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BACTERIOPHAGE: LABORATORIAL DIAGNOSIS AND PHAGE THERAPY

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ABSTRACT

Bacteriophages have been researched as a new alternative to antibiotics. These viruses inject their genetic material into bacteria and use their host machinery to multiply themselves. The research of bacteriophages in Brazil will certainly provide low-cost treatment of multidrug resistant bacteria, new microbiological diagnosis and advantages for the Brazilian food industry.

Key words: Phage-based therapy, bacterial diseases, antibiotic resistant bacteria

Phage therapy is the use of lytic phages to treat or to prevent bacterial infections. The knowledge about phage therapy obtained so far permit us to consider these viruses as a powerful weapon against bacteria (6). During billions of years the Nature has shaped these natural killers leaving for us the responsibility of making use of them for our own cure . The discovery of antibiotics shrunk phage therapy research in the west countries in that phage biology was not satisfactory understood and antibiotic-based treatment provided more accurate results in diseased patients (6).

The widespread use of antibiotics for many years in hospitals and farms precipitated the rise of multidrug resistance bacteria forcing the development of new ways of dealing with them Phage-based treatment has been shown as an attractive opportunity to cope with persistent bacterial infections (7).

Although it is clear that phages are effective against bacteria, the lack of data on phage pharmacokinetics is a hurdle to overcome. Their self replicating ability, ecological characteristics and density-dependent thresholds are still to be better understood considering these entities as pharmaceutical agents (3).

Data obtained by McVay *et al*. (7) treating thermally injured mice infected with *Pseudomonas aeruginosa* indicated that intraperitoneal administration was more efficient to deliver phages than the intramuscular and subcutaneous routes suggesting that the administration method is crucial for the success of phage treatment in this thermal injured model. Indeed, this research reinforced the statement that cocktail of phages greatly reduces the emergence of resistant bacteria.

Knowing that phages are rapidly recognized by the reticuloendothelial system, techniques to select long-circulating viruses are being developed. One important step

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into the solution of this problem was given by Merril *et al.* (8) who developed a serial-passage technique and produced phages capable of resisting the mice immune system longer then their wild type. Similar results were obtained by Capparelli *et al.* (4) with *Staphylococcus aureus* phages. These techniques will certainly reduce the number of phage doses needed to be taken during treatments.

The use of bacteriophages in developing countries to prevent and treat post-burn microbial infection was suggested by Ahmad (1). Certainly, this approach suits Brazil in its struggle to improve public health assistance without having the cost of foreign technology. Producing phage cocktails is less expensive than developing new drugs because they are commonplace, and tools used to find them are simple.

Miedzybrodzki *et al*. (9) took into account all the elements needed to carry out phage therapy and reported that the mean cost for treating patients using phages is about half the cost of 10-day-vancomycin therapy. Surely, this average cost increases along with the treatment length if patients are required to stay longer at the hospital. Yet, these prolonged stay open up the door for nosocomial infections contributing to the spread of antibiotic resistance.

Though there is a lack of data in Brazil about hospital-acquired infections, some reports give us insights into this problem (12). Phage therapy might help Brazil to control the widespread use of antibiotics, replace them in case of they fail and reduce the National Public Health Service expenditure.

A well studied phage-based technology is the use of bacteriophages to detect bacteria. This approach has been applied to identify *Mycobacterium tuberculosis* (PhageTek MB, FASTPlaque-TB ®) and for drug resistance assays (*FASTPlaque-TB-MDRi* ®, *FASTPlaque-TB-Response* ®). After infecting the target bacteria, the progeny of mycobacteriophages can be detected by plating the progeny on a lawn of *Mycobacterium smegamtis* (2). Recombinant phages expressing fluorescent proteins to detect bacteria have also been reported (5).

Phages used as a processing-aid product have become a suitable alternative to control bacteria in food without changing its properties (10).

As it is still common to eat raw cheese in Brazil as well as to imbibe unprocessed milk, there is a high probability of having outbreaks of food borne diseases (11). Consumers will be protected against a variety of diseases by associating techniques currently used with phage cocktail to improve the quality of raw cheese.

Brazilian cheese industry will benefit from phage preparations. As an example, Minas frescal cheese, one of the most popular product in Brazil, spoil rapidly due to its high humidity (11). This shrunk the industry profit and raises the possibility of food borne diseases. By adding phage cocktail to Minas frescal cheese, it would be easier to keep its quality on the supermarket shelf.

Not only will the cheese market take advantages from phage preparations but the whole food chain. Phage-based technology can be applied to prevent any bacterial contamination reducing the impact of food borne infection on public health.

Bacteriophages are an option to control bacteria in a variety of fields. It is clear that these entites can benefit the Brazilian food industry in its effort to reduce food contamination. These viruses are not to replace antibiotics completely, but to augment our weapons against resistant bacteria. Additionaly, they have shown good sensibility and specificity in detecting bacterial pathogens which make them suitable for clinical laboratories.

RESUMO

Bacteriofagos: diagnóstico laboratorial e terapia fágica

Bacteriófagos têm sido pesquisados como uma alternativa ao uso de antibióticos. Estes vírus infectam as bactérias e utilizam a maquinaria celular para multiplicar o próprio material genético. O estudo de bacteriófagos no Brasil levará ao desenvolvimento de tratamentos de baixo custo, novos testes diagnósticos e vantagens para a industria alimentícia.

Palavras-chave: Terapia fágica, Infecção Bacteriana, resistência bacteriana

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