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Enhanced antibacterial activity of ceftazidime against *pseudomonas aeruginosa* using poly (propyleneimine) dendrimer as a nanocarrier

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Pseudomonas aeruginosa;
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Ceftazidime;
Sustained release;
Antibacterial activity.

Abstract. The aim of the current study is the loading of ceftazidime into the first generation of poly(propyleneimine) dendrimer (PPI-G1) to produce an effective drug delivery system against *Pseudomonas aeruginosa*. The mechanism of ceftazidime-PPI-G1 dendrimer complex formation is based on interaction between amine groups of dendrimers and carboxylic groups of ceftazidime. PPI-G1 was dissolved in dry tetrahydrofuran (THF), and ceftazidime was added to the solution to prepare the nanodrug. The series of tests, including size, zeta potential, drug release, stability and kinetic evaluation, as well as Scanning Electron Microscopy (SEM) and Fourier transform infrared (FT-IR) spectroscopy, were performed for characterization of the ceftazidime-loaded PPI-G1. The Minimum Inhibitory Concentration (MIC) and Minimum Bactericidal Concentration (MBC) of the nanodrug were determined, with respect to *Pseudomonas aeruginosa* as the test microorganism. Ceftazidime-PPI-G1 complex was synthesized with the size of 156.6 nm and −10.2 mV zeta potential. The value of loaded ceftazidime was determined to be about 38.46 mol%. A gradual drug release was observed within three days; up to 92% of the loaded ceftazidime. The macrodilution assay demonstrated that PPI-G1 enhances the antibacterial activity of ceftazidime. A new drug delivery system was improved against *P. aeruginosa* with sustained release and enhanced antibacterial activity.

1. Introduction

Pseudomonas aeruginosa is a leading cause of health care associated infections, ranking second among gram-negative pathogens, as reported by the United States national nosocomial infection surveillance system. *P. aeruginosa* contributes substantially to wound-related morbidity and mortality worldwide, and infections due to this organism are often difficult to treat. The organism enters into the blood, causing sepsis that may spread to the skin and leads to ecthymagangrenosum, a black necrotic lesion [1,2]. Ceftazidime, a third-generation of cephalosporins, is an important and effective antimicrobial agent for the therapy of serious infections due to *P. aeruginosa* (Figure 1). However, in recent years, antibiotic resistance is a pervasive and growing clinical problem in the treatment of this organism [3].

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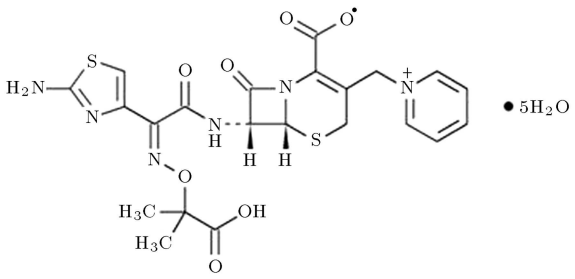

Figure 1. The schematic molecular structure of ceftazidime.

The widespread problem of antibiotic resistance in pathogens has prompted a search for new antimicrobial approaches [4,5]. The use of drug carriers, especially nanoparticles-based carriers, is a good idea to overwhelm this problem. Dendrimers are defined as highly ordered and regularly branched globular macromolecules. In recent years, many antibacterial drugs have been successfully loaded into dendrimer nanoparticles with improved solubility and therapeutic efficacy. These include penicillin [6,7], azithromycin [8], sulfamethoxazole [9], nadifloxacin and prulifloxacin [10]. The structure of dendrimers consists of three distinct architectural regions: a focal moiety or a core, layers of branched repeat units emerging from the core, and functional end groups on the outer layer of the repeat units [11]. They can be made from a wide variety of biocompatible materials, such as polyamidoamine (PAMAM), polyethylene oxide (PEO), poly(propyleneimine) (PPI), polyethyleneimine (PEI) and polyethylene glycol (PEG) [12]. For this study, we used the first generation of PPI (PPI-G1) as a dendritic nano-carrier. These dendrimers closely resemble PAMAM dendrimers (except repeating units). This indicates that PPI dendrimers also hold promise as solubilizing agents. Surprisingly, however, very few studies are available exploring PPI dendrimer abilities in this field [13,14]. The structure of PPI-G1 is shown in Figure 2 [15]. The specific molecular structure of PPI enables it to carry various drugs through its multivalent surface by covalent conjugation or electrostatic adsorption. Its surface can be also engineered to provide precise spacing of surface molecules and to conjugate targeting molecules [16]. Also, denderimers can be developed as a dual drug container for multidrug delivery systems [17].

After the preparation of ceftazidime-loaded PPI-G1 (the properties of the new nanodrug), the quantity of loaded ceftazidime and the release profile were investigated. The antibacterial activity of the complex was evaluated against *P. aeruginosa* (ATCC 15442) as the indicator too. This is the first official report of the preparation of ceftazidime-PPI-G1 complex using the slightly modified method [18].

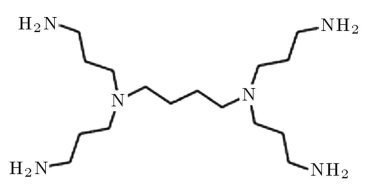

Figure 2. The schematic molecular structure of first generation of PPI dendrimer.

2. Materials and methods

2.1. Materials

PPI-G1dendrimer, and a DO405 dialysis tube 23 × 15 mm (cut-off: 10-12 KD) were purchased from Sigma-Aldrich, USA. Tetrahydrofuran, *n*-hexane, dichloromethane, diethyl ether, nutrient agar and nutrient broth media were purchased from Merck, Germany. *Pseudomonas aeruginosa* (ATCC 15442) was obtained from the microbial bank of the Pasteur Institute, Tehran, Iran. Ceftazidimepentahydrate was obtained from Alborz/Darou Pharmaceuticals, Qazvin, Iran.

2.2. Loading of ceftazidime onto PPI-G1 dendrimer

0.52 mL of PPI-G1dendrimer was dissolved in 20 mL of dry THF (dried by heating under reflux over sodium wire in the presence of benzophenone as the indicator) [19]. Then, 1 g of ceftazidime was added to 10 mL of the solution and stirred at 500 rpm for 2 h. The complex was precipitated in *n*-hexane and dissolved in dichloromethane. Then, the solution was precipitated in diethyl ether. Eventually, the final product was filtered and the powder of the ceftazidime-PPI-G1 nanodrug was prepared.

2.3. Size and zeta potential of ceftazidime-loaded PPI-G1 dendrimer

Particles size distribution and particle surface potential (the zeta potential) were measured using a laser scattering-based particle size analyzer (Nano ZS3000; Malvern Instruments, Malvern, UK), working on a Photon Correlation Spectroscopy (PCS) platform with a laser wavelength of 633 nm. Triplicate samples were analyzed in each case, including the control sample.

2.4. Chemical characterization and morphology study

Fourier transform infrared spectroscopy (FTIR) was used for chemical characterization of ceftazidime loaded PPI-G1 dendrimer. The IR spectrum was obtained with a KBr pellet using a JascoFT-IR 6300 spectrometer. Particle morphology was investigated by Scanning Electron Microscopy (SEM). The specimens were mounted on aluminum stubs of appropriate size, sputter coated with a thin layer of gold-palladium, and examined using SEM (Philips XL30; Philips, Almelo, The Netherlands).

2.5. Calculating the amount of loaded ceftazidime

The amount of loaded ceftazidime was calculated by measuring the weight of the PPI-G1 dendrimer before and after complexation (drug/dendrimer complex). The difference between the measured weights gives the quantity of loaded ceftazidime in the dendritic compound [20].

α = weight of PPI-G1dendrimer after the complexation;
β = weight of PPI-G1dendrimer before the complexation;
$(\alpha - \beta)$ = weight of loaded ceftazidime onto PPI-G1.

2.6. In vitro release assessment

The release study was performed using the dialysis method. The sediment of the ceftazidime-dendrimer complex, separated from the reaction solution by centrifugation, was redispersed in phosphate buffer saline (pH 7.4) and poured into a DO405 dialysis tube. The tube was immersed into a small glass beaker containing 40 mL of PBS (pH 7.4). Then, one mL samples were withdrawn from the beaker at predetermined time intervals up to 96 h. Ceftazidime concentration was analyzed using UV-spectrophotometry at a wavelength of 256 nm.

2.7. Stability study

In order to evaluate the stability of the ceftazidime-PPI-G1 dendrimer, the complex was prepared and divided into two portions: one portion was kept at room temperature and another was refrigerated at 2-8°C. The samples were withdrawn after 1, 2, 4, 8, 12, 24, 48 and 72 h, and subjected to particle size measurement using the zeta sizer.

2.8. Antibacterial activity

The ceftazidime-dendrimer complex was tested for its antibacterial activity against *Pseudomonas aeruginosa* (ATCC 15442) by the agar diffusion method. The bacterial suspensions, with a cell density equivalent to 0.5 McFarland (1.5×10^8 CFU/mL), were transferred individually onto the surface of Muller-Hinton agar plates. Then, hollow wells of 5 millimeter diameter were cut from the agar using a sterile cork-borer. 0.1 mL of ceftazidime-PPI-G1 dendrimer complex, free ceftazidime, unloaded PPI-G1, the blend of ceftazidime and dendrimer (non-conjugated) and normal saline (negative control) were poured into the wells separately. The zones of inhibition around the wells were measured in mm using a caliper 48 h post incubation at 35-37°C. All experiments were performed three times.

2.9. MIC and MBC determination

The antibacterial activity of the ceftazidime-PPI-G1 dendrimer complex was evaluated through the determination of MIC and MBC in culture broth, according to the macrodilution guidelines of the Clinical and Laboratory Standards Institute. The complex was prepared and serially diluted in 5 ml of Muller-Hinton broth to reach the concentration range of 0.05, 0.1, 0.25, 0.5, 1, 2, 4, 8, 16, 32, 64, 128 and 256 μg/ml (the equivalent ceftazidime concentration was calculated based on the loading ratio). Then, 50 μl of *P. aeruginosa* inoculum was added to each tube to reach a final concentration of 2×10^8 CFU/mL [21]. The MIC and MBC were determined after 24 h incubation at 37°C. Simultaneously, all steps were repeated for a stock solution of free ceftazidime for MIC and MBC determination via the serial dilution method. All experiments were performed three times.

2.10. Data analysis and statistics

The results were presented as mean ±SD. Statistical comparisons were performed as analysis of variance (ANOVA), whenever applicable, using SPSS 18. The level of significance was taken to be 0.05.

3. Results

3.1. Size and zeta potential of ceftazidime-PPI-G1 dendrimer complex

The typical particle size of the ceftazidime-PPI-G1 complex was found to be 156.6 nm (Figure 3(a)). The

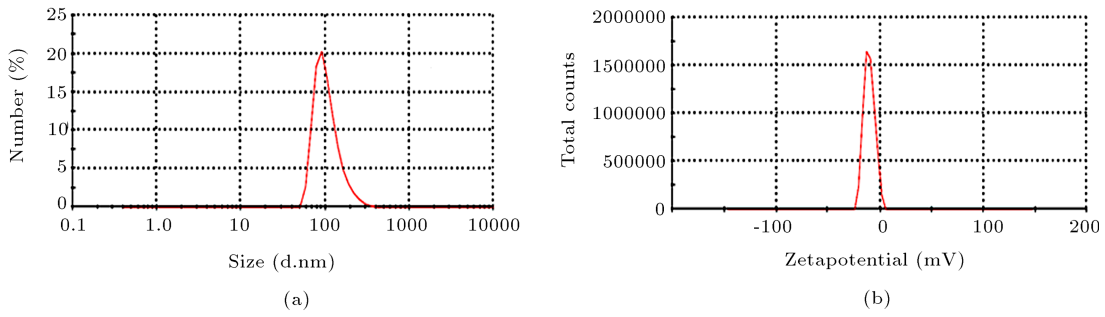

Figure 3. The size distribution diagram and zeta potential of ceftazidime-loaded PPI nanocarriers. The average size is approximately 156 nm and zeta potential is -10.2 mV.

zeta potential distribution curve was determined as −10 mV (Figure 3(b)).

3.2. Calculating the amount of trapped ceftazidime molecules

The amount of loaded ceftazidime onto PPI-G1 was calculated as follows:

$\alpha = 0.1343$ g,

$\beta = 0.1243$, g $= 0.00039$ mol,

$(\alpha - \beta) = 0.01$, g $= 0.000157$ mol.

Then, the mol proportion of ceftazidime was obtained to 38.46 mol% with a simple calculation.

3.3. Chemical characterization

Figure 4 shows the IR spectra of unloaded PPI-G1 nanocarrier (a), free ceftazidime (b) and ceftazidime-loaded PPI-G1 complex (c). It seems that there are electrostatic interactions between carboxylate groups of ceftazidime and NH_3^+ groups of PPI-G1 dendrimer. In the formation of ceftazidime loaded PPI-G1, a proton is transferred from the COOH group of ceftazidime to the NH_2 group of PPI-G1. The N-H bending vibration of the NH_2 group in ceftazidime appears at 1620 cm^{-1}, while, in ceftazidime loaded PPI-G1, the symmetrical and asymmetrical N-H bending vibration of the NH_3^+ group appears at 1536 and 1619 cm^{-1}, respectively.

3.4. Morphology study

The SEM micrograph approved the formation of ceftazidime-loaded PPI-G1 complex in the size range of 100-200 nm, with more or less spherical morphology (Figure 5).

3.5. In vitro release of ceftazidime from the dendrimer nanocarrier

The release profile of ceftazidime from PPI-G1dendrimer was analyzed with UV-spectrophotometry (Figure 6), in which a biphasic pattern can be seen: 1) an initial rapid drug releasing phase in the first 15 h, in which about 50 percent of the total loaded ceftazidime is released, and 2) a gradually increasing drug releasing phase after 15 h extending up to 72 h (up to 100 percent of the drug content). This is an acceptable model for a controlled drug release system.

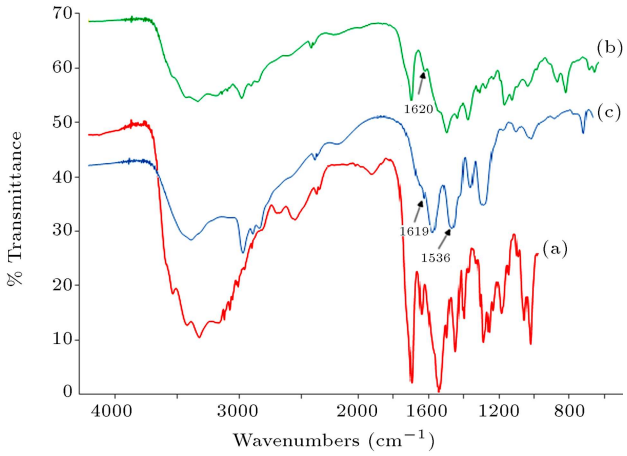

Figure 4. FTIR spectra of (a) unloaded nanocarriers, (b) ceftazidime loaded nanocarriers, and (c) ceftazidime.

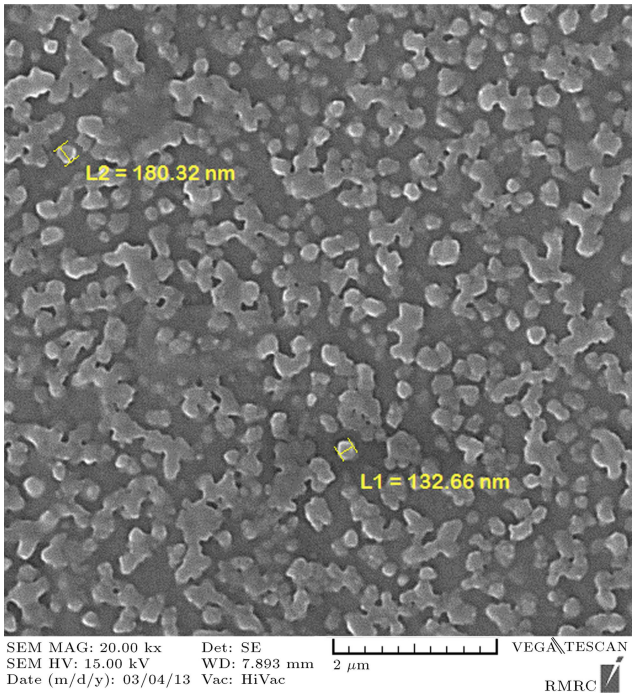

Figure 5. SEM photograph of ceftazidime-loaded PPI nanocarriers.

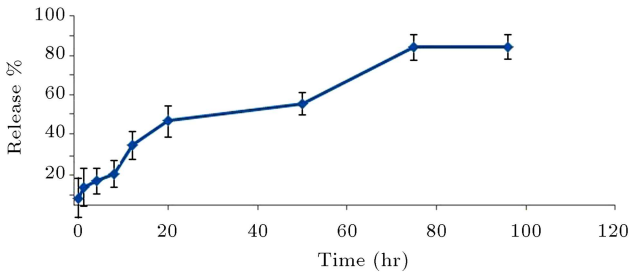

Figure 6. *In vitro* release profile of ceftazidime from PPI nanocarriers. The results were expressed as percentage of released gentamicin with three replicates.

3.6. Stability of ceftazidime-PPI-G1 dendrimer

According to the findings, the size of the ceftazidime-PPI-G1 complex remained unchanged for 72 h with no sensitivity to temperature (Figure 7).

3.7. Antimicrobial activity

An antimicrobial susceptibility test was performed on Mueller-Hinton agar using the agar diffusion method. Ceftazidime-loaded PPI-G1 displayed greater antimicrobial activity against target bacteria than free cef-

Table 1. Antimicrobial susceptibility study by measurement of bacterial inhibition zone around the wells.

Groups	Inhibition zone around the well (mm)
Ceftazidime-loaded PPI nanocarriers	23.66±1.15
Free ceftazidime	9±1
Unloaded PPI nanocarriers	20.33±0.57
Blend of ceftazidime and PPI dendrimer (non-conjugated)	30.66±1.52
Normal saline solution as negative control	0

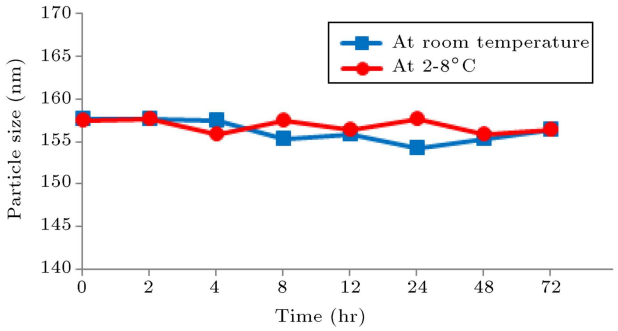

Figure 7. The particle size of ceftazidime-loaded PPI nanocarriers was remained stable during the stability test.

Table 2. MIC and MBC for free ceftazidime and PPI nanocarriers loaded by ceftazidime.

	Free ceftazidime (μg/mL)	Ceftazidime-loaded dendrimer (μg/mL)
MIC	0.5	0.25
MBC	1	0.5

tazidime (p value>0.05). The results were shown in Table 1.

3.8. MIC and MBC determination

The results of MIC and MBC determination are shown in Table 2. There is an observable difference between the MIC and MBC of ceftazidime-loaded PPI-G1 and free ceftazidime against *P. aeruginosa*, which is mostly due to the enhanced antibacterial effect caused by PPI-G1dendrimer.

4. Discussion

Dendrimers are repeatedly branched macromolecules or nano-sized, radially symmetric molecules, with a well-defined, homogenous and monodisperse structure consisting of treelike arms or branches [22]. Medical application is one of the private behaviors of the dendrimers [23]. In this study, the loading of ceftazidime in the dendrimeric system was accomplished. The results of FTIR suggested electrostatic interaction between carboxylate groups of ceftazidime and NH_3^+ groups of PPI-G1. Characterization studies showed the following characteristics for the new drug delivery system: ideal monodispersed particle size of 156.6 nm, with no significant out-of-range particles, and slightly negative zeta potential, both of which are suitable for a nanocarrier to be used for drug delivery purposes. The zeta potential obtained in this study was near the neutral zeta value (-10 to 10 mV) or the zeta value of zero (isoelectric point) [24]. The slightly negative zeta potential may be explained by the superiority of the contribution of carboxyl groups of ceftazidime in the surface of the nanoparticles. The release of ceftazidime from the PPI-G1 nanocarrier was prolonged up to 72 h, which, apparently, indicates a controlled-release of the loaded drug. According to the results obtained from the stability study, nanoparticle size remained unchanged for 3 days, which is quite acceptable. In addition, no observable swellability of the particles in aqueous media were seen; both features being very important in the stability of the complex. The morphology and chemical characterization of the prepared complex were examined in this study too. The SEM image shows that each particle unit exhibits a nanostructure size, and also shows the agglomeration of particles. Agglomeration is a phenomenon which arises from the particles gluing together one by one. One reason for this phenomenon could be due to the incomplete drying process, owing mainly to the hydrophilic nature of ceftazidim. One of the main parts of this study is evaluation of the antimicrobial activity of the ceftazidime-dendrimer complex. For this purpose, agar diffusion and macrodilution methods were used and the results compared with free ceftazidime. In the agar diffusion technique, the ceftazidime-loaded PPI-G1 dendrimer demonstrated superior antimicrobial activity compared to free ceftazidime. One probable reason might be the high density of active ceftazidime molecules present on the dendrimer surfaces. On the other hand, the polycationic structure of dendrimer biocides facilitates the initial electrostatic adsorption to negatively charged bacteria. Consequently, the absorption increases membrane permeability and allows more ceftazidime molecules to enter the bacteria, leading to a leakage of potassium ions and, eventually, complete disintegration of the bacterial membrane [25]. The comparative study using a macrodilution method indicated that ceftazidime-dendrimer nanoparticles were

more effective than free ceftazidime against *P. aeruginosa*, and can clear the infection with less adverse effects and more safety.

5. Conclusion

Based on the findings in this paper, we suggest the great potential of PPI-G1 for ceftazidime delivery with the ability to enhance antibacterial activity against *P. aeruginosa*.

References

1. Khan, J.A., Iqbal, Z., Rahman, S.U., Farzana, K. and Khan, A. "Report: Prevalence and resistance pattern of Pseudomonas aeruginosa against various antibiotics", *Pak. J. Pharm. Sci.*, **21**, pp. 311-315 (2008).
2. Snitkin, E.S. and Segre, J.A."Pseudomon asaeruginosa adaptation to human hosts", *Nature Genetics*, **47**, pp. 2-3 (2015).
3. Du, S.J., Kuo, H.C., Cheng, C.H., Fei, A.C.Y., Wei, H.W. and Chang, S.K. "Molecular mechanisms of ceftazidime resistance in *Pseudomonas aeruginosa* isolates from canine and human infections", *Veterinarni Medicina*, **55**(4), pp. 172-182 (2010).
4. Zolfaghari, P.S., Packer, S., Singer, M., Nair, S.P., Bennett, J., Street, C. and Wilson, M. "In vivo killing of Staphylococcus aureus using a light activated antimicrobial agent", *B.M.C. Microbiology*, **9**, p. 27 (2009).
5. Maddahi, P., Shahtahmasebi, N., Kompany, A. and Mashreghib, M. "Dopant induced changes in physical properties of ZnO: Mg nanosuspensions: Study of antibacterial activity", *Scientia Iranica, F.*, **20**(6), pp. 2375-2381 (2013).
6. Khandare, J. and Calderón, M. "Dendritic polymers for smart drug delivery applications", *Nanoscale*, **7**, pp. 3806-3807 (2015).
7. Gupta, U., Agashe, H.B. and Jain, N.K. "Poly (propylene imine) dendrimers mediated solubility enhancement, effect of pH and functional groups of hydrophobes", *J. Pharm. Sci.*, **10**, pp. 358-367 (2007).
8. Mishra, M.K., Kotta, K., Hali, M., Wykes, S., Gerard, H.C., Hudson, A.P., WhittumHudson, J.A. and Kannan, R.M. "PAMAM dendrimer-azithromycin conjugates for the treatment of Chlamydia trachomatis infections", *Nanomedicine*, **7**, pp. 935-944 (2011).
9. Abeylath, S.C., Turos, E., Dickey, S. and Lim, D.V. "Glyconanobiotics: Novel carbohydrated nanoparticle antibiotics for MRSA and Bacillus anthracis", *Bioorg. Med. Chem.*, **16**, pp. 2412-2418 (2008).
10. Heng, Y., Qu, H., Ma, M., Xu, Z., Xu, P., Fang, Y. and Xu, T. "Polyamidoamine (PAMAM) dendrimers as biocompatible carriers of quinolone antimicrobials: An in vitro study", *Eur. J. Med. Chem.*, **42**, pp. 1032-1038 (2007).
11. Grayson, S.M. and Frechet, J.M. "Convergent dendrons and dendrimers: From synthesis to applications", *Chem. Rev.*, **101**, pp. 3819-3868 (2001).
12. Tsartsalis, S. and Tzouveleki, M.M. "New challenges in nanotechnology: The use of dendrimers in drug administration", *Aristotle University Medical Journal*, **36**, pp. 47-52 (2009).
13. Pistolis, G. and Malliaris, A. "Study of poly (propylene imine) dendrimers in water, by exciplex formation", *Langmuir*, **18**, pp. 246-251 (2002).
14. Baars, M.W.P.L., Kleppinger, R., Koch, M.H.J., Yeu, S.L. and Meijer, E.W. "The localization of guests in water soluble oligoethyleneoxy modified poly(propylene imine) dendrimers", *Angew. Chem. Int. Ed.*, **39**(7), pp. 1285-1288 (2000).
15. Yang, H. and Lopina, S.T. "Penicillin V-conjugated PEG-PAMAM star polymers", *J. Biomat. Sci. Polymer. Ed.*, **14**, pp. 1043-1056 (2003).
16. Wang, A.Z., Gu, F., Zhang, L., Chan, J.M., Radovic-Moreno, A., Shaikh, M.R. and Farokhzad, O.C. "Biofunctionalized targeted nanoparticles for therapeutic applications. Expert", *Opin. Biol. Ther.*, **8**(8), pp. 1063-1070 (2008).
17. Hai, H., Yao, W., Hao, W. and Xinru, J. "Dendrimer-based multilayer nanocarrier for potential synergistic paclitaxel-doxorubicin combination drug delivery", *RSC. Adv.*, **4**, pp. 3643-3652 (2014).
18. Torok, M.E., Chantratita, N. and Peacock, S.J. "Bacterial gene loss as A mechanism for gain of antimicrobial resistance", *Current Opinion in Microbiology*, **15**, pp. 583-587 (2012).
19. Perrin, D.D. and Armarego, W.L.F., *Purification of Laboratory Chemicals*, pp. 72-73, Pergamon Press New York (1980).
20. Namazi, H., Motamedi, S. and Namvari, M. "Synthesis of new functionalized citric acid-based dendrimers as nanocarrier agents for drug delivery", *BioImpacts*, **1**, pp. 63-69 (2011).
21. Ahangari, A., Salouti, M., Heidari, Z., Kazemizadeh, A.R. and Safari, A.A. "Development of gentamicin-gold nanospheres for antimicrobial drug delivery to Staphylococcal infected foci", *Drug Deliv.*, **20**(1), pp. 34-39 (2013).
22. Hari, B.N.V., Kalaimagal, K., Porkodi, R., Gajula, P.K. and Ajay, J.Y. "Dendrimer: Globular nanostructured materials for drug delivery", *Int. J. Pharm. Tech. Res.*, **4**, pp. 432-451 (2012).
23. Didehban, K., Namazi, H. and Entezami, A.A. "Dendrimer-based hydrogen-bonded liquid crystalline complexes: Synthesis and characterization", *European Polymer Journal*, **45**(6), pp. 1836-1844 (2009).
24. Clogston, D.J. and Patri, K.A. "Zeta potential measurement", *Methods in Molecular Biology.*, **697**, pp. 63-70 (2011).
25. Chen, C.Z. and Cooper, S.L. "Interactions between dendrimer biocides and bacterial membranes", *Biomaterials.*, **23**, pp. 3359-3368 (2002).

Biographies

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Dr. Salouti serves as Chief Editor of the International Journal of Bioscience and Biotechnological Research, and is editorial board member of several international journals in related fields. He has published more than 60 peer reviewed articles and 3 book chapters (international), mostly on aspects related to nanotechnology. He has also been a member of the scientific committee of many national and international conferences and also as an invited speaker. His research interests include bioconjugation of monoclonal antibodies/peptides/antibiotics with nanoparticles/radionuclides to produce targeting agents for the diagnosis/therapy of breast cancer and infectious diseases.

Ali Reza Kazemizadeh was born in Sabzevar, Iran, in 1970. He obtained a BS degree in Chemistry from Zanjan University in 1994 and his MS degree in Organic Chemistry from Tabriz University in 1998. He earned a PhD degree in Organic Chemistry from Zanjan University in 2009. He is currently Assistant Professor in the Department of Chemistry at the Islamic Azad University, Zanjan, Iran. His main research interests include synthesis of organic compounds by multicomponent reactions.

Arash Zabihian was born in 1985. He obtained an MS degree in Microbiology from the Islamic Azad University, Zanjan, Iran. His thesis is entitled, "Preparation of Hydrogel Nanoparticles Loaded by Gentamicin: Physicochemical Characterization and Antimicrobial Effects". He currently works at Kish Medipharm Pharmaceutical Company as supervisor of the microbiology laboratory. His research interests include pharmaceutical microbiology, drug delivery and nanobiotechnology.

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