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Research Article

A Facile Nanodelivery Platform Based on Functionalized Hyperbranched Poly(ether-ester) for Individualized Antitumor Drugs: Pingyangmycin as a Model

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Nanodelivery of antitumor drugs is a new treatment mode for cancer. The aim of this investigation was to construct and evaluate a facile nanodelivery platform for individualized antitumor drugs based on functionalized hyperbranched poly(ether-ester)s. Poly(ether-ester)s, as a kind of hyperbranched polymers, have received extensive attention. Three terminal-functionalized (OH–, NH_2– and COOH–) hyperbranched poly(ether-ester)s were prepared and characterized by dynamic light scattering and attenuated total reflectance Fourier transform infrared spectroscopy. The relationship between chemical terminal variation and physical surface charges was investigated. Biocompatibility of these polymers was confirmed by methyl tetrazolium assays and scanning electron microscopy. As a model drug, pingyangmycin has antitumor and antiangiogenic effects. In the paper, pingyangmycin was mixed with carboxyl-modified hyperbranched poly(ether-ester) through ionic binding. Polymer-mixed pingyangmycin exhibited significant inhibition of HN-6 head and neck cancer human cells *in vitro*. These studies demonstrate that functionalized hyperbranched (ether-ester)s can be exploited as a facile nanodelivery platform for antitumor therapy.

1. Introduction

Although nanodelivery of antitumor drugs has numerous advantages, such as improved solubility [1], accurate targeting [2–5], increased permeability of tumor vasculature to macromolecules, and decreased lymphatic drainage from the tumor; the complicated techniques involved in nanodelivery development have impeded individualized nanodelivery of numerous antitumor drugs. Even dendritic polymers, which have been used for nanodelivery for years, involve complicated techniques and high costs associated with the crystal architecture [6, 7].

Over the past two decades hyperbranched polymers have received a great deal of attention [8–10]. Since the first intentional preparation of hyperbranched polymers, many types have been synthesized, including polyimide, polyether, polymethacrylate, polyphenylene, poly(ether ketone), polyester, and polyurethane [11]. As a novel generation of dendritic polymers, hyperbranched polymers (HBP), which have characteristic incomplete branching and irregular dimensions, provide a facile substitute for the preparation and screening of nanocarriers. Distinct from their linear analogues, hyperbranched polymers have structures and topologies similar to dendrimers and possess some strikingly superior material properties [9, 10]. Due to their low dispersity and excellent biocompatibility and biodegradability [1, 12–16] hyperbranched polymers have been applied in the field of pharmaceutical delivery. In our previous studies, hyperbranched poly(ether-ester) (HPEE) was prepared, characterized [17, 18], and applied as a nanocarrier of antitumor drug [1, 19]. In the present study, a series of terminal-functionalized derivatives were established based on the HPEE backbone, thus

providing a facile platform for optimization of individualized antitumor drug delivery. Pingyangmycin is a water-soluble glycopeptide produced by *Streptomyces pingyangensisn*. It is chemically similar to bleomycin with antitumor and antiangiogenic effects. In this paper pingyangmycin is used as an example to assess the efficacy of this nanodelivery platform.

2. Materials and Methods

2.1. Synthesis of End-Functionalized HPEE Derivatives. A suspension of potassium hydride (KH, Aldrich) in mineral oil (30% in weight) was placed in a dry preweighed 100 mL Schlenk flask under nitrogen. The mineral oil was removed by three extractions with tetrahydrofuran (THF), which was added to the flask by syringe. Completely dried KH (0.58 g, 14.46 mmol) was added to 40 mL dimethyl sulfoxide (DMSO) and tetra (ethylene glycol) (TTEG; 5.62 g, 28.92 mmol) (Aldrich, ShangHai). The solution was stirred for 30 min to form the alcoholate potassium. Subsequently, glycidyl methacrylate (GMA; 4.12 g, 29.98 mmol) (Sigma, USA) was added and polymerization was conducted for 24 h at 80°C. The resultant mixture was precipitated in 1000 mL of acetone/diethyl ether (v/v 1/4) and then redissolved in methanol and neutralized by filtration over cation-exchange resin. The polymer was precipitated twice from methanol solution into cold diethyl ether and subsequently dried under vacuum at 50°C for 24 h. The purified HPEE-OH was obtained as a highly viscous polymer. For HPEE-NH_2 synthesis, 2 g of HPEE-OH was dissolved into 25 mL of DMF. Fmoc-glycine (2.97 g, 10 mmol), dicyclohexylcarbodiimide (DCC; 4.13 g, 20 mmol), 4-dimethylaminopyridine (DMAP; 0.61 g, 5 mmol), and hydration p-toluene sulfonic acid (PTSA; 0.95 g, 5 mmol) were added to the solution. The mixture was dissolved in 20% piperidine to remove fmoc-protected groups. For HPEE-COOH synthesis, 1 g HPEE-OH was dissolved in 15 mL dichloromethane (CH_2Cl_2) under moderate stirring at room temperature. When it was completely dissolved, 1 g of succinic anhydride and 360 μL dried piperidine were added to the flask under the same conditions. For comparison and confirmation purposes, the nonbiodegradable structural analogue hyper-branched poly(ether) (HPE) and its functionalized derivatives were concurrently synthesized and analyzed (details are provided in Supplementary Material available online at http://dx.doi.org/10.1155/2014/601272). *The same synthesis protocols were used for preparation of HPE and its functionalized derivatives.*

2.2. Characterization. Nuclear magnetic resonance (NMR): ^{1}H NMR spectra of the polymers were recorded on an Advanced III 400 M spectrometer (Bruker, Germany) in D_2O as the solvent. Fourier infrared spectra were mefasured on an EQUINOX55 (Bruker, Germany). Respective potentials were tested using NaCl titrant (25°C, 100 mmol/L, pH = 7) on Malvern Instruments Zesasizer 2000. Dynamic light scattering (DLS) was assessed on Zetasizer Nano S (Malvern Instruments Ltd., Malvern, Worcestershire, UK) at 25°C.

2.3. Cell Cultures. NIH/3T3 normal cells (a mouse embryonic fibroblast cell line) were cultured in DMEM supplemented with 10% FBS and antibiotics (50 units/mL penicillin and 50 units/mL streptomycin) at 37°C in a humidified atmosphere containing 5% CO_2. After 48 h logarithmic growth the attached cells were collected by enzymatic digestion (0.25% pancreatin and 0.02% EDTA) for further assay. HN-6 cancer cells (a human head and neck squamous carcinoma cell line) were cultured in PRMI-1640 supplemented with 10% FBS and antibiotics (200 units/mL penicillin and 50 units/mL streptomycin) at 37°C in a humidified atmosphere containing 5% CO_2. Using enzymatic digestion (0.25% pancreatin and 0.02% EDTA), cells were passaged with a 1 : 3 ratio every 2-3 days for numerous cell generations.

2.4. In Vitro MTT Assay for Cytotoxicity Assessment. *In vitro* cytotoxicity of a serial dilution of polymer solution against NIH/3T3 cells was measured by the MTT viability assay. Synthesized HPEE-OH, HPEE-NH_2, and HPEE-COOH were compared with their structural analogues (HPE-OH, HPE-NH_2, and HPE-COOH). All solutions were dissolved in PBS with serial dilutions of 0.001 mg/mL, 0.01 mg/mL, 0.1 mg/mL, 1 mg/mL, and 10 mg/mL. The same concentration series of dextran and PEI were also prepared as negative and positive controls, respectively. NIH/3T3 cells were seeded into 96-well plates at a seeding density of 4.0×10^3 cells per well in 50 μL. After 24 h of incubation, the culture medium was removed and replaced with 50 μL polymer solution at different concentrations. After treatment with polymers for 24 h, 48 h, and 96 h, 20 μL of 5 mg/mL MTT stock solution in PBS was added to each well. After addition of 200 μL DMSO to each well and shaking for 5–10 min, the absorbance was measured at a wavelength of 490 nm using BioTek SynergyH4. Cytotoxicity was determined by the absorbance relative to the blank control.

The *in vitro* inhibitory effect of pingyangmycin-mixed polymers against HN-6 cells was also evaluated by MTT assay. After incubation of HN-6 cells (8.0×10^3 cells/well) for 24 h, the culture medium was removed and replaced with 200 μL of medium containing pingyangmycin-mixed polymer. Pingyangmycin was tested at serial concentrations of 0.01, 0.1, 1.0, 10, and 100 μg/mL.

2.5. Surface Morphological Features of 3T3 Cells. 3T3 cells (2×10^5/mL) were separately cultured with solutions of three end-modified HPEE derivatives and three end-modified HPE analogues. To strengthen the results, each polymer was tested at low concentration (10 μg/mL) and high concentration (1 mg/mL) and the corresponding data were compared. Cells that were simultaneously incubated with HPEE derivatives for 1 h are shown in Figure 4(a) (low concentration subgroup) and Figure 4(b) (high concentration subgroup). At the same time, two control experiments were performed: polyethyleneimine (PEI), an accepted cell toxicant, was used as a positive control and dextran with polymer structure was used as a negative control. Normal 3T3 cells incubated with PBS are also shown as a blank control. Cells of each subgroup were collected and fixed with 2.5% glutaraldehyde for 24 h. Morphological features of the cell surface were observed by scanning electron microscopy (SEM) (FEI Corp. USA).

2.6. Self-Assembly of Pingyangmycin-Mixed Micelle Preparation. Based on pingyangmycin's physical and chemical

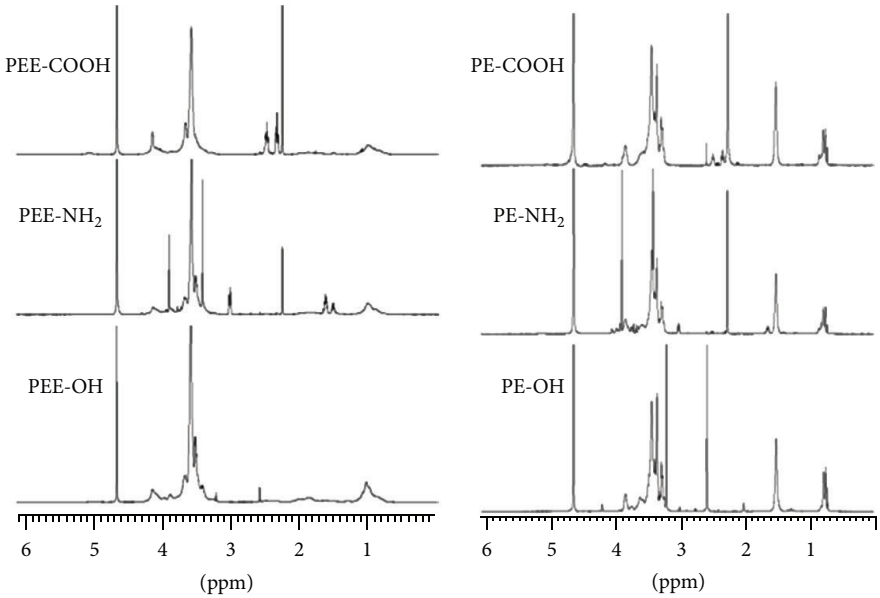


Figure 1: Comparison of ^{1}H NMR spectra between three PEE-derivatives and three PE-analogues.

characteristics, anionic carboxyl-functionalized HPEE was selected for preparation of micelles. Two functionalized mixtures (HPEE : carboxyl = 1 : 1 or 1 : 1.02) were separately added to 10 mL ultrapure water. Pingyangmycin (Bolai Pharmacy Company, China) was then added to each flask with increasing polymer/pingyangmycin ratios of 1 : 1, 1 : 2, 1 : 3, 1 : 4, and 1 : 5. All mixtures were stirred at room temperature for 24 h to form a transparent aqueous solution.

2.7. Visualization of Self-Assembled Micelles by Transmission Electron Microscopy. Prepared micelle samples that had been dried for 24 h in a vacuum were observed by transmission electron microscopy (TEM) (JEOL2010) at 200 KV.

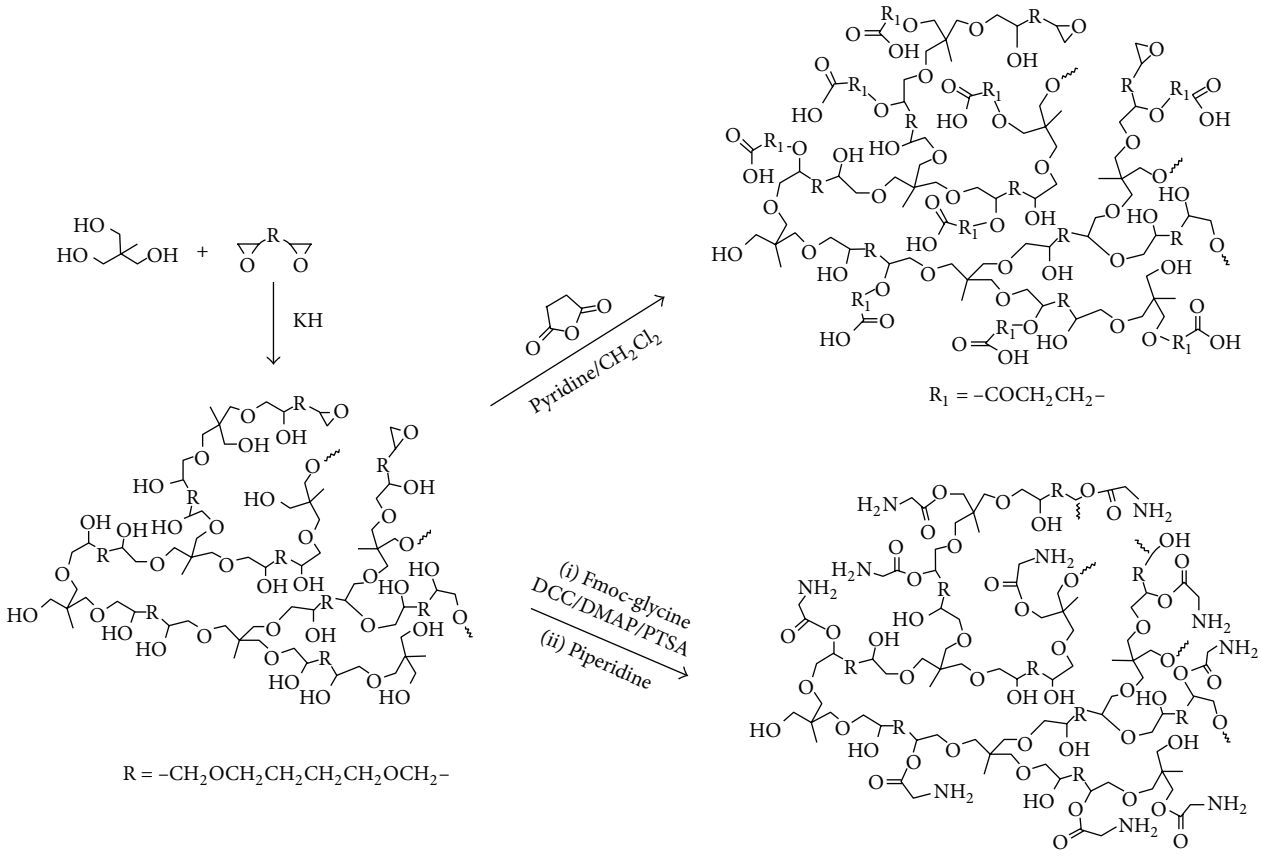
3. Results

3.1. Synthesis of End-Modified Hyper-Branched Poly(ether-ester)/HPEE Derivatives. Characterization of the HPEE backbone has been intensively documented in a previous study [20], therefore terminal-modified hyper-branched poly(ether-ester)s could be easily synthesized based on the HPEE backbone according to Scheme 1. Supplemental data address the scheme for preparing structure-matched HPE derivatives.

3.2. Characterization of Functionalized Hyper-Branched Poly(ether-ester)s/HPEE by ^{1}H NMR. According to the quantitative ^{1}H NMR spectrum of HPEE (Figure 1, Left), the shift of methyl protons was found to be 1.05 ppm. The backbone of HPEE was observed at 1.80–2.10 ppm and revealed a spectrum of $-CH_2-CH(CH_2-)-O-$ or $-CH_2-C(CH_3)-$ structural subunits. A proton peak of methine adjacent to alcohol oxygen and methylene adjacent to ether oxygen was observed at 4.2–3.3 ppm. Novel peaks could be observed at 2.50 ppm ($-OCOCH_2CH_2COOH-$) and 2.30 ppm ($-OCOCH_2CH_2COOH-$) after the carboxyl group was grafted onto HPEE. When a glycine residue ($-OCOCH_2NH_2-$) was grafted onto HPEE, a novel 3.9 ppm peak that indicated the methylene proton from the amino group could be observed. Similar variation of ^{1}H NMR peak-to-terminal could be observed when the same terminals were added to the HPE backbone (Figure 1, Right). The degree of ($-OCH_2CH_2CH_2CH_2O-$) in HPE was found to be 1.59 ppm. ^{1}H NMR distributions were 0.70–0.85.17–4.12 ppm (hydroxyl protons), 0.70–0.85 ppm (methyl protons), and 3.15–3.70 ppm (methylene and methane adjacent to ether oxygen and alcohol oxygen).

3.3. Fourier Transform Infrared (FT-IR) Spectra of the Poly(ether-ester) Derivatives. FT-IR spectra of PEE-OH, PEE-NH_2 and PEE-COOH are shown in Figure 2 (Left). Characteristic ether bond and ester bond absorption bands were shown at 1100 cm^{-1} and 1725 cm^{-1}, respectively. A band at 1668 cm^{-1} could be seen after grafting of amidogen, whereas the 1557 cm^{-1} band could only be seen after the carboxyl group was grafted. For comparison purposes, FT-R spectra of HPE-analogues are also shown in the same figure (Figure 2, Right). Similarly, the 1100 cm^{-1} FTIR band in the top HPE-OH figure was produced by asymmetric stretching vibration originating from C–O–C groups. An amidogen absorption band at 1660 cm^{-1} and a carbonyl absorption band at 1740 cm^{-1} appeared when $-NH_2$ was polymerized into HPE-OH. For HPE-COOH, the carbonyl and carboxyl bands could be observed at 1730 cm^{-1} and 1555 cm^{-1}, respectively.

3.4. Correlation between Surface Potentials and Terminal Groups. Surface charge varied with chemical terminal functionalization, thus reflecting an interrelationship between physical and chemical variations. As shown in Table 1, the negative potential carried by hydroxyl on the surface of



Scheme 1: End-functionalization between HPEE and amino group/carbonyl group.

PEE changed to a positive charge when the hydroxyl was replaced by amidogen; conversely, the negative potential of PEE-OH decreased to a more negative value when hydroxyl was replaced by carboxyl. The PE analogues exhibited similar variation in charge-terminal relationships.

3.5. In Vitro Cytotoxicity against 3T3 Cells. The results of MTT assays for 3T3 cells following incubation for 24 h, 48 h, and 96 h with various concentrations of the HPEE end-functionalized derivatives are shown in Figure 3. In general, HPEE derivatives demonstrated low cytotoxicity against 3T3 cells. Even 3T3 cells treated with 10 mg/mL HPEE-NH_2, which was predicted to have the greatest cytotoxicity, for a long incubation time of 96 h retained good viability. The experiment was repeated using the HPE analogues at the same concentrations. Similar MTT results were obtained for HPE-derivatives, as shown in Supplementary Data 2.1.

3.6. Visualization of 3T3 Cell Surface Morphological Changes by SEM. Cell surface morphological features were visualized by scanning electron microscopy (SEM). As shown in Figure 4, we observed an extraordinarily smooth surface in normal 3T3 cells, except for a scattering of microvilli and some ruffles at the ends of the pseudopodia. Compared with PBS controls, cells treated with hyperbranched polymers showed notable changes in scattered microvilli and irregular ruffle distributions on cell surfaces that reflected mild adaptation rather than cell injury. None of the cell membranes lost their integrity during the whole incubation period. As a positive control, severely damaged 3T3 cells cultured in a high concentration of PEI totally lost their fibroblastic shape and the surface topography appeared to be very irregular and destroyed. Similar SEM observations of HPE-derivatives are shown in Supplementary Data 2.1.

3.7. Self-Assembly of Pingyangmycin into Functionalized HPEE. To verify the nanocarrier platform based on HPEE functionalized derivants for individualized antitumor drug delivery, we used pingyangmycin as a model drug. Based on the physical and chemical characteristics of pingyangmycin, carboxyl-terminated hyperbranched poly(ether-ester) was selected for bioconjugation as shown in Scheme 2.

After screening, the self-assembly protocol was performed. As shown in Figure 5 and Figure 6, successfully conjugated spherical micelles (Sample 3 and Sample 5) with average diameters of 156 ± 9.6 nm (Sample 3/S3) and 173 ± 12.4 nm (Sample 5/S5) were observed by DLS and TEM visualization.

3.8. In Vitro Cytotoxicity of Carboxyl-HPEE-Pingyangmycin Micelles against HN-6 Cells. To evaluate the potential therapeutic efficiency of the carboxyl-terminal-HPEE-pingyangmycin nanocarrier, an *in vitro* MTT assay was performed using HN6 human neck and head carcinoma cells. Both carboxyl-terminated-HPEE-pingyangmycin nanocarriers (S3 and S5) displayed concentration-dependent and time-dependent cytotoxicity as shown in Figure 7. For 24 h

Table 1: Correlation between surface potential and end-functionalized polymers.

Delivery vehicle (PEE)	Potential	Comparable analogue (PE)	Potential
PEE-OH	2.1 ± 1.2	PE-OH	−1.3 ± 1.1
PEE-NH_2	5.4 ± 2.5	PE-NH_2	4.2 ± 0.8
PEE-COOH	−11.8 ± 3.5	PE-COOH	−11.7 ± 2.2

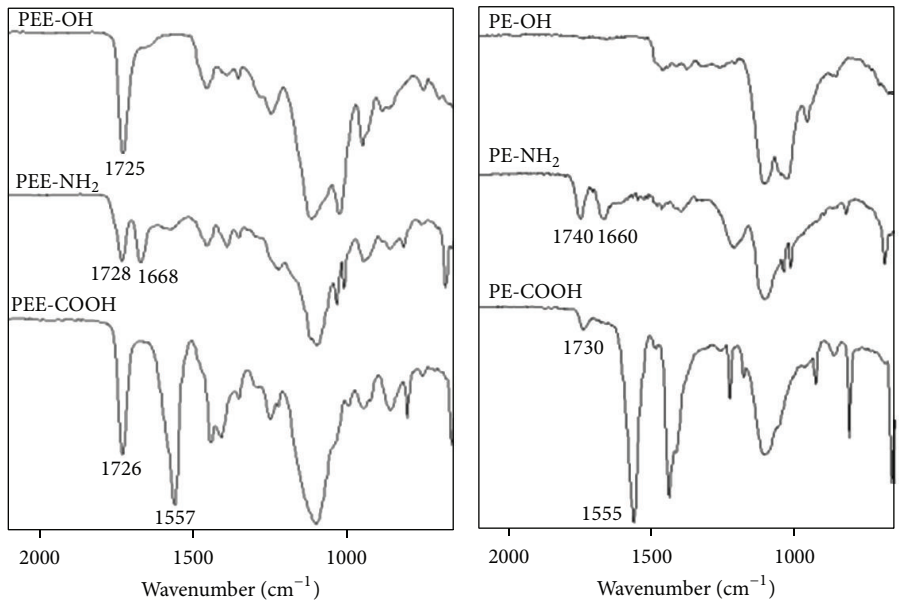


Figure 2: Comparison of FT-IR spectra between three PEE-derivatives and three PE-analogues.

treatment, cell viabilities were decreased by 25% for both pingyangmycin alone and pingyangmycin-nanocarrier complexes at concentrations of 0.1 mg/mL to 1 mg/mL. As the concentration increased to 100 mg/mL, cell viabilities significantly reduced. When the time of treatment extended to 48 h, the viability of HN-6 cells was slightly lower than that observed for 24 h treatment.

4. Discussion

Theoretically, a facile platform could be constructed using functionalized hyperbranched polymer derivatives such that a series of nanocarriers could be obtained for optimization of individualized antitumor-drug delivery. Hyperbranched polymers are characterized by three-dimensional cavities with abundant surface terminals and therefore represent an ideal candidate backbone [1, 21–23]. As shown in Scheme 1, ion-transfer polymerization was observed during HPEE terminal functionalization. A hydroxyl group initially reacted with butanedioic anhydride to form a carboxyl group [24, 25]. The carboxyl end then reacted with the glycine that was protected by the 9-carbonyl methoxycarbonyl group to generate an amino group by subsequent esterification [26], after which methoxycarbonyl protection was rapidly removed. Using the facile polymerization procedure presented here, a series of terminal-functionalized polymers were simultaneously prepared. Subsequent studies revealed physical-chemical interrelationships during functionalization. For confirmation purposes, HPEEs and their HPE structural analogues were simultaneously observed. The similar results confirmed a correlation between physical surface charge and chemical terminal structure; thus, tunable modification of physical charges could be easily achieved by chemical functionalization. Based on this physical-chemical correlation, a tunable nanodelivery platform based on a functionalized HPEE backboned was initially constructed for individualized antitumor drug delivery.

Although good biocompatibility of hyperbranched polymers has been reported [27], the potential cytotoxicity of functionalized HPEE has not been documented. According to the MTT assays, all HPEE derivatives demonstrated excellent biocompatibility even when high concentrations of polymers were used. Furthermore, the biocompatibility of end-modified HPEEs was confirmed by SEM visualization. Previous studies have found that cationic charge of polymers was one of the risk factors for increased cytotoxicity. Due to complicated mechanisms including interactions between cell membranes [28], generation-related clearance [29], and inherent toxicity [30], a strong positive charge of primary amino groups significantly increased the cytotoxicity [28]. Overall, the greatest cytotoxicity of the entire platform was indeed observed for high concentrations of the HPE-NH_2 subgroup, consistent with the previous study. Similarly, mildly enhanced cytotoxicity was observed when the ionic HPEE-COOH subgroup was substituted by the cationic HPEE-NH_2 subgroup. However, relatively good biocompatibility was demonstrated for all HPEE-derivatives in the plat-

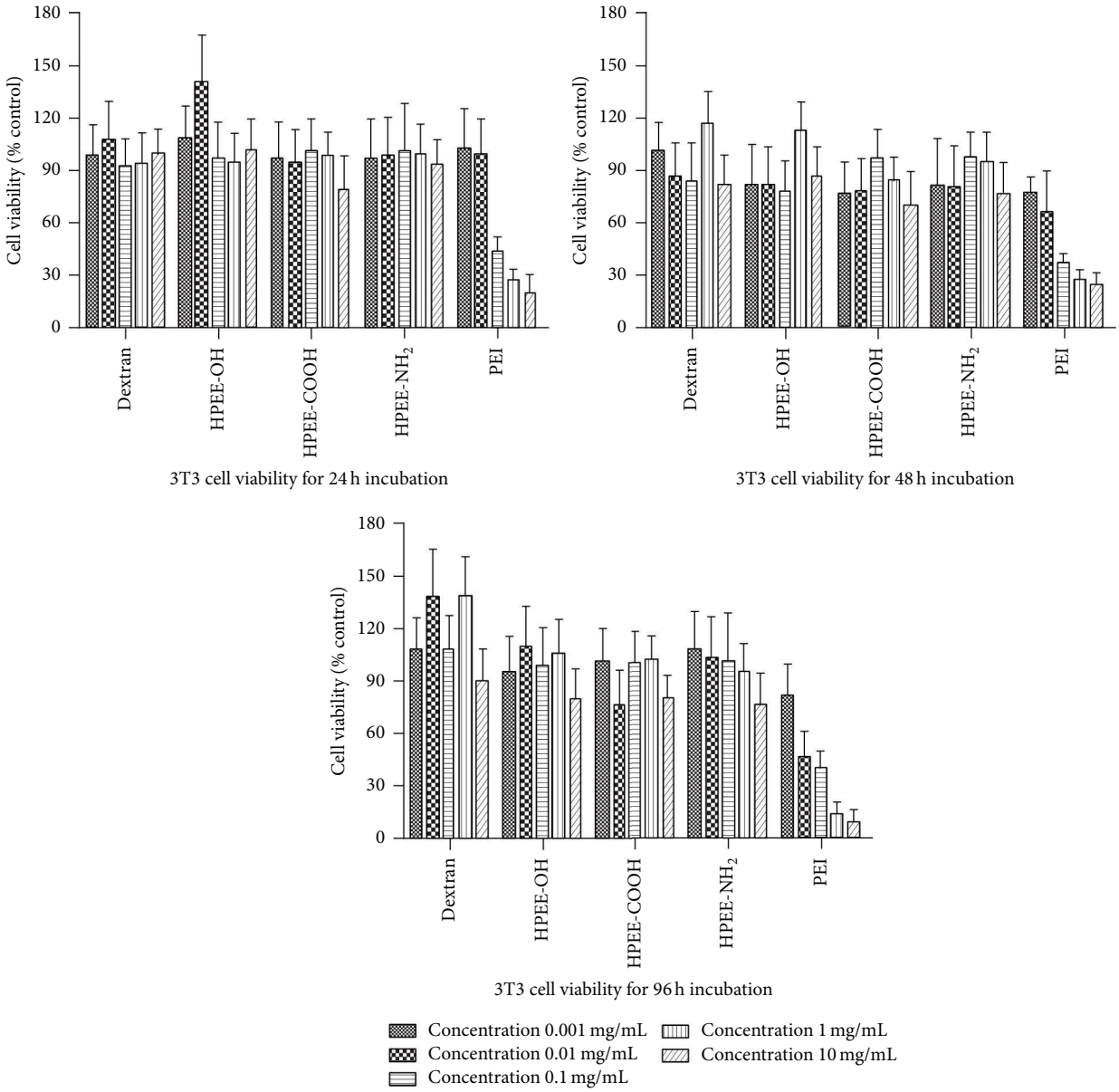


Figure 3: 3T3 cell viability following treatment with various concentrations of HPEE-derivatives.

form, including cationic HPEE derivatives despite previous reports of time- and concentration-dependent cytotoxicity of cationic polymers [28]. The mechanism of the reduced cytotoxicity of cationic HPEE functionalization was attributed to scattered surface charge density and the unique uncompleted hyperbranched architecture.

To evaluate potential application of the present nanodelivery platform, an anticancer drug, pingyangmycin (Bleomycin A5), was used as a model agent to assess assembly capability. Pingyangmycin is an antibiotic that was initially isolated from the culture medium of *Streptomyces pingyangensisn spp.* in China and has been known for a long time to exhibit significant cytotoxicity to tumor cells [31–34]. Despite its effective antitumor activity, the systemic toxicity and short half-life time of pingyangmycin have largely prevented its widespread clinical application. Therefore, hydrophilic pingyangmycin has only been used *in situ* to treat head and neck cancers [31–34]. The specific benefits of nanocarriers, such as passive and accurate targeted therapy with decreased systemic toxicity and long circulation [16], could increase the clinical application of pingyangmycin. As shown in Scheme 2, taking into account the amino-bonding surface of pingyangmycin, electrostatic interactions would theoretically be formed between the positive-charged protonated amines of pingyangmycin and the surface carboxyl groups on the oxidized HPEE [35]; therefore, a self-assembled micelle could potentially be constructed in water. Although it is well documented that hyperbranched polymers possess great capability for self-assembly in solution, the issue of interfacial self-assembly and hybrid self-assembly [18, 36–38] and whether and how functionalized HPEE could successfully mix with pingyangmycin was unknown. In addition, some properties

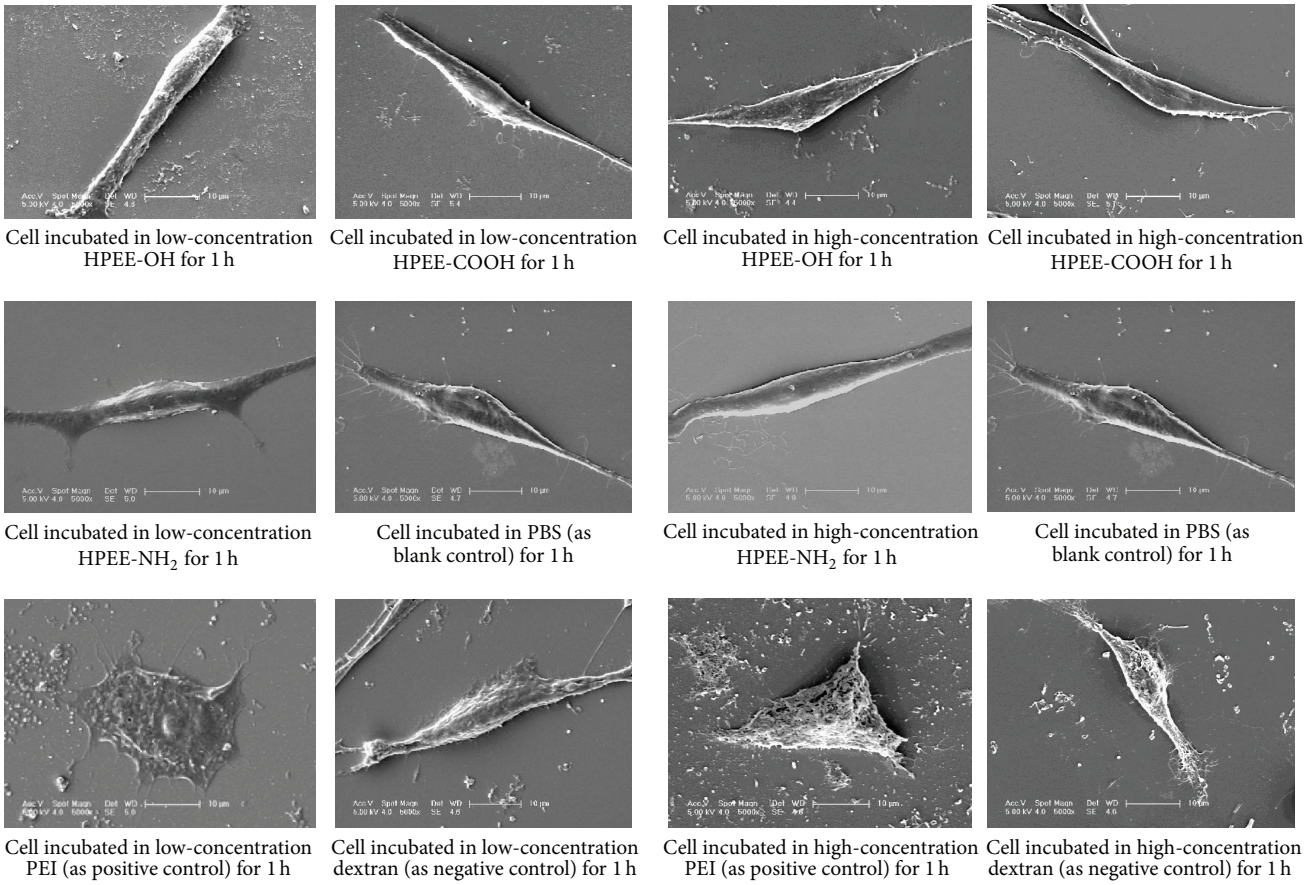
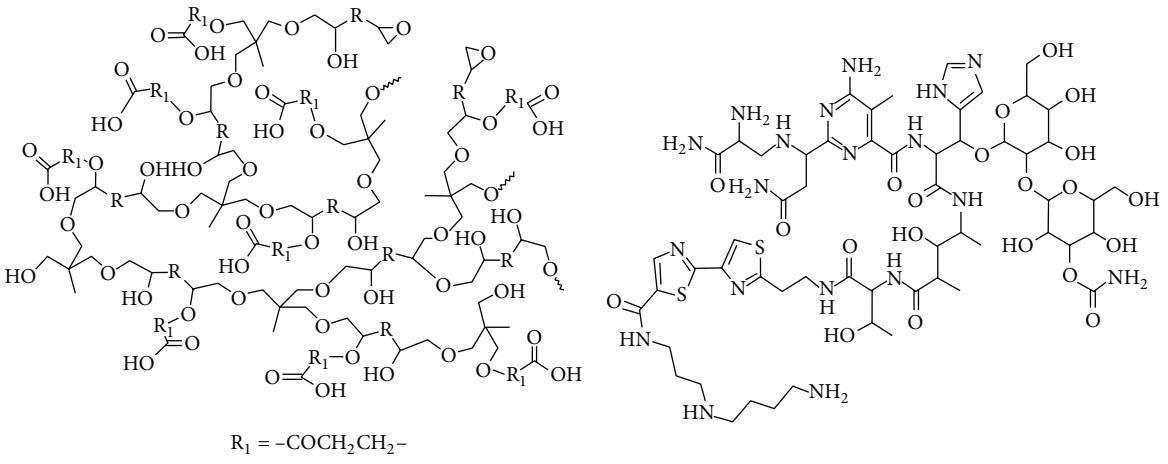


Figure 4: (a) SEM visualization of surface morphological features of 3T3 cells following incubation with low concentration (10 μg/mL) of functionalized HPEE-derivatives and controls. (b) SEM visualization of surface morphological features of 3T3 cells following incubation with a high concentration (1 mg/mL) of functionalized HPEE-derivatives and controls.



Scheme 2: Structure of COOH-HPEE (a) and pingyangmycin (b).

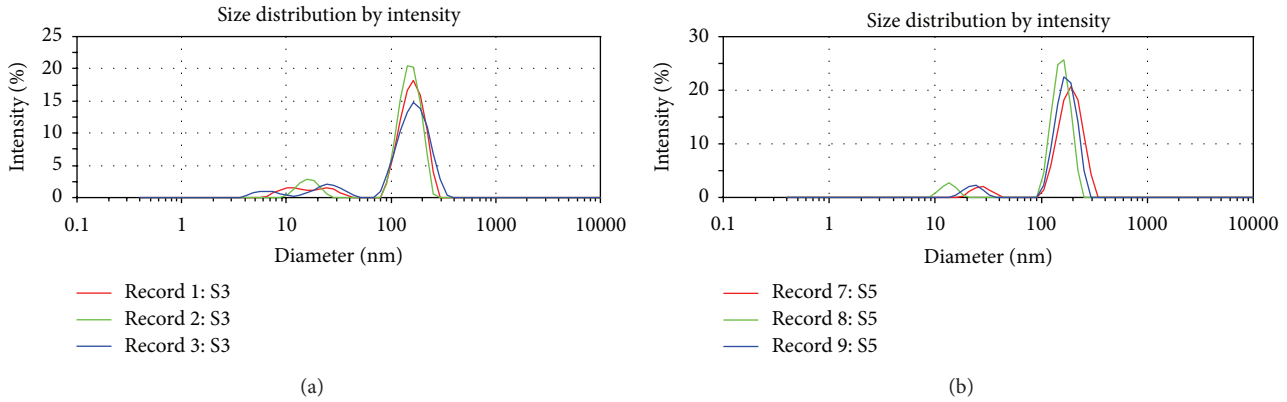


FIGURE 5: (a) Diameter of Sample 3 analyzed by dynamic light scattering assay. (b) Diameter of Sample 5 analyzed by dynamic light scattering assay.

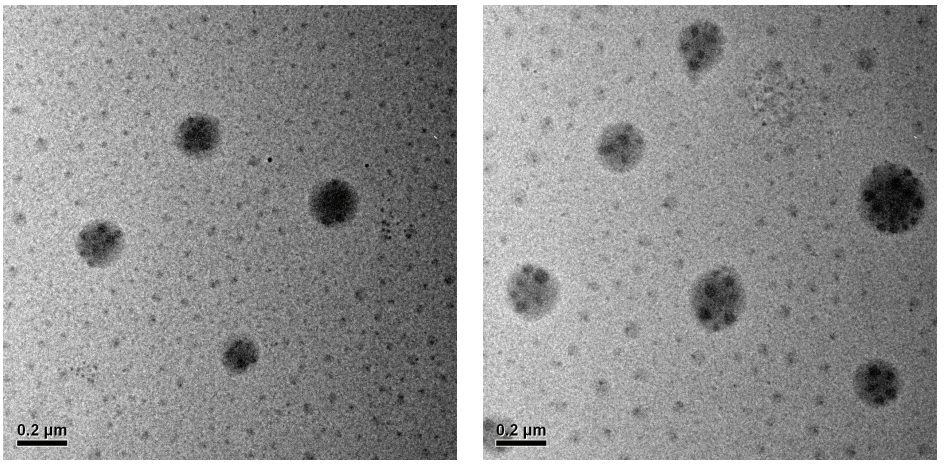


FIGURE 6: Transmission electron microscopy (TEM) visualization of two micelles of pingyangmycin conjugated into carboxyl-terminated HPEE that were successfully self-assembled in water ((a), *S3;* (b), *S5*).

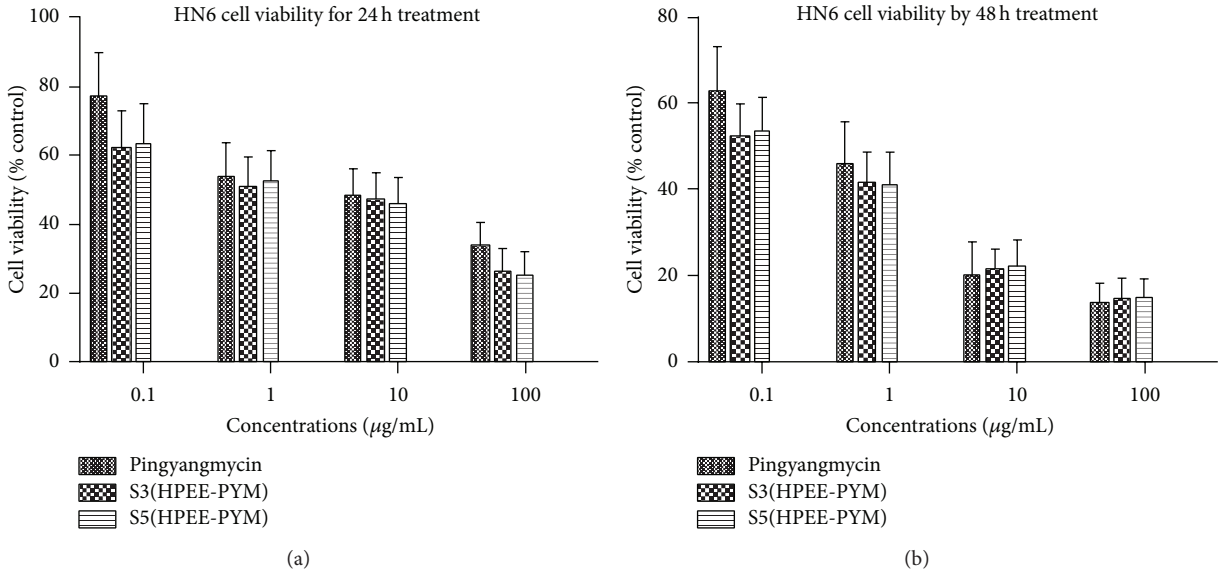


FIGURE 7: (a) HN6 cell viability following treatment with various concentrations of HPEE-pingyangmycin nanocarriers or pingyangmycin alone for 24 h. (b) HN6 cell viability following treatment with various concentrations of HPEE-pingyangmycin nanocarriers or pingyangmycin alone for 48 h.

of hyperbranched polymers have been found to be modulated by terminal-backbone interactions [39]; therefore, confirmation of successful self-assembly was required. For the purpose of comparison, in the present study functionalized HPEE was initially prepared at two different dissolving ratios to give appropriately modified polymer and excessively modified polymer. Accordingly, comparison between these subgroups allowed us to understand the contribution of physical charges. After preparation of functionalized-HPEE with distinct terminal/backbone ratios, pingyangmycin solutions of various concentrations were added for nanocarrier copolymerization. Based on the present results, stable micelles could only be successfully mixed at a ratio of carboxyl-HPEE : pingyangmycin of 5 : 1, irrespective of terminal/backbone functionalized ratios, suggesting that the terminal-backbone interaction exerted a mild effect on surface charge modification. The polymer : drug ratio meant that one pingyangmycin molecule was appropriately combined with five HPEE-COOH molecules in the water. Notably, numerous multimolecular compounds sized approximately 10 to 50 nm were also observed in the coconjugated solution. The size of these smaller particles was approximately that of HPEE [1], and the particles were considered to be redundant carboxyl-terminal HPEE. The final assembled delivery particles were equivalent to nanoparticles, which can be efficiently taken up by tumor cells due to passive targeting, known as the enhanced permeation and retention (EPR) effect. Therefore, appropriately sized HPEE-pingyangmycin nanocarriers have high potential for targeted antitumor therapy *in vivo*. A previous study revealed that acute cytotoxicity could be eliminated by chemical modification involving replacement of cationic amino-dendrimers on the surface by neutral copolymers [40]. The *in vitro* cytotoxicity of nanocarrier against tumor cells was assessed by MTT assays. Slight differences in tumor cell inhibition were observed between pingyangmycin-HPEE conjugation and pingyangmycin alone, indicating that the HPEE-COOH used in the nanodelivery system based on electrostatic interaction exerted little pharmacological effect, at least in an *in vitro* assay.

5. Conclusions

Due to the facile synthesis and inexpensive costs, individualized nanodelivery systems for antitumor drugs could be optimized using the present platform of functionalized hyperbranched poly(ether-ester)s. Based on the observed relationship between the chemically modified end group and physically variations in surface charge, tunable drug delivery seems easily achievable. After the physical-chemical interrelationship between surface terminal and charge loading of HPEE was revealed, pingyangmycin, a potent antitumor drug, was used as a model drug to assess the HPEE-dependent nanocarrier system. Negative-charged carboxyl-functionalized HPEE was chosen because it was expected to form ionic bonds with the positive-charged pingyangmycin. Mixture between carboxyl-HPEE and pingyangmycin was successfully achieved by self-assembly and confirmed by DLS and TMS. The resultant nanoparticles exhibited promising antitumor cytotoxicity as assessed by MTT assays. The facile platform presented here provides an attractive pathway for individualized drug delivery based on functionalized-HPEEs.

Abbreviations

HPEE: Hyper-branched poly(ether-ester)
HPE: Hyper-branched poly(ether)
PEE: Poly(ether-ester)
PE: Poly(ether)
HBP: Hyper-branched polymers
PYM: Pingyangmycin.

Conflict of Interests

This work is sponsored by the National Natural Science Foundation of China (20974062) and China Postdoctoral Scientific Foundation (20100470692), Shanghai Jiao Tong University Med-Science Cross Research Foundation (YG2007MS11), and China National Funds for Distinguished Young Scientists (21025417). No conflict of interests has been claimed.

Authors' Contribution

Xing-ai Jin and Yan-wu Li are joint first authors.

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