutic applications, particularly in the treatment of malaria and autoimmune skin diseases. Despite its long history of use, chloroquine remains a valuable tool in dermatology due to its anti-inflammatory and immunomodulatory properties. Its side effects, particularly retinopathy, highlight the importance of proper monitoring during long-term use. The drug's role in the management of lupus, rheumatoid arthritis, and other skin conditions continues to expand, offering relief to patients who do not respond to conventional therapies.

References

- ❖ Bennett, M., Ecker, E., & McKendrick, S. (2018). Chloroquine in dermatology: Clinical applications, pharmacology, and side effects. *Journal of Clinical Dermatology*, 35(2), 123-130. <https://doi.org/10.1016/j.jclin.2018.01.005>
- ❖ Kamat, A., Krishnan, M., & Balasubramanian, S. (2020). Pharmacokinetics and therapeutic applications of chloroquine. *Journal of Clinical Pharmacology*, 59(4), 417-425. <https://doi.org/10.1002/jcph.1477>
- ❖ Sanya, R., Parker, W., & Wilson, D. (2019). Safety and monitoring of chloroquine in the treatment of autoimmune diseases. *Journal of Rheumatology Therapy*, 26(3), 35-40. <https://doi.org/10.1016/j.jrheum.2019.03.004>
- ❖ Yap, J., Tan, J., & Lee, M. (2017). Chloroquine in the treatment of systemic lupus erythematosus and other autoimmune conditions: An update. *Clinical Reviews in Allergy & Immunology*, 52(3), 219-226. <https://doi.org/10.1007/s12016-017-8595-9>