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REVIEW

Dendrimer porphyrin-based self-assembled nano-devices for biomedical applications

Young-Hwan Jeong, Hee-Jae Yoon and Woo-Dong Jang

Dendrimers have attracted great interest for the design of functional materials. Because the core porphyrin unit in dendrimer porphyrin (DP) is surrounded by large poly(benzyl ether) dendritic wedges with ionic peripheries, the resulting electrostatic interaction with oppositely charged polymeric materials has been used to create various functional nano-devices. In this paper, we briefly review DP-based self-assembled biomedical nano-devices, including DP-loaded polyion complex micelles, the ternary complex systems used for gene delivery, polymer-metal complex micelles, the hollow nanocapsules used for combination cancer therapy, and the DP-immobilized surfaces used for diagnostic tools.
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Keywords: biomedical; dendrimer; nano-device; photodynamic therapy; phthalocyanine; polymeric micelle; porphyrin

INTRODUCTION

Because of their well-characterized, three-dimensional structure, dendritic macromolecules are of interest for a wide range of applications.[1–5] For biomedical applications in particular, dendrimers are promising materials because functional nano-devices require a controlled three-dimensional architecture with appropriate functional groups at designated sites.[6–11] Because dendrimers are synthesized by precisely controlled stepwise reactions, designers have the freedom to introduce functional groups at specific sites.[12–14] A typical dendrimer comprises three different topological parts: a focal core, layered building blocks, and multiple peripheral groups, which provide fascinating chemical characteristics.[15,16] The focal core can be isolated from the outer environment by large dendritic wedges, the layered building blocks provide the dendrimer with its three-dimensional structure, and the multivalent surface can integrate functionalities in a small space. In addition, only the congested surface functionalities interact with the external environment; therefore, the peripheral functional groups can be used to control the solution properties of the dendrimers.[17–19] To date, a great number of dendritic macromolecules have been developed and investigated. Among them, we have designed poly(benzyl ether) dendrimers with a photofunctional porphyrin or phthalocyanine core for use in biomedical nano-devices. Herein, we review recent research on dendrimer porphyrin-based nano-devices for biomedical applications.

STRUCTURE AND CHARACTERISTICS OF DENDRIMER PORPHYRIN AND PHTHALOCYANINE

Synthesizing dendrimer porphyrin (DP) and dendrimer phthalocyanine (DPc) uses convergent synthetic strategies to prepare a defect-free dendritic structure (Scheme 1).[20,21] Because porphyrin and phthalocyanine have unique photofunctional properties, such as a large absorption cross-section, fluorescence emission, and photosensitizing properties, DP and DPc can be used as photofunctional nano-devices.[22–25] Upon excitation by light, porphyrin and phthalocyanine can fluoresce or transfer their excitation energy or an electron to an appropriate acceptor molecule.[25] This unique property makes these molecules useful for probing micro-environments or as photosensitizers for photodynamic therapy (PDT).[26–29] However, because porphyrin and phthalocyanine are strongly hydrophobic and because they have a large π conjugation domain, they often form aggregates. Aggregated porphyrin and phthalocyanine eventually lose their photofunctional properties.[30] The dendrimer forms of these molecules, DP and DPc, remain soluble in aqueous medium because of the large number of anionic functional groups on their periphery. In addition, large dendritic wedges effectively prevent aggregation.[31–34] The high solubility of DP and DPc permits their use in PDT, a promising technology for less invasive cancer treatments. PDT involves the systemic administration of photosensitizers (PS) followed by the irradiation of the target tissue with laser light. The irradiation excites PSs, which transfer their excitation energy or electrons to oxygen molecules in the target tissue to generate highly toxic reactive oxygen species (ROS). The ROS eventually destroy the target tissue (Figure 1). Because DP and DPc exhibit successful solubility in aqueous medium, we can utilize them as effective PSs. When DP was used as a PS, it exhibited 10–100 times higher photocytotoxicity than protoporphyrin IX, a conventional PS, for treating Lewis lung carcinoma (LLC).[33] Moreover, the ionic surfaces of DP and DPc have been used to form polyion complex (PIC) micelles through electrostatic interactions. *In vitro* and *in vivo*

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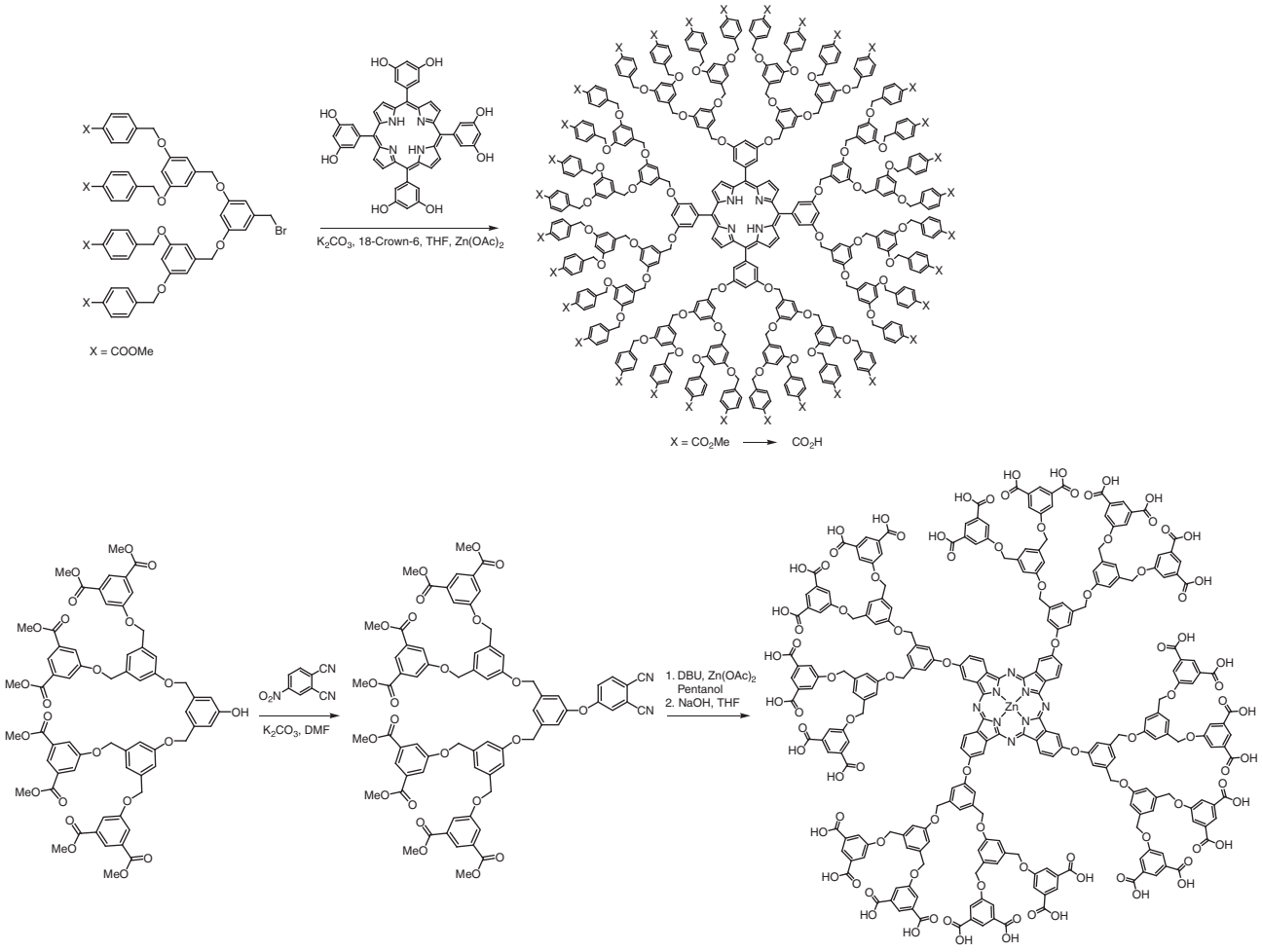

Scheme 1 Synthesis of dendrimer porphyrins (DP) and dendrimer phthalocyanine (DPc).

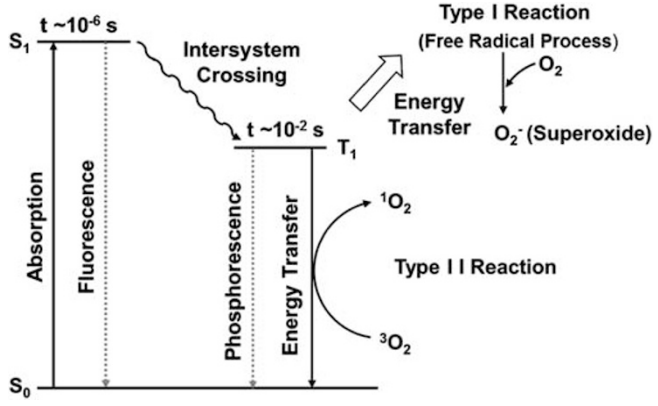

Figure 1 Photodynamic process. A full color version of this figure is available at *Polymer Journal* online.

experiments have demonstrated that PIC micelles are successful formulations for use in PDT.

FORMATION OF DP-LOADED PIC MICELLES

Because the peripheries of DP and DPc contain negatively charged carboxylic acid groups, PIC micelles can be formed through electrostatic interactions with positively charged block copolymers. When DP is mixed with poly(ethylene glycol)-block-poly(L-lysine) (PEG-b-PLL) in a stoichiometric charge ratio, PIC micelles form spontaneously with a diameter of approximately 60 nm (Figure 2).[35] The PIC micelles prepared from DP and PEG-b-PLL have an extremely narrow size distribution in physiological saline solution. The spherical shape of DP-incorporated micelles was confirmed by atomic force microscopy (AFM) and field emission-transmission electron microscopy (FE-TEM). Static light scattering (SLS) revealed that each PIC micelle contains an average of 38 DP molecules.[35] The PIC micelles remain stable in remarkably high NaCl concentrations. Although the local DP concentration is high in the micellar core, the PIC micelles did not exhibit fluorescent quenching.[34] Moreover, fluorescent quenching did not occur when PIC micelles containing DP were incubated with cells, suggesting an effective photochemical reaction in the living cells. These unique photochemical properties might not be achieved with other conventional PSs. We have investigated the efficiency of oxygen depletion under light irradiation. PIC micelles containing DP exhibited an oxygen depletion rate comparable to that of free DP in PBS containing fetal bovine serum (FBS) as a singlet oxygen acceptor, suggesting that the singlet oxygen molecules produced by DP effectively escape the micellar structure and react with proteins in FBS (Figure 3).[34] DP-loaded PIC micelles exhibited approximately 280 times higher

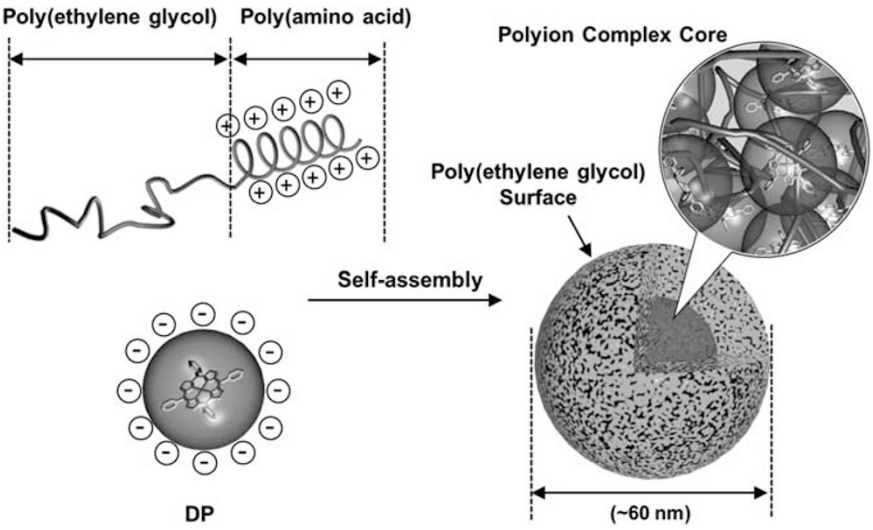

Figure 2 Formation of polyion complex micelle. A full color version of this figure is available at *Polymer Journal* online.

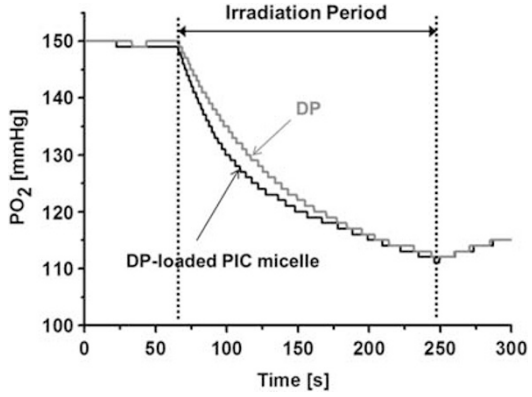

Figure 3 Oxygen depletion profiles by free DP (–) and the DP-loaded PIC micelle (—) in PBS containing 10% FBS. The light irradiation and the oxygen partial pressure measurements were performed using a Hg lamp and a Clark-type oxygen microelectrode, respectively (Jang *et al.*,[34] with permission. Copyright Wiley-VCH). A full color version of this figure is available at *Polymer Journal* online.

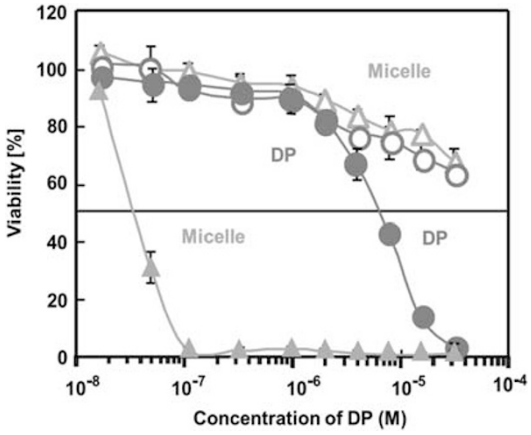

Figure 4 The cytotoxicity of LLC cells incubated with free DP (circle) and the DP-incorporated PIC micelles (triangle) compared with that of LLC cells under dark conditions (open symbol) and photoirradiation (closed symbol). Cells were photoirradiated for 10 min using broadband visible light from a xenon lamp (150 W) equipped with a filter passing light of 400–700 nm (fluence: 180 kJ cm^{-2}). The cell viability was evaluated using the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay. A full color version of this figure is available at *Polymer Journal* online.

photocytotoxicity against LLC cells than free, anionic DP, although the cells only take up 6–8 times more DP-incorporated PIC micelles than free anionic DP (Figure 4).[34] This strong photocytotoxicity can be explained by a high local concentration of singlet oxygen generation at the local site.

The formation of PIC micelles was again investigated using different generations of DPs. Using small dendrimers to form PIC micelles resulted in aggregates with a large size distribution, indicating that the relatively open architectures and small dendritic wedges may not completely prevent π-π interactions between the porphyrin cores.[36] Additionally, aggregates of small dendrimers had shorter fluorescence lifetimes and decreased oxygen depletion. Therefore, we conclude that the dendritic wedges in third-generation DPs might be sufficiently large to prevent focal photosensitizing units in the micellar core from self-quenching. The *in vitro* PDT effect of various sized DP-loaded micelles has been tested for HeLa (human cervical adenocarcinoma) cells.[36] Micelles loaded with third-generation DPs exhibited the highest photocytotoxicity.

To evaluate PDT with DP-loaded micelles *in vivo*, animal models of exclusive age-related macular degeneration (AMD) were prepared by photocoagulation using semiconductor laser irradiation. AMD, which is caused by abnormal neovascularization (CNV) from the choroidal membrane to the macula, is a major cause of vision loss in developed countries.[37] For PDT to be effective against AMD, PSs need to selectively accumulate in CNV lesions.[38] PDT was performed using DP-loaded PIC micelles in an AMD model.[39] After 7 days of photocoagulation in rats, 400 μl of DP-loaded PIC micelles or free DP (including 1.5 mg ml^{-1} of DP) was administered by tail vein injection.[39] When DP fluorescence was observed in the eyes, DP-loaded micelles effectively and selectively accumulated in the CNV lesions. The selective accumulation of DP-loaded micelles indicates that the CNV lesions may have features similar to solid tumor vasculatures, such as hyperpermeability and impaired lymphatic

drainage.[40–43] Additionally, DP-loaded micelle accumulation in CNV lesions significantly enhanced PDT, as confirmed by fluorescein angiography. When the laser irradiation was performed after 15 min of the DP-loaded micelle injection, 78% of fluorescein leakage in the CNV lesions was blocked after 1 day of PDT.[39] More importantly, no macroscopic photodamage was observed on the skin when the rats were exposed to broadband visible light after 4 h of the DP-loaded micelles injection (a Xenon lamp equipped with a 377 to 700 nm bandpass filter with power of 30 mW cm^{-2}). In sharp contrast, administering Photofrin, a conventional PS, has resulted in severe skin burns under the same conditions, indicating that DP-loaded micelles may not be hypersensitive to light exposure.

Corneal neovascularization is another major cause of vision loss. A wide range of inflammatory, infectious, degenerative, and traumatic disorders can induce corneal neovascularization. Similar to AMD, DP-loaded micelles selectively accumulate in neovascular corneal tissue. PDT using a fluence of 10 J cm^{-2} after injecting DP-loaded PIC micelles resulted in complete regression of neovascular lesions after 7 days. From these *in vivo* results, we conclude that DP has great potential as a PS to treat several ophthalmologic diseases.

FORMATION OF DPc-LOADED PIC MICELLES

Although the aforementioned results indicate that DP has great potential as a PS for PDT in transparent ophthalmologic diseases, the absorption maximum of DP, 430 nm (soret band) and 560 nm (Q band), might limit its use in solid tumors because of problems with light delivery. Melanin dyes in the skin absorb short wavelength light to prevent genetic disorders, and heme proteins in the blood also absorb light in the visible range. Therefore, PSs for solid tumors must absorb long wavelength light that can penetrate deeper lesions. DPc-loaded PIC micelles were prepared and tested in a solid tumor model.[28,44–46] DPc-loaded micelles, approximately 50 nm in diameter, were prepared from DPc and PEG-b-PLL in a manner similar to the DP-loaded micelles.[47] Unlike DP, loading DPc into micelles shifted the absorption maximum from 685 to 630 nm, indicating possible interactions between the phthalocyanine units in the micellar core. The relatively small dendritic wedges in DPc may not be sufficient to prevent such interactions. Consequently, DPc-loaded micelles consume less oxygen than DPc alone.[47]

DPc-loaded micelles, however, significantly enhanced photocytotoxicity, which relies on the photoirradiation time. DPc-loaded micelles exhibited approximately 100 times higher photocytotoxicity than free DPc upon 60 min of photoirradiation. DPc-loaded PIC micelles were 3.9 times more effective than Photofrin, as indicated by the number of photosensitizing units. Significant differences in the light-induced morphological changes of the cells were observed when the cells were treated with IC_{99} of DPc or DPc-loaded micelles.[48] DPc-loaded PIC micelles induced rapid cell death accompanied by morphological changes, including swelling and membrane blebbing, whereas free DPc induced gradual shrinkage of the cells.

The morphological changes induced by DPc-loaded micelles are characteristic of oncosis, which is induced by several pathological conditions, such as hypoxia, inhibition of ATP production, and increased permeability of the plasma membrane.[48] Through detailed observation with a fluorescence microscope, we observed that DPc-loaded micelles induce photodamage to mitochondria, which results in oncosis-like cell death through exhaustion of ATP. In addition to the unique intracellular localization and photochemical reactions, the high local concentration of DPc in the micellar core may also contribute to the high PDT efficiency. The high local concentration of DPc might generate a high local concentration of ROS, generating enough photochemical oxidation to exceed the threshold of cell death.[49]

To test phototoxicity induced by DPc-loaded micelles *in vivo*, mice with subcutaneous A549 tumors received DPc-loaded micelles (0.37 μmol kg^{-1}), free DPc, or Photofrin (2.7 μmol kg^{-1}) through tail vain injection.[49] The tumor volumes were monitored after the PDT treatment. DPc-loaded micelles exhibited significantly higher antitumor activity than DPc or Photofrin. Furthermore, the DPc-loaded micelle dose, in PS units, was 7.3 times lower than that of Photofrin (Figure 5). The enhanced PDT efficacy of DPc-loaded micelles might be attributed to their increased accumulation in tumors and enhanced photocytotoxicity. Similar to DP-loaded micelles, DPc-loaded micelles resulted in minimal skin toxicity upon broadband white light irradiation. DP- and DPc-loaded micelles may

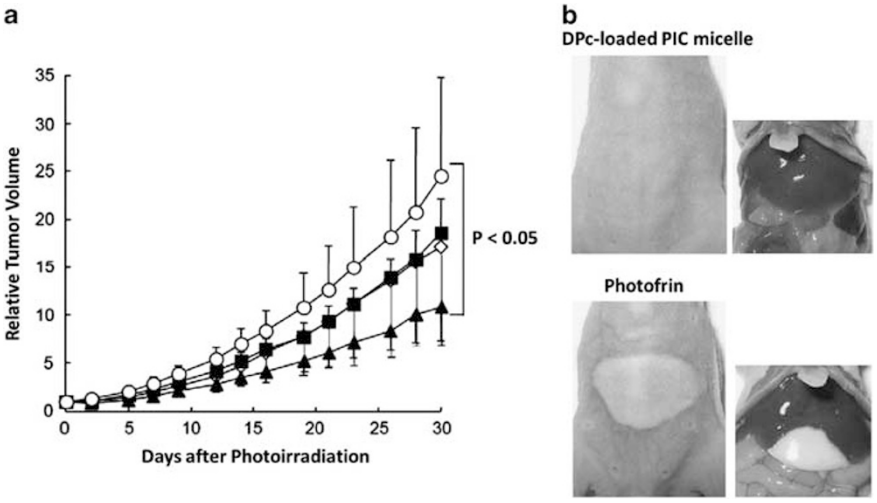

Figure 5 (**a**) Growth curves of subcutaneous A549 tumors in control mice (open circles) and mice administered 0.37 μmol kg^{-1} DPc (closed squares), 0.37 μmol kg^{-1} DPc-loaded PIC micelle (closed triangles) and 2.7 μmol kg^{-1} Photofrin (open diamonds) ($n=6$). After 24 h photosensitizer administration, the tumors were photoirradiated using a diode laser (fluence: 100 J cm^{-2}). (**b**) Macroscopic observation of the skin and organs in the mice treated with 4.2 μmol kg^{-1} DPc-loaded PIC micelle and 8.1 μmol kg^{-1} Photofrin 4 days after light irradiation to the abdominal skin using a halogen lamp (fluence: 60 J cm^{-2}). A full color version of this figure is available at *Polymer Journal* online.

produce low phototoxicity in the skin because fewer of the micelles accumulate in the skin and other normal organs.

Irradiating PSs with light generates ROS, which disrupt tissues and organelles. PSs then accumulate in endo/lysosomal compartments, and photoirradiation selectively disrupts the endo/lysosomal lipid bilayer. Recently, this concept has been applied to drug delivery.[50] Because the endosomal escape of drugs is a major obstacle in drug delivery for drugs that are taken up by endocytosis, light-induced drug delivery would allow for site-specific drug delivery. Cells take up DPc-loaded PIC micelles through endocytosis; therefore, DPc-loaded PIC micelles are preferentially localized in the endo/lysosomes. Upon photoirradiation, DPc-loaded PIC micelles disrupt the endo/lysosomal membranes and translocate to other organelles.

This concept has been used for the light-induced delivery of several compounds, including plasmid DNA (pDNA) and camptothecin (CPT), to the cytoplasm. The light dose for light-induced drug delivery is much lower than that for PDT. Light-induced transfection was performed using a combination of micelles loaded with DPc and pDNA. Transgene expression increased 100-fold while maintaining 80% cell viability.[50] More recently, a polymeric micelle containing CPT, a hydrophobic anticancer agent, was designed as a stimulus-responsive drug carrier. CPT is covalently conjugated to block copolymers via a disulfide bond, which is cleaved under reductive conditions in the cytosol. To evaluate *in vitro* cytotoxicity, HeLa cells were incubated with CPT-loaded micelles and a non-toxic concentration of DPc-loaded PIC micelles.[51] Upon light irradiation, the CPT-loaded micelles internalized and the disulfide bonds were cleaved, significantly enhancing the cytotoxicity of the CPT (Figure 6). Photo-induced drug delivery has an added benefit of controlling drug localization in the body. In addition, a strong potential exists for overcoming the multidrug resistance present in many *in vivo* tumor models.

TERNARY COMPLEX SYSTEM FOR GENE DELIVERY

To deliver genes, ternary complexes composed of pDNA, quadruple cationic Tat peptide (CP4), and DPc have been designed (Figure 7).[52] The ternary complex was prepared by simply adding DPc to the cationic pDNA–CP4 complex, which was obtained by mixing pDNA

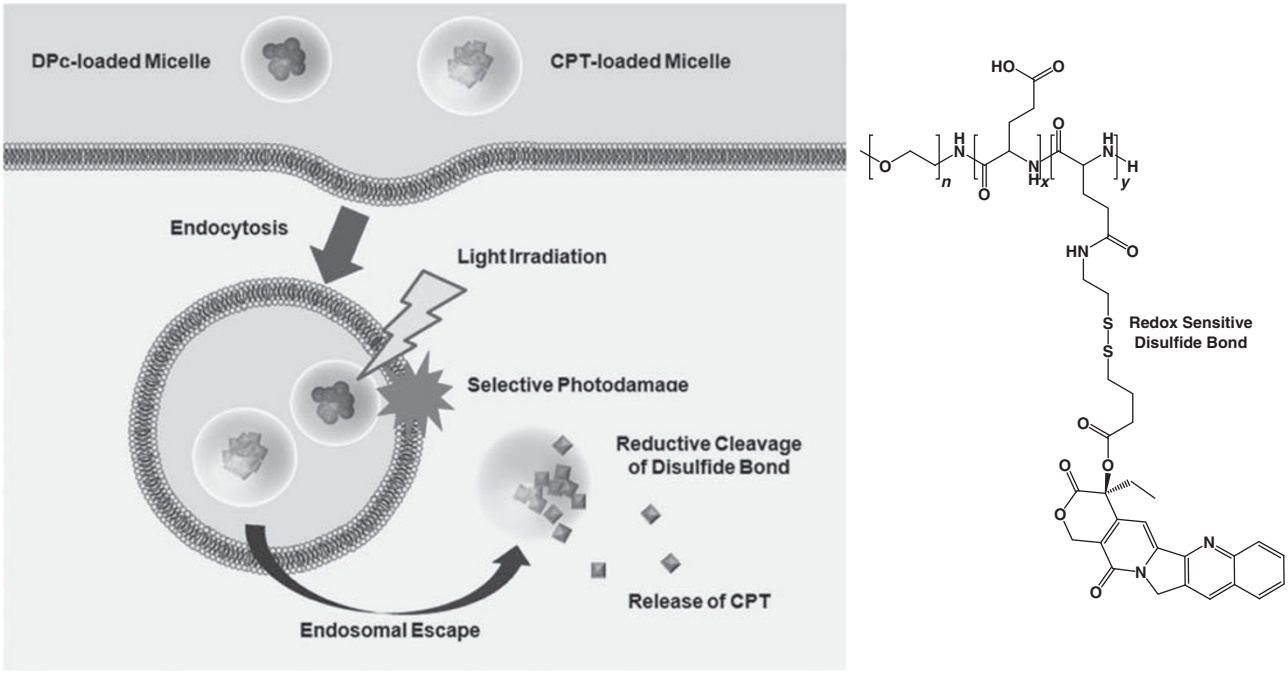

Figure 6 Photochemical delivery of CPT using DPc-loaded PIC and CPT-loaded micelles. A full color version of this figure is available at *Polymer Journal* online.

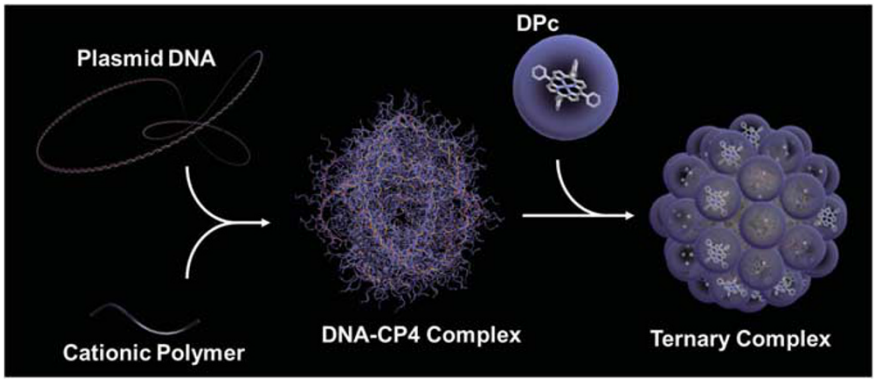

Figure 7 Formation of the pDNA–CP4–DPc ternary complexes as light-responsive gene carriers for site-directed gene transfer.

and CP4 with negative and positive charge in a 1:2 ratio. Adding DPc to the cationic pDNA–CP4 complex creates a ternary complex 130 nm in diameter with a narrow size distribution.[52] In contrast, linear poly(aspartic acid) (degree of polymerization = 26) does not form spherical nanoparticles when added to pDNA–CP4 complexes, suggesting that the three-dimensional structure of DPc plays an essential role in forming the ternary complex. The ternary complex enhanced *in vitro* transgene expression more than 100-fold following light irradiation, without severe photocytotoxicity. In contrast, AlPcS2a (aluminum phthalocyanine with two sulfonate groups) mixed with the pDNA–CP4 complex, causing severe cytotoxicity, possibly because of the non-selective adhesion of AlPcS2a to cells. The ternary complex was used for subconjunctival injection in rats and was irradiated with a semiconductor laser (689 nm) 2 h after injection. The gene, encoding a fluorescent protein, was only expressed at the laser-irradiated site in the conjunctiva, indicating that we can control gene expression in a light-directed manner.

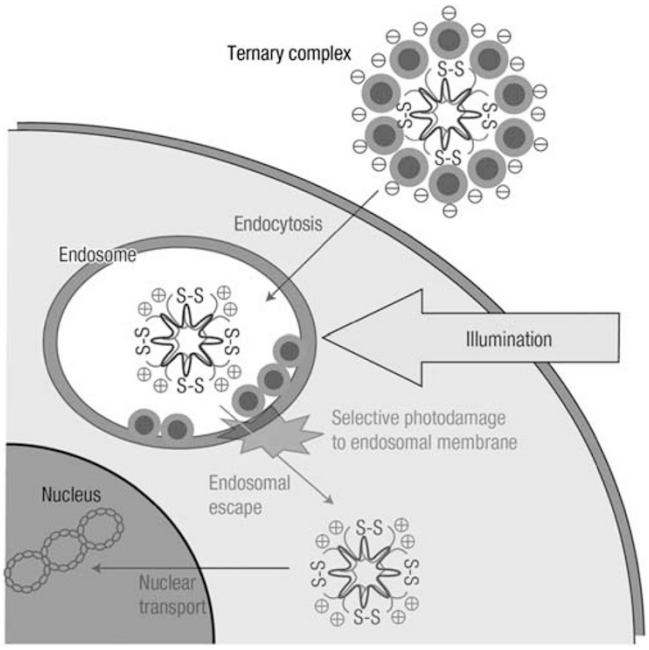

Figure 8 Proposed mechanism for transgene expression by the ternary complex. A full color version of this figure is available at *Polymer Journal* online.

Transgene expression by the ternary complex can be explained by the following mechanism (Figure 8): Cells internalize the ternary complex through endocytosis. Once internalized, DPc is released from the ternary complex as its peripheral carboxyl groups are protonated under the acidic conditions in the endosome. The hydrophobic nature of the dendritic framework causes DPc to then associate with the endosomal membrane. Finally, light-induced disruption of the endosomal membrane allows the pDNA–CP4 complex to escape to the cytosol. The Tat peptides in CP4 then transport the pDNA to the nucleus.

POLYMER-METAL COMPLEX MICELLE

Although PDT is a promising technology to treat malignant tumors, improving its effectiveness could expand its application to a wide range of cancer modalities. In this regard, several nano-devices have been designed for combination cancer therapy. Recently, we designed polymer-metal complex micelles (PMCM) by coordinating cisplatin [*cis*-dichlorodiammineplatinum (II); CDDP] with DPc and poly(ethylene glycol)-block-poly(L-aspartic acid) (PEG-b-PLA, n;

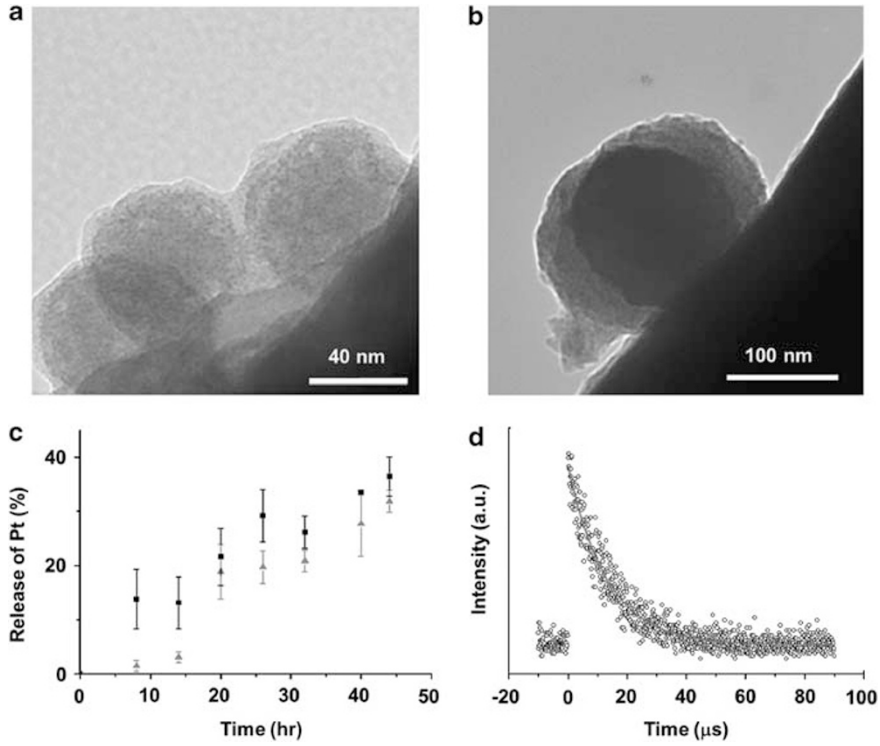

Figure 9 TEM images of (**a**) PMCM68, (**b**) PMCM96, (**c**) release of CDDP from PMCM68 and PMCM96, and (**d**) time-resolved photo-luminescence of singlet oxygen. (Kim *et al.*,[54] reproduced with permission from the Royal Society of Chemistry). A full color version of this figure is available at *Polymer Journal* online.

molecular weight of the PEG segment = 12 000 g mol^{-1}; polymerization degrees of the aspartic acid segment $n = 68$, 96).[45,53,54] The formation of PMCMs was confirmed by TEM and LLS, where PMCM68 and PMCM96 were 97 and 140 nm in diameter, respectively (Figure 9).[54] The PMCMs were highly stable in 10 mM PBS without NaCl and maintained their shape and size for over a month. The PMCMs slowly released CDDP in physiological PBS at 37 °C. Under pulsed laser light (615 nm), the PMCMs generated singlet oxygen, which was evidenced by the photo-luminescence from the singlet oxygen at 1270 nm (Figure 9). Because the PMCMs exhibited sustained release of CDDP with generation of singlet oxygen, they are potential biomedical nano-device for combination therapy.

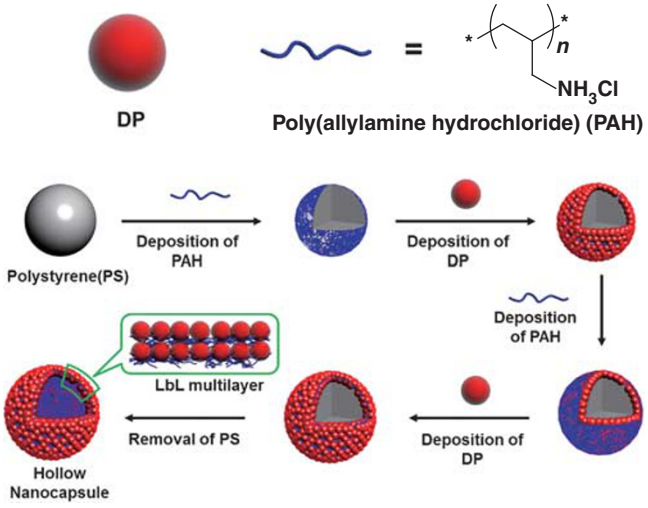

Figure 10 Procedure for the preparation of multilayer hollow nano-capsules. [Son *et al.*,[58] with permission. Copyright Wiley-VCH.].

LbL NANOCAPSULES FOR COMBINATION THERAPY

Recently, we reported a new hollow nanocapsule (NC) as a biomedical nano-device for combination cancer therapy.[55] Hollow NCs were designed using layer-by-layer (LbL) deposition of polyelectrolytes on a sacrificial template.[56,57] DP and poly(allylamine hydrochloride) (PAH) were used as negative and positive electrolytes, respectively.[58] PAH and DP were alternatively deposited on a negatively charged polystyrene (PS) nanoparticle, which was removed to form a hollow structure (Figure 10). The stepwise formation of multilayer shells on PS was monitored by the ζ-potential of the particles after each deposition. The deposition of PAH and DP results in discrete ζ-potential values, alternatively positive or negative, depending on the outermost layer.[58] Formation of the multilayer can also be monitored by changes in the UV-Vis absorbance and FL emission because of the strong UV-Vis absorption and fluorescence emission properties of DP. TEM and FE-SEM were used to directly observe the formation of the multilayered hollow NC_n (n = numbers of LbL bilayer) (Figure 11). Even a single bilayer had sufficient stability to maintain its globular shape after the template PS nanoparticle was removed. Drug encapsulation was tested using doxorubicin hydrochloride (DOX). Through a simple diffusion method, a large amount of DOX was encapsulated in a time-dependent manner. To control the drug release, the shells were crosslinked using N-hydroxysuccinimide (NHS) and 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide (EDC). As a result, the release rate of DOX depended on the degree of cross-linking. When light

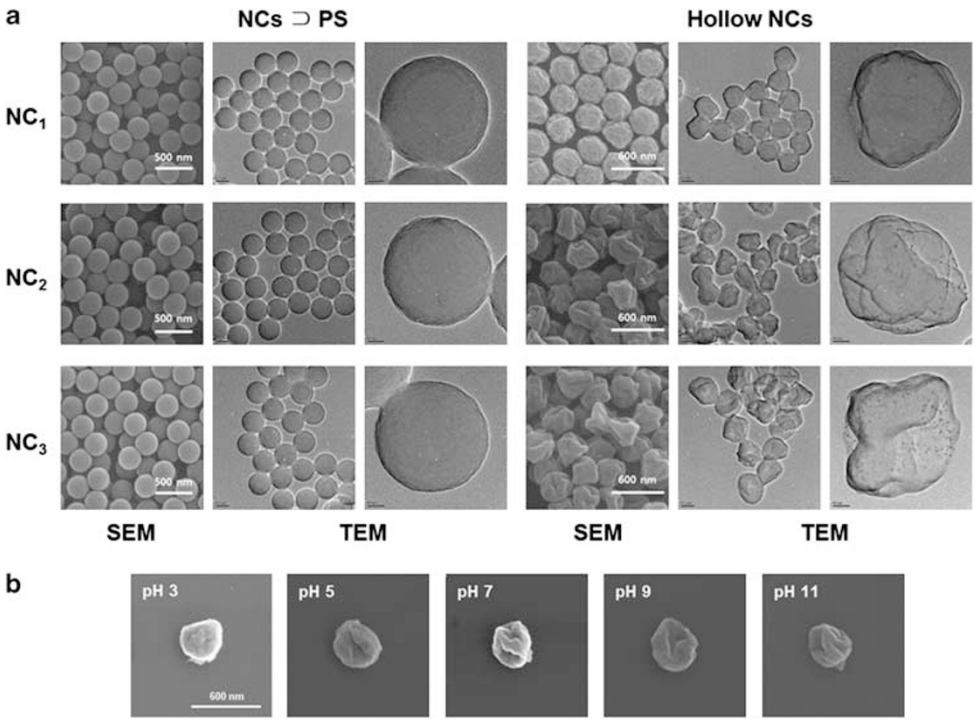

Figure 11 SEM and TEM images of NCs. (**a**) SEM and TEM images of NCs before and after removal of PS nanoparticles. (**b**) SEM images of hollow nanocapsules (NC_3) treated with solutions of different pH values for 1 day. Scale bars are 500 nm except for the right-hand TEM images, whose scale bars are 100 nm (Son *et al.*,[58] with permission. Copyright Wiley-VCH).

irradiated this NC, it was strongly photocytotoxic, indicating that NCs can be successfully used as photosensitizers for PDT. When light irradiated NCs with DOX, they were much more cytotoxic than either chemotherapy or PDT alone, indicating that NCs are possible nano-devices for combinational cancer therapy.

DP-IMMOBILIZED SURFACES FOR DIAGNOSTIC TOOLS

Protein microarrays are a promising technology for protein-based high-throughput assays to analyze interactions between proteins and analytes.[59–63] To design protein microarrays, we used DP as a protein support because the many carboxylic acid moieties on the periphery can effectively immobilize target proteins. DP-coated surfaces can load more proteins and more protein activity than planar surfaces.[64–67] Furthermore, we determined the relative amounts of dendrimer immobilized on the surface and monitored the enzyme-catalyzed reactions using fluorescence microscopy by means of the fluorescent properties of the DP.[66] To prepare a DP-coated surface, the surface of a silicon wafer was covered with positively charged amine groups using 3-aminopropyltriethoxysilane deposited DP via electrostatic interaction in a silanization reaction (Figure 12). FITC-labeled bovine serum albumin (FITC-BSA) or glucose oxidase (GOx) was then immobilized on the DP-coated surface using EDC/NHS chemistry. The DP-coated surface had a higher loading efficacy than the linear poly(acrylic acid)-immobilized surface control. More interestingly, we could directly observe GOx activity from the fluorescence emission intensity of DP. Increasing the glucose concentration caused a gradual decrease in the fluorescence emission intensity of DP. This unique property can be used to develop glucose sensors for medical and industrial applications.

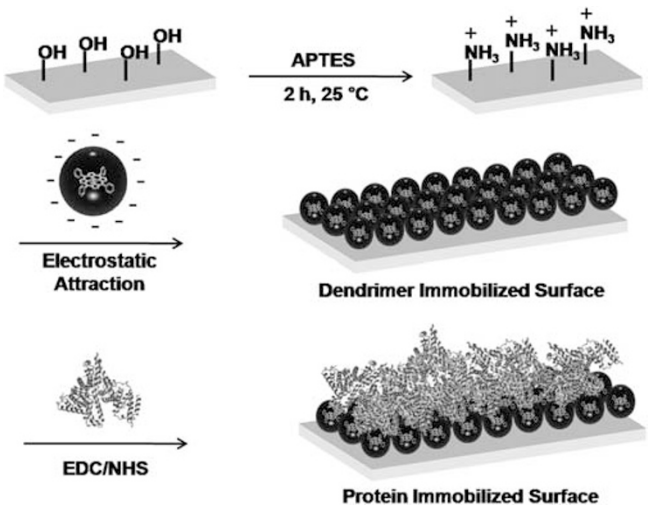

Figure 12 Schematic representation of protein immobilization on silicon/glass substrates coated with dendrimer porphyrin. (Lee *et al.*,[66] reproduced with permission from the Royal Society of Chemistry). A full color version of this figure is available at *Polymer Journal* online.

As another application, we prepared patterned protein microarrays for immunoassays using the LbL technique and used DP to immobilize the proteins on the substrate (Figure 13).[67]

By combining spin-assisted LbL self-assembly and the lift-off method, micropatterns can be fabricated that consist of multilayer films. DP was immobilized on these micropatterns via electrostatic adsorption, and the fluorescence intensity was confirmed by microscopy and AFM. Finally, immunoglobulin was immobilized on the DP-immobilized micropatterns using EDC/NHS chemistry. The DP-immobilized micropatterns exhibited significantly enhanced protein-loading efficacy.[67] Furthermore, the microarray prepared by combining the multilayer micropatterns and DP exhibited drastically improved sensitivity as immunosensors compared with conventional systems.

CONCLUSIONS

In this paper, we have briefly reviewed recent research related to DP and DPc applications in biomedical fields. Owing to the unique

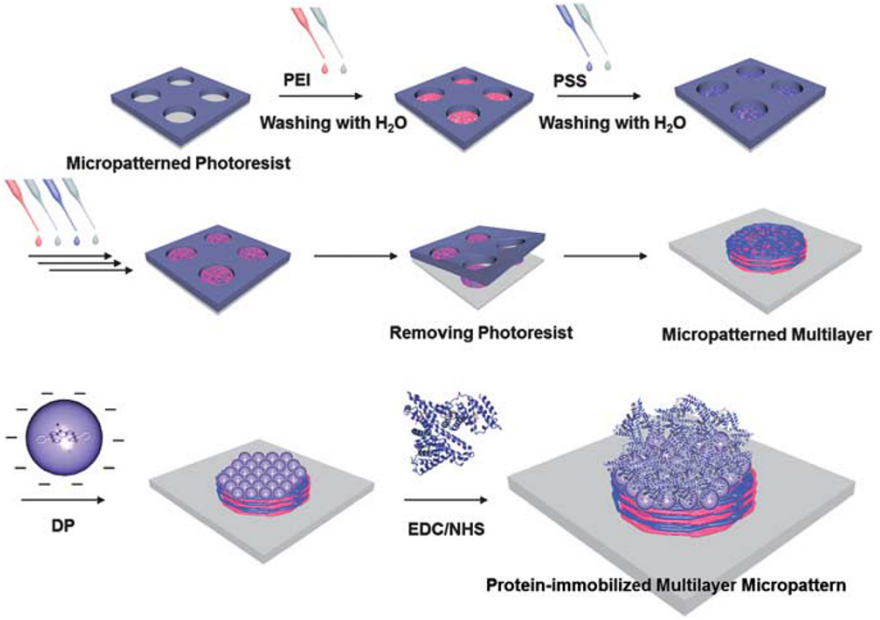

Figure 13 Schematic diagram of protein microarray preparation using micropatterned multilayer films coated with dendrimer porphyrin. (Son *et al.*,[67] reproduced with permission from the Royal Society of Chemistry).

photophysical properties of porphyrin and phthalocyanine in the cores, we have successfully used DP and DPc as photosensitizers for PDT. Moreover, the multivalent functionality on the periphery can be used to build up various nano-devices, including PIC micelles, ternary complexes, PMCMs, hollow NCs, and protein arrays. These unique applications of DP and DPc cannot be achieved using linear polymeric materials. We expect that the continuous effort in designing dendritic materials will be justified and will open a new paradigm in the design of biomedical nano-devices.

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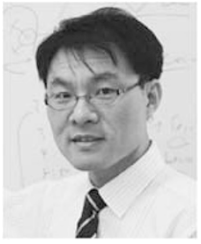

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