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**EDITORIAL**

# Clofazimine: what can tuberculosis to teach for leprosy?

## Clofazimina: o que a tuberculose pode ensinar para a hanseníase?

## Clofazimina: ¿que puede enseñar la tuberculosis para la lepra?

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Clofazimine, a riminophenazine dye, synthesized in 1957, as antimicrobial agents, initially was used in the treatment of tuberculosis[1]. The antimycobacterial activity against M. tuberculosis in vitro was very effective. However, experimental studies in mice and as monothaerapy, its activity was considered unsuccessful, for *M. tuberculosis* and *M. leprae*.

In the early 1960s, a preliminary clinical study with only 16 borderline Virchovian patients treated with clofazimine for 6 months was considered satisfactory in terms of clinical improvement and reduction in bacteriological indices, in addition to a synergism in the group of patients who received clofazimine plus dapsone. These effects have also been seen in subsequent studies; so that the WHO, in 1982, recommended its inclusion as one of the components of multidrug therapy for leprosy[2].

The antimicrobial and anti-inflammatory properties of clofazimine have provided considerable benefits to individuals affected by *M. leprae* infection and reduced the manifestations

of erythema nodosum leprosum. These benefits are also observed in infection by *Lacazia loboi*, Jorge Lobo's disease, and other dermatological pathologies of unspecific and/or immune-mediated etiology.

The pharmacological actions of clofazimine are probably due, in part, to its high lipophilic property, which facilitates penetration and deposition in various tissues, especially in macrophages, where *M. leprae* is found. In summary, clofazimine's antimycobacterial activity results from the activation of bacterial phospholipase A2 and the consequent release of lysophospholipids, a toxic product for mycobacteria. Promotes DNA fragmentation during the apoptosis process. It induces the generation of reactive oxygen species (ROS), which competes with menaquinone, by transferring electrons in the respiratory chain, reducing the production of ATP, which corroborates the antimicrobial activity.[3-6]

The absorption of CFZ in the digestive system rate from 45 to 70%, and it can be increased if administered with a meal rich in fats and proteins. Its lipophilic character determines high affinity for tissues rich in fat, macrophages, breast milk and most other biological compartments. The tissue half-life of a single dose is around 10 days and multiple doses are estimated at 25 to 90 days; it is eliminated predominantly by biliary route, in feces and small amounts are excreted by the sebaceous, sweat and mammary glands.[7] The most common adverse effects are the reddish skin and secretions; deposition in the cornea and lens, requiring ophthalmological monitoring.[8]

Considering that the tuberculosis and leprosy are two diseases that provide bilateral teachings and learning, that is, a certain "symbiosis", the text on screen was nourished by knowledge related to clofazimine in the context of tuberculosis. The reasons for this fact are some of the biological characteristics of *M. tuberculosis*, which, as it rapidly multiplies in vitro help the development experimental in mice, which is not fast with *M. leprae*, because it is not cultivated and only multiplies in some animal model, and even then, very slowly, which constitutes a limiting factor for pharmacological studies.

Both diseases are considered a major public health problem and control and elimination measures have not achieved the proposed goals. Pharmacological therapy has not been successful and, consequently, many cases of multiple resistance to multidrug therapy have been occurring in tuberculosis and leprosy. However, in tuberculosis the severity is more impactful due to the speed of evolution of the disease.

The pharmacotherapeutic resources is limited in both cases. Howev-

er, in this regard, tuberculosis has fostered greater boldness to evaluate new protocols using old drugs, in particular clofazimine. The results show that the association of clofazimine with classic antituberculosis chemotherapy induces a synergism in the bactericidal and sterilizing action on *M. tuberculosis* inoculated in mice,[4-5] which could constitute a promising and motivating perspective for the investigation of new protocols with this drug in therapy tuberculosis and leprosy.

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