

## Heme-induced anti-leishmanial activity in the sand fly model *Lutzomyia longipalpis*

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**Introduction:** A successful *Leishmania* colonization of the sand fly midgut is dependent on several aspects such as physiological, physical and microbiological factors. The protozoa *Leishmania* needs to overcome initially the action of digestive enzymes. The peritrophic matrix (PM) is a semi-permeable structure that encases the food bolus. This PM plays important roles such as compartmentalizes the digestive process and also protects the gut wall from the direct contact of food-derived molecules and potential pathogens. **Objectives:** The aim of this work is to investigate the effect of heme on ROS production and *Leishmania mexicana* survival in the midgut of *L. longipalpis*. **Material and Methods:** The sand flies were fed on sheep blood or phosphate buffer agarose solution with or without heme through chicken skin using an artificial feeder. In order to disrupt PM formation, we fed sand flies sheep blood supplemented with 1µg/mL chitinase. Amplex red Kit was used to quantify hydrogen peroxide. Sand flies were also fed either on blood or plasma, with and without heme, seeded with  $2 \times 10^6$  amastigotes/mL. Parasites were counted 6 days post-infection in a hemocytometer. **Results and Discussion:** The number of total *L. mexicana* was reduced in the midgut of chitinase treated sand flies. However, when sand flies were fed *ad libitum* from emergence on uric acid-containing 70% sucrose prior infection, the total number of parasites was rescued to levels similar to control. Heme led to an increase of hydrogen peroxide concentration in the midgut. When flies were fed on plasma seeded with amastigotes *L. mexicana*, the addition of heme caused a reduction of the total number of parasites per midgut. **Conclusions:** Heme can induce ROS production when in contact with the gut wall, what is dangerous to the parasites. The PM protects the parasites against the attack of ROS during the initial stage of blood digestion.

Keywords: *Lutzomyia longipalpis*, *Leishmania Mexicana*, heme, hydrogen peroxide

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