



Bovine Lactoferrin and Lactoferrin-Derived Peptides Inhibit the Growth of *Vibrio cholerae* and Other *Vibrio* species

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Vibrio is a genus of Gram-negative bacteria, some of which can cause serious infectious diseases. *Vibrio* infections are associated with the consumption of contaminated food and classified in *Vibrio cholera* infections and non-*cholera Vibrio* infections. In the present study, we investigate whether bovine lactoferrin (bLF) and several synthetic peptides corresponding to bLF sequences, are able to inhibit the growth or have bactericidal effect against *V. cholerae* and other *Vibrio* species. The antibacterial activity of LF and LF-peptides was assessed by kinetics of growth or determination of colony forming unit in bacteria treated with the peptides and antibiotics. To get insight in the mode of action, the interaction between bLF and bLF-peptides (coupled to FITC) and *V. cholera* was evaluated. The damage of effector-induced bacterial membrane permeability was measured by inclusion of the fluorescent dye propidium iodide using flow cytometry, whereas the bacterial ultrastructural damage in bacteria treated was observed by transmission electron microscopy. The results showed that bLF and LFchimera inhibited the growth of the *V. cholerae* strains; LFchimera permeabilized the bacteria which membranes were seriously damaged. Assays with a multidrug-resistant strain of *Vibrio* species indicated that combination of sub-lethal doses of LFchimera with ampicillin or tetracycline strongly reduced the concentration of the antibiotics to reach 95% growth inhibition. Furthermore, LFchimera were effective to inhibit the *V. cholerae* counts and damage due to this bacterium in a model mice. These data suggest that LFchimera and bLF are potential candidates to combat the *V. cholerae* and other multidrug resistant *Vibrio* species.

Keywords: lactoferrin, lactoferrin peptides, LFchimera, bactericide, *Vibrio cholerae*