INDIAN INSTITUTE OF TECHNOLOGY GUWAHATI
SHORT ABSTRACT OF THESIS

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SHORT ABSTRACT

Bacterial infections in the gastrointestinal tract is a critical healthcare issue. In this context, the use of antibiotic-mediated therapy to achieve pathogen clearance from the gastrointestinal milieu is counterproductive since, beneficial gut microbes are likely to be abrogated by collateral damage rendered by therapeutic antibiotics. This fact reinforces the need to develop a radical therapeutic intervention that can selectively target gut pathogens. The present investigation reports the potential of native isolates of lactic acid bacteria (LAB) and its secreted metabolite, bacteriocin, as antibacterial agents for selectively targeting gastrointestinal pathogens. Initial *in vitro* assays on bacteriocin-producing LAB isolated from *dahi*, dried fish and salt-fermented cucumber indicated that *Lactobacillus plantarum* CRA21, CRA38, CRA52 and DF9 displayed characteristic probiotic attributes. Fluorescence-based *in vitro* adhesion assays indicated that *L. plantarum* CRA21, CRA38 and CRA52 displayed high *in vitro* adhesion to extracellular matrix (ECM) proteins collagen and mucin, while adhesion inhibition assays suggested that the highest inhibition of *Listeria monocytogenes* Scott A, *Enterococcus faecalis* and *Staphylococcus aureus* adhesion onto ECM by bacteriocin-producing *L. plantarum* strains was observed in the exclusion mode. Exposure of ECM-adhered pathogens to plantaricin A extract from *L. plantarum* strains also rendered reduction in viability of the pathogens. A dual label flow cytometry (FCM)-based host cell adhesion assay indicated that *L. plantarum* DF9 could impede *E. faecalis* MTCC 439 adhesion onto HT-29 cells, a model intestinal cell. Estimation of the adhesion process parameters in conjunction with a principal component analysis provided a means to screen and select LAB strains that may hold potential in anti-adhesion therapy. Interestingly, bacteriocins from LAB could selectively abrogate adhered cells of *E. faecalis* MTCC 439 and had no effect on adhered *L. plantarum* DF9, unlike antibiotic exposure, which led to a profound elimination of adhered *L. plantarum* DF9. In order to hinder proteolytic inactivation of bacteriocin by enzymes present in the gastrointestinal milieu, a novel milk protein nanoparticle (MNP) was generated by desolvation of the decaseinated fraction of milk. Mechanistic studies indicated that the decaseinated milk protein extract (MPE) as well as MNP had a strong proclivity to interact and inhibit pepsin, present in simulated gastric fluid (SGF). Interestingly, pediocin-loaded milk protein nanocomposite (Ped-MNC) demonstrated significant retention of bacteriocin activity in SGF and could also render notable elimination of model gastrointestinal pathogens in a simulated gastric transit experiment. Combinatorial deployment of Ped-MNC and *L. plantarum* DF9 led to a heightened decline in the population of *E. faecalis* MTCC 439 adhering onto HT-29 cells, in contrast to that observed for *L. plantarum* DF9 or Ped-MNC alone. It can be envisaged that the present study, which describes the potential of LAB and bacteriocin-loaded nanomaterial, can serve as a promising avenue for development of niche specific therapy for selective mitigation of gastrointestinal pathogens.