Synthesis and characterization of new polyamides derived from alanine and valine derivatives

Ayman El-Faham1,2*, Hammed HAM Hassan2 and Sherine N Khattab2

Abstract

Background: Many efforts have been recently devoted to design, investigate and synthesize biocompatible, biodegradable polymers for applications in medicine for either the fabrication of biodegradable devices or as drug delivery systems. Many of them consist of condensation of polymers having incorporated peptide linkages susceptible to enzymatic cleavage. Polyamides (PAs) containing α-amino acid residues such as L-leucine, L-alanine and L-phenylalanine have been reported as biodegradable materials. Furthermore, polyamides (PAs) derived from C10 and C14 dicarboxylic acids and amide-diamines derived from 1,6-hexanediame or 1,12-dodecanediamine and L-phenylalanine, L-valyl-L-phenylalanine or L-phenylalanyl-L-valine residues have been reported as biocompatible polymers. We have previously described the synthesis and thermal properties of a new type of polyamides-containing amino acids based on eight new symmetric meta-oriented protected diamines derived from coupling of amino acids namely; Fomc-glycine, Fmoc-alanine, Fomc-valine and Fomc-leucine with m-phenylene diamine or 2,6-diaminopyridine. Results revealed that incorporation of pyridine onto the polymeric backbone of all series decreases the thermal stability.

Here we describe another family of polyamides based on benzene dicarboxylic acid, pyridine dicarboxylic acid, and α-amino acid linked to benzidine and 4,4'-oxydianiline to study the effect of the dicarboxylic acid as well as the amino acids on the nature and thermal stability of the polymers.

Results: We report here the preparation of a new type of polyamides based on benzene dicarboxylic acid, pyridine dicarboxylic acid, and α-amino acid linked to benzidine and 4,4'-oxydianiline to study the effect of the dicarboxylic acid as well as the amino acids on the nature and thermal stability of polymers. The thermal properties of the polymers were evaluated by different techniques. Results revealed that structure-thermal property correlation based on changing the dicarboxylic acid monomer or the diamine monomer demonstrated an interesting connection between a single change (changing the dicarboxylic acids in each series while the diamine is fixed) and thermal properties. The newly prepared polymers may possess biodegradability and thus may find some applications as novel biomaterials.

(Continued on next page)
Conclusions: The thermal properties of the new type of polyamides based on benzene dicarboxylic acid, pyridine dicarboxylic acid, and α-amino acid (alanine and valine) linked to benzidine and 4,4′-oxydianiline were evaluated by thermal gravimetric (TG), differential thermal gravimetric (DTG) and differential thermal analysis (DTA) techniques. Results revealed that the structure-thermal property correlation based on changing the dicarboxylic acid monomer or the diamine monomer demonstrated an interesting connection between a single change (changing the dicarboxylic acids in each series while the diamine is fixed) and thermal properties. In addition, pyridine-containing polymers exhibited semicrystalline characteristic with melting temperature, \( T_m \), where none of the valine-containing polymers showed a melting and crystallization peak indicating that the polymers were amorphous. This is expected since L-valine side chain can inhibit close packing and eliminate crystallization. The newly prepared polymers may possess biodegradability and thus may find some applications as novel biomaterials.

Background
Many efforts have been recently devoted to design, investigate and synthesize biocompatible, biodegradable polymers for applications in medicine for either the fabrication of biodegradable devices or as drug delivery systems [1-5]. Many of them consist of condensation polymers having incorporated peptide linkages susceptible to enzymatic cleavage. Polyamides (PAs) containing α-amino acid residues such as L-leucine, L-alanine and L-phenylalanine have been reported as biodegradable materials [6,7], Jin et al. [8] prepared polyamides, and polyureas containing L-leucine and L-tyrosine residues in the chain. Polyester amides derived from α-amino acids and α-hydroxyacids, the polydepsipeptides, have also been investigated as biodegradable polymers [9,10]. Polyamides (PAs) derived from C₁₀ and C₁₄ dicarboxylic acids and amide-diamines derived from 1,6-hexanediamine or 1,12-dodecandiamine and L-phenylalanine, L-valyl-L-phenylalanine or L-phenylalanyl-L-valine residues have been reported as biocompatible polymers [11-13]. Furthermore, an appropriate choice of the number and sequence of the α-amino acids, as well as a balance of hydrophilic and hydrophobic characteristics of the other constituents, makes these polymers susceptible to enzymatic cleavage of the peptide bonds by specific enzymes [6,14-19].

Diamine type monomers derived from glycine [20], (D, L)- and (L)-alanine [21-30], (D, L-) and (L)-phenylalanine [31,32] and various aliphatic diols or from tyrosine–leucine–dipeptide [19,33] and different diamines, were utilized to obtain the polyester amides or polyamides. In general, it is expected that derivatives of L-alanine could be highly crystalline with extensive hydrogen bonding in contrast to the amorphous character of polymers that could be synthesized from α-amino acids with bulky side groups [8,34,35].

We have previously [36] described the synthesis and thermal properties of a new type of polyamides-containing amino acids based on eight new symmetric meta-oriented protected diamines derived from coupling of four types of Fmoc-amino acids namely; Fomc-glycine, Fomc-alanine, Fomc-valine and Fomc-leucine with m-phenylene diamine or 2,6-diaminopyridine. Results revealed that incorporation of pyridine onto the polymeric backbone of all series decreases the thermal stability [36].

Here we describe another family of polyamides based of benzene dicarboxylic acid, pyridine dicarboxylic acid, and α-amino acid linked to benzidine and 4,4′-oxydianiline to study the effect of the dicarboxylic acid as well as the amino acids on the nature and thermal stability of the polymer.

Experimental
Materials and methods
The solvents used were were of HPLC reagent grade. The commercial isophthalic acid (Merck), pyridine-2,6-dicarboxylic acid (Aldrich), pyridine-3,5-dicarboxylic acid (Aldrich), Fmoc-amino acids namely Fmoc-Ala-OH, Fmoc-Val-OH, and (O-(7-azabenzotriazol-1-yl)-1,1,3,3-tetramethyloxuronium hexafluorophosphate) (HATU) (IRIS Biotech, Germany), benzidine (Aldrich) 3, 4, 4′-oxydianiline (Aldrich) 4 and the solvents triethylamine (Et₃N), N,N-dimethylacetamide (DMAc), N,N-dimethylformamide (DMF), 1-Methyl-2-pyrrolidone (NMP) (Fluka), diethylamine, acetonitrile, chloroform, n-hexane, ethyl alcohol were used as purchased without purification.

Melting points were determined with a Mel-Temp apparatus and are uncorrected. Infrared spectra (IR) were recorded on a FTIR-8400S Shimadzu-Japan or on a Perkin-Elmer 1600 series, Fourier transform instrument as KBr pellets. Absorption spectra were measured with a UV 500 UV–vis spectrometer at room temperature (rt) in DMSO with a polymer concentration of 1 mg/10 mL. Magnetic resonance spectra (¹H NMR and ¹³C NMR spectra) were recorded on a JEOL 500 MHz spectrometer with chemical shift values reported in δ units (ppm) relative to an internal standard. Follow-up of the reactions and checks of the purity of the compounds was done by thin layer chromatography (TLC) on silica gel-protected aluminum sheets (Type 60 GF254, Merck) and the spots were detected by exposure to UV-lamp at λ 254 nm for a
few seconds. Differential thermogravimetric (DTG) analyses were carried out in the temperature range from 20°C to 500°C in a stream of nitrogen atmosphere by Shimadzu DTG 60H thermal analyzer. The experimental conditions were: platinum crucible, nitrogen atmosphere with a 30 ml/min flow rate and a heating rate 10°C/min. Differential thermal analysis (TGA/DTA) analyses were carried out using SDT-Q600-V20.5-Build at the Institute for Graduate Studies and Research, Alexandria University and at the Microanalysis Center, Cairo University, Giza, Egypt. Elemental analyses were performed at the Microanalytical Unit, Cairo University and Center for mycology and biotechnology, Alazhar University, Cairo.

Synthesis of Bis Fmoc-protected diamines 5–8 (general method)

To a solution of Fmoc–Ala-OH 1 (0.623 g, 2 mmol) or Fmoc–Val-OH 2 (0.679 g, 2 mmol); diisopropylethylamine (DIEA, 0.7 mL, 4 mmol) in 5 ml DMF. The reaction mixture was stirred overnight and then the mixture was poured over water. The precipitate was filtered, washed with 5% citric acid (3 x 20 mL), saturated NaHCO3 (3 x 20 mL) and water. The crude product was recrystallized from CH2Cl2/hexane.

Bis(9H-fluoren-9-yl)methyl)-1,1’-(4,4’-oxybis(4,1-phenylene)bis(azanediyl))bis(1-oxopropane-2,1-diyl)dicarbamate 7 (FT-IR, 1H NMR and 13C NMR are attached as supporting information; Additional files 7, 8, 9 respectively)

The reaction of Fmoc–Ala-OH 1 with 4,4’-oxydianiline 4 gave compound 7. The product was obtained as a white powder, mp 133-134°C, in yield 0.66 g (84%). IR (KBr): 3452, 3288 (NH), 1668 (C=O, amide) cm⁻1. 1H-NMR (CDCl3, 500Hz): δ 1.11-1.23 (m, 6H, 2 CH3), 2.60-2.69 (2brs, 2H, NH, D2O exchangeable), 4.18-4.24 (m, 4H, 4 CH). 13C-NMR (CDCl3, 125Hz): δ 21.66, 51.17, 110.31, 119.22, 120.47, 121.67, 121.87, 127.94, 129.57, 134.63, 137.94, 139.94, 143.08, 153.15, 175.46. Anal. Calcd for C48H42N4O7: C, 73.27; H, 5.09; N, 6.87. Found: C, 73.64; H, 5.09; N, 6.87.

Bis(9H-fluoren-9-yl)methyl)-1,1’-(4,4’-oxybis(4,1-phenylene)bis(azanediyl))bis(3-methyl-1-oxobutane-2,1-diyl)dicarbamate 8 (FT-IR, 1H NMR and 13C NMR are attached as supporting information; Additional files 10, 11, 12 respectively)

The reaction of Fmoc–Val-OH 2 with 4,4’-oxydianiline 4 gave compound 8. The product was obtained as a white powder, mp 193-194°C, in yield 0.75 g (89%). IR (KBr): 3289 (NH), 1692, 1660 (C=O, amide) cm⁻1. 1H-NMR (CDCl3, 500Hz): δ 1.58-1.63 (m, 6H, 2 CH3), 2.60-2.69 (2brs, 2H, NH, D2O exchangeable). 13C-NMR (CDCl3, 125Hz): δ 21.66, 51.17, 110.31, 119.22, 120.50, 121.67, 121.87, 127.94, 129.57, 134.63, 137.83, 139.93, 142.93, 153.15, 175.46. Anal. Calcd for C48H42N4O7: C, 73.27; H, 5.09; N, 6.87.
General procedure for the deblocking of the Fmoc-protecting groups: preparation of the diamines 9–12

Protected diamine (0.5 mmol) 5–8 was stirred with 40 ml (30% Et$_2$NH / CH$_3$CN) at r.t. for 14h. The progress of the reaction was monitored by using TLC using ethyl acetate / hexane 4:6 v/v as eluent. The solvent and volatiles were removed under reduced pressure and the crude residue was washed thoroughly with hexane to get rid from the deblocked dibenzofulvene byproduct to produce the desired diamine 9–12 which is used directly to the next step.

Preparation of polymers 16–25 by low-temperature solution polycondensation (general method)

To a mechanically stirred cold (ice bath) solution of the diamine 9–12 (1.0 mmol) dissolved in 5.0 mL DMA, a solution of 1.0 mmol of the acid dichloride 13, 14, 15 dissolved in 5.0 mL DMA was added dropwise. The reaction mixture was allowed to stir for 2h then the mixture was poured into iced water. The formed polymer precipitate was filtered under vacuum, washed thoroughly with water, ethyl alcohol and water again, dried and kept in the desiccator.

Poly[3-acetyl-N-((2S)-1-(4-(3-methyl-2-(methylamino)propanamido)phenoxy)phenylamino)-1-oxopropan-2-yl]picolinamide 16

The polymerization of the diamine 9 with isophthaloyl dichloride 13 produced the polymer 16 as a black solid, yield 59.0%, m. p. > 300°C, UV (DMSO): \(\lambda_{\max} = 272\) nm (\(\epsilon = 1569\)), \(\lambda_{\max} = 304\) nm (\(\epsilon = 1684\)), IR (cm$^{-1}$): 3230 (N-H, amide), 3064 (\(\geq C-H\), aromatic), 2921 (\(\geq C-H\), aliphatic), 1658 (C=O, amide), 1599 and 1497 (C=C, aromatic), 1114 and 1071 (C-N, aliphatic). Calculated for C$_{26}$H$_{26}$N$_4$O$_5$; C, 65.52; H, 5.78; N, 11.55.

Poly[3-acetyl-N-((2S)-1-(4-(3-(methylamino)butanamido)phenoxy)phenylamino)-1-oxopropan-2-yl]benzamide 17

The polymerization of the diamine 10 with isophthaloyl dichloride 13 produced the polymer 17 as a black solid, yield 56.0%, m. p. > 300°C, UV (DMSO): \(\lambda_{\max} = 275\) nm (\(\epsilon = 2244\)), \(\lambda_{\max} = 300\) nm (\(\epsilon = 2156\)), IR (cm$^{-1}$): 3430 (N-H, amide), 3039 (\(\geq C-H\), aromatic), 2921 (\(\geq C-H\), aliphatic), 1658 (C=O, amide), 1607 and 1446 (C=C, aromatic), 1249 and 1113 (C-N, aliphatic). Calculated for C$_{26}$H$_{26}$N$_4$O$_5$; C, 67.91; H, 6.46; N, 10.56; Found: C, 67.72; H, 6.70; N, 10.77.

Poly[3-acetyl-N-((2S)-1-(4-(4-(2-(methylamino)propanamido)phenoxy)phenylamino)-1-oxopropan-2-yl]benzamide 18

The polymerization of the diamine 11 with isophthaloyl dichloride 13 produced the polymer 18 as a black solid, yield 68.0%, m. p. > 300°C, UV (DMSO): \(\lambda_{\max} = 268\) nm (\(\epsilon = 1539\)), \(\lambda_{\max} = 276\) nm (\(\epsilon = 1169\)), \(\lambda_{\max} = 362\) nm (\(\epsilon = 86\)), IR (cm$^{-1}$): 3439 (N-H, amide), 2935 (C-H, aromatic), 1669 (C=O, amide), 1592 and 1490 (C=C, aromatic), 1114 and 1070 (C-N, aliphatic). Calculated for C$_{32}$H$_{32}$N$_4$O$_6$; C, 63.66; H, 5.34; N, 11.42; Found: C, 63.29; H, 5.08; N, 11.73.

Poly[3-acetyl-N-((2S)-3-methyl-1-(4-(3-methyl-2-(methylamino)butanamido)phenoxy)phenylamino)-1-oxobutan-2-yl]benzamide 19

The polymerization of the diamine 12 with isophthaloyl dichloride 13 produced the polymer 19 as a black solid, yield 60.0%, m. p. > 300°C, UV (DMSO): \(\lambda_{\max} = 268\) nm (\(\epsilon = 1754\)), \(\lambda_{max} = 330\) nm (\(\epsilon = 158\)), IR (cm$^{-1}$): 3477 (N-H, amide), 3036 (\(\geq C-H\), aromatic), 2887 (C=H, aromatic), 1640 (C=O, amide), 1610 and 1475 (C=C, aromatic), 1216 and 1150 (C-N, aliphatic). Calculated for C$_{32}$H$_{32}$N$_4$O$_6$; C, 65.92; H, 6.27; N, 10.25; Found: C, 66.28; H, 6.61; N, 10.60.

Poly[6-acetyl-N-((2S)-1-(4-(2-(methylamino)propanamido)biphenyl-4-ylamino)-1-oxopropan-2-yl]picolinamide 20

The polymerization of the diamine 9 with pyridine-2,6-dicarbonyl dichloride 14 produced the polymer 20 as a black solid, yield 56.0%, m. p. > 300°C, UV (DMSO): \(\lambda_{\max} = 268\) nm (\(\epsilon = 1930\)), \(\lambda_{max} = 321\) nm (\(\epsilon = 459\)), IR (cm$^{-1}$): 3400 (N-H, amide), 3063 (\(\geq C-H\), aromatic), 2934 (C=H, aromatic), 1668 (C=O, amide), 1590 and 1489 (C=C, aromatic), 1440 (C=C, aromatic), 1113 and 1070 (C=N, aliphatic). Calculated for C$_{26}$H$_{34}$N$_5$O$_5$; C, 63.15; H, 5.30; N, 14.73; Found: C, 63.41; H, 5.06; N, 14.61.

Poly[6-acetyl-N-((2S)-3-methyl-1-(4-(3-(methyl-2-(methylamino)butanamido)biphenyl-4-ylamino)-1-oxobutan-2-yl]picolinamide 21

The polymerization of the diamine 10 with pyridine-2,6-dicarbonyl dichloride 14 produced the polymer 21 as a black solid, yield 62.0%, m. p. > 300°C, UV (DMSO): \(\lambda_{\max} = 275\) nm (\(\epsilon = 2162\)), \(\lambda_{max} = 299\) nm (\(\epsilon = 2106\)), IR (cm$^{-1}$): 3416 (N-H, amide), 3039 (\(\geq C-H\), aromatic), 2890 (C=H, aromatic), 1642 (C=O, amide), 1613 and 1477 (C=C, aromatic), 1445 (C=C, aromatic), 1215 and 1150 (C=N, aliphatic). Calculated for C$_{30}$H$_{34}$N$_5$O$_5$; C, 65.52; H, 6.26; N, 13.17; Found: C, 65.85; H, 5.96; N, 12.89.

Poly[6-acetyl-N-((2S)-1-(4-(4-(2-(methylamino)propanamido)phenoxy)phenylamino)-1-oxopropan-2-yl]picolinamide 22

The polymerization of the diamine 11 with pyridine-2,6-dicarbonyl dichloride 14 produced the polymer 22 as a black solid, yield 58.0%, m. p. > 300°C, UV (DMSO): \(\lambda_{\max} = 268\) nm (\(\epsilon = 767\)), \(\lambda_{max} = 276\) nm (\(\epsilon = 651\)), IR (cm$^{-1}$): 3440 (N-H, amide), 3096 (\(\geq C-H\), aromatic), 2936 (C=H, aromatic), 1692 (C=O, amide), 1591 and 1490 (C=C, aromatic), 1441 (C=C, aromatic), 1113 and 1070 (C=N, aromatic).
Poly[5-acetyl-N-(25)-1-(4′-2-(methylamino)propanamido) biphenyl-4-ylamino]-1-oxopropan-2-yl)nictotinamide] 23  
The polymerization of the diamine 9 with pyridine-3,5-dicarboxylic acid chloride 15 produced the polymer 23 as a black solid, yield 67.0%, m. p. >300°C, UV (DMSO): $\lambda_{\text{max}}$ = 268 nm ($\varepsilon$ = 957), $\lambda_{\text{max}}$ = 276 nm ($\varepsilon$ = 860), $\lambda_{\text{max}}$ = 322 nm ($\varepsilon$ = 179), IR (cm$^{-1}$): 3416 (N-H, amide), 3087 (=C-H, aromatic), 2936 (C-H, aliphatic), 1669 (C=O, amide), 1593 and 1490 (C=C, aromatic), 1441 (C-N, aromatic), 1113 and 1070 (C-N, aliphatic). Calculated for $\text{C}_{25}\text{H}_{25}\text{N}_{5}\text{O}_{6}$; C, 65.52; H, 6.26; N, 13.17 Found: C, 65.17; H, 6.54; N, 13.51.

Poly[5-acetyl-N-(25)-3-methyl-1,4′-(3-methyl-2-(methylamino) butanamido)biphenyl-4-ylamino]-1-oxobutan-2-yl)nictotinamide] 24  
The polymerization of the diamine 10 with pyridine-3,5-dicarboxylic acid chloride 15 produced the polymer 24 as a black solid, yield 58.0%, m. p. >300°C, UV (DMSO): $\lambda_{\text{max}}$ = 269 nm ($\varepsilon$ = 888), $\lambda_{\text{max}}$ = 276 nm ($\varepsilon$ = 731), IR (cm$^{-1}$): 3420 (N-H, amide), 3036 (=C-H, aromatic), 2881 (C-H, aliphatic), 1639 (C=O, amide), 1612 and 1475 (C=C, aromatic), 1444 (C-N, aromatic), 1215 and 1150 (C-N, aliphatic). Calculated for $\text{C}_{29}\text{H}_{33}\text{N}_{5}\text{O}_{5}$; C, 61.32; H, 5.44; N, 13.98. Found: C, 60.98; H, 4.96; N, 14.63.

Results and discussion  

Chemical preparation of the polyamides containing amino acids  

Preparation of the Fmoc-protected diamines 5–8  
The preparation of the new symmetric diamines 9–12, Scheme 1, for the stepwise polymerization was our first target. Fmoc-alanine (Fmoc-Ala-OH) 1 and Fmoc-valine (Fmoc-Val-OH) 2 were used in this investigation. Reactions of two equivalent amounts of the aforementioned amino acids with benzidine 3, or 4,4′-oxydianiline 4 were performed using two equivalents of HATU [37] as coupling reagent in presence of four equivalent of diisopropylethyl amine (DIEA) as base in dimethylformamide (DMF) to furnish the corresponding bis-Fmoc-protected diamines (5–8) in good yield and purity. The structures of the prepared protected diamines 5–8 were fully characterized by IR, $^1$H-NMR, $^{13}$C-NMR and elemental analyses. IR spectra of the protected diamines exhibited characteristic absorption bands in the range 3452–3288 cm$^{-1}$ corresponding to the N-H bond. In addition the bands corresponding to the amide CONH group is observed in the range 1692–1668 cm$^{-1}$. $^1$H-NMR spectra of compounds 5–8 in DMSO-d$_6$ showed signals corresponding to four NH protons. The signals at the range δ 6.82-7.80 ppm correspond to two NH protons, and the other two NH protons are observed at the range δ 9.83-10.47 ppm. The 13C-NMR spectra of compounds 5–8 in DMSO-d$_6$ show two signals corresponding to the four carbonyl groups at the range 152.99-154.00 ppm and at the range 174.29-175.60.

Preparation of the diamines-containing amino acids 9–12  

Treatment of the protected diamines 5–8 with (3:7 Et$_2$NH/CH$_3$CN ν/ν) easily furnished the required diamines 9–12, respectively, in high yield, Scheme 1. Noteworthy, the byproduct dibenzofulvene was easily removed from the crude materials by washing with n-hexane. The crude products obtained were used as such without further purification.

Preparation of the polyamides 16–25 by low temperature solution polycondensation  

The aromatic acid chlorides, namely isophthaloyl dichloride 13, pyridine-2,6-dicarboxylic dichloride 14, and pyridine-3,5-dicarboxylic dichloride 15 used in this investigation were prepared by the reaction of their corresponding dicarboxylic acids, isophthalic acid, pyridine-2,6-dicarboxylic acid, and pyridine-3,5-dicarboxylic acid respectively, with thionyl chloride in the presence of few drops of DMF. Direct polycondensation reaction of an equimolar mixture of the acid chloride 13 with the diamines 9–12 in DMAC solution at 0–5°C furnished the corresponding polyamides containing amino acids 16–19, respectively in high yields, Scheme 2. In a similar manner, reactions of the acid chlorides 14 and 15 with the diamines-containing amino acids 9–11 furnished the corresponding polyamides 20–22 and 23–25, Scheme 2. The polymer structures were confirmed by elemental analysis, IR and UV spectroscopy.

Physical properties of the prepared polyamides containing amino acids  

Solubility  
The prepared polymers 16–25 showed similar solubility behavior in different organic solvents. Moderate to
complete dissolution was observed in a variety of aprotic solvents such as NMP, DMSO, DMAC, boiling alcoholic solvents such as methanol, ethanol while insoluble in halogenated solvents such as CHCl₃, CCl₄, CH₂Cl₂, ClCH₂CH₂Cl or in ethers such as Et₂O, THF, 1,4-dioxane or 1,2-dimethoxyethane (DME).

**FTIR Spectroscopy**

The FTIR spectra of the polymers exhibited characteristic absorbance at the range of υ 3477–3230 cm⁻¹ and 1692–1639 cm⁻¹, corresponding to the N-H and C = O stretching of the amide group, respectively. Bands around υ 2900 cm⁻¹ were assigned to the alkyl H-C stretching, while bands appeared around υ 3050, 1598 and υ 1524 cm⁻¹ assigned to the aromatic C-H and C=C aromatic, respectively.

**Optical properties**

The optical properties of polymers 16–25 were investigated by UV–vis spectroscopy in DMSO with a polymer concentration of 1 mg/10 mL. The spectra were recorded from 600 nm to 200 nm and the maximum absorbances (λmax) of the prepared polymers were recorded. Ala-containing polymers 18, 20, 23 and 25 exhibited bathochromic or red shifted peaks maxima at λ 362 nm, 321 nm, 322 nm and 367 nm, respectively may be attributed to the n→π transition while peaks at lower wavelengths appeared, respectively at 276 nm, 268 nm, 276 nm and 269 nm and could be attributed to the π→π transitions. Ala-containing polymers 16 and 22 exhibited peaks at wavelengths, appeared respectively at 304 nm and 276 nm which could be attributed to the n→π transitions. They also showed additional peak maxima at 272 nm and 268 nm due to π→π transitions.

Val-containing polymers 17, 19, 21 and 24 showed redshifted peaks maxima at λ 300 nm, 330 nm, 299 nm and 276 nm corresponding to the expected n→π, and similar peaks maxima at λ 275 nm, 268 nm, 275 nm and 269 nm, respectively due to π→π transitions.

**Thermal properties**

The thermal properties of these new materials were carried out in the temperature range from 20°C to 500°C in
a stream of nitrogen atmosphere. Because many of the polymers containing amino acids were rather hydrophilic and could absorb atmospheric moisture during preparations, samples were heated to remove the absorbed water, cooled, and reheated again at a heating/cooling rate of 20°C/min.

Figures 1 and 2 show the TGA/DTG and DSC curves of the alanine-containing polymers 16, 20, 23 and valine-containing polymers 17, 21, 24, derived from the diamine 3, respectively. Structure-thermal property correlation based on changing the diacid residue revealed that the prepared polymers have comparable thermal stabilities. Alanine-containing polymers 16, 20, 23 exhibited subsequent degradation and their major amide linkage degradation processes appeared at 365°C (77.12% wt loss), 380°C (81.94% wt loss) and 375°C (86.74% wt loss) leaving 20.69%, 12.64% and 11.39%, respectively, as remaining mass residues. Valine-containing polymers 17, 21, 24 exhibited two subsequent major degradation processes appeared at [256°C (46.91% wt loss), 339°C (37.71% wt loss)] and [260°C (48.77% wt loss), 340°C (39.70% wt loss)] and [168°C (38.00% wt loss), 293°C (35.09% wt loss)] leaving 11.70%, 7.18% and 24.83%, respectively, as remaining mass residues. On the other hand, alanine-containing polymers 22 and 25 derived from the diamine 4 exhibited subsequent degradation processes appeared in the temperature ranges 219°C - 439°C (58.99% wt loss) and 300°C - 495°C (50.53% wt loss).
Figure 1 TGA/DTG curves of the alanine-containing polymers 16, 20, 23 and valine-containing polymers 17, 21, 24.

Figure 2 DSC curves of the alanine-containing polymers 16, 20, 23 and valine-containing polymers 17, 21, 24.
leaving 19.69% and 37.57%, respectively, as remaining mass residues.

The glass transition temperature, \( T_g \), of the newly synthesized polymers ranged from 200°C to 225°C, and most of them were amorphous. In case of alanine-containing polymers 16, 20, 23, it is interesting to note that the change of the diacid had a noticeable \( T_g \) difference. In addition, pyridine-containing polymers 20 and 23 exhibited semicrystalline characteristic with melting temperature, \( T_m \), 383°C and 378°C, respectively. None of the valine-containing polymers 17, 21, 24 showed a melting and crystallization peak indicating that the polymers were amorphous. This is expected since L-valine side chain can inhibit close packing and eliminate crystallization.

Conclusions

The thermal properties of the new types of polyamides based on benzene dicarboxylic acid, pyridine dicarboxylic acid, and \( \alpha \)-amino acid (Alanine and Valine) linked to benzidine and 4,4'-oxydianiline were evaluated by thermal gravimetric (TG), differential thermal gravimetric (DTG) and differential thermal analysis (DTA) techniques. Results revealed that structure-thermal property correlation based on changing the dicarboxylic acid monomer or the diamine monomer demonstrated an interesting connection between a single change (changing the dicarboxylic acids in each series while the diamine is fixed) and thermal properties. In addition, pyridine-containing polymers exhibited semicrystalline characteristic with melting temperature, \( T_m \), where none of the valine-containing polymers showed a melting and crystallization peak indicating that the polymers were amorphous. This is expected since L-valine side chain can inhibit close packing and eliminate crystallization. The newly prepared polymers may possess biodegradability and thus may find some applications as novel biomaterials.

Additional files

Additional file 1: FT-IR spectra of compound 5.
Additional file 2: 1H NMR spectra of compound of compound 5.
Additional file 3: 13C NMR spectra of compound of compound 5.
Additional file 4: FT-IR spectra of compound 6.
Additional file 5: 1H NMR spectra of compound of compound 6.
Additional file 6: 13C NMR spectra of compound of compound 6.
Additional file 7: FT-IR spectra of compound 7.
Additional file 8: 1H NMR spectra of compound of compound 7.
Additional file 9: 13C NMR spectra of compound of compound 7.
Additional file 10: FT-IR of compound 8.
Additional file 11: 1H NMR spectra of compound of compound 8.
Additional file 12: 13C NMR spectra of compound of compound 8.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

HAMH carried out the polymerization, SNK carried out the preparation of the monomers. AEF, HAMH and SNK designed the proposed methods and analyzed the data statistically together. All authors read and approved the final manuscript.

Acknowledgment

This project was supported by King Saud University, Deanship of Scientific Research, College of Science Research Center.

Received: 3 August 2012 Accepted: 15 October 2012
Published: 2 November 2012

References

1. Chasin M, Langer R: Biodegradable polymers as drug delivery systems. NY: Marcel Dekker Inc; 1990.
2. Huang SJ, Roby MS, Macri CA, Cameron JA: The effects of structure and morphology on the degradation of polymers with multiple groups. In Biodegradable polymers and plastics. Edited by Vert M, Feijen J, Albertsson A, Scott G, Chieffini E: Cambridge: The Royal Soc. of Chem; 1992:149–157.
3. Bechaouch S, Coutin B, Sekiguchi H: Improvement of the synthesis of poly (L-cystyl-L-cystine): a new biodegradable polymer. Macromol Chem Phys 1996, 197:1661–1668.
4. Bechaouch S, Gachard I, Coutin B, Sekiguchi H: Synthesis and degradation of nonpeptide \( \alpha \)-amino-acid-containing polyamides. Polym Bull 1997, 38:365–370.
5. Pascual S, Gachard I, Coutin B, Sekiguchi H: Synthesis of new polyamides from natural monomers: L-malic acid and L-Lysine. Macromol Chem Phys 2001, 252:873–881.
6. Mungara PM, Gonsalves KE: Synthesis of polyamides containing sites targeted for enzymatic cleavage. Polymer 1994, 35:663–666.
7. Nagata M, Kiyotsumi T: Nylon-6 copolymers: copolymerization with \( \omega \)-amino acids. Eur Polym J 1992, 28:1069–1072.
8. Jin S, Mungara PM, Gonsalves KE: Synthesis of polyamides and polyureas containing leucine-tyrosine linkages. J Polym Sci Part A Polym Chem 1997, 35:499–507.
9. Langer R, Baera DA, Zylstra E, Lansbury PT: Synthesis and RGD peptide modification of a new biodegradable copolymer – poly(lactic acid-co-lysine). J Am Chem Soc 1993, 115:1010–11011.
10. Noga DE, Petrie TA, Kumar A, Weck M, Garcia AJ, Collard DM: Synthesis and modification of functional poly(lactide) copolymers: toward biofunctional materials. Biomacromolecules 2008, 9:2056–2062.
11. Yoshida M, Asano M, Kumakura M, Katakai R, Mashimo T, Yuasa H, Yamaika H: Sequential polydepsipeptides containing tripeptide sequences and \( \omega \)-hydroxy acids as biodegradable carriers. Eur Polym J 1991, 27:325–329.
12. Bianco B, Castaldo L, Del Gaudio A, Maglio G, Palumbo R, La Cara F, Peluso G, Petito O: Biocompatible \( \omega \)-amino acids based aliphatic polyamides. Polymer Bull. 1997, 39:279–286.
13. Castaldo L, Corbo P, Maglio G, Palumbo R: Synthesis and preliminary characterization of polyesteramides containing enzymatically degradable amide bonds. Polymer Bull. 1999, 28:301–307.
14. Maglio G, Maglio P, Oliva A, Palumbo R: Polyamides containing \( \omega \)-aminocids and hydrophilic oxygeny groups along the chain. Polymer Bull. 1999, 43:91–198.
15. Al-Khafaji JK, Ahmid MR, Al-Mousayy WA: Preparation and characterization of new poly (l-hexamethylene diamine – polyoxyethylene) copolymers. Titr J Pure Sci 2011, 16:31–41.
16. Huang SJ, Barkshey DA, Knox JR: Biodegradable polymers: Chymotrypsin degradation of a low molecular weight poly(ester-urea) containing phenylalanine. J Appl Polym Sci 1979, 23:429–437.
17. Kartveilishvili T, Ttitlanadze G, Edilashvili L, Japaridze N, Katsarava R: Amino acid based bioanalogous polymers. Novel regular poly(ester urethane) diesters, Macromol Chem Phys 1997, 198:1921–1932.
18. Sviridova LA, Leshcheva IF, Vertelov GK: Reaction of 1-acetyl-5-hydroxy-2-phenylpyrazolidine with amino acid esters. Chem Heterocycl Compd 1999, 36:1154–1160.
19. Katsarava R, Beridze V, Arabuli N, Kharadze D, Chul CC, Wox CY: Amino acid-based bioanalogous polymers. Synthesis, and study of regular poly(ester amide)s based on bis(\( \alpha \)-amino acid) di, \( \omega \)-alkylene diesters, and aliphatic dicarboxylic acids. J Polym Sci (A) Polym Chem 1999, 37:391–407.
20. Ulbrich K, Strolham J, Kopecek J. Polymers containing enzymatically degradable bonds. 10. Poly(ethylene glycol) containing enzymatically degradable bonds. *Makromol Chem-Macromol Chem.* 1986, 187:1131–1144.

21. Paredes N, Rodriguez-Galan A, Puigalli J. Synthesis and characterization of a family of biodegradable poly(ester amide)s derived from glycine. *J Polym Sci Part A: Polym Chem* 1998, 36:271–282.

22. Paredes N, Casas MT, Puigalli J, Lotz B. Structural data on the packing of poly(ester amide)s derived from glycine, hexanediol, and odd-numbered dicarboxylic acids. *J Polym Sci Part B: Polym Phys* 1999, 37:2521–2533.

23. Ash L, Armelin E, Montané J, Rodríguez-Galán A, Puiggali J. Sequential poly(ester amide)s based on glycine, diols, and dicarboxylic acids: thermal polyesterification versus interfacial polyamidation. Characterization of polymers containing stiff units. *J Polym Sci Part A Polym Chem* 2001, 39:4283–4293.

24. Armelin E, Paracuellos N, Rodriguez-Galan A, Puigalli J. Study on the degradability of poly(ester amide)s derived from the α-amino acids glycine, and L-alanine containing a variable amide/ester ratio. *Polym 2001,* 42:7023–7032.

25. Botines E, Rodriguez-Galan A, Puigalli J. Poly(ester amide)s derived from 1,4-butanediol, adipic acid and 1,6-aminohexanoic acid: characterization and degradation studies. *Polym 2002,* 43:s6073–6084.

26. Ciangia L. Synthesis and characterization of optically active polymers containing azo groups and (R)-α-amino acid moieties. *Eur Polym J* 2003, 39:2271–2282.

27. Karimi P, Risdalla AS, Mequanint K. Versatile biodegradable poly(ester amide)s derived from α-amino acids for vascular tissue engineering. *Materials* 2010, 3:2346–2368.

28. Puiggali J, Subirana JA. Synthetic polymers containing α-amino acids: from polyamides to poly(ester amide). *J Pep Sci* 2005, 11:247–249.

29. Mallakpour S, Dinari M. Progress in synthetic polymers based on natural amino acids. *J Macromol Sci Part A Pure and Applied Chemistry* 2011, 48:644–679.

30. Smath D, Lin S, Knight DK, Risdalla AS, Mequanint K. Fibrous biodegradable L-alanine-based scaffolds for vascular tissue engineering. *Tissue Eng Regen Med* 2012, doi:10.1002/term.1562. Article first published online: 17 AUG 2012.

31. Paredes N, Rodriguez-Galan A, Puigalli J, Peraire C. Studies on the biodegradation and biocompatibility of a new poly(ester amide) derived from L-alanine. *J Appl Polym Sci* 1998, 69:1537–1549.

32. Rodriguez-Galan A, Pelfort M, Aceituno JE, Puigalli J. Comparative studies on the degradability of poly(ester amide)s derived from L- and L,D-alanine. *J Appl Polym Sci* 1999, 74:2312–2320.

33. Lips PAM, Broos R, van Heeringen MJM, Dijkstra PJ, Feijen J. Incorporation of different crystallizable amide blocks in segmented poly(ester amide)s. *Polymer* 2005, 46:7834–7842.

34. Puiggali J, Subirana JA. Synthetic polymers containing α-amino acids: from polyamides to poly(ester amide). *J Pep Sci* 2005, 11:247–249.

35. Mallakpour S, Zadehnazari A. Simple and efficient microwave-assisted polycondensation for preparation of chiral polyamide-imide having pendant phenol moiety. *Polym Sci (B) Polym Chem* 2012, 54:5–6.

36. Hassan HHAM, El-Husseiny AF, Abo-Elfadl AG, El-Faham A, Albericio F. Synthesis and thermal properties of Novel polyamides containing α-amino acid moieties: structure–property relationship. *J Macromol Sci Part A* 2012, 49:41–54.

37. Carpino IA, El-Faham A. The diisopropylcarbodiimide-1-hydroxy-7-azabenzo triazole system: segment coupling and stepwise peptide assembly. *Tetrahedron* 1999, 55:6813–6830.

---

**Publish with ChemistryCentral and every scientist can read your work free of charge**

“Open access provides opportunities to our colleagues in other parts of the globe, by allowing anyone to view the content free of charge.”

W. Jeffery Hurst, The Hershey Company.

- available free of charge to the entire scientific community
- peer reviewed and published immediately upon acceptance
- cited in PubMed and archived on PubMed Central
- yours—you keep the copyright

Submit your manuscript here: http://www.chemistrycentral.com/manuscript/