TITLE: β-LAPACHONE ENCAPSULATED INTO LIPOSOMES INHIBIT METHICILLIN-RESISTANT *Staphylococcus aureus* BIOFILM

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ABSTRACT:

Methicillin-resistant *Staphylococcus aureus* (MRSA) has been one of the main pathogens involved in serious hospital infections, with high rates of morbidity and mortality, due to its resistance to current antibiotics and production of biofilm. Thus, the scientific community looks for new therapeutic options that inhibit biofilm and therefore its clinical manifestations. β-lapachone (β-lap), a molecule extracted by "Ipê-roxo" tree (*Tabebuia avellanedae*), becomes a viable alternative due to its pharmacological properties, including the activity antibacterial. However, this molecule has limitations such as low water solubility and toxicity. Therefore nanosystems, such as, liposomes appear as options to overcome these limitations. Liposomes are vesicles that consist of one or more concentric phospholipidic bilayers organized around an aqueous inner compartment. The liposomes can enhanced the solubility of drugs, as well as decrease their toxicity. Thus, this study aimed to evaluate the effect of β-lapachone encapsulated into conventional (β-lap_SACL) and stealthy liposomes (β-lap_NSL) to inhibit MRSA biofilm. The liposomes containing β-lap were prepared by the hydration of thin lipid film method followed by sonication. These liposomes were characterized by measuring the pH, particle size, polydispersion index (PDI) and encapsulation efficiency (%EE). The antimicrobial activity of β-lap_SACL and β-lap_NSL against MRSA clinical isolates was investigated by the microdilution method according to the *Clinical and Laboratory Standards Institute* (CLSI). The inhibition of MRSA biofilm was evaluated by determining the minimum biofilm inhibitory Concentration (MBIC) and Minimum Biofilm Eradication Concentration (MBEC) by crystal violet staining method. β-lap_SACL and β-lap_NSL exhibit pH, particle size, PDI and %EE of 7.5 and 7.5, 113.15 ± 1.35 nm, and 84.2 ± 8.9 nm, 0.30 and 0.28, 97.9 ± 0.9% and 98.7 ± 0.6%, respectively. β-lap_SACL and β-lap_NSL presented Minimum Inhibitory Concentrations (MICs) values ranged for 4 to 16 µg/ml. The liposomes containing β-lap exhibit MBIC and MBEC values ranged from 4 to 16 µg/ml and 4 to 64 µg/ml, respectively. These results suggest that β-lap encapsulated into liposomes is a promising drug to inhibit MRSA biofilm.

Keywords: β-lapachone, bacterial resistance, biofilm, liposomes, MRSA,
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