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Drug Delivery Cationic Nano-Containers Based on Pseudo-Proteins

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Abstract : The elaboration of effective drug delivery vehicles is still topical nowadays since targeted drug delivery is one of the most important challenges of the modern nanomedicine. The last decade has witnessed enormous research focused on synthetic cationic polymers (CPs) due to their flexible properties, in particular as non-viral gene delivery systems, facile synthesis, robustness, not oncogenic and proven gene delivery efficiency. However, the toxicity is still an obstacle to the application in pharmacotherapy. For overcoming the problem, creation of new cationic compounds including the polymeric nano-size particles – nano-containers (NCs) loading with different pharmaceuticals and biologicals is still relevant. In this regard, a variety of NCs-based drug delivery systems have been developed. We have found that amino acid-based biodegradable polymers called as pseudo-proteins (PPs), which can be cleared from the body after the fulfillment of their function are highly suitable for designing pharmaceutical NCs. Among them, one of the most promising are NCs made of biodegradable Cationic PPs (CPPs). For preparing new cationic NCs (CNCs), we used CPPs composed of positively charged amino acid L-arginine (R). The CNCs were fabricated by two approaches using: (1) R-based homo-CPPs; (2) Blends of R-based CPPs with regular (neutral) PPs. According to the first approach NCs we prepared from CPPs 8R3 (composed of R, sebacic acid and 1,3-propanediol) and 8R6 (composed of R, sebacic acid and 1,6-hexanediol). The NCs prepared from these CPPs were 72-101 nm in size with zeta potential within +30 ÷ +35 mV at a concentration 6 mg/mL. According to the second approach, CPPs 8R6 was blended in organic phase with neutral PPs 8L6 (composed of leucine, sebacic acid and 1,6-hexanediol). The NCs prepared from the blends were 130-140 nm in size with zeta potential within +20 ÷ +28 mV depending on 8R6/8L6 ratio. The stability studies of fabricated NCs showed that no substantial change of the particle size and distribution and no big particles' formation is observed after three months storage. In vitro biocompatibility study of the obtained NPs with four different stable cell lines: A549 (human), U-937 (human), RAW264.7 (murine), Hepa 1-6 (murine) showed both type cathionic NCs are biocompatible. The obtained data allow concluding that the obtained CNCs are promising for the application as biodegradable drug delivery vehicles. This work was supported by the joint grant from the Science and Technology Center in Ukraine and Shota Rustaveli National Science Foundation of Georgia #6298 'New biodegradable cationic polymers composed of arginine and spermine-versatile biomaterials for various biomedical applications'.

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