

TITLE: ANTIMICROBIAL AND ANTIOXIDANT ACTIVITY OF *ILEX PARAGUARIENSIS* IN MURINE MODEL OF SEPSIS.

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ABSTRACT:

Sepsis is an organ dysfunction caused by a dysregulated immune response from the host to an infection. During the therapeutic approach to sepsis, antimicrobials are used that are not sufficient to control infection, and associations with other therapies are necessary. *Ilex paraguariensis* is described as a potent antimicrobial and antioxidant. Thus, this work aimed to evaluate the antimicrobial and antioxidant effect of *Ilex paraguariensis* 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 *I. paraguariensis* (22,2 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 bacterial load, production of nitric oxide (NO), malonaldehyde (MDA), total antioxidant capacity (TEAC) and in ex vivo was evaluated phagocytic capacity and EROs by DCFH. To evaluate survival, the animals were observed for 16 days. 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 by day 6 and those with *I. paraguariensis* survived by the 16th day. Animals with sepsis present high bacterial load on the peritoneum, whereas animals that were pre-treated with *I. paraguariensis* had a reduction in the tissues evaluated. Regarding NO production, the septic animals that were pretreated with *I. paraguariensis* were observed the reduction of NO in the peritoneum. In relation to the release of ROS, the septic mice pretreated with the extract presented similar levels to the sham group, and in the presence of tBHP, *I. paraguariensis* was also able to inhibit the release of ROS induced by the stimulus, confirming the antioxidant activity of *I. paraguariensis*. In addition the animals presented high antioxidant levels in the peritoneal lavage and reduced MDA. The phagocytic capacity of the extract group was high, which may have contributed to the increase in survival of the animals and reduction of bacterial load. *I. paraguariensis* was shown to be promising as adjunctive therapy in sepsis, due to its high antimicrobial and antioxidant activity in the CLP sepsis model.

Keywords: Sepsis, *Ilex paraguariensis*, Antimicrobial, Antioxidant.

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