

Study on Synthesis and Characterization of Unsaturated Poly (ester-amide) as Bone Fixation Materials

AI, Yong-Ping; XIE, Shi-Kun*⁺

New Low-Carbon Green Building Materials Institute, School of Mechanical and Electrical Engineering, Jinggangshan University, Ji'an, Jiangxi 343009, P.R. CHINA

ABSTRACT: A new type of unsaturated poly ester-amide was prepared by melt polycondensation and characterized completely. Influence of heat treatment conditions and cross-linking content on mechanical and degradation properties of unsaturated polyester-amide were studied. Results suggested that the newly synthesized unsaturated poly(ester-amide) possessed good heat stabilization properties. Mechanical and degradation properties of cross-linked poly (ester-amide) were determined by heat treatment conditions and cross-linker content. Different initiation-accelerating agent systems and their content differences have an insignificant influence on the cross-linking time at Room Temperature (RT). Increasing heat treatment time increased the retention rate of mechanical properties during the degradation process and decreased hydrolysis rate in alkaline solution.

KEYWORDS: Unsaturated poly(ester-amide); Heat treatment; Mechanical properties; Degradation properties.

INTRODUCTION

In contrast to metallic implants, biodegradable polymers used as bone fixation materials eliminate the second surgery for removal and avoid some problems caused by stress shielding. At present, some main biodegradable polymers used as fracture fixation materials are poly(L-Lactic acid)(PLLA), poly(glycolic acid)(PGA) and their copolymers[1-3]. The study of such materials is still the focus content of biodegradable bone fixation polymer. Polymerization of 2-p-dioxanone (PDS)^[4] occurs via ring opening polymerization because it is a flexible polymer and can only be used in the non-mechanical eroding degradable mechanism. Poly (orthoester) (POE) [5, 6] can maintain its mechanical strength in the degradation process, while its mechanical strength is only

one half of that of PLG. For cross-linked polyanhydrides [7], the double bonds can be broken by ultraviolet light to form a cross-linked network structure, which can greatly improve its mechanical properties. However, all reported polymers have been limited to low-load bearing applications due to insufficient strength.

Degradable ester groups and high polarity N-H bonds are included in poly ester-amide which renders the polymer with good mechanical properties. However, the reported unsaturated polyester-amide after cross-linking has low mechanical properties and can degrade easily [8]. Compared to unsaturated poly ester-amide, the saturated poly ester-amide is an elastomer with lower mechanical properties and higher degradation rate [9]. In the present

* To whom correspondence should be addressed.

+ E-mail: 27440767@qq.com

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work, a new type of unsaturated poly ester-amide, namely "maleic anhydride-phthalic anhydride-ethylene glycol-neopentylene glycol-glycin" copolymer was synthesized via polycondensation and was mixed with some cross-linker and initiation-accelerating agent to generate cross-linking at room temperature. This was followed by heat treatment to extend the cross-linking inside the polymer to increase its mechanical properties. The mechanical, degradation and hydrolysis properties of the newly synthesized cross-linked unsaturated poly ester-amide were studied after the heat treatment.

EXPERIMENTAL SECTION

Materials

Phthalic anhydride and maleic anhydride were purchased from Tianjing Central Pharmaceutical Corp. Ltd (Tianjing, China). Ethylene glycol, benzyl alcohol, neopentylene glycol, and vinyl acetate were purchased from Zibo Guangtong Chemical Co. Ltd. (Zibo, China).

Unsaturated poly (ester-amide) synthesis

In the synthesis process, maleic anhydride was polymerized via the addition of unsaturated C=C double bonds and further cross-linked with vinyl acetate. In the absence of phthalic anhydride, the cross-linking occurs at a temperature higher than 180°C. On the other hand, excess of phthalic anhydride can reduce the C=C double bonds content which in turn influence the mechanical strength of cross-linked samples. Ethylene glycol can increase the mechanical strength of cross-linked samples, and neopentylene glycol has good water resistance which reduces strength loss in Simulated Body Fluid (SBF).

To study the mechanical and degradation properties, the following reaction was done. Briefly, 0.024 mol (3.59 g) phthalic anhydride, 0.046 mol (3.49 g) ethylene glycol and 0.049 mol (5.09 g) neopentylene glycol were added to a 3-necked flask. The mixture was subjected to electrodynamic stirring, followed by oil water separation and polymerization at 160°C for 1 h. After cooling to 120°C and letting the product to stand at that temperature for 1h, 0.076 mol (7.42 g) maleic anhydride and 0.0125 mol (0.937 g) glycin were added, The reaction temperature was further raised to 180°C and maintained at that temperature for 1 h. Polymerization was done at 195°C for 4 h under a flow of argon. After cooling to 120°C, 2.05 g benzyl alcohol was added and reacted for 1 h. Again, the temperature was raised to 180 °C

kept for 1 h after reaction at 160°C for 1 h. When the temperature dropped to 100°C, the liquid products were stored in a P₂O₅ desiccator before use. The structure formula of synthesized unsaturated poly (ester-amide) is shown:

Unsaturated poly (ester-amide) cross-linking

Briefly, 8 g unsaturated poly (ester-amide) was added to 2 g vinyl acetate containing 0.06g benzoyl peroxide BPO and 0.005g N, N-Dimethylaniline until the vinyl acetate is fully dissolved in the unsaturated poly(ester-amide). The mixture was allowed to cross-link completely at room temperature. The cross-linked samples were placed under 195 °C heat treatment for 22 hours.

Synthesized unsaturated poly (ester-amide) characterization Methods

By GB/T2895 -82 "unsaturated polyester resin acid number" test acid number:

$$\text{The acid number before reaction} = \frac{\text{Mol mass} \times 56.1 \times 1000}{\text{Total mass}} \quad (1)$$

$$\text{Account acid number during reaction process} = \frac{C \times V \times 56.1}{M} \quad (2)$$

C is KOH- ethanol concentration (mol/L) ; V is consumption volume of KOH-ethanol solution (ml/L) ; M is removed sample mass (g).

InfraRed (IR) spectroscopy was done with a Bruker EQUINOX55FT-IR spectrometer. Synthesized unsaturated poly (ester-amide) samples were placed on NaCl plates directly for recording IR spectra.

Mechanical properties test

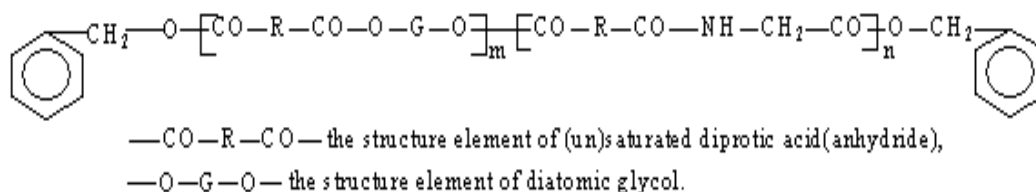
(1) Flexural properties

Flexural properties were measured on a Micro controls tension, at a load speed of 1mm/min, sample size 5×5×45mm

$$\sigma_b = \frac{3FL}{2BH^2} \quad (3)$$

$$E_b = \frac{FL^3}{4BH^3Y} \quad (4)$$

Where σ_b is flexural strength (MPa); E_b is flexural modulus, F is span; B and H stand for the breadth and ply, respectively and Y is camber.



Scheme 1

(2) Compressive properties

Calculation of compressive strength:

$$X_c = \frac{P_{\max}}{A} \quad (5)$$

Where P_{\max} is maximal compressive load and F is cross section area.

Calculation of compressive modulus:

$$E_c = \frac{P_2 - P_1}{(\Delta L_2 / L_0 - \Delta L_1 / L_0) F_0} \quad (6)$$

Where E_c is compressive modulus (MPa), P_2 is load with 0.3% strain; P_1 is load with 0.1% strain, ΔL_2 is 0.3% strain, ΔL_1 is 0.1% strain, L_0 is initialized length and F_0 is initialize area.

(3) Impact strength

$$\sigma = \frac{Q}{S} \quad (7)$$

σ is impact strength, Q is impacted energy, S is cross section area of impact sample

(4) Shear strength

Load speed: 2mm/min

$$Y_c = \frac{P_{\max}}{A} \quad (8)$$

P_{\max} is maximal sheet load and A is sheet cross section area.

RESULTS AND DISCUSSION

Acid number changes in the reaction process

The acid number of a reaction compound not only indicates the degree of esterification but also reflects the molecular weight. Acid number changes with reaction time are shown in Table 1. As shown in Table 1, in early reaction, the acid number dropped rapidly with

the passage of time. In the pre-primary reaction, the system contained monomers and low molecular weight oligomers and keep the reaction moving on. After 90 min, the speed of the reaction reduced and the molecular weight increased, which led to an increase in viscosity. High viscosity caused an increased collision of functional groups and became more difficult, which hampered smooth progress of the polycondensation reaction.

Synthesized unsaturated poly (ester-amide) characterization

The IR spectrum of the synthesized unsaturated polyester-amide showed strong absorption peaks at 1710–1735 cm^{-1} , which are characteristic absorptions of carbonyl stretching vibrations of ester groups. Such peaks were found in the IR spectra of all the products. The absorption bands at 1645 cm^{-1} are characteristic of C=C stretching vibrations. Those at 1454 cm^{-1} were attributed to =CH plane swing vibrations, and those at 982 cm^{-1} were attributed to =CH non-plane swing vibrations (Fig. 1) which indicated that the double bonds of maleic anhydride and became highly active double bonds. Such highly active double bonds favored the cross-linking of unsaturated poly (ester-amide).

Influence of Initiation-accelerating agent on cross-linking time of unsaturated poly (ester-amide)

The initiation-accelerating agent was used to initiating cross-linking of the unsaturated poly (ester-amide) monomers to a solid so that the cross-linking can be continued further after heat treatment. However, initiation-accelerating agent influenced cross-linking time at room temperature. The influence of accelerating agent on cross-linking time at room temperature is shown in Tables 2 and 3. As shown in Tables 2 and 3, with an increase in the amount of initiation-accelerating agents, the cross-linking time decreased, especially when N, N-Dimethylanillize was used as the accelerating agent.

Table 1: Changes in the acid number of reaction compound at 195 °C.

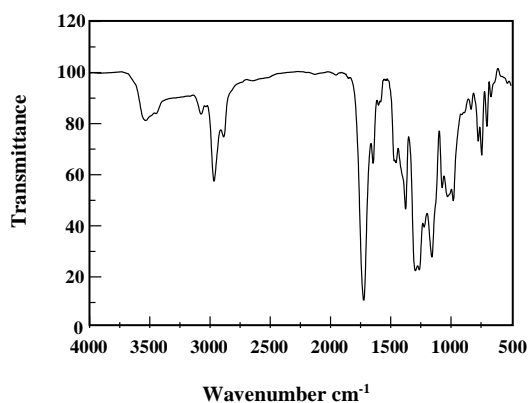
R	Reaction time (min)	0	30	60	90	120	150	180
A	Acid number (mgKOH/g)	235	190	156	135	117	102	76

Table 2: Influence of initiation-accelerating agent on cross-linking time of unsaturated poly (ester-amide).

B	BPO(Wt%)	1.0	0.8	0.6	0.4
A	Ascorbic acid(Wt%)	0.5	0.4	0.3	0.2
Cr	Cross-linking time(h)	6.0	8.0	9.0	12.0

Table 3: Influence of initiation-accelerating agent on cross linking time of unsaturated poly (ester-amide).

B	BPO(Wt%)	0.6	0.6	0.6	0.6
N	N,N-Dimethylaniline(Wt%)	0.2	0.1	0.05	0.02
Cr	Cross-linking time(h)	0.15	0.35	0.6	1.0

**Fig. 1: Infrared spectrum of unsaturated poly ester-amide.**

Mechanical properties of cross-linked unsaturated poly (ester-amide) with different vinyl acetate (cross-linker) content

As shown in Table 4, when the amount of vinyl acetate was over 20 Wt%, mechanical properties of the cross-linked unsaturated poly (ester-amide) did not show any obvious change. However, when the amount of vinyl acetate was less than 20 Wt% in the unsaturated poly (ester-amide), the mechanical properties became very poor. Therefore, 20 wt% of vinyl acetate was the best choice. In the present report, if not specifically mentioned, all the cross-linked unsaturated poly (ester-amide) have 20% vinyl acetate content. Furthermore, since the viscosity of the synthesized unsaturated poly (ester-amide) was very large and the initiator did not dissolve

in the unsaturated poly (ester-amide), vinyl acetate also helped to dilute the unsaturated poly (ester-amide) and dissolve the initiator.

Mechanical strength of the cross-linked unsaturated poly (ester-amide)

Mechanical strength of cross-linked unsaturated poly (ester-amide) improved gradually with increasing heat treatment temperature or time (Figs. 2 and 3). However, when the heat treatment time was more than 20 h at 195°C, the mechanical strength started to decrease. Moreover, as the heat treatment time was extended at 195°C, the compressive strength of the cross-linked unsaturated poly (ester-amide) improved faster than flexural strength showing that the heat treatment temperature had a large influence in improving the flexural strength. However, when the heat treatment temperature was over 220°C, the unsaturated poly (ester-amide) disintegrated.

As shown in Table 5, heat treatment time or temperature had a little effect on shear strength. The shear strength of the samples showed only a slight increase with the increase in the heat treatment time when the heat treatment temperature was over 170 °C, particularly at 195 °C. With an increase in heat treatment time, the impact strength of the samples also showed a rapid increase.

After heat treatment, the modulus of the samples was extremely low which was because the plastic itself possessed good flexibility. The modulus of the samples changed with heat treatment conditions, as shown in Table 6.

Table 4: Mechanical properties of cross-linked unsaturated poly(ester-amide) with different cross-linker content after heat treatment at 195 °C for 14 h.

Vinyl acetate (Wt%)	Flexural strength (MPa)	Flexural modulus (GPa)	compressive strength (MPa)	compressive modulus (GPa)
10	94.2	0.95	69.3	0.84
20	114.1	1.35	99.3	1.23
30	116.5	1.15	97.1	1.21
40	116.2	1.01	94.2	1.11
50	117.3	0.98	89.9	1.02

Table 5: Changes in mechanical strength of cross-linked unsaturated poly (ester-amide) at different heat treatment temperature and time.

Heat treatment temperature (°C)	150				170				195					
Heat treatment time	14	18	20	22	8	12	14	18	8	10	14	18	22	24
Sh Shear strength (MPa)	29.9	32.9	34.7	36.5	29.1	31.2	32.1	33.8	33.2	33.5	33.9	34.6	41.9	38.7
Im Impact strength(J/cm ²)	1.22	1.26	1.87	2.11	2.47	3.31	3.39	6.38	3.82	4.31	5.39	6.93	8.84	7.88

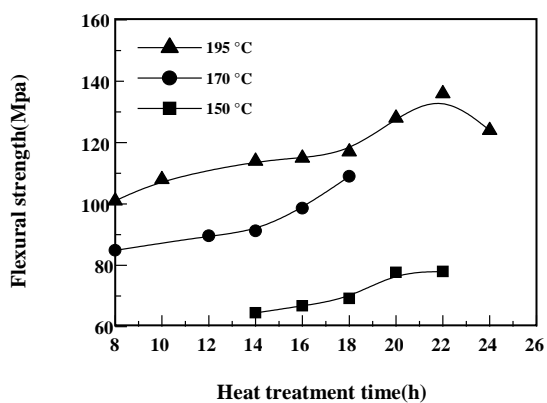


Fig. 2: Flexural strength changes of the cross-linked unsaturated poly (ester-amide) containing 20% cross-linker at different heat treatment time and temperature.

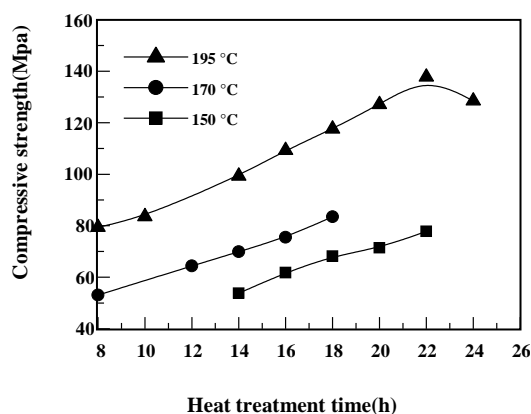


Fig. 3: Compressive strength changes of the cross-linked unsaturated poly (ester-amide) containing 20% cross-linker at different heat treatment time and temperature.

As shown in Table.6, the flexural modulus showed a larger growth rate than the compressive modulus under the same heat treatment conditions.

Degradation properties

Loss of mechanical properties of the cross-linked unsaturated poly (ester-amide) in pH 7.4 phosphate buffer at 37°C with 20wt% cross-linker at 195°C heat treatment for different time is shown in Tables 7 and 8. Mechanical properties of the cross-linked unsaturated poly (ester-amide) reduced with increase in the degradation time. Furthermore, longer heat treatment time showed a lower

mechanical properties loss rate. This is because with an increase in the heat treatment time, the degree of cross-linking of the copolymer also improved which in turn reduced mechanical properties loss rate. At the same time, it demonstrated that the degree of cross-linking of the copolymer played an important role in controlling properties loss rate, after degradation of 3 months in pH 7.4 phosphate buffer at 37°C. The flexural and compressive strength of the cross-linked unsaturated poly (ester-amide) were 99.5 MPa and 102.3 MPa, respectively when the heat treatment was done at 195°C for 22 h with 20 Wt% cross-linker. Therefore, it is

Table 6: Changes in mechanical modulus of cross-linked unsaturated poly(ester-amide) at different heat treatment temperature and time.

He Heat treatment temperature(°C)	150				170				195					
He Heat treatment time(h)	14	18	20	22	8	12	14	18	8	10	14	18	22	24
Fle Flexural modulus(GPa)	0.48	0.77	0.89	1.03	0.55	0.65	0.72	1.04	0.88	1.21	1.35	1.43	1.49	1.21
Co Compressive modulus(GPa)	0.37	0.67	0.69	0.71	0.47	0.56	0.68	0.85	0.89	1.01	1.23	1.58	1.11	0.98

Table 7: Changes in mechanical properties of cross-linked unsaturated poly(ester-amide) at different degradation time in simulated body fluid (SBF) at pH 7.4 and 37 °C after heat treatment at 195 °C for 14h.

Degr Degradable time(weeks)	0	1	2	3	5	7	9	11	13
Fle Flexural strength(MPa)	114.0	98.4	87.3	87.1	86.5	80.3	78.5	73.6	65.3
Co Compressive strength (MPa)	99.3	84.5	81.1	78.3	73.4	68.1	62.8	58.3	54.6
Fle Flexural modulus (GPa)	1.35	1.18	1.08	1.01	0.97	0.91	0.91	0.88	0.87
Com Compressive modulus (GPa)	1.23	1.03	0.96	0.91	0.88	0.81	0.75	0.70	0.65

Table 8: Changes in mechanical properties of cross-linked unsaturated poly(ester-amide) at different degradation time in simulated body fluid (SBF) at pH 7.4 and 37 °C. after heat treatment at 195 °C for 22 h.

Deg Degradable time(weeks)	0	1	2	3	5	7	9	11	13
Fle Flexural strength (MPa)	136.6	125.2	122.1	121.7	117.8	115.4	107.7	104.5	99.5
Co Compressiv strength(MPa)	137.8	121.1	121.0	118.2	116.6	112.4	107.5	104.3	102.3
Fle Flexural modulus(GPa)	1.49	1.25	1.24	1.23	1.21	1.18	1.15	1.14	1.12
Co Compressive modulus (GPa)	1.11	0.99	0.96	0.93	0.91	0.88	0.88	0.84	0.84

Table 9: Rate of mass loss of cross-linked unsaturated poly(ester-amide) in 1.0 mol/L NaOH standard solution at room temperature at different heat treatment time and cross-linker content at 195 °C after hydrolyzed for 15 days.

He Heat treatment time(h)	8	14	18	22	14	14	14
Cr Cross-linker content(Wt%)	20	20	20	20	30	40	50
M Mass loss rate(Wt%)	50.12	14.71	15.5	7.71	9.67	18.42	23.51

possible to use the copolymer material as a new type of cancellous bone (flexural strength 10-20 MPa, compressive strength 5-20 MPa) fixation device, and to meet the needs of cortical bone (flexural strength 120-180 MPa, compressive strength 110-167 MPa) by adjusting the chemical composition in the cross-linking copolymer network.

Hydrolysis behavior of cross-linked unsaturated poly(ester-amide)

In vitro, degradation properties of the cross-linked unsaturated poly(ester-amide) were studied in phosphate buffer solutions (pH 7.4) at 37°C and the result showed

that the polymer mass had only lost a little after degradation in 3 months. In order to accelerate its degradation process, hydrolysis behavior of copolymer with 20 Wt% cross-linker content and under different heat treatment conditions was determined by quantitative analysis of the mass loss in 1.0 mol/L NaOH standard solution at room temperature, as shown in Table 9. During the tested periods, the dimension of the devices was decreased step by step with the mass loss, while the surface of the devices remained slick during the hydrolysis process. It showed surface erosion property. After about 40 days hydrolysis, the dimension of the cross-linked unsaturated poly(ester-amide) that

contained 20 Wt% cross-linker and heat treated at 195°C for 22 hours decreased about a quarter, and then gradually vanished.

CONCLUSIONS

The following conclusions can be drawn from the current research.

(1) Novel unsaturated poly (ester-amide) showed good thermal stability and can be used to heat treatment.

(2) Heat treatment conditions or cross-linker content had a large influence on the mechanical properties of cross-linked unsaturated poly (ester-amide).

(3) Different initiation-accelerating agent systems or their content had a significant effect on the cross-linking time of unsaturated poly (ester-amide) at room temperature.

(4) Extending heat treatment time or increasing the temperature can increase the mechanical properties of cross-linked unsaturated poly (ester-amide) and reduce the hydrolysis rate of cross-linked unsaturated poly (ester-amide).

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REFERENCES

- [1] Kousa P., Jarvinen T.L., Kannus P., Järvinen M., [Initial Fixation Strength of Bioabsorbable and Titanium Interference Screws in Anterior Cruciate Ligament Reconstruction. Biomechanical Evaluation by Single Cycle and Cyclic Loading](#), *Am. J. Sports. Med.*, **29**(4): 420-425 (2001).
- [2] Suzuki T., Kawamura H., Kasahara T., Nagasaka H., [Resorbable Poly- L-Lactide Plates and Screws for the Treatment of Mandibular Condylar Process Fractures: a Clinical and Radiologic Follow-up Study](#), *J. Oral. Maxillofac Surg.*, **62**(8): 919-924 (2004)
- [3] Belligundu S., Shiakolas P.S., Pandey A., Pranesh B., [A Systemic Approach Toward Optimization of the Hot Embossing of Poly-L-Lactic Acid for Biomedical Applications](#), *J. Biomed. Mater. Res. B. Appl. Biomater.*, **5**: 201-207 (2007).
- [4] Boenisch M., Tamas H., Nolst Trenité G.J., [Morphological and Histological Findings after Typical Surgical Manipulations on Growing Septal Cartilage in Rabbits](#), *Facial. Plast. Surg.*, **23**(4): 231-232 (2007).
- [5] Sinha V.R., Khosla L., [Bioabsorbable Polymers for Implantable Therapeutic Systems](#), *Drug. Dev. Ind. Pharm.*, **24**(12): 1129-38. Review (1998).
- [6] Munford R.S., [Detoxification of Bacterial Lipopolysaccharides\(endotoxins\) by a Human Neutrophil Enzyme](#), *Science*, **234**: 203-205 (1986).
- [7] Amy K.B., Anseth K.S., [A Review of Photocrosslinked Polyamides: in Situ Forming Degradable Networks](#), *Biomaterials*, **21**: 2395-2404 (2000).
- [8] Guo K., Chu C.C., [Synthesis, Characterization, and Biodegradation of Novel Poly \(ether ester amide\) s Based on L-Phenylalanine and Oligoethylene Glycol](#), *Biomacromolecules*, **8**(9): 2851-2861 (2007).
- [9] Han S.I., Kim B.S., Kang S.W., Shirai H., Im S.S., [Cellular Interactions and Degradation of Aliphatic Poly \(Ester-Amide\) s Derived from Glycine and/or 4-Amino Butyric Acid](#), *Biomaterials*, **24**: 3453-3462 (2003).