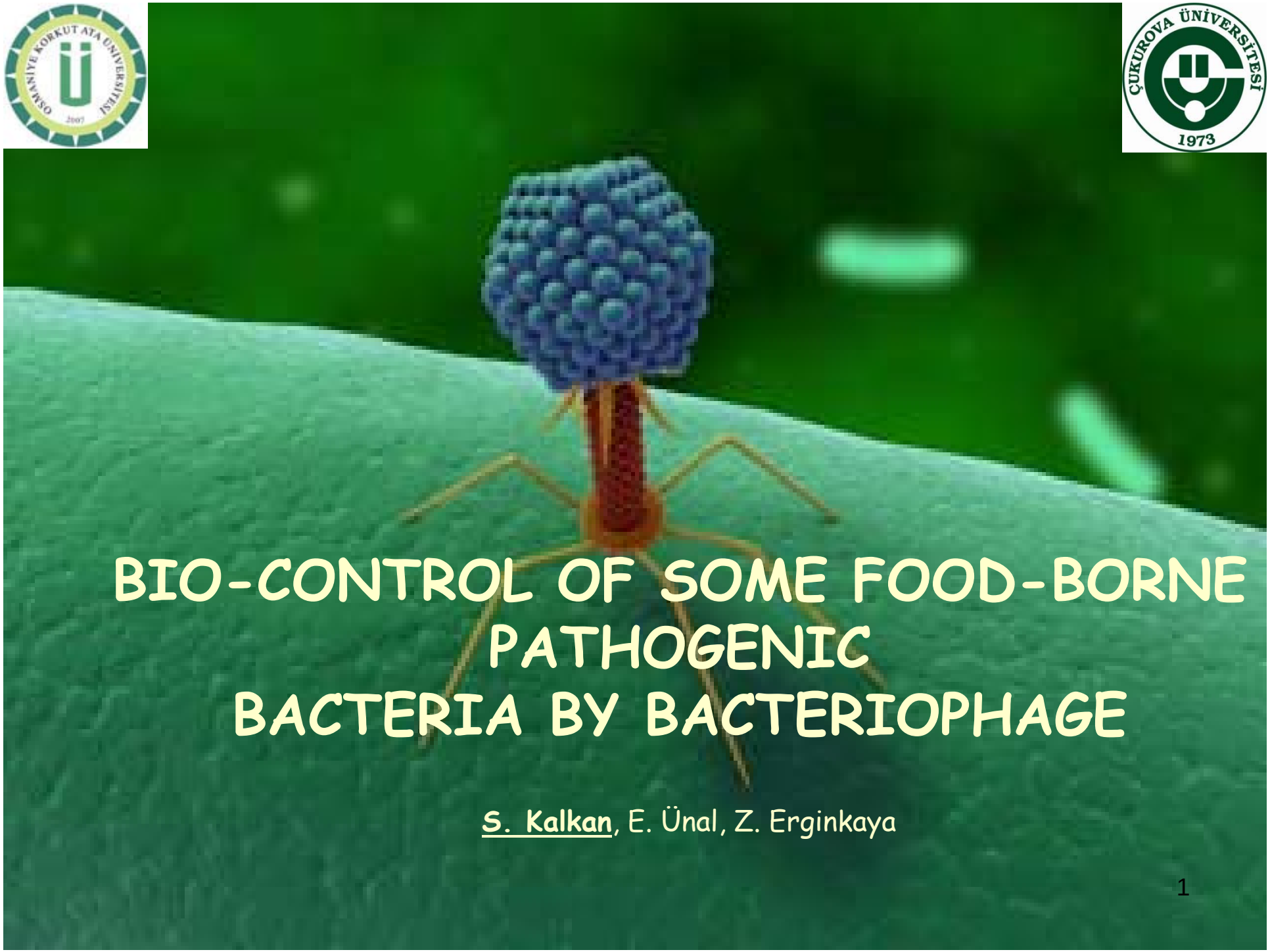

BIO-CONTROL OF SOME FOOD-BORNE PATHOGENIC BACTERIA BY BACTERIOPHAGE

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In this review given some information to explain the importance of bio-control of bacteriophages;

- General properties of bacteriophages,
- Antimicrobial Spectrum of bacteriophages,
- The antimicrobial effects of bacteriophages against severel food-borne pathogenic bacteria

In the view of these informations, it was discussed advantages and disadvantages about use of bacteriophages by taking into antimicrobial characteristics of them

The usage of biological factors against various pathogenic and saprophyte microorganisms, especially pathogenic bacteria, is defined as a

"bio-control"

The usage of bacteriophage as a bio-control factor proposed shortly after the discovery of bacteriophage independently by Twort (1915) and d'Herelle (1917).

Bacteriophage, also know as phage, is a type of virus that infects only bacteria cells. Phages are very tiny and measure 20 to 200 nanometres, which is approximately 100 times smaller than most bacteria.

They ara obligate intracelluler parasites that infect bacteria and reproduce by hijacking their host's biosynthetic pathway (Walker, K.,2006).

Phages are very specific toward their target bacteria; they only effect that particular type or strain, and have no effect on any other type cell including human, animal and plant cells.

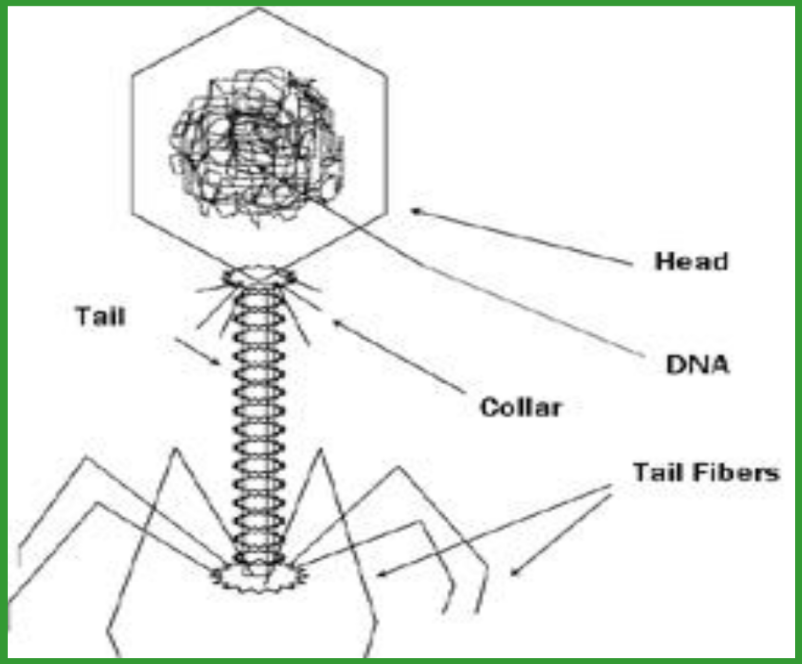

Figure 1. A representative shematic of structure of a bacteriophages (Bassett, K. D., 2007)

Usually, bio-control by bacteriophages studies are concentrated about food safety, especially food pathogens such as *Salmonella*, *Campylobacter*, *E. coli* O157:H7 and *Listeria* causing epidemics of disease (Hangens and Loessner, 2007)

But the researchers have two major concerns about the use of bacteriophages on food products;

*consumption of bacteriophages with food whether harmful or not on human health

* how to overcome phage resistance of bacteria against bacteriophages

Relatively high numbers of phages are natural habitat, such as sea water, fresh water, soil, plants and even food.

The hypothesis confirmed that bacteriophages have broad habitat by the isolation of phages in human feces (Hangens and Loessner, 2007).

An oral toxicity study in rat receiving high doses of *Listeria* phage P100 because of resolving the concerns and did not reveal any side effects

In a similar study in humans with *E. coli*-specific phages also indicated that phages are safe for oral administration.

In accordance with these results were also examined defense mechanisms against bacteria and have been identified host systems of phages continuously adapt to changing conditions. Furthermore, technical measures such as the alternating use of different phages, either in a cocktail or in consecutive treatments, may also reduce the frequency of resistance (Hangens and Loessner, 2007).

Phages are classified as either lytic or lysogenic based upon their replication strategy (Walker, K., 2006).

When a lytic phage and a host meet there needs to be a match between structures on both, and this confers specificity on the interaction, i.e. any given phage will only infect a specific group of hosts.

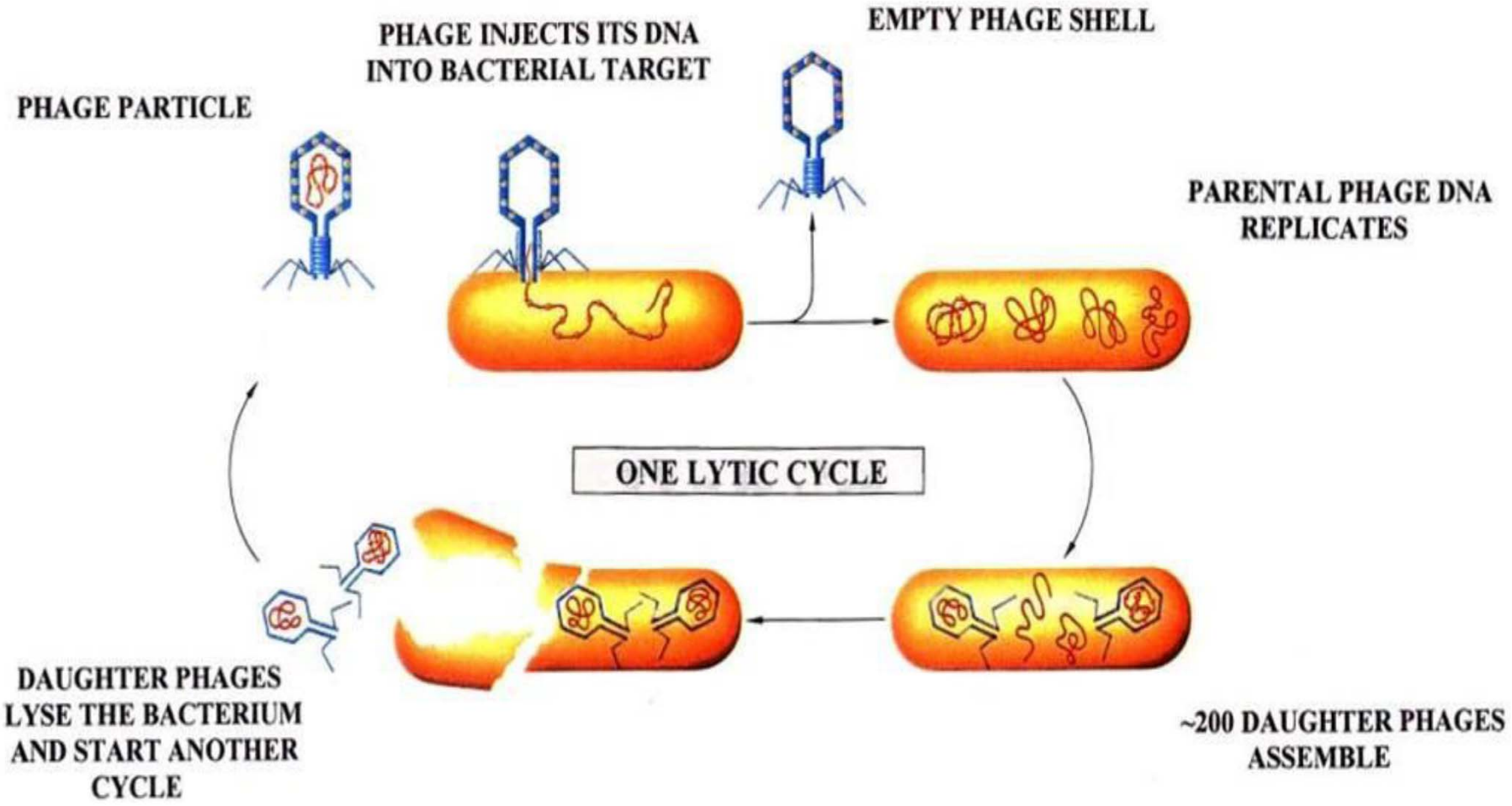

Figure 2. Flow diagram of the lytic cycle of a bacteriophages (Bassett, K.D., 2007).

One of the remarkable factors in many food studies inactivation is only achieved by **using a high phage to host ratio** (the multiplicity of infection, or MOI) with food pathogens. In addition, inactivation has been reported to occur at temperatures beneath the growth minimum of the host.

- In a study published by Atterbury et al. (2003) was achieved rate of 95-99% success *C. jejuni* inactivation from chicken skin by bacteriophages.

- In another study has been reduced numerical of *Listeria monocytogenes* by phages in infected melon and soft cheeses.

- However, *Salmonella* Enteritidis were followed after the application of phage therapy in raw and pasteurized milk and cheeses and were encountered in cheeses made form pasteurized milk after 89 days of storage.

- In a different study with *Salmonella* in chicken carcasses which inoculated with *Salmonella*, *Salmonella* phages infected rate of > 10^8 PFU ml and was achieved inactivation varying from 7% to 100%. Similarly, the turkey carcasses have been used successfully in the application of phage (Bigwood *et al.*, 2008).

- A cocktail of three phages was effective in reducing *E. coli* O157:H7 on meat incubated at 37°C (O'Flynn *et al.*, 2004). The host was not detectable by enrichment in seven of nine samples, while two samples yielded counts of < 10 CFU ml^{-1} after treatment.

- The first phage preparation is used commercially contained a mixture of phages against *Listeria monocytogenes*
- In the Federal Register of August 18, 2006, the US Food and Drug Administration (FDA) announced that it had approved the use of a phage preparation made from six purified phages to be used on ready-to-eat meat and poultry products as an antimicrobial agent against *L. monocytogenes*

The approval of the phage preparation, developed from a company in USA, followed studies in which the effectiveness of the phage preparation against the pathogen on food was proven and a spray application in meat and poultry processing plants was permitted. The approved phage cocktail has antimicrobial activity against 170 strains of *L. monocytogenes.*

Another phage designated Listex P100, developed from a Netherlands company against *Listeria monocytogenes* and has also a potential to be widely used in the food industry.

P100 demonstrate to be effective against a wide range of *Listeria* strains and a bio-informatic analysis of the total genomic sequence did not reveal any similarities of P100 genes or gene products to any genes or proteins or other factors known or believed to play a role in the pathogenicity or virulence of *L. monocytogenes*.

As a proof of concept, the application of P100 in the ripening process of soft cheese (red-smear soft cheese) was performed. The surface of the cheese was artificially contaminated with *Listeria* and a significant reduction (at least 3.5 log10 units) or complete eradication of *Listeria* viable counts were achieved. Listex P100 bacteriophage product also received approval from the FDA for use on cheese. The approval was granted under the FDA's GRAS (Generally Recognized as Safe) procedure for use on cheese (Strauch *et al.*, 2007).

The advantages of phage therapy over antibiotic therapy as follows;

(i) it is effective against multidrug-resistant pathogenic bacteria;

(ii) substitution of the normal microbial flora does not occur because the phages kills only the targeted pathogenic bacteria;

(iii) it can respond quickly to the appearance of phage-resistant bacterial mutants because the frequency of phage mutation is significantly higher than that of bacteria;

(iv) developing costs for a phage treatment is cheaper than that of new antibiotics;

(v) side-effects are very rare.

However, there are still some concerns such as;

(i) rapid cell lysis of bacteria may result in the release of large amount of bacterial membrane-bound endotoxins;

(ii) some phages may encode toxins;

(iii) lack of pharmacokinetic data;

(iv) neutralization of phages by the host immune system may lead to failure of phage therapy;

(v) conversion of lytic phages to lysogenic phages (prophages) leads to bacterial immunity to attacks by the corresponding lytic phages and may also change the virulence of the bacteria (Parisien *et al.*, 2008).

As a result ;

Bacteriophages known as "new" antimicrobial agents in food industry and studies concentrates to expand which using in food. Inactivation of pathogenic bacteria leading to outbreaks of very successful results to be retrieved by infected bacteriophages food consumption can hold an important place in human nutrition in future.

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THANKS FOR YOUR ATTENTION