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Characterisation of Physical-chemical and Self-assembling Properties of Pyridinium Moieties Containing 1,4-dihydropyridine and Pyridine Derivatives as NADH/NAD Analogues for Development of Gene Delivery Systems

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Introduction. Over the past decades, development of new non-viral vectors as delivery systems has resulted in elaboration of various nanopharmaceutical applications and become a competitive field for different researcher groups. Polyfunctional pyridinium derivatives on the 1,4-dihydropyridine (1,4-DHP) scaffold possess self-assembling properties. Cationic 1,4-DHP derivatives form liposomes and efficiently act as gene delivery agents. The parent compound of this class is 1,4-DHP [Hyvönen et al., 2000; Hyvönen et al., 2004]. The influence of lipids head-group on transfection activity [Pajuste et al., 2013] and properties of formed liposomes [Rucins et al., 2013] were studied.

Aim, Material and Methods. The aim of the study was to characterise the physical-chemical and self-assembling properties for individual compounds and clarify their relationships with biological activity. Synthesis of amphiphiles were perfomed according to Pajuste [Pajuste et al., 2011] and Petrichenko [Petrichenko et al., 2015]; free radical quenching activity was evaluated by 1,1-diphenyl-2-picrylhydrazyl radical method after Abdelwahed [Abdelwahed et al., 2007]; determination of pKa values using UV-Vis method – by Furdui [Furdui et al., 2012]. Preparation and studies of liposomes by transmission electron microscopy (TEM) and dynamic light scattering (DLS) – by Pajuste [Pajuste et al., 2013].

Results. Two main groups of new amphiphiles: derivatives of cationic 1,4-DHP with variations of substituents at different positions of 1,4-DHP cycle and other class, oxidated form, fully aromatised compounds with head-group variations were designed and synthesised as putative delivery agents. The structures of all newly synthesised compounds were established and confirmed by NMR, MS and elemental analysis data. Molecular weights of 1,4-DHP derivatives measured by LC/MS technique were in good agreement with the calculated values for all compounds. The purities of the studied compounds were at least 97% according to high-performance liquid chromatography (HPLC) data. Studies of physical-chemical and self-assembling properties of them were performed. All derivatives of cationic 1,4-DHP possess free radical quenching activity and the buffering capacity of studied N-unsubstituted 1,4-DHPs were in the pH range 6.8–8.8.

Conclusions. Some of 1,4-DHP have significant radical scavenging activity. It can be concluded that structure of substituents of positions at 2 and 6 of 1,4-DHP molecule are important for radical scavenging properties. According to DLS measurements, all compounds form nanoparticles with the average size 79–532 nm, depending on the structure of the compound; values of zeta-potentials for the nanoparticles were in the range of 48–89 mV.

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