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Drug development for cutaneous leishmaniasis: on the importance of relating anti-parasitic efficacy to skin pharmacokinetics

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Today, a small arsenal of drugs is available for the treatment of the parasitic skin infection cutaneous leishmaniasis (CL), but the unmet medical need for this disease of poverty remains high. While there has been recent progress in the discovery and development of new drugs for visceral leishmaniasis, the search for new drugs to cure CL remains a neglected area. One aspect of the problem is the vast challenges that the complex biology of CL poses to effective pharmacology: from drug penetration into the infected dermal skin tissue and macrophage host cells, to exerting activity against the plethora of pathogenic *Leishmania* parasite species. Taking the evaluation of a number of new drug candidates as an example, we will present a strategy to take compounds across the drug development pipeline from hit identification to preclinical development. We will focus in particular on the PK/PD relation between skin pharmacokinetics (tissue homogenates, microdialysis) and antileishmanial pharmacodynamics (qPCR, in vivo imaging). With this approach, we aim to develop new oral or topical treatments for CL that are safe, effective, affordable and patient-friendly.

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