Sudiarta et al. 2010). Also, they form monomers (e.g. *Pseudomonas* phage φ6) (Caldentey and Bamford 1992), dodecamer (e.g. *Salmonella* phage P22) (Tang et al. 2011), and oligomers. The latter are the most reported state in the virus particle. Biologically, VALs are proteins that digest the peptidoglycan of actively growing cells from the outside, and endolysins digest the peptidoglycan from within of an already dead cell by the pre-action of holins. Enzymatically, VALs usually possess domains conferring glycosidase or endopeptidase activity that are shared with endolysins, being the latter often observed in Gram-positive phage VALs. Interestingly, the endopeptidase (M23 family) is almost exclusively found on VALs. This domain is also found by analogous bacterial enzymes (e.g. lysostaphin and enterolysin A) that also degrade the cell wall from outside, suggesting being more prepared to degrade the peptidoglycan from actively growing cells (Khan et al. 2013). The absence of an identifiable binding domain is another distinctive feature of VALs. The approach of these proteins to the cell wall is ensured by other embedded subdomains found in the same open reading frame where VALs are found (e.g. tail fiber, tail spikes). VALs have also been found to be highly thermostable, which contrasts with the mesophilic properties of most endolysins. For instance, the *P. aeruginosa* φKMV VAL has the ability to resist temperatures up to 100 °C and even to autoclaving (Lavigne et al. 2004). This is probably explained by the fact that being anchored to the phage particle, these proteins have evolved to endure harsh external conditions where phage inhabits, ensuring their infectivity and survival. Therefore, VALs may find several biotechnological applications when thermic processing is applied.

Moreover, the role of VALs goes beyond what was previously anticipated. Some VALs (e.g. *S. aureus* phage φ11 and *E. coli* phage T7) are reported to be dispensable for phage infection and to degrade highly cross-linked peptidoglycan, which is found in stationary phase cells (Moak and Molineux 2000; Rodriguez-Rubio et al. 2013c; Stockdale et al. 2013). These observations suggest that VALs offer competitive advantages to degrade the peptidoglycan in the initial step of phage infection under specific physiological conditions.

15.3.1.2 VALs as Antimicrobials

The natural lytic activity of VALs causes "lysis from without," a phenomenon that was first documented in 1940. This phenomenon occurs when several phages are drilling holes in the peptidoglycan of the same cell through enzymatic degradation of the VALs, causing premature death of the host. After this observation, VALs have emerged as novel antibacterial agents being mostly applied to kill *S. aureus* (Table 15.2). For instance, *S. aureus* phage φIPLA88 and P68 VALs demonstrated to kill 99% of methicillin-resistant *S. aureus* (MRSA) strains 20 minutes after exposure (Takac and Blasi 2005; Rodríguez et al. 2011). The thermostability of VALs confers them high potential to control undesirable bacteria for example in pasteurized milk or other dairy products