Title	Dodecylated and non-dodecylated polycations as promising siRNA complexing agents for skin diseases treatment
Keywords (up to 5)	Gene Therapy, polymer synthesis, lipid nanoparticles, skin
Authors	Marcelo KRAVICZ [1], Debora T BALOGH [2], Juliana S ROSA [1], Angelo L CARON[1], Isabella L SUZUKI [1,2], Maria Vitoria L B BENTLEY [1] *[1] School of Pharmaceutical Sciences of Ribeirao Preto, University of Sao Paulo, Brazil* *[2] Sao Carlos Institute of Physics, University of Sao Paulo, Brazil*
Abstract	Although lipid nanoparticles (LNP) are an interesting platform for skin diseases treatment, we observe formulation instability, especially when polyethyleneimine (PEI) is used as a complexing agent. Hence, we proposed synthesizing two small groups of cationic polymers via aminolysis of poly(succinimide) (PSI), a non-dodecylated group, $1A_n$, and a dodecylated group $2A_n$, in which A_n represents different amines from A_1 to A_6. Previously, DNA polyplexes were formed by complexing a plasmid DNA pEGFP-N3 encoding a green fluorescent protein (GFP). Transfection was carried out in HeLa cells and GFP expression was measured by flow cytometer after 48 hours. Dodecylated PSI derivatives showed lower CMC than their non-dodecylated counterparts, suggesting polymer-polymer interactions by hydrophobic interactions and micelle-like structures formation. Furthermore, $2A_n$ group had higher buffering capacities β (β > 40%) than $1A_n$ and bPEI 25 (β, 23%). Polyplexes formed with non-dodecylated polycation containing A_3 and A_4 moieties provided higher GFP expressing HeLa cells. Polyanion competition assay with heparin for polyplexes at N:P 5 showed no release of the plasmid from the polyplex for all dodecylated polymers. Cytotoxicity of all plain polymers showed that dodecylated polycations do not decrease cellular viability, also all polyplexes at N:P 5 have negligible cytotoxicity. Although no GFP expressing was observed for dodecylated polycations polyplexes, we hypothesize a different complexation behaviour in siRNA polyplexes and other lipid systems. We gratefully acknowledge INCT-NANOFARMA CNPq 300235/2018-6 and FAPESP
References	1. Roberts, M. S., Mohammed, Y., Pastore, M. N., Namjoshi, S., Yousef, S., Alinaghi, A., Grice, J. E. (2017). Topical and cutaneous delivery using nanosystems. Journal of Controlled Release, 247, 86-105. 2. Dorrani, M., Garbuzenko, O. B., Minko, T., & Michniak-Kohn, B. (2016). Development of edge-activated liposomes for siRNA delivery to human basal epidermis for melanoma therapy. Journal of Controlled Release, 228, 150-158.