Photoresponsive transformation from spherical to nanotubular assemblies: anticancer drug delivery using macrocyclic cationic gemini amphiphiles

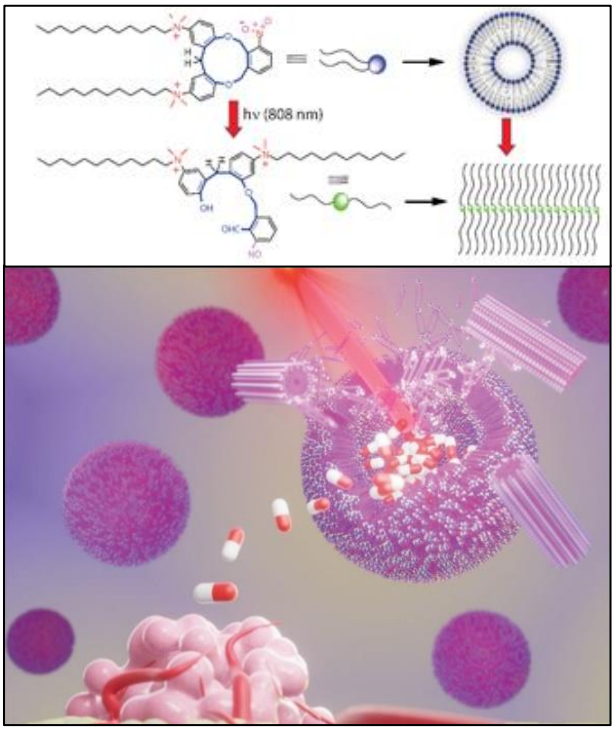
Subhasis Dey,[a] Soumya Chatterjee,[b] Anjali Patel,[c] Nirmalya Pradhan,[a] Diship Srivastava,[d] Niladri Patra,[d] Arindam Bhattacharyya[b] and Debasis Manna [ac,*]

[a].*Department of Chemistry, Indian Institute of Technology Guwahati, Assam 781039, India.* [b]*Calcutta University, Zoology, Kolkata, West Bengal, India.* [c]*Indian Institute of Technology Guwahati, Centre for the Environment, Guwahati, Assam, India.* [d]*Indian Institute of Technology (Indian School of Mines) Dhanbad, Chemistry, Dhanbad, Jharkhand, India*

*dmanna@iitg.ac.in

Abstract

Currently, significant efforts are being dedicated to early diagnosis and developing various biocompatible drug delivery strategies to fight against cancer. Lipid-based nanocarriers represent effective agents for efficiently delivering appropriate therapeutic doses of various chemotherapeutic drugs to targeted cancer cells or tissues. Besides lower toxicity, biodegradability, prolonged circulation properties, and non-immunogenicity are also the remarkable advantages of lipid-based drug delivery system (DDSs). However, the slow-drug release profiles of various lipid-based DDSs at disease sites significantly compromise their clinical efficiency. It is challenging to control the delivery of appropriate doses of the drug at the right time. Moreover, precisely controlled release of drug molecules into deep tumors is a prerequisite for enhancing the therapeutic efficiency of lipid-based DDSs. Hence, the development of facile methods to synthesize novel lipid-based nanocarriers with excellent drug release profiile has been of significant interest. Lipid-based nanocarriers represent effective agents for efficiently delivering



appropriate therapeutic doses of various chemotherapeutic drugs to targeted cancer cells or tissues. Though it has suitable biophysical properties, still it is a challange to control the delivery of appropriate doses of the drug at the right time. Moreover, precisely controlled release of drug molecules into deep tumors is a prerequisite for enhancing the therapeutic efficiency of lipid-based DDSs. Furthermore, installation of stimuli-responsive cleavable covalent linkers to the lipid molecules provides a controllable tool for triggering the release of encapsulated drug molecules. However, most of the cleavages mediated by these endogenous stimuli are restricted by the limiting conditions obligatory for the release, as they rely on differences in properties between cells. The use of a near-infrared (NIR; exogenous stimulus) light-responsive DDS is one of the attractive strategies as it can be used over long distances with excellent spatial and temporal resolutions. Here we introduce a 2-nitrobenzyl containing 11-membered strained macrocyclic amphiphiles. We hypothesized that the installation of the UV-active, 2-nitrobenzyl moiety within the highly strained macrocyclic moiety would make it NIR sensitive and endow it with substantial structural changeInterestingly, our synthesized macrocycle lipid molecule easily formed liposomal aggregate and upon 15 minutes NIR light irradiation turns into nanotubular assembly. The potent synthesized gemini cationic amphiphile showed successful encapsulation and delivery of the most widely used hydrophobic chemotherapeutic drug Dox to cancer cells.

Keywords: Photoresponsive amphiphile; nanotube; drug delivery; Lipid; stimuli-responsive**.**

References:

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