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Abstract

Resveratrol-Loaded Glycosylated Liposomes for Targeting Bacteria †

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Biofilm-associated bacterial diseases are a major health problem due to the high antibiotic resistance of biofilm infections [1,2]. In recent years, several methods, some of which rely on nanotechnology [3], have been developed to tackle this problem. The search for non-antibiotic strategies has renewed interest in natural molecules that exploit alternative bacterial-fighting mechanisms and, above all, do not induce resistance. In this context, we have developed two sets of cationic glycosylated liposomes for the targeted delivery of *trans*-resveratrol (RSV), a secondary plant metabolite with antimicrobial properties, to bacteria that express carbohydrate-specific proteins able to recognize monosaccharides, namely *Staphylococcus epidermidis* [4] and *Methicillin Resistant Staphylococcus Aureus* (MRSA) [5]. Liposome physico-chemical properties (diameter, polidispersity index-PDI-, charge, and RSV entrapment efficiency) were measured by dynamic light scattering (DLS), electrophoretic mobility, and high-performance liquid chromatography (HPLC). Liposomes used in the experiments on MRSA were composed of 1,2-dioleoyl-*sn*-glycero-3-phosphocholine, cholesterol (Chol), and glycoamphiphiles featuring a galactosyl, mannosyl, or glucosyl moiety [5]. The objective was to identify the best sugar moiety to target MRSA biofilm. Microbiological tests carried out to monitor the demolition effect of RSV-loaded liposomes on MRSA mature biofilms showed that RSV-galactosylated liposomes are the most effective at an RSV concentration 60 times below the minimum inhibitory concentration (MIC). Liposomes used

in the experiments on *S. epidermidis* were formulated with 1,2-dipalmitoyl-*sn*-glycero-3-phosphocholine, Chol, and the glycoamphiphile featuring the glucose residue [4]. The ability of RSV-loaded liposomes to inhibit the growth of a slime-positive and a slime-negative strain of *S. epidermidis* was evaluated. Glucosylated liposomes, which are non-toxic, kill bacteria at concentrations tenfold under the MIC of RSV.

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