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DNA compaction to multi-molecular DNA condensation induced by cationic imidazolium gemini surfactants

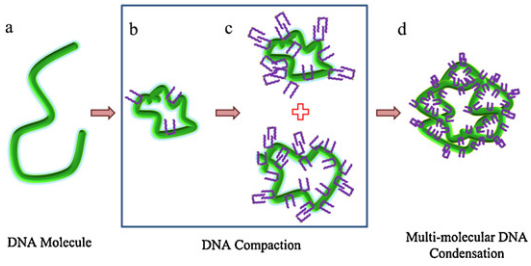
Ting Zhou[a,b], Guiying Xu[a,*], Mingqi Ao[a], Yanlian Yang[b,**], Chen Wang[b]

[a] Key Laboratory of Colloid and Interface Chemistry, Ministry of Education, Shandong University, Jinan 250100, PR China
[b] National Center for Nanoscience and Technology, Beijing 100190, PR China

HIGHLIGHTS

- An evolution from DNA compaction to multi-molecular DNA condensation induced by $[C_n\text{-}4\text{-}C_n\text{im}]Br_2$ is identified and its mechanism is discussed.
- $[C_n\text{-}4\text{-}C_n\text{im}]Br_2$ as novel imidazolium gemini surfactants can interact with DNA *via* electrostatic, hydrophobic and π–π interaction.
- The stronger interaction between DNA and $[C_n\text{-}4\text{-}C_n\text{im}]Br_2$ with longer tails demonstrates the important contribution of the hydrophobic interaction.

GRAPHICAL ABSTRACT



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ABSTRACT

The compaction and condensation of DNA induced by cationic imidazolium gemini surfactants ($[C_n\text{-}4\text{-}C_n\text{im}]Br_2$, $n = 10, 12, 14$) at different charge ratios have been investigated by dynamic light scattering (DLS), *zeta* potential, circular dichroism (CD), and ethidium bromide exclusion assay. Upon addition of $[C_n\text{-}4\text{-}C_n\text{im}]Br_2$, DNA molecules undergo the process from compaction to multi-molecular condensation accompanied by conformation change, which could be proved by the DLS and CD results. The charge density changes in *zeta* potential measurements indicated the impact of the electrostatic interaction in DNA–surfactant complex. The comparison between DNA compaction and condensation by $[C_n\text{-}4\text{-}C_n\text{im}]Br_2$ with different tail lengths demonstrated the important contribution of the hydrophobic interaction. The EtBr exclusion assay indicates the π–π interaction between imidazolium groups of $[C_n\text{-}4\text{-}C_n\text{im}]Br_2$ and DNA aromatic rings also plays a role in the DNA/$[C_n\text{-}4\text{-}C_n\text{im}]Br_2$ complex formation. The impact of the different interactions on the DNA compaction and condensation by gemini surfactants would shed light on their potential applications in gene delivery.

1. Introduction

Gene therapy has been demonstrated as a potential treatment of both genetic and acquired diseases, while the effective delivery of the therapeutic genes into target cells *in vitro* and *in vivo* is still one of the greatest challenges in gene therapy. It has been confirmed that the key parameters for achieving effective gene therapy is the size of the DNA condensates [1,2]. It is also necessary to neutralize the negative charges of DNA, because an overall positive charge significantly improves the docking of the DNA condensate on the primarily negatively charged cell membranes [3]. As an anionic polyelectrolyte, due to the highly negative charge of phosphate backbone, DNA can bind a variety of cationic agents, such as simple lipid-like cations [4,5], cationic surfactants [6–9], polycations [10], dendrimers [11], nanoparticles [12], and peptides

* Corresponding author. Tel.: +86 531 88365436; fax: +86 531 88564750.
** Co-corresponding author. Tel.: +86 10 82545559.
E-mail addresses: xuguiying@sdu.edu.cn (G. Xu), yangyl@nanoctr.cn (Y. Yang).

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