RESUMO SIMPLES - PROTOZOÁRIOS E AGENTES TRANSMITIDOS POR VETORES DE IMPORTÂNCIA EM SAÚDE

# THE IMMUNOMODULATORY EFFECT OF STOMOXYS CALCITRANS (L.) SALIVA

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Both male and female Stomoxys calcitrans (L.), popularly known as the stable fly, are hematophagous. The fly is considered of great veterinary importance, and although it is most active around cattle farms, it can also be found in residential areas near agricultural production. The fly's painful bite causes stress to animals and may lead to weight loss and decreased dairy and meat production, resulting in negative livestock economic impacts. During blood feeding, the insect can mechanically transmit several pathogens to the host causing further losses. The saliva of hematophagous insects contains various pharmacologically active molecules that facilitate feeding and can also affect pathogen infection through immunomodulatory effects on their hosts. This immunomodulatory potential may influence different cells of the immune system, including macrophages, which have the capacity to secrete large amounts of cytokines and pro-inflammatory mediators. The genus Herpetomonas is a monophyletic group with representatives on almost all

continents and is associated with many individuals from different insect classes, such as Diptera, Hemiptera, Hymenoptera, and Siphonaptera. Recently, the species H. muscarum was isolated from S. calcitrans for the first time by our group. Leishmaniases comprise a group of diseases with distinct clinical manifestations depending on the parasite species (cutaneous, diffuse cutaneous, mucocutaneous, and visceral leishmaniasis). These diseases remain on the World Health Organization's list of neglected tropical diseases. Brazil, where leishmaniases have a high incidence, is among the 10 countries with the highest number of cutaneous leishmaniasis cases and among the 6 with the highest incidence of visceral leishmaniasis in the world. Visceral leishmaniasis, also known as kala-azar, is a systemic and chronic disease. In Brazil, it is caused by Leishmania infantum and transmitted by phlebotomine sandfly vectors. Humans are accidental hosts of the disease, contracting it when they come into contact with its transmission cycle. VL is a zoonotic disease known to affect various animal species, such as marsupials, rodents, edentates, and canids, with dogs being the main reservoir and source of human infection in urban areas. Given this context, the present study aims to analyze the immunomodulatory effect of the salivary gland extract of S. calcitrans on promastigote forms of L. infantum and opistomastigote forms of H. muscarum, as well as to assess the cytotoxicity of the salivary gland extract toward macrophages, the host cells of L. infantum using a colorimetric assay. We also intend to elucidate the possible mechanisms of action of the salivary gland extract through the production of nitric oxide, reactive oxygen species, cytokine production, flow cytometry, and evaluation of the parasitic load in macrophages infected with L. infantum in the presence and absence of fly saliva. Preliminary results demonstrated that the salivary gland extract of S. calcitrans is not cytotoxic to macrophages. The saliva showed no significant effect on binding or phagocytosis in macrophages infected with L. infantum, although an increase in NO was observed in macrophages previously treated with saliva, whether stimulated with IFN and LPS or not. When assessing the direct effect of the extract on L. infantum promastigotes and H. muscarum opistomastigotes, increased proliferation of H. muscarum and a lower survival rate of L. infantum were observed compared to untreated controls. Infection of macrophages with L. infantum will soon be carried out to evaluate the remaining parameters. Our data suggest that S. calcitrans saliva plays an important role in the parasitic control of L. infantum and in the establishment of H. muscarum in the fly.

Palavras-chave: vector insects; immune system; macrophages.