PHARMACOLOGICAL PROSPECTING OF THERMORECEPTORS IN *LEISHMANIA* SPP.

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Leishmania spp. are dimorphic parasites with a heteroxenic life cycle. In the invertebrate host, the promastigote form resides in the vector's digestive tract, where the pH varies from neutral to slightly acidic, and the temperature is around 26°C. Upon infecting the vertebrate host, the parasite encounters an acidic pH in the parasitophorous vacuole and a temperature of 35–37°C. Both forms have evolved to survive within these environments. In mammals, Transient Receptor Potential (TRP) channels detect environmental stimuli, including temperature changes. This study aims to functionally characterize the receptor used by *Leishmania* spp. to sense temperature fluctuations and trigger differentiation between promastigote and amastigote forms. We performed phenotypic screening using TRPV1 and TRPM8 receptor agonists and antagonists to "mimic temperature," assess morphological changes, and determine IC_{50} values. The key compounds and their IC_{50} values for promastigotes of *L. amazonensis* and *L. infantum* were: olvanil (>128 and 15.23 µM), capsazepine (22.9 and 43.37 µM), AMTB (6.64 and 15.28 µM), M8-B (21.15 and 19.38 µM), and icilin (15.97 and 53.30 µM). In initial scanning microscopy assays, *L. infantum* promastigotes treated with icilin (128 µM) displayed morphological changes similar to axenic amastigotes. Since icilin is a cold-sensitive channel agonist, we further examined the effects of low temperatures. After 72 hours at 16°C, promastigotes adopted a rounded morphology, distinct from their elongated shape at 26°C. These findings suggest that both icilin and cold conditions act as environmental stressors, triggering adaptive responses in promastigotes. Although preliminary, our results also indicate the possible presence of temperature receptors in Leishmania spp.

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