Photo-Triggered Localized Nitric Oxide Release from Polyprodrug Vesicles for Corneal Wound Healing

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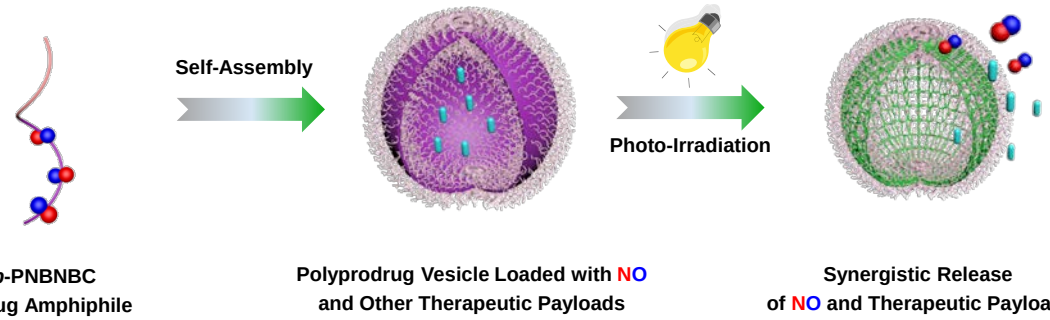
Nitric oxide (NO), an endogenous ubiquitous transmitter, exerts unique therapeutic effects in the treatment of tumors, bacterial infections, and wound healing and so on. The site-specific delivery of NO is of crucial importance to achieve optimal therapeutic outcomes. However, it remains challengeable to deliver NO in a spatiotemporally controlled manner. Herein, we propose a prodrug strategy to deliver NO that can be selectively activated by light irradiation. NO was first caged by the formation of *N*-nitrosoaniline-based prodrug monomers; these monomers with excellent stability can be polymerized with the formation of polyprodrug amphiphiles, which can further self-assemble into vesicular assemblies. The photo-cleavage of N-NO bonds of *N*-nitrosoaniline moieties within the vesicle bilayers led to the release of NO, which subsequently activated the azaquinone-methide elimination, thereby permeating and cross-linking the vesicular bilayers. We demonstrated the photo-mediated spatiotemporal NO release could be used for the treatment of corneal wound healing and the synergistic delivery of NO and other therapeutic payloads could be achieved.



Scheme 1: Schematic illustration of the formation of vesicles assembled from nitric oxide (NO)-containing polyprodrug amphiphiles, PEO-*b*-PNBNBC. The resulting vesicles encompass NO donors in the hydrophobic bilayers and hydrophilic therapeutic payloads can be loaded into the aqueous lumens. Under light irradiation, the N-N bonds were cleaved and NO was released; subsequently, the spontaneous 1,6-elimination reaction occurred, concomitant cross-linking and permeating the bilayers, which gave rise to the synergistic release of encapsulated payloads.

References

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