

TITLE: ANTIMICROBIAL AND IMMUNOMODULATOR ACTIVITY OF *AGARICUS BRASILIENSIS* IN MURINE MODEL OF SEPSIS.

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ABSTRACT:

Sepsis is an organ dysfunction caused by a dysregulated immune response to an infection. In the initial therapeutic approach of sepsis, broad-spectrum antimicrobials are used, which are not sufficient to control infection, and associations with other therapies are necessary. Thus, the search for new therapies that aim to improve the immune response and reduce the burden of the pathogen is necessary. The mushroom *Agaricus brasiliensis* is rich in polysaccharides that have immunomodulatory and anti-inflammatory properties. Thus, the present study aimed to evaluate its antimicrobial and immunomodulatory effect in a murine sepsis model. Male Swiss mice weighing 20 to 30 g were divided into four groups, in which three groups were pre-treated orally with *A. brasiliensis* aqueous extract (135 mg/kg) or 0.9% saline and other group intraperitoneally with Ceftriaxone (20mg/kg) and had sepsis induced by cecal ligation puncture procedure (CLP) and the fourth group had a surgical procedure without CLP induction (Sham). The animals were euthanized after 12 and 24 hours and the samples were collected for evaluation of leukocyte migration and bacterial load. In the survival tests, after induction of CLP, the animals were observed for 16 days every 12 hours, recording the weights and date of death. All procedures were approved by the Ethics Committee on the Use of Animals (CEUA/UFPA - no 02/15). In the survival test, saline-treated animals died between days 5 and 6 and those treated with ceftriaxone between days 6 and 7, whereas those treated with *A. brasiliensis* survived to 16th day. Regarding leukocyte migration, treatment with *A. brasiliensis* in animals with sepsis inhibited leukocyte migration in the peritoneal lavage induced by bacterial infection. The fact that *A. brasiliensis* reduces leukocyte migration may be important during the initial sepsis, since the proinflammatory response is initially dominant, and the excess neutrophil infiltration may lead to the exacerbated production of pro-inflammatory mediators. The bacterial load of the *A. brasiliensis* group at the inflammatory site compared to the group pretreated with saline was reduced, and with 24 hours after CLP it was not possible to detect the presence of bacteria, and in the other tissues there was a significant decrease. The aqueous extract of *A. brasiliensis* was shown to be promising as adjunctive therapy in sepsis due to its high antimicrobial and anti-inflammatory activity in vivo.

Keywords: Sepsis, *Agaricus brasiliensis*, Antimicrobial

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