Vol 2 No.3 2018

ISSN Online : 2709-4030
ISSN Print : 2709-4022

Synthesis, Characterization of Poly[bis(diethyl amino phenol)phosphazenes] and Biomedical Applications for Social Benefit of Humanity

Amin Abid*

Department of Basic Sciences and Humanities, University of Engineering and Technology,
Lahore Narowal Campus, Pakistan

Abstract

Recently, biomedical applications gained much attention due to their application and significance for humanity such as drugs deliver, tissue engineering etc. Researcher found that polymers are the best materials for biomedical applications, but polyphosphazenes are the versatile class of biomaterials being extensively applied in multitude of biomedical applications due to their unique properties such as easily biodegradable and non-toxicity, biocompatible and meet the requirement of human body. In this study, poly[bis(diethyl amino phenol)phosphazenes] is synthesized in two steps. In the first step polydichlorophosphazenes (PDCP) is synthesized from hexacholorocyclotriphosphazenes (HCCP) using $AlCl_3$ catalyst and then chlorines groups of PDCP are replaced with hydroxy groups of phenol and diethylamine respectively. HNMR and GPC proved the successful synthesis of poly[bis(diethyl amino phenol)phosphazenes]. Later, hydrolytic degradation of Poly[bis(diethyl amino phenol)phosphazenes] is investigated for biomedical applications such as hydrolytic degradation for drugs delivery etc for the social benefit of human beings.

Keywords: Polyphosphazenes, synthesis, characterization, biodegradable polymers, biomedical applications

1. Introduction

At present, many types of materials are under investigation for biomedical applications, but polymers showed unique applications due to their properties and applications, such as biocompatibility, biodegradation and non-toxicity etc. **[1-5]**. Due to these significant properties, polymers showed its dire need of advancement for the modern medicine. Many types of polymers are using for clinical purpose such as surgical sutures and implants **[6-10].**

Corresponding Author: E-mail: mabiduet@gmail.com

Among these polymers, polyphosphazenes is unique class due to combination of organic and inorganic and attracted the researchers due to their novel characteristics and applications. Polyphosphazenes are combination of inorganic backbone and organic side groups so have wide range of application such as hydrogels, drug delivery, membranes, biomaterials, fiber and film forming, elastomers, ionic conductors, flame retardant, and optical applications **[11-15]**.

PPhosphazenes can be replaced with hydrophobic and hydrophilic side groups and degradation rte can be controlled. For the fast degradation, polyphosphazenes are replaced with amino acid ester as substituents **[16-22]**.

Poly[bis(diethyl amino phenol)phosphazenes] is synthesized in two steps, in first step, hexachlococyclotriphosphazenes (HCCP) was converted into polydichlorophosphazenes (PDCP) by thermal ring opening polymerization heating upto 250°C under vacuum and then chlorines side groups of PDCP are replaced with hydroxy groups of phenol and diethyl amine respectively. Furthermore, hydrolytic degradation study was investigated for biomedical applications.

Synthesis of PDCP from HCCP and Synthesis of Poly[bis(diethyl amino phenol)phosphazenes]

Poly[bis(diethyl amino phenol)phosphazenes] is syntheized in two steps. In the first step, monomer HCCP (2.0g, 5.75mmol) and catalyst AlCl$_3$ (0.1g, 0.75mmol) are added respectively in clean and dry glass tube and then sealed under vacuum. Sealed sample tube is heated in oil bath at 250°C for 6 hours.It was found that during heating HCCP converted into viscous mobile liquid. The Reaction is shown in Figure 1. PDCP is purified and dried under vacuum and then dissolved in refluxed tetrahydrofuran. In the second step, poly[bis(diethyl amino phenol)phosphazenes] is synthesized. Purified PDCP is dissolved in THF and phenol and diethyl amine added respectively (Cl:OH, 1:2). The reaction mixture is refluxed at 67°C for 48hrs shown in Figure 2. The resultant mixture filtered, and polymer precipitated and dried under vacuum.

3. Results and Discussion

After purification of HCCP, PDCP was synthesized by thermal ring opening polymerization as we reported previously [2-6]. The Reaction is shown in Figure 1.

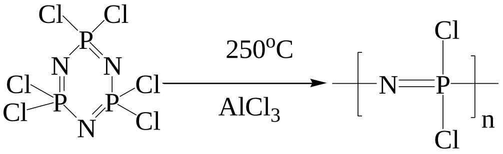

Figure 1. Synthesis of PDCP from HCCP in the presence of catalyst

In second step, poly[bis(diethyl amino phenol)phosphazenes**]** is synthesized by the replacement of chlorines from PDCP with hydroxyl group phenol and diethylamine in THF solvent by refluxing 48 hours..

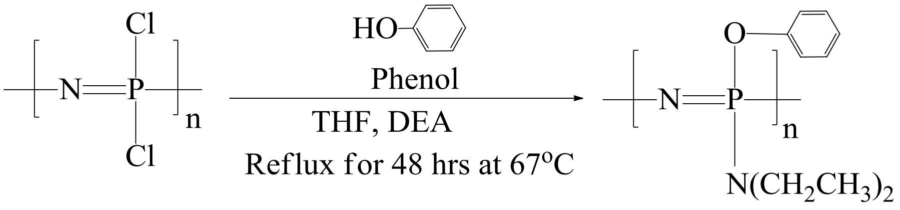

Figure 2. Synthesis of poly[bis(diethyl amino phenol)phosphazenes**]**

The ^{1}H NMR spectrum showed peaks with the following shifts: 6.63-6.84ppm (2H of C_6H_4), 7.13-7.38ppm (2H of C_6H_4), 7.57-7.69ppm (2H of C_6H_4), 7.70-7.82ppm (2H of C_6H_4), and 3.55-3.80ppm (2H of CH_2) and from 2.49-2.52ppm (3H of CH_3) represented the diethylamine as shown in Figure 3. Molecular weight of polymer was Mw, 1768490, PDI 2.6, Mn, 265865 as shown in Figure 4.

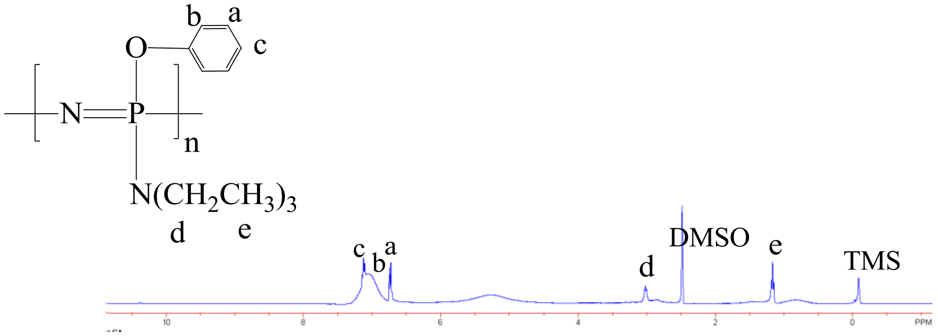

Figure 3. H NMR of poly[bis(diethyl amino phenol)phosphazenes**]**

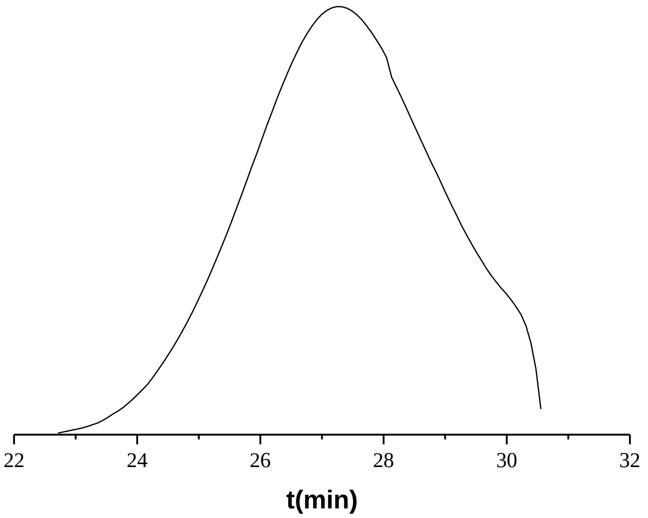

Figure 3. GPC of poly[bis(diethyl amino phenol)phosphazenes**]**

The hydrolytic degradation of polymer was investigated in acidic, basic and neutral medium at human body temperature 37^{o}C for biomedical application such as drugs delivery **[11-15]**. Polymer sample was placed into buffer solution and degradation study was noted with the polymer breakdown side groups and then loss of weight was observed with balance. Ammonia, phosphoric acid and other by products were produced after degradation which was tested via Ninhydrin test by the appearance of violet color.

Degradation of the polymer depended on side groups as we proved in our previous studies and here our purposes is to fast the degradation time. The degradation of polymer was very fast in acidic medium, basic and slow in neutral medium. Possible degradation mechanism of polymer is shown in Figure 5. Moreover, this data will be analyzed by mathematical and computational modeling.

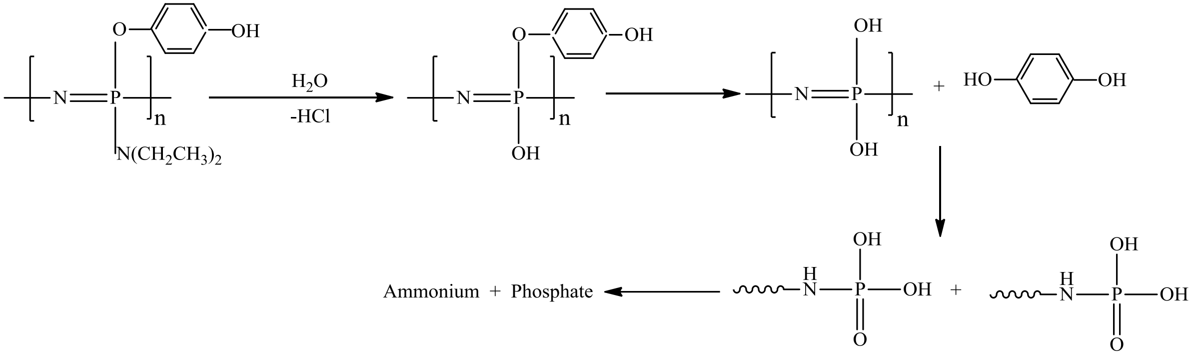

Figure 5. Possible degradation mechanism of poly[bis(diethyl amino phenol)phosphazenes]

Conclusion

Poly[bis(diethyl amino phenol)phosphazenes] is syntheized in different two steps. In first step, the polydichlorophosphazenes (PDCP) was synthesized from hexachlorocyclotriphosphazene (HCCP) by thermal ring opening polymerization in the presence of $AlCl_3$ catalyst and in second step chlorine atoms from PDCP were substituted by hydroxy groups of phenol and diethyl amine respectively. HNMR and GPC confirmed the successful synthesis of poly[bis(diethyl amino phenol)phosphazenes]. Further, degraded polymeric data will be analyzed by mathematical modeling.

References

1) Amin AM, Wang L, Yu H, Amer WA, Gao J, Huo J, Tai Y, Zhang L. Synthesis and Characterization of Poly [bis (ethyl salicylate) phosphazenes] and Poly [bis (ethyl salicylate diethylamino) phosphazenes] and Their Hydrolytic Degradation. Journal of Inorganic and Organometallic Polymers and Materials, **2012**, 22 (1):196-204
2) Akram M, Wang L, Yu H, Amer WA, Khalid H, Abbasi NM, Chen Y, Saleem M, Tong R Polyphophazenes as anti-cancer drug carriers: From synthesis to application. Progress in polymer science, **2014**, 39 (12):1987-2009.
3) Kondiah PJ, Choonara YE, Kondiah PP, Marimuthu T, Kumar P, Du Toit LC, Pillay V. A review of injectable polymeric hydrogel systems for application in bone tissue engineering. Molecules, **2016**, 21 (11):1580.
4) Amin AM, Wang L, Wang J, Amer WA, Huo J, Yu H, Gao J. Synthesis and characterization of poly [bis (resorcinol monobenzoate) phosphazenes] and poly [bis (resorcinol monobenzoate diethylamino) phosphazenes] and their self assembly behaviors. Journal of Inorganic and Organometallic Polymers and Materials, **2011**, 21 (2):283-290
5) Rothemund S, Teasdale I Preparation of polyphosphazenes: a tutorial review. Chemical Society Reviews, **2016**, 45 (19):5200-5215.

6) Amin AM, Wang L, Wang J, Yu H, Huo J, Gao J, Xiao A Recent research progress in the synthesis of polyphosphazene and their applications. Designed monomers and polymers, **2009,** 12 (5):357-375
7) Amin AM, Wang L, Yu H, Amer WA, Gao J, Yulei T, Huo J, Zhang Y, Zhang L Synthesis and Characterization of Poly [bis (p-oxybenzaldehyde diethylamino) phosphazenes], Poly [bis (p-oxybenzaldehyde) phosphazenes], Poly [bis (diethylamino) phosphazenes] and their Self-assembly Behaviors. Journal of Macromolecular Science, Part A, **2011**, 48 (11):937-946
8) Azam Rahimi. Inorganic andorganometallic polymers: A review. Iranian polymer Journal **2004**, 13(2), 149-164.
9) Amin AM, Wang L, Wang J, Yu H, Gao J, Li C, Huo J, Amer WA, Yan G, Ma L. Recent research progress in the synthesis of polyphosphazene elastomers and their applications. Polymer-Plastics Technology and Engineering, **2010,** 49 (14):1399-1405
10) Allcock, H. R.; Kugel, R. L.; Valan, K. Phosphonitrilic Compounds. VI. High Molecular Weight Poly(a1koxy- and aryloxyphosphazenes. J. Inorg. Chem. **1966**, 5, 10, 1709-1715.
11) Harry R. Allcock, Gayann S. McDonnell, and James L. Desorcie. Synthesis of New Polyphosphazene Elastomers. Macromolecules, **1990**, 23, 17, 3873-3877.
12) Akram M, Yu H, Wang L, Khalid H, Abbasi NM, Chen Y, Ren F, Saleem M Sustained release of hydrophilic drug from polyphosphazenes/poly (methyl methacrylate) based microspheres and their degradation study. Materials Science and Engineering: C , **2016**, 58:169-179.
13) Allcock, H. R.; Kugel, R. L. Synthesis of High Polymeric Alkoxy and Aryloxy phosphonitriles. J. Am. Chem. SOC.**1965**, 87, 4216.
14) Harry R. Allcock, Karyn B. Visscher, and Young-Baek Kim. New polyphosphazenes with Unsaturated Side Groups: Use as Reaction Intermediates, Cross-Linkable Polymers, and Components of Interpenetrating Polymer Networks. Macromolecules, **1996**, 29, 2721-2728.
15) Hengameh Honarkar, Azam Rahimi. Applications of inorganic polymeric materials III: polyphosphazenes. Review. Monatshefte fur Chemie, **2007**, 138, 923-933.
16) Stewart FF, Harrup MK, Luther TA, Orme CJ, Lash RP J Appl Polym Sci, **2001**, 80: 422.
17) Alexander K. Andrianov. Water-Soluble Polyphosphazenes for Biomedical Applications. Journal of Inorganic and Organometallic Polymers and Materials, **2006,**16, 4, 397-406.
18) Ko¨tz, J.; Kosmella, S.; Beitz, T. Prog. Polym. Sci**. 2001**, *26*, 1199–1232.
19) C. W. Cairo, J. E. Gestwick, M. Kanai, and L. L. Kiessling,J. Am. Chem. Soc. **2002,** 124, 1615.
20) H. R. Allcock, Chemistry and Applications of Polyphosphazenes (John Wiley and Sons, Hoboken, NJ, **2003**).
21) Yap, H. P.; Quinn, J. F.; Johnston, A. P. R.; Caruso, F. Macromolecules **2007**, 40, 7581–7589.
22) Jianhua Ding, Li Wang, Haojie Yu, Qiang Yang, Jia Huo, Libo Deng, Qingquan Liu, et al. Controllable Formation of Nanorods through Electrostatic-Assisted Assembly of Star Poly(methacrylic acid) Induced by Surfactants. *J. Phys. Chem. C*, **2009**, *113* (9), pp 3471–3477.