efficacy and safety. In a murine model of *P. aeruginosa* chronic lung infections, PELP20 was able to penetrate and kill bacteria within a biofilm-associated cystic-fibrosis lung-like environment. In a mice model, intraperitoneal injection of bacteriophage efficiently rescued bacteremia caused by imipenem-resistant *Pseudomonas*. A bacteriophage in the form of eye-drop showed high efficacy against *Pseudomonas* keratitis.

Numerous virulent phages of *Staphylococcus* have been described to have the ability to kill different *S. aureus* strains – such as phage f812. Phage Sb-1 was used to successfully treat patients in the United States with diabetic foot ulcers infected with MRSA. In the food industry, phages have been employed to decontaminate food by removing *E. coli, Salmonella*, or *Listeria* and played important role in food production and cattle raising. They are used to control foodborne diseases associated with *Salmonella* (salmonellosis), *Campylobacter* (campylobacteriosis in poultry), *Listeria monocytogenes,* or *E. coli*. Phages have been used to ensure food safety since they allow removal of bacterial infections in animals and thus prevent consumption of contaminated food. Phage CEVI successfully reduced the pathogenic *E. coli* strain in sheep.

19.5.3 Phage Enzymes

Phages produce several enzymes, for example, the holin and endolysin (lysins), used by most of the lytic phage to destroy the host cell. Endolysins, which degrade the peptidoglycan in the cell wall, are a new class of antimicrobials for treatment of infections caused by MDR strains due to their rapid actions, low evidence of resistance development, and cytotoxicity to mammalians cells. This activity is particularly against Gram-positive bacteria; since the outer membrane of Gram-negative bacteria provides protection to the peptidoglycan layer. Several endolysins have showed bactericidal activity *in vitro* against *Enterococcus faecalis* and *E. faecium* including vancomycin-resistant strains. The endolysin PlySs2 from a phage infecting *Streptococcus suis* exhibited activity against vancomycin-intermediate *S. aureus*, MRSA, *Staphylococcus epidermidis*, different species of *Streptococcus*, and *Listeria* spp. The phage lysine is used to treat infection caused by *B. anthracis*. To improve efficacy against Gram-negative bacteria, researchers have been looking for endolysins with the natural ability to degrade Gram-negative bacteria; in addition the combination of lysins with other agents has been shown to destabilize the outer membrane.

Holins are commonly small proteins that elicit a variety of effects and serve various functions. Their function involves bacterial cell lysis, a process used to form open or tightly sealed channels in the host bacterial cell membrane, releasing an autolysin and ultimately, following lysis of the cell, releasing the phage progeny. The combined use of holin and endolysin may be an effective strategy to cure infections and prevent bacterial resistance to antibiotics. Holin