Biotechnological production of sialylated solid lipid microparticles as Influenza virus inhibitors

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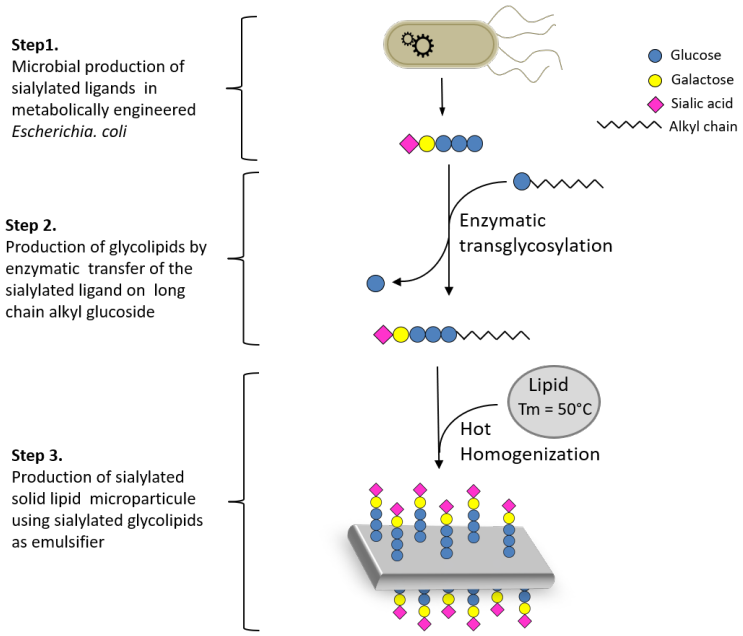
Influenza viruses bind to their target through a multivalent interaction of their hemagglutinins with sialosides at the host cell surface[1]. To fight the virus, one therapeutic approach consists in developing sialylated multivalent structures that can saturate the virus hemagglutinins and prevent the binding to host cells[2,3]. We describe herein the biotechnological production of sialylated solid lipid microparticles (SSLMs) in three steps: (i) a microbiological step leading to the large-scale production of sialylated maltodextrins by metabolic engineering of an *Escherichia coli* strain, (ii) a new *in vitro* glycosylation process using the amylomaltase MalQ, based on the transglycosylation of the terminal sialoside ligand of the sialylated maltodextrin onto a long-chain alkyl glucoside, and (iii) the formulation of the final SSLMs presenting a multivalent sialic acid. We also describe the morphology and structure of the SSLMs and demonstrate their very promising properties as influenza virus inhibitors using hemagglutination inhibition and microneutralization assays on the human A/H1N1 pdm09 virus.



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Bibliographic references:

[1] U. Karakus, MO Pohl, S. Stertz (2020), J. Virol. (94)
[2] J. Kingery-Wood, KW. Williams, GB. Sigal, GM. Whitesides (1992), J. Am. Chem. Soc. (114) 7303-7305.
[3] A. S. Gambaryan, E. Y. Boravleva, TY. Matrosovich, M. N. Matrosovich, H. D. Klenk, E. V. Moiseeva, A. B. Tuzikov, A. A. Chinarev, G. V. Pazynina, N. V. Bovin (2005), Antivir. Res. (68) 116-123.