Thymus vulgaris L. (thyme) extract helps murine macrophages (RAW 264.7) to eliminate *Staphylococcus aureus* during *in vitro* infection

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Introduction: Bacteria have several mechanisms to overcome the host's defense barriers, invade the organism, and proliferate in the target tissue. Some can opportunely cause infections such as S. aureus (Sa), a bacterium from the human microbiota which is related to high rates of systemic infection and mortality, mainly due to accumulations in medical devices. In addition, it is essential finding integrative and complementary ways to help the defense cells to fight pathogens, such as the use of plant products. Thus, in this study, the effect of thyme extract (TE) was evaluated on the interaction of RAW 264.7 with Sa in an in vitro infection model. Material and Methods: The minimum inhibitory concentration (MIC) of TE was determined by microdilution in broth. RAW 264.7 was cultured (37 °C; 5% CO₂; 24 h) in 24-well plates and challenged with Sa suspension (MOI of 1:5) containing TE, 1% penicillin-streptomycin (PS) or DMEM (n = 6/group). After 30 min, the phagocytosis was paralyzed using ice-cold PBS, which was also used to discard non-phagocyted bacteria. The macrophages were lysed with sterile distilled water and the supernatant was added on BHI agar. After 24 h of incubation, the concentration of colony forming units per milliliter (CFU/mL) was determined. The results were analyzed by ANOVA and Tukey's test ($P \le 0.05$). Discussion of Results: A MIC of 100 mg/mL of TE was able to promote a significant Sa reduction of $43 \pm 9\%$. In contrast, PS provided a reduction of $78 \pm 3\%$. However, both products acted effectively in the control of the infection, when compared with the DMEM group (P < 0.05). Thus, it was evidenced that the natural product contributed effectively to eliminate bacteria internalized by macrophages. The plant extract showed an effective biological activity of destruction of bacteria that can survive inside macrophages. It is known that there are strains of Sa able to neutralize the enzymatic action of phagolysosomes and live protected in the cytoplasm of the infected cell. In addition, some strains can also evade phagocytosis. Conclusion: Thyme extract helped RAW 264.7 to eliminate S. aureus during in vitro infection. With this, it could be used in an integrative and complementary way to control infections caused by this bacterium.

Keywords: Host-pathogen interaction; Macrophages; RAW 264.7; *Staphylococcus aureus*; *Thymus vulgaris* L.

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