Heparin Immobilized on Multiwalled Carbon Nanotubes for Catalytic Conversion of Fructose in Water with High Yield and Selectivity

Chenyu Wang, Wei Gong, Xingyuan Lu, Yang Xiang, and Peijun Ji

Department of Chemical Engineering, Beijing University of Chemical Technology, Beijing 100029, China

ABSTRACT: Being a member of the glycosaminoglycan family of carbohydrates, native heparin is a highly sulfated polysaccharide. Herein, heparin was grafted onto polydopamine (PDA)- and poly(ethylene imine) (PEI)-coated multiwalled carbon nanotubes (MWCNTs) (heparin–PEI@PDA@MWCNT). The immobilized heparin consists of a sulfated repeating disaccharide unit, conferring a unique microenvironment when catalyzing fructose dehydration into 5-hydroxymethylfurfural (HMF). The hydrogen bonding interactions naturally occur between the disaccharide unit of heparin and the monosaccharide fructose, and the adjacent sulfonic acid groups catalyze the fructose dehydration. The reactions were performed in water, and heparin–PEI@PDA@MWCNT achieved an HMF yield of 46.2% and an HMF selectivity of 82.2%. For the dehydration of fructose in water, heparin–PEI@PDA@MWCNT exhibits advantages over published heterogeneous catalysts on the basis of HMF yield and HMF selectivity. Three aspects contribute to the environmentally benign processing: (1) the catalyst heparin is a natural sulfated polysaccharide; (2) the catalysis is carried out in water and not in organic solvents; and (3) fructose can be produced from a biomass resource.

INTRODUCTION

As an important platform chemical, HMF can be used for production of monomers and fuels with high heating values.

Catalytic conversion of biomass resources into HMF has attracted great attention. Fructose dehydration into HMF is one of the major steps utilizing biomass resources. Fructose dehydration is an acid-catalyzed reaction. Compared to homogeneous acids, heterogeneous solid acid catalysts are more desirable because they are less corrosive, more ready to separate, and more easily adapted in environmentally benign processes.

Aside from catalysts, the reaction media can also influence the dehydration of fructose into HMF. In organic reaction media, such as ionic liquids and dimethyl sulfoxide (DMSO), a high conversion and selectivity can be achieved. The organic reaction media need to be removed after reaction. However, removing ionic liquids and DMSO from the reaction systems is extremely difficult or requires tremendous energy cost due to the fact that they are miscible with water and not volatile or having a high boiling point. Using organic reaction media does not meet the demand of sustainable processes. In contrast, being an environmentally benign solvent, water is more preferred than organic solvents as the reaction media for fructose dehydration.

Various heterogeneous catalysts have been investigated for catalyzing fructose dehydration in water. A chromium-based heteropoly acid achieved an HMF yield of 33.4% from fructose dehydration at 130 °C. The catalyst Nb-P/SBA-15 exhibited an HMF yield of 31.2% after reaction at 130 °C for 3 h.

Catalysts consisting of sulfonic acid groups are capable of catalyzing fructose dehydration. Functionalized porous organic hyper-cross-linked polymers were grafted with sulfonic acid groups. The HMF yield was 9.8% under the catalysis of a sulfonated polymer. Polyethylene fibers were grafted with sulfonic acid groups (HSO3−-fiber), achieving an HMF yield of 34% at 120 °C. Silica particles grafted with a poly(4-styrenesulfonic acid) brush were applied for catalytic conversion of fructose to HMF in water. The particles exhibited a high activity with the HMF yield up to 31%. Sulfonic acid supported on porous solids has shown activity for the fructose dehydration in neat water. Unfortunately, deactivation of catalysts in water was unavoidable because of leaching of the acid sites. Dehydration of fructose in water requires developing efficient catalysts to overcome the contradiction between the dehydration reaction and its media of water.

Heparin is a natural and safe biomaterial, which is a highly sulfated and anionic glycosaminoglycan consisting of a variably sulfated repeating disaccharide unit, as illustrated in Scheme 1. In this work, heparin immobilized on multiwalled carbon nanotubes (MWCNTs) was investigated as a catalyst for fructose dehydration in water. Multiwalled carbon nanotubes...
exhibit properties such as good stability, enhanced mechanical strength, excellent electronic properties, and high specific surface area. MWCNTs were used as the support of heparin. MWCNTs were first coated with polydopamine (PDA) followed by wrapping poly(ethylene imine) (PEI). Heparin was then grafted on PEI@PDA@MWCNT through amidation reaction between the amine groups of PEI and the carboxyl groups of heparin. The conjugate heparin−PEI@PDA@MWCNT comprises sulfonic acid groups and repeating disaccharide units, possessing a unique microenvironment. Fructose, a monosaccharide, can have hydrogen bonding interactions with the disaccharide units, and the adjacent sulfonic acid groups catalyze the fructose dehydration.

RESULTS AND DISCUSSION

Characterization of the Catalyst. Dopamine polymerization and coating on MWCNTs resulted in a thin layer of polydopamine (PDA) formed on the surface of MWCNTs, as illustrated in Figure 1b, in contrast to the transmission electron microscope (TEM) image of purified MWCNTs (Figure 1a). Binding of PEI to PDA@MWCNT (PEI@PDA@MWCNT) was accomplished by the Schiff base formation reaction between the primary amine groups of PEI and the catechol groups of PDA. Figure 1c shows that a thicker layer was formed after grafting PEI. The surface of PEI@PDA@MWCNT contains primary amine, secondary amine, and tertiary amine groups. The carboxyl groups of heparin reacted with the primary amine groups of PEI@PDA@MWCNT, and heparin was grafted. Figure 1d shows that after grafting heparin, the surface of heparin−PEI@PDA@MWCNT becomes rough, and the layer becomes thicker.

FTIR and XPS Spectra. Figure 2 shows the X-ray photoelectron spectroscopy (XPS) spectra for the samples. PDA@MWCNT exhibited a relatively increased intensity of O 1s, and the peak of N 1s appeared, in comparison to MWCNTs. It is ascribed to the formation of a PDA layer on the MWCNTs. Compared to PDA@MWCNTs, the intensities of C 1s and N 1s of PEI@PDA@CNT are relatively increased due to binding PEI. After grafting heparin, the peak for S 2p appears, ascribed to the sulfonate groups of heparin. Based on the XPS spectra, the distribution of functional groups was analyzed, as shown in Figure 3. The C 1s regions were fitted with Lorentzian and Gaussian lines of variable proportions.

Figure 1. TEM image of the (a) purified MWCNT, (b) PDA@MWCNT, (c) PEI@PDA@MWCNT, and (d) heparin−PEI@PDA@MWCNT.

Scheme 1. Schematic Presentation of the Fructose Dehydration under the Catalysis of Heparin−PEI@PDA@MWCNT
assigned to the binding energies for C−H, C=N/C=O, C=O/C=N, and π → π* shakeup satellites, respectively. PDA@MWCNT exhibited a wide peak of π → π*, ascribed to the energy loss feature for aromatic carbon species from PDA. The prominent peak of C=O/C=N is also ascribed to PDA. After grafting PEI on PDA@MWCNT, the fraction of the π → π* peak is decreased, and the intensity of the C=O/C=N peak is relatively increased due to the amine groups of PEI. After grafting heparin on PEI@PDA@MWCNT, the π → π* peak disappears, and the intensity of the C−H peak is relatively increased. The S 2p peak of heparin−PEI@PDA@MWCNT is shown with two split peaks of S 2p1/2 and S 2p3/2 centered at 168.1 and 169.2 eV, respectively. The peak area ratio of 2:1 provides evidence of sulfonic acid groups of heparin. The XPS spectra (Figures 2−4) confirmed the grafting of heparin on the functionalized MWCNTs.

Appearance of these peaks is consistent with the chemical structure of PEI. In the spectrum of heparin−PEI@PDA@MWCNT, the peaks at 1200 and 1028 cm−1 were assigned to the asymmetric vibration and the symmetric stretching vibration of the −SO3 groups of heparin, confirming the grafting of heparin on PEI@PDA@MWCNT. An acid−base titration method was used to determine the sulfonic acid group content of heparin−PEI@PDA@MWCNT. Heparin−PEI@PDA@MWCNT (50 mg) was stirred in 10 mL of 2 M NaCl at room temperature for 24 h. Then, 1 mM NaOH solution was used to titrate the filtrate of NaCl suspension. The sulfonic acid group content of heparin−PEI@PDA@MWCNT was determined to be 0.85 ± 0.04 mmol/g. The molecular weight of native heparin was determined to be 11.4 ± 0.5 kg/mol; thus, the amount of sulfonic acid groups in native heparin is 5.2 mmol/g. According to the sulfonic acid group content of heparin, the loading of heparin on heparin−PEI@PDA@MWCNT is 16.3 wt %.

Native heparin consists of sulfated repeating disaccharide units. Fructose is a monosaccharide. Hydrogen bonding interactions can occur between heparin−PEI@PDA@MWCNT and fructose. To investigate the types of the hydrogen bond interactions, the infrared spectra of adsorption at the νOH band from 3000 to 3700 cm−1 were analyzed. The νOH region has been investigated to effectively identify specific hydrogen bond interactions within and between molecules. Figure 6 shows the FTIR spectra in the hydroxyl stretching region.
region from 3700 to 3000 cm$^{-1}$ for heparin and heparin−PEI@PDA@MWCNT + fructose. The band at $\sim$3484 cm$^{-1}$ is attributed to the intramolecular hydrogen bonds within heparin. The relative intensity at $\sim$3484 cm$^{-1}$ of heparin (21.5%) is larger than that of heparin−PEI@PDA@MWCNT + fructose (8.9%). The band at $\sim$3415 cm$^{-1}$ arises from formation of multiple intermolecular hydrogen bonds between hydroxyl groups, between hydroxyl and glycosidic and ring oxygen, and between hydroxyl and sulfonic acid groups. The relative intensity at $\sim$3415 cm$^{-1}$ of heparin (16.2%) is larger than that of heparin−PEI@PDA@MWCNT + fructose (12.6%). The band at $\sim$3350 cm$^{-1}$ is ascribed to the intermolecular hydrogen bonds between hydroxyl groups and between hydroxyl and sulfonic acid groups. The relative intensity at $\sim$3350 cm$^{-1}$ of heparin (35.7%) is larger than that of heparin−PEI@PDA@MWCNT + fructose (24.6%). The band at $\sim$3240 cm$^{-1}$ is attributed to the intermolecular hydrogen bonds between hydroxyl and glycosidic and ring oxygen. The NH comes from both heparin and PEI. The relative intensity at $\sim$3240 cm$^{-1}$ of heparin−PEI@PDA@MWCNT + fructose (18.6%) is larger than that of heparin (13.6%). Analysis of the FTIR spectra indicates that upon adding fructose to the solution of heparin−PEI@PDA@MWCNT, the number of intramolecular hydrogen bonds within heparin decreased, and that for the multiple intermolecular hydrogen bonds also decreased. That for the intermolecular hydrogen bonds increased due to the hydrogen bonding interactions between heparin−PEI@PDA@MWCNT and fructose. The FTIR spectra in Figure 6 confirmed the hydrogen bonding interaction between fructose and heparin−PEI@PDA@MWCNT.

The dispersibility of purified MWCNTs, PEI@PDA@MWCNT, and heparin−PEI@PDA@MWCNT was monitored by UV−vis spectroscopy (Shimadzu UV 2550). The higher UV−vis absorbance, the larger the dispersibility of the sample in water is. Figure 7 shows the UV−vis spectra for the samples. After grafting heparin, the conjugate heparin−PEI@PDA@MWCNT exhibited the highest dispersibility in water compared to other samples due to the sulfated repeating disaccharide unit of heparin. This is favorable for the interaction of heparin−PEI@PDA@MWCNT with fructose.

Catalytic Activity. Figure 8 illustrates the fructose dehydration under the catalysis of heparin−PEI@PDA@MWCNT in water at different temperatures. The weight ratio of fructose to catalyst was 4.0. The fructose dehydration was performed for 3 h.

MWNT at different temperatures in water. With increasing temperature, the fructose conversion increased. At 140 °C, the HMF selectivity was the highest one (88.3%), the corresponding fructose conversion was 43%, indicating that the side reactions were significantly suppressed. At 160 °C, the conversion of fructose and the selectivity of HMF were 56.2 and 82.2%, respectively. Considering the conversion of fructose and the selectivity of HMF, the temperature 160 °C was determined as the appropriate temperature.

Figure 9 shows the conversion of fructose and the selectivity of HMF as a function of reaction time. The highest HMF yield of 46.2% was achieved after 3 h of reaction. As the reaction time was prolonged, the yield of HMF decreased due to the formation of byproducts. The weight ratio of fructose to the conjugate was 4, which is equivalent to the weight ratio of fructose to heparin of 24.7. When using native heparin as the
catalyst with a weight ratio of fructose to heparin of 24.7, native heparin achieved the yield and selectivity of HMF being 47.4 and 82.6%, respectively. Under the same reaction condition, the HMF conversion was not observed under the catalysis of PEI@PDA@MWCNT. It has been confirmed that the catalytic activity of heparin–PEI@PDA@MWCNT comes from the heparin of the conjugate heparin–PEI@PDA@MWCNT. The formed humin impurities are insoluble in water. The soluble portion, containing HMF and unreacted fructose, was recovered by filtration and washed with water. Using hexane/EtOAc (1:1) as the mobile phase, HMF was purified with flash column chromatography.

For the stability test, native heparin was incubated in aqueous solution at reaction conditions (160 °C for 3 h). Then, heparin was precipitated from the solution with ethanol. The FTIR spectrum of the recovered heparin shows peaks at 1200 and 1025 cm⁻¹ (Figure S1), which were assigned to the asymmetric vibration and the symmetric stretching vibration of the −SO₃ groups of heparin. The peaks at 1720 cm⁻¹ were assigned to the absorption of carboxyl groups of heparin. The molecular weights of native heparin and recovered heparin were measured to be 11.4 ± 0.5 and 11.2 ± 0.4 kg/mol, respectively. The molecular weight distributions of native heparin and recovered heparin were narrow with polydispersities of 1.20 and 1.22, respectively. These results confirm the stability of heparin under the reaction condition.

Heparin–PEI@PDA@MWCNT was reused to test its stability. Heparin–PEI@PDA@MWCNT exhibited negligible loss in activity after five cycles of reuse, as shown in Figure 10. EDS spectra of heparin–PEI@PDA@MWCNT after reuse were measured. Figure S2 shows that the intensity of elements for the fresh catalyst and the catalyst recycled was almost the same, indicating that heparin–PEI@PDA@MWCNT did not change after the reuse.

Various heterogeneous catalysts had been investigated in organic solvents such as isopropanol, N,N-dimethylformamide (DMF), isopropanol, and dimethyl sulfoxide (DMSO). Herein, these organic solvents were used in the fructose dehydration under the catalysis of heparin–PEI@PDA@MWCNT. DMSO is a versatile solvent. Fructose can be dissolved in DMSO, and the conjugate heparin–PEI@PDA@MWCNT can be dispersed well in DMSO. Thus, the hydrogen bonding interactions between fructose and heparin–PEI@PDA@MWCNT occurred naturally, promoting the contact of fructose with the catalyst. The generated water arising from the dehydration is miscible with DMSO, reducing the inhibition effect of water. In addition, DMSO can inhibit the side reactions that often occurred when using water as the reaction media. Attributed to the above reasons, the fructose dehydration in DMSO with heparin–PEI@PDA@MWCNT had excellent fructose conversion and selectivity (Table 1).

However, DMSO has a high boiling point and is difficult to remove from the system afterward. In other organic solvents such as DMF and isopropanol, fructose has a lower solubility, making them not favorable for the interaction of fructose with heparin–PEI@PDA@MWCNT through the hydrogen bonding interactions. Possibly, this is the reason why the fructose conversion and selectivity in the organic solvents are lower than those in water. Researchers have always paid much attention to fructose dehydration in water. Table 2 lists the published results of fructose dehydration in water under various heterogeneous catalysts. Compared to the published heterogeneous catalysts, heparin–PEI@PDA@MWCNT exhibited advantages in terms of yield and selectivity of HMF.

**CONCLUSIONS**

Native heparin was grafted onto PEI- and PDA-functionalized multiwalled carbon nanotubes and used for catalyzing the fructose dehydration into HMF in water. Multiwalled carbon nanotubes exhibit properties such as good stability, excellent electronic properties, enhanced mechanical strength, and high specific surface area. The synthesis of heparin–PEI@PDA@MWCNT utilized four different raw materials. Polydopamine (PDA) has a strong adhesion coating on various surfaces. In situ formation of polydopamine on the MWCNTs confers a solid basis for further grafting poly(ethylene imine) (PEI). The amino groups of PEI were the functional groups to react with the carboxyl groups of heparin for grafting heparin. Heparin

**Figure 9.** Fructose conversion, HMF yield, and lactic acid yields under the catalysis of heparin–PEI@PDA@MWCNT in water. The weight ratio of fructose to catalyst was 4.0. The fructose dehydration was performed at 160 °C.

**Figure 10.** Consecutive test of heparin–PEI@PDA@MWCNT for fructose conversion into HMF in water. The consecutive test was performed at 160 °C for 3 h. The catalyst after run was recovered by filtration, washed with ethanol and water thoroughly, and then vacuum dried at 60 °C for 12 h.

**Table 1. Fructose Dehydration Catalyzed by Heparin–PEI@PDA@MWCNT in Various Solvents**

| solvent     | fructose conv. (%) | HMF selectivity (%) | HMF yield (%) |
|-------------|--------------------|---------------------|---------------|
| water       | 56.2               | 82.2                | 46.2          |
| DMSO        | 100                | 99.2                | 99.2          |
| DMF         | 48                 | 41.7                | 20            |
| isopropanol | 25                 | 36                  | 9             |

*Heparin–PEI@PDA@MWCNT (25 mg), fructose (100 mg), temperature of 160 °C, and time of 3 h.*
possesses a sulfated repeating disaccharide unit, conferring a unique microenvironment for the hydrogen bonding interactions and subsequent fructose dehydration. It has been demonstrated that heparin–PEI@PDA@MWCNT achieved a high HMF yield and selectivity in water, in comparison to published heterogeneous catalysts. The conjugate can be recycled to catalyze the fructose dehydration. Using heparin as the catalyst for fructose dehydration in water meets the demand of sustainable development.

**METHODOLOGY**

**General Information.** Multiwalled carbon nanotubes (MWCNTs) were obtained from Nanotech Port Co., Ltd. (Shenzhen, China). Other chemical reagents were obtained from Sigma Aldrich and Sinopharm Chemical Reagent Co. Ltd. The chemical reagents were used without further purification.

**Polydopamine Coating of MWCNTs (PDA@MWCNT).** MWCNTs were purified in 3 M HNO₃ for 12 h, then recovered by filtering with a polycarbonate membrane, and then washed with deionized water. The samples were vacuum-dried at 60 °C. The purified MWCNTs (100 mg) were dispersed in water/ethanol (40 mL/50 mL) after sonication for 15 min. Then, dopamine (400 mg) and Tris buffer (100 mL, pH 8.5) were added. The solution was stirred at room temperature for 1 day. The polydopamine-coated MWCNTs (PDA@MWCNT) were collected by filtration with a polycarbonate membrane and washed with deionized water. Then, the conjugate was dried under vacuum at 60 °C overnight.

**Poly(ethylene imine) Coating of PDA@MWCNT (PEI@PDA@MWCNT).** PDA@MWCNT (50 mg) was added to 25 mL of the PEI aqueous solution (2.0 mg/mL) and sonicated for 15 min. Then, the conjugate PEI@PDA@MWCNT was recovered by filtering through a polycarbonate membrane, washed with deionized water, and then dried under vacuum at 80 °C for 12 h.

**Grafting of Heparin on PEI@PDA@MWCNT (Heparin–PEI@PDA@MWCNT).** Heparin was grafted on PEI@PDA@MWCNT through the reaction between the amino groups of PEI and the carboxyl groups of heparin. Briefly, heparin sodium (200 mg) was dispersed in 2-(N-morpholino)ethanesulfonic acid (MES) buffer (20 mL, pH 6.2) under sonication. Then, 0.12 g of N-hydroxysuccinimide (NHS) and 0.38 g of N-ethyl-N-(3-(dimethylamino)propyl) carbodiimide hydrochloride (EDC) were added to the mixture separately. The resulting mixture was then sonicated for 10 min. The solution of activated heparin (10 mg/mL) was added to the suspension of PEI@PDA@MWCNT (4 mg/mL, 15 mL). The mixture was then shaken (130 rpm) at 25 °C for 8 h. Then, the mixture was centrifuged at 8000 rpm for 15 min, and the precipitate was washed with deionized water five times to remove heparin that was not grafted. Finally, heparin–PEI@PDA@MWCNT was obtained after drying under vacuum at 80 °C for 12 h.

**Characterization and Measurement.** Thermo VG ESCALAB250 was used to measure XPS spectra of the samples. The measurement was performed at a pressure of 2 × 10⁻⁹ Pa with Mg Kα X-rays as the excitation source. FTIR spectra of the samples were measured with a Bruker Tensor 27 spectrometer with a resolution of 2 cm⁻¹. The molecular weight and molecular weight distribution of heparin were estimated by size exclusion chromatography using a Shimadzu HPLC system equipped with a multangle light-scattering detector.

**Dehydration of Fructose to HMF.** Fructose (0.1 g) was dissolved in 10 mL of water, and then 25 mg of heparin–PEI@PDA@MWCNT was added to the solution. The air inside the reactor was purged with Ar, and the pressure was kept at 0.4 MPa to prevent boiling. After reacting for a certain time at a desirable temperature, samples were taken out. Insoluble particulates were removed from the samples via centrifugation. A portion of samples was taken for analysis.

### Table 2. Fructose Dehydration in Water under Various Heterogeneous Catalysts Published

| fructose | catalyst | temp (°C) | fructose conv. (%) | HMF yield (%) | selectivity (%) | ref |
|----------|----------|-----------|--------------------|---------------|----------------|-----|
| 2 mmol   | GO (20 mg)| 100       | 70                 | 14            | 20             | 7   |
| 2.8 mmol | ZrPO (50 mg)| 180       | 76.4               | 36.6          | 48             | 11  |
| 3.5 mmol | H-beta (620 mg)| 150       | 78                 | 18            | 23             | 13  |
| 2.8 mmol | Nb-P/SBA-15 (100 mg)| 130       | 59.5               | 31.2          | 52.4           | 14  |
| 0.28 mmol| HCP-2.0 (10 mg)| 140       | 61.9               | 9.8           | 15.8           | 15  |
| 5.6 wt %| HSO₃⁻ fiber (8.6 wt %)| 120       | 72                 | 34            | 47             | 16  |
| 6.5 wt %| PSSH/Sio₂ (100 mg)| 120       | 80                 | 27            | 34             | 39  |
| 10 wt % | α-Sr(PO₄)₂ (10 mg)| 200       | 89                 | 35            | 39             | 39  |
| 1 mmol   | HSiW/SiO₂ (18 mg)| 170       | 77.7               | 50.2          | 64.6           | 43  |
| 2.8 mmol | HY (500 mg)| 150       | 69.8               | 19.8          | 28.4           | 44  |
| 0.08 mol | Amberlyst-15 (1000 mg)| 100       | 73                 | 43.8          | 60             | 45  |
| 0.3 M    | Si-Nb (3000 mg)| 100       | 80                 | 15            | 18.7           | 46  |
| 3.3 mmol | Nb₂O₅ (80 mg)| 130       | 80                 | 36            | 45             | 47  |
| 0.6 mmol | TiO₂ (20 mg)| 200       | 90.4               | 41.2          | 45.6           | 48  |
| 3.3 mmol | WO₃/ZrO₂ (80 mg)| 130       | 69                 | 12            | 17.4           | 49  |
| 5 wt %   | PMC₅ (250 mg)| 120       | 68                 | 43            | 63.2           | 50  |
| 10 wt %  | ZrPO (66 mg)| 180       | 84.2               | 39.5          | 46.9           | 51  |
| 0.56 mmol| SO₄²⁻-ZrO₂ (20 mg)| 200       | 79.9               | 29.9          | 37.4           | 52  |
| 10 wt %  | H-USY (80 mg)| 130       | 70                 | 7             | 10             | 53  |
| 0.06 mmol| Nb₆₂-WO₃ (100 mg)| 120       | 100                | 30            | 30             | 54  |
| 3.3 mmol | (C₁₆H₁₈)₆N₃PW₁₁Ti (2300 mg)| 130 | 90                 | 47.9          | 48.8           | 55  |
| 1.0 mmol | Cr₁ (5 mg)| 170       | 270                | 55.0          | 55.0           | 56  |
The samples were analyzed by high performance liquid chromatography (Shimadzu LC-10A). Fructose, levulinic acid, and formic acid were detected using a refractive index detector with an Aminex HPX 87H ion exclusion column. H₂SO₄ (5 mM) flowing at 0.6 mL/min was used as the mobile phase. The yield of HMF was measured using a UV–vis detector with a DiomnisS C18 column. Methanol/water (70:30 (v/v)) flowing at 1.0 mL/min was used as the mobile phase. Each reaction was carried out at least three times. The error bars shown in the figures reflect the differences between runs.

**ASSOCIATED CONTENT**

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acsomega.9b01607.

FTIR spectrum of heparin recovered after dissolution in 160 °C for 3 h and EDS analysis for the catalyst heparin–PEI@PDA@MWCNT after reuse (PDF)

**AUTHOR INFORMATION**

**Corresponding Author**

*E-mail: pipj@mail.buct.edu.cn. Phone: +86-10-64423254.

**ORCID**

Peijun Ji: 0000-0003-1994-1639

**Notes**

The authors declare no competing financial interest.

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