Liposome nanoencapsulation can increase efficacy of bacteriophages in oral phage therapy

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Scientists at the Universitat Autònoma de Barcelona (UAB) and the Catalan Institute for Nanoscience and Nanotechnology (ICN2) have developed a nanoencapsulation system with a liposome coating in order to increase the efficacy of bacteriophages in oral phage therapy. The research demonstrated that a liposome nanoencapsulation provides the bacteriophage with greater resistance to stomach acids and increases residence time in the intestinal tract of model broiler chickens in simulated poultry farming conditions. The technology developed could be applied to bacteriophages with different morphologies to be used in phage therapy, in both animals and humans.

The efficacy of encapsulated bacteriophages has been tested with animals treated with specific bacteriophages to fight against the zoonotic bacteria Salmonella. The results demonstrated a significant reduction in the concentration of Salmonella in the intestinal tract and prolonged effects when the treatment was administered using encapsulated bacteriophages, in comparison to the effects of nonencapsulated phages.

Oral phage therapy has demonstrated to be a feasible and effective tool in the control of infections caused by different bacterial pathogens. In previous studies, the UAB Molecular Microbiology Group had published the isolation and characterisation of three virulent bacteriophages (UAB_Phi20, UAB_Phi78, and UAB_Phi87) specific to Salmonella, and demonstrated their efficacy in the reduction of the concentration of this zoonotic bacteria in models of specific pathogen-free (SPF) White Leghorn chickens, and in several experimentally contaminated food matrices. Nevertheless, in this research two limitations were observed in the use of orally administered bacteriophages: the reduced stability of the phages in extremely acid environments, such as the stomach, and short residence time in the intestinal tract.

To overcome these limitations, researchers developed a nanoencapsulation system using liposome capsules and applied them to the three aforementioned virulent bacteriophages in order to compare the effects of liposome-encapsulated phages and nonencapsulated phages on the concentration of Salmonella in model broiler chickens experimentally contaminated with the bacteria. The experiment was conducted at the UAB Farms and Experimental Fields Services, with all the conditions of a real poultry farm.

Thanks to the study, nanometric capsules were developed, with an average diameter of 320 nm and a positive charge of 33mV. The nanocapsules containing the bacteriophages were observed using a cryo-electron microscope (Cryo-TEM) and confocal microscope. Researchers observed how the liposome coating allowed the encapsulated bacteriophages to be significantly more stable in the gastric fluids. The coating also significantly improved the time the bacteriophages stayed inside the intestinal tract of the chickens. After 72 hours encapsulated bacteriophages were detected in 38.1% of animals, while only 9.5% of animals showed signs of still containing the nonencapsulated bacteriophages.

In oral therapy experiments, once the treatment was suspended, the protection provided by nonencapsulated bacteriophages disappeared, while the encapsulated ones were effective for at least another week.

The methodology developed allows encapsulating bacteriophages of different sizes and morphologies, demonstrates the advantages of using encapsulated bacteriophages for oral phage therapy and, moreover, the nanometric size allows adding it to potable water and fodder.

Source:
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