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Treatment strategy by lactoperoxidase and lactoferrin combination:
Immunomodulatory and antibacterial activity against multidrug-resistant *Acinetobacter baumannii*

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Treatment Strategy by Lactoperoxidase and Lactoferrin Combination: Immunomodulatory and Antibacterial Activity against Multidrug-Resistant *Acinetobacter baumannii*

Abstract

Lactoperoxidase (Lpo) and Lactoferrin (Lf) were extracted from camel colostrum milk and purified. The antibacterial activity of the two purified proteins was estimated against 14 isolates of multidrug resistance *Acinetobacter baumannii*. A combination of Lpo and Lf exhibited bactericidal action against *A. baumannii in vitro*. A mouse model of acute *A. baumannii* pneumonia was improved. The injection of combined Lpo and Lf after infection leads to significant clearance of *A. baumannii* rates in lung as well as blood culture $P < 0.05$ in comparing with control. Furthermore, the results showed a significant $P < 0.05$ reduction in the Bronchoalveolar lavage albumin concentration, lung injury and lactate dehydrogenase activity in comparing with control. In addition, the combination of Lpo and Lf treatment induced substantial elevation of IL-4 and IL10 concentrations $p < 0.05$ that helped to prevent damage caused by the inflammatory response. We concluded that combination of Lpo and Lf had a major inhibition effect against *A. baumannii* in comparing with imipenem as well as their immunomodulatory activity against resistant *A. baumannii* was increased by a synergistic effect of them as a crude combination. This study indicated two combined proteins consider as crucial strategy for practical treatment of pneumonia in the future.

Key words: Lactoperoxidase, lactoferrin, *A. baumannii*, Immunomodulation.

Introduction

A. baumannii is known for heavy nosocomial and community-acquired pneumonia, difficult-to-treat hence, its produce infections which are the consequence of a common propagation of strains in hospitals and their enhancing resistance to antibiotics [1]. Colostrum, the chief milk component created by the mammary glands of mammals after childbirth, include elements with immunomodulatory, these elements have attracted the interest of some medical and food manufacture as a dietary complements [2]. Lactoperoxidase is an effective antimicrobial agent and important enzyme in many industrial applications. This enzyme LPO E.C. 1.11.1.7 is a glycoprotein produced in human and other mammalian milk, as a natural antimicrobial factor and function as a significant part in the innate immune system by killing bacteria in milk. Lactoferrin is known an iron-binding protein with molecular weight of 80 KDa, present in mammalian milk and liberation the potent antimicrobial peptide lactoferricin (LFcin) by hydrolysis with pepsin [3,4]. In an investigation for new antibacterial drugs, Lf displays a novel source with a powerful medical implementation by targeting several mechanisms of resistance, integration treatment might assistance slow the evolution of impedance. Moreover it has been proposed that any cooperation between these treatments and the immune restraint must be utilized in the therapy of bacterial contagions [4]. Lactoferrin and other human peptides are considered to participate in protection or repair of damages in the immune system by promoting the immune response, Some immunomodulators, can be nonspecific to certain pathogens such as cytokines and antimicrobial peptides which used to produce a favorable host immune response[5,6]. There are new perspectives in the conception of the mechanisms implied the several functions of Lf. LPO provides a future view on its powerful prophylactic and remedial applications[2,7]. Consequently, industrial applications of lactoperoxidase are being found in canning food, beauty products, and optic solutions, wound healing and LPO removal from whey or milk is based on the well-developed manufacturing revolutions [7]. Thus this study aimed to extract and purify Lactoperoxidase and lactoferrin from camel colostrum milk to study the antimicrobial activity of them *in vitro* and *in vivo* against clinically important antibiotic resistant bacteria of *A. baumannii* to find alternative treatment for its infections like pneumonia.

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