Biocontrol of *Salmonella* in the food industry using phage therapy

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BACKGROUND

Food is an essential requirement of everyday life, but occasionally, contamination with pathogenic bacteria can result in illness and even death. According to the European Food Safety Authority (EFSA), food-borne illnesses are one of the leading causes of morbidity and mortality in the world, and it was estimated that approximately one third of the population may be affected by such diseases in developed countries every year.

Ensuring food safety involves a wide range of microbial control measures applied to relevant steps in the food chain. Currently, the most effective means to limit microbial growth are good hygiene in the production and proper use of biocides and disinfectants. However, these treatments are inefficient and can produce organoleptic variations or the possibility of leaving toxic waste. Consequently, the development of effective and safe natural methods has been an interesting topic during the last years. Phage therapy emerges as one of the solutions becoming a good approach to reduce the incidence of food-borne diseases.

PHAGE THERAPY

Historically, phage therapy arose to control resistant bacteria because of the widespread problem of antibiotic resistance coupled with the paucity of new antibacterial drugs. Even so, the interest has been renewed for the control of bacteria in other areas, including food.

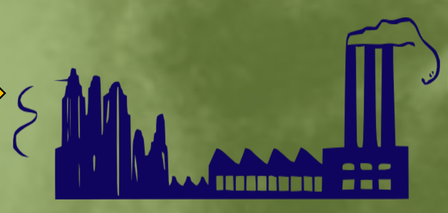
Advantages and disadvantages of phage therapy

Advantages	Disadvantages
Highly specific, rapid bacterial killing, ability to self-replicate and natural.	Narrow host range. Mixture (cocktail) usually required.
Minimal disruption to regular microbiota.	Knowledge of biology often required.
Does not affect organolpetic properties.	Negative consumer perception.
Abundant in natural environments.	
Effective in biofilms.	

BACTERIOPHAGES IN FOOD INDUSTRY

The use of bacteriophages to promote food safety can be mainly done at three different stages along the food chain.

To reduce pathogen colonization in animals during **primary production.**



Disinfection of food contact surfaces and equipments.

Directly in **postharvest food**, such as meat carcasses, fresh fruit, vegetables and processed ready-to-eat (RTE) foods.

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BIOCONTROL OF *Salmonella*

In the European Union, salmonellosis is the second reported zoonotic disease in humans. Although the numbers of reported outbreaks caused by vegetables and products has increased, poultry and derivates are still the common sources of *Salmonella*. The following table shows several studies concerning phage therapy against *Salmonella*.

Biocontrol of Salmonella in primary production

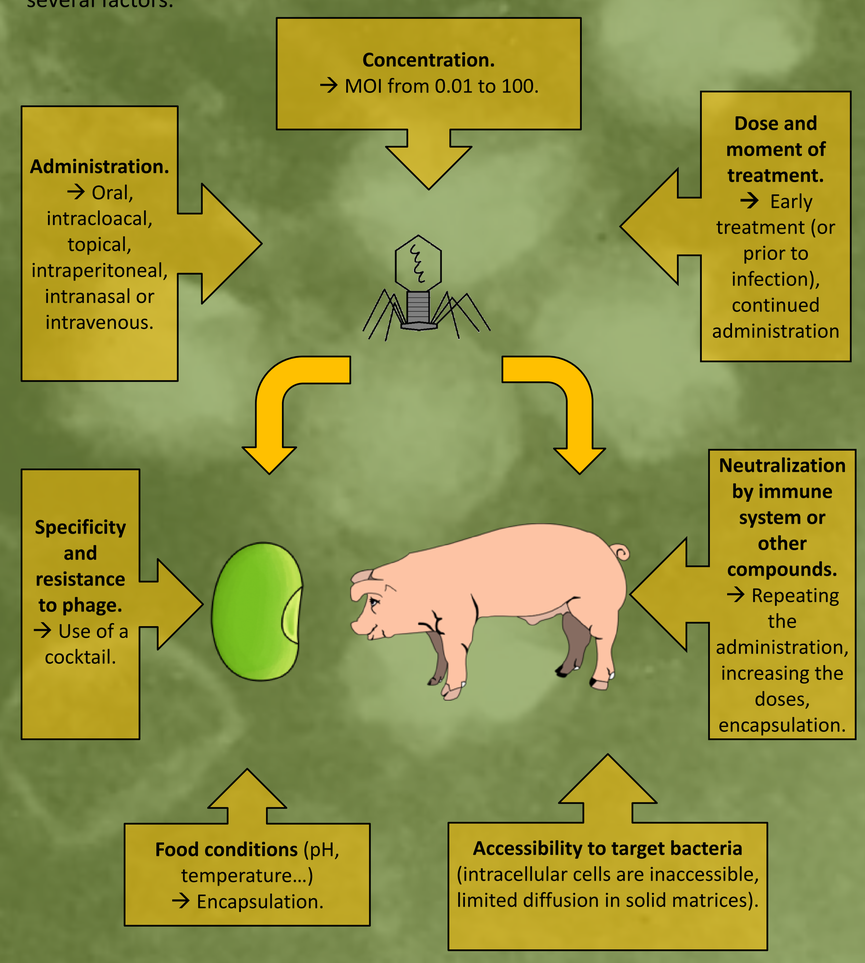
Year	Product	Phage(s)	Strategy	Conclusions
2007	Poultry	ϕ151, ϕ25, ϕ10	Oral delivery	Reduction of CFU with phages ϕ151 and ϕ10, not observed with ϕ25. Significant numbers of phages are required to adsorb to individual host cells. Importance of accessible receptors on cell surface to allow adsorption.
2007	Poultry	CB4ϕ, WT45ϕ (cocktail)	Oral delivery	Significant reduction at 24h, not at 48h. Emergence of resistant cells.
2012	Poultry	UAB_Phi20, UAB_Phi78, UAB_Phi87(cocktail)	Oral delivery	Importance of administering the phage prior to infection and continued administration to achieve significant protection.
2012	Poultry	ϕCJ07	Oral delivery (via feed)	CFU reduction in uninfected chickens. ΦCJ07 to prevent cross contamination in poultry.
2013	Poultry	ϕst1	Intracloacal delivery	*Salmonella* was not detected at and after 24h. Intracloacal administration avoids contact with stomach.
2013	Poultry (eggs)	F1O55S, F12013S (cocktail)	Spray delivery	F1O55S and F12013S reduce *Salmonella* horizontal transmission during egg incubation.
2011	Swine	Phage cocktail	Oral delivery	Reduction of *Salmonella* within 96h. Bacteriophages can reduce *Salmonella* in swine.

Biocontrol of *Salmonella* in postharvest food

Year	Product	Phage(s)	Strategy	Conclusions
2003	Chicken skin	P22, 29C	Applied on top	MOI (multiplicity of infection) 100-1000 caused more reduction than MOI 1 and eradicated resistant strains.
2001	Fresh-cut fruit	Phage cocktail	Added to foods	Significant CFU reduction on melon but not on apple. pH of apples inactive bacteriophages.
2004	Sprouting seeds	Phage cocktail	Applied by immersion	Significant reduction. It is important to develop phage cocktails to control a wide range of contaminants.
2012	Ready-to-eat food	F01-E2	Added to foods	Significant reduction of CFU in hot dogs, cooked sliced turkey breast, mixed seafood and chocolate milk at 15ºC.

FACTORS AFFECTING THE EFFECTIVENESS OF PHAGE THERAPY

The effectiveness of phage applications against pathogenic bacteria depends on several factors.



CONCLUDING REMARKS AND FUTURE PERSPECTIVES

- This work reflects that bacteriophages are a remarkable alternative to control and eradicate pathogenic bacteria in primary production and postharvest food.
- The application of phage therapy is strengthened by the number of companies around the world investing in the production of phage-based products for use in the food industry. SALMONELEX™, for example, is a phage-based product to control *Salmonella* in the food chain.
- However, regulatory agencies are careful with the application of bacteriophages because of the lack of scientific evidence through clinical trials fully supervised by ethics committees and regulatory compliance standards.

REFERENCES

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