The Synthesis and Characterization of Heparin-Doped Polypyrrole for Biomedical Applications

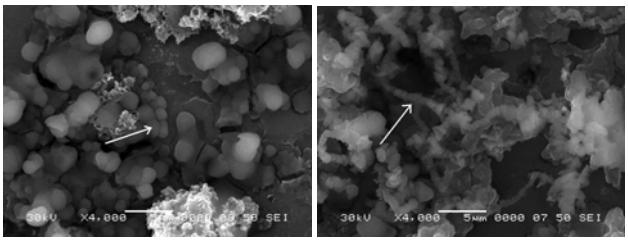
Shiyun Meng[1], Guixin Shi[1], Mahmoud Rouabhia[2], Ze Zhang[1]
[1] Faculté de médecine, Université Laval; Centre de recherche, Hôpital St-François d'Assise, CHUQ, Québec, Canada
[2] Faculté de médecine dentaire, Université Laval, Québec, Canada

Introduction: Conducting polymers like polypyrrole (PPy) are useful in biomedical applications to facilitate electrical stimulation and recording. However, the lack of long-term electrical stability and the relatively poor cell adhesion remain the major issues that limit the application of the conductive PPy [1]. It is known that polyanion can be used as dopant and form counterions with PPy. Because of the multiple electrical interactions and the high molecular weight, these polyanions are difficult to be excluded from PPy upon reduction, ensuring a better electrical stability. Heparin is a linear polysaccharide made of repeating disaccharide units of sulfate derivatives of N-acetyl-D-glucosamine and D-iduronate. Heparin sulphate presents in extracellular matrix and on cell surface to modulate cell adhesion. Heparin also carries strong negative charges which make it possible to bind to positively charged PPy as counterions [2]. Previously, heparin was introduced into PPy as counterions only through electrochemical method. In this work, we present a novel chemical synthesis approach, by which heparin-doped PPy showed high doping ratio and moderate conductivity.

Methods: PPy was synthesized through a water-in-oil emulsion polymerization. In brief, pyrrole was introduced dropwise into the emulsion system that contained oxidant and heparin. The reaction was kept at room temperature for 24h. Four types of PPy were synthesized, i.e., PPy/Cl, PPy/Cl/HE0.05, PPy/Cl/HE0.25 and PPy/Cl/HE0.5, where HE represents heparin and the number indicates the initial weight ratio of pyrrole to heparin. The synthesized PPy materials were pressed into wafers for conductivity measurement. A Jeol JSM-360LV scanning electron microscope (SEM) was used to observe the shape and surface morphology of the PPy powder. A Perkin Elmer PHI model 5600 X-ray photoelectron spectroscope (XPS) was used to measure surface elemental composition and the oxidation state of the elements. Attenuated total reflectance Fourier transform infrared (ATR-FTIR) (Nicolet Magna-IR^{TM} Spectrophotometer 550) was performed to investigate the surface chemistry of the PPy.

Results/Discussion: The resistivity of the PPy wafers measured 1×10^{-2} Ω·m, which was moderate and appropriate for biological application. SEM photomicrographs showed spherical and irregular PPy particles, with spherical size ranging from a few hundreds nanometers to approximately 10 microns, depending on the heparin content. Interestingly, the PPy also formed rod-like structures micrometers in dimension (Fig.1b), which was contrary to the particulate and irregular flake-like morphologies commonly experienced in emulsion and solution polymerization, respectively (Fig.1a). The heparin counterions were considered responsible for the various morphologies [3]. XPS measurement revealed that the ratio of the positively charged nitrogen to neutral nitrogen was as high as 32% for the heparin-doped PPy, compared to about 25% of the PPy doped by Cl^-. The increasing of sulfur and oxygen content in the heparin doped PPy evidenced the successful incorporation of heparin into PPy. The presence of heparin in PPy was also supported by infrared. ATR-FTIR spectra showed that the stretching of C-N bond in PPy shifted from 1444cm^{-1} (υ_{C-N}) to 1415cm^{-1} , and the band at 1287cm^{-1} (υ_{C-H}) moved to 1275cm^{-1} with the increasing of heparin content. Also, a shoulder of strong S=O vibration appeared at 1242cm^{-1} and became stronger when shifted to 1275cm^{-1} with the increasing of heparin content.

Because of the high molecular weight and multiple charged nature of the heparin, the heparin-doped PPy is expected to have higher electrical stability than the PPy doped by Cl^-. In addition, the heparin-doped PPy is also likely to have improved cell adhesion ability.



a b

Fig.1 The SEM photomicrographs of PPy/Cl (a) and PPy/Cl/HE0.5 (b)

Conclusion: Heparin was successfully incorporated into PPy as counterions through water-in-oil emulsion polymerization. The heparin-doped PPy showed various morphologies that were likely related to heparin content. The heparin-doped PPy showed high doping ratio and moderate conductivity. This material could be a promising candidate to prepare conductive biodegradable or nonbiodegeadable polymer composites for biomedical applications.

References:

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