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Anti-microbial therapeutic potential of encapsulated Fe-saturated lactoferrin on alginate gel-encapsulated ceramic nanocarriers (ACN's)

Jagat R. Kanwar[1], Isha Gupta[1], Rupinder K. Kanwar[1], Kusum Joshi[2] and Rakesh Sehgal[2]
[1]Nanomedicine-Laboratory of Immunology and Molecular Biomedical Research (NLIMBR), Deakin University, Australia
[2]Postgraduate Institute of Medical Education and Research (PGIMER), India

We studied the antimicrobial activity of various forms of Australian bovine Lf (bLf) against some pathogenic gram negative bacteria *Eschirichia coli* (*MTCC 729*), *Shigella flexneri* (MTCC 1457) & *Shigella dysenteriae*, *Salmonella typhimurium* (wild strain) *in vitro*); a gram positive bacteria *Staphylococcus aureus* (MTCC 737) and encapsulated bovine Fe-Lf^{+} on alginate gel-encapsulated ceramic nanocarriers (ACN's) *in vivo* on the bacteria *Salmonella typhimurium* (wild strain). Multiple *in vitro* and animal studies have shown a protective effect of lactoferrin on infections with enteric microorganisms, including rotavirus, *Giardia, Shigella*, *Salmonella* and the diarrheagenic *Escherichia coli*.

Our aim was to develop combination nanotherapeutic strategies for drug delivery to provide more potent & targeted therapeutic especially against *Salmonella typhimurium*, bacteria mainly responsible for causing enteric fever, gastroenteritis, septicemia, with/without focal suppuration in humans. Food-borne bacterial infections caused by Salmonella remain a serious threat to human health in both developing and industrialized countries. *Salmonella* infections cause an estimated 1.4 million human illnesses and 400 deaths annually in the United States. In 2007, there were 9,484 cases of *Salmonella* infection, a rate of 45 cases per 100,000 population, which is a 15% increase over the mean of the previous 5 years. In 2007, the most commonly notified *Salmonella* serotype was *S. Typhimurium*. Due to emerging resistance of bacterial strains to the existing antibiotics or multi drug resistance (MDR) and chronic toxicity associated with them, the search for alternative chemotherapeutic agents against bacteria is the need of the hour.

Our results for bLf in bacteria *in vitro* showed that this protein can be either microbicidal or used as an iron source for growth, depending on the Lf saturation. Experimentally it was also observed that oral feeding of nanoformulated Lf diet to BALB/c mice, 3 days after challenge with *Salmonella typhimurium* (200µl of 10^8 CFU/ml suspension) was efficient in eliminating the infection from mice within 2 days of treatment/ 6 days post infection, reducing the duration of the disease preventing the *Salmonella* -infected phagocytes to gain access to the lymphatics and bloodstream and spread to the liver and the spleen. Same results were observed in the mice fed with bLf alone 3 days post infection with the bacteria where mice became pathogen free within 2 days of treatment/ 6 days post infection. While chronic infection developed in the infected group of mice which didn't receive any drug treatment and the mice treated with Ciprofloxacin as persistence of bacteria was observed in the sera, small intestine, liver, spleen and their mesenteric lymph nodes, continued till 20 days post infection after which the infection almost resolved in all the groups of mice. Histological examination and ultrastructural studies by Transmission Electron microscopy showed the recovery of pathological profile of mice, further confirming the protection of mice dosed with nanoformulated Lf diet and bLf after being infected with *Salmonella typhimurium* after 3 days and receiving various treatments thereafter. The study concludes that bovine lactoferrin and nanoformulated Fe-Lf^{+} are more effective in the treatment than that of ciprofloxacin dose used in this trial in the animals too.

Biography

Jagat Kanwar is an Immunologist and molecular biochemist. He is group leader of the Laboratory of Immunology and Molecular Biomedical Research has an international reputation in investigating fundamental and applied molecular aspects of cancer and chronic inflammation. He has extensive training and expertise in studying the molecular mechanisms and devising treatments for human diseases like cancer and chronic inflammatory diseases such as asthma, atherosclerosis, inflammatory bowel disease (IBD), arthritis and multiple sclerosis in both *in vivo* and *in vitro* models. The research approach employed monotherapy (gene therapy, immunotherapy) or combinational therapy with commercially available chemotherapeutic agents including peptides.

jagat.kanwar@deakin.edu.au