Introduction: β-lapachone (β-lap) is a compound which can be naturally extracted from the bark of *Tabebuia avellanedae*. This molecule has attracted increasing attention due to its different pharmacological activities with therapeutic potential, such as antibacterial, antifungal, as well as anticancer properties. Even β-lap presenting a significant pharmacological activity, their therapeutic application is limited due to its low water solubility (0.038 mg mL\(^{-1}\) or 0.16 mM). This limitation had been overcome by forming inclusion complexes of β-lap with 2-hydroxypropyl-β-cyclodextrin (β-lap:HPβ-CD) and it entrapped into liposomes. Thus, the aim of this study was to evaluate the antimicrobial activity of β-lapachone (β-lap) or β-lap:2-hydroxypropyl-β-cyclodextrin inclusion complexes (β-lap:HPβ-CD) encapsulated into conventional and stealth liposomes. Material and Methods: Liposomes were prepared using the hydration of thin lipid film and the *in vitro* antimicrobial activity against methicillin/oxacillin-resistant and -susceptible *Staphylococcus aureus* (MRSA and MSSA, respectively) was performed by microdilution method according to the *Clinical and Laboratory Standards Institute* (CLSI). Results and Discussion: The liposomes presented mean particle size ranged from 88.7 ± 1.5 nm to 132.6 ± 3.3 nm and drug encapsulation efficiency ranged from 97.4 ± 0.3 % to 99.2 ± 0.2 %. The antimicrobial activity test proved that β-lap and β-lap:HPβ-CD presented the same activity with MICs ranging from 1 to 2 mg/L and MBCs ranging from 1 to 16 mg/L against bacteria. MICs of the stable liposomes encapsulating β-lap or β-lap:HPβ-CD varied from 2 to 32 mg/L. Our results of β-lap and β-lap:HPβ-CD antimicrobial activities is comparable to linezolid, an antibiotic approved by the FDA and currently available in the market. Emphasis should be done that β-lap as well as its liposomal formulations presented bacteriostatic and bactericidal activity. Conclusions: Thus β-lap, β-lap:HPβ-CD and the newly developed liposomes can significantly contribute to the treatment of infections caused by multiresistant bacteria, specially MRSA.

Keywords: β-lapachone; liposomes; antimicrobial activity.

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