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论文

聚[(甲氧基乙氧基乙氧基)$_{1.0}$(乙氧基吡咯烷酮)$_{1.0}$]膦腈的合成及性能研究

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摘要:

用三氯化铝催化六氯三聚膦腈开环聚合制得线性聚二氯膦腈(PDCP), 通过PDCP磷原子上的亲核取代反应, 合成了新的水溶性高分子聚[(甲氧基乙氧基乙氧基)$_{1.0}$(乙氧基吡咯烷酮)$_{1.0}$]膦腈(P3), 用^{31}P NMR, ^{1}H NMR, ^{13}C NMR和IR对其结构进行了确证, 用DSC测定了其玻璃化转变温度T_g和熔融温度T_m, 用蒸汽压渗透法(VPO)测定了其数均分子量. 改进了聚二(乙氧基吡咯烷酮)膦腈(P2)的合成方法. 体外降解实验表明, P3具有和P2类似的pH响应性降解行为, 降解速率在pH=5.0时最快, 而在pH=7.4和8.0时较慢. P3在所测试的3个pH缓冲溶液中均比P2降解慢. 用^{31}P NMR、薄层色谱(TLC)和滴定法对降解产物进行了检测, 初步推断了P3在不同pH介质中的水解机理, 其在pH=5.0的缓冲溶液中的降解, 除侧链断裂外, 聚膦腈的骨架也裂解; 而在pH=7.4和8.0时的降解仅为侧链的断裂. 用噻唑蓝(MTT)比色法进行的体外细胞毒性评价实验表明, P3及其在pH=5.0的缓冲溶液中降解49 d后的产物均对细胞表现出了很好的生物相容性, 而且其降解产物在浓度为800 μg/mL时还表现出一定的促进细胞增殖作用.

关键词: 聚膦腈 乙氧基吡咯烷酮 甲氧基乙氧基乙氧基 pH响应性降解 水解机理 体外细胞毒性

Synthesis, Characterization, *in Vitro* Degradation and Cytotoxicity of Poly{[2-(2-oxy-1-pyrrolidiny) ethoxy]$_{1.0}$(methoxyethoxyethoxy)$_{1.0}$] phosphazene}

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Abstract:

Polydichlophosphazene(PDCP) was prepared by the ring-opening polymerization of hexachlorocyclotriphosphazene in the presence of 2%$AlCl_3$. A new mixed substituent poly (organophosphazene) bearing 2-(2-oxy-1-pyrrolidiny) ethoxy and methoxyethoxyethoxy side groups was synthesized *via* the macromolecular substitution reactions of poly(dichlorophosphazene) with the sodium salt of 1-(2-hydroxyethyl)-2-pyrrolidone and sodium methoxyethoxyethoxide. Its structure was verified by ^{31}P NMR, ^{1}H NMR, ^{13}C NMR, IR and DSC. Its molecular weight was determined by vapor pressure osmometry(VPO). 18-Crown-6 was used in the synthesis of poly[di(2-oxy-1-pyrrolidiny) ethoxyphophazene](PYRP) as phase transfer catalysis in order to improve its synthetic method. The new polymer and PYRP were water-soluble and their *in vitro* degradation behavior was studied at varied pH conditions. The results indicate that the degradation of poly(organophosphazenes) with (2-oxy-1-pyrrolidiny)ethoxy side groups is dependent on pH of the buffer solution. The rate of hydrolysis was more rapid at pH=5.0 than at pH=7.4 and pH=8.0. It was shown that addition of methoxyethoxyethoxy side group to PYRP structure resulted in a decrease in the rate of hydrolysis. The hydrolysis products of the poly(organophosphazenes) were analyzed by ^{31}P NMR, thin layer chromatography(TLC) and titration methods. A hydrolysis pathway of the new polymer in buffer solutions with pH=5.0, 7.4 and 8.0 was proposed. The degradation of the polymers at pH=5.0 involved a hydrolytic cleavage of (2-oxy-1-pyrrolidiny)ethoxy from the chain followed by the degradation of the phosphorus-nitrogen backbone to form phosphate and ammonium. However, the degradation of the polymers at pH=7.4 and pH=8.0 was only cleavage of the side group. The MTT test for the new polymer and its hydrolysis products at pH=5.0 in HepG2 cell revealed that an increase in polymer concentration from 1.3 to 800 μg/mL was not harmful for the cell survival. The hydrolysis products of the new polymer at 800 μg/mL were able to promote cell proliferation.

Keywords: Polyphosphazene 2-(2-Oxy-1-pyrrolidiny)ethoxy Methoxyethoxyethoxy pH-sensitive hydrolytic degradation property Hydrolysis pathway *In vitro* cytotoxicity

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