

Synthesis and characterization of new biodegradable polymers and study of some properties in phosphate buffers

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Abstract

Copolymers between polylactic acid and polyethylene glycol, also alganic acid and polyethylene glycol were synthesized and diisocyanate (MDI) were prepared and characterized. Swelling behaviors and loss of weight of these polyurethanes were studied by immersion of the gels in various buffer solutions. Particularly the polyurethane foam showed the highest EWC (equilibrium water constant) in time-dependent and pH-dependent swelling.

Key words: copolymer, hydrogels, swelling.

Introduction

Biodegradable polymeric materials have been used in medicine with the major purpose to assist damaged tissues for their healing. The most widely accepted application is wound closure by absorbable sutures (Kada, 1989). Although the biodegradable materials have a great advantage over the non degradable in which we do not need re-operation to remove the implanted foreign body. First, not only the starting materials but also the biodegradation by-product should not be toxic Second, the minimum mechanical properties required for the biodegradable materials as a scaffold of tissue ingrowths or fixation of fractured bones should be maintained until regeneration of the defective tissues Third, the starting materials as well as the degradation and hopefully may accelerate the tissue healing (Kada,1991). Although

a large number of biodegradable materials have been studied for medical application, very few kinds of biodegradable polymers are currently used for surgery. The clinically applied absorbable polymers are mostly synthetic aliphatic polyesters such as polyglycolic acid (PGA) and polylactic (PLA)(Kada,1991). Wound dressing based on alginic martial is well known (Fual and Nelson,2004; Nurs,1997 and Piacquadio,1992). Calcium alginates being a natural hemostat, alginate based dressings are indicated for bleeding wounds. The gel forming property of alginate in removing the dressing without much trauma and reduces the pain experienced by the patient during dressing changes. It provides a moist environment that leads to rapid granulation and reepithelialization, therefore its improvement in healing split skin graft donor sites(Ezio,1994). In another study with burn patients, calcium alginate significantly reduced the pain severity and was favored by the nursing personal because of its ease of care. The combined use or calcium sodium alginate and bio-occlusive membrane dressing in the management of split thickness skin graft donor sites eliminated the pain and the problem of seroma formation and leakage seen routinely with the use of boi-occlusive dressing alone (Disa *et al.*, 2001). Bulk commodity polymers refer to polymers that have been developed for other purpose and then adapted for biomedical applications. It should be noted however that there is not necessarily only one material solution for particular medical problem, polymers are often used in combination to provide the desired spectrum of properties, and the polymeric materials are often surface modified primarily to aid biocompatibility (Dumitriu,2004).The goal is synthesis of new biodegradable polymers for biological application such as suture,tendons,..etc.

Materials and Instruments

Polyethylene glycol (PEG) (Mwt.300) (Merch co.), L.lactic acid (Mwt.90.08) (BDH co), sodium alginate (Mwt.200000) (BDH co), buffer solution (Fluka co), ammo-nium hydroxide (Fluka co), hydrochloric acid (Merch co), sodium carbonate (Fluka co), tetrahydrofuran (THF) (Merch co), polyol(Mwt.30000)(BDH co), and Methylendiisocyanate (MDI) (Merch co). Infrared (IR) Spectrophotometer (Shimadzu Bruker mod guin ox55).

Experimental- Preparation of poly lactic acid (1)

Three necked flask equipped with mechanical stirrer, gas outlet tube, and nitrogen gas tube in bottom of flask, was charged with (0.13 mmole, 10 ml) of L-lactic acid, five drops of diluted 1% HCl was add. The reaction mixture was stirred for 3 hrs at 130 °C and the nitrogen gas was passed through the mixture to get of the water. Then the reaction mixture was cooled and neutralized by washed with 0.1% of NaHCO₃ then with water. The product was dried in vacuum- oven for 24 hrs at 0.1 mm Hg and 40°C to give a yellow oily product.

2- Preparation of Alginic acid (2)

The more direct method of precipitation is by using acid directly. Sodium alginate was dissolved in water and diluted (1%) HCl was added drop by drop until alginic acid was precipitated. The colloidal mixture was centrifuged then dried in vacuum-oven at 50 °C for 24 hrs.

3- Preparation of PLA-AA copolymers (3)

3-1-Preparation of LA-AA Copolymer

Polymerization was carried out in sterilized glass ampoules. Polyactic and alginic acid were mixed to a 1:1 mole ratio. Under vacuum the ampoule was heat sealed .The polymerization mixture was homogenized at polymerization temperature. Polymerization was continued for 10 days at 110 °C.

4- Preparation of PEG-AA Copolymer (4)

Alginic acid was powdered .One gram (0.013 m mole) of Alginic acid was suspension in 50 ml THF in 250 ml three necked flask, 10 g(0.013 moles) of polytheneglycol was added . The mixture was reflected with vigorously mechanical stirred for 3 hrs. The solvent was evaporated under reduced pressure. The copolymer was characterized by IR spectrophotometer.

5- Preparation of Poly Urethane Resins (6,7)

2 grams (0.025 moles) of copolymer (3and 4) was dissolved in 8 grams (10 mmoles) of polyol under heating with stirred for 1 hrs. The mixture was cooled in ice water, and then 10 grams (0.001) of

MDI was added with vigorously stirred. The foam was cured in oven for 3 hrs at 100 °C.

6- Study of hydro gel and loss of weight in Phosphate Buffer.

The stability and hydrogelesity of polyurethane foam (6,7) of phosphate buffer was studied. The one diameter disc of polyurethane was coated. The Phosphate buffer in different pH (6.5, 7, and 7.4) was prepared. The equilibrium water constant (EWC) per weighted was estimated. The discs were immersed in various phosphate buffer solutions. The weight of swollen sample was measured at various time intervals after excessive surface water was removed with the filter paper. The procedure was reported until was no further weight increase. EWC was determined according to the following equation: $EWC (\%) = (W_s - W_d) / W_s \times 100$ Where W_s and W_d represent the weight of swollen and dry state, Sample, respectively. Also the loss of weight at different time in different phosphate buffer was determined.

Results

Characterization of polymeric compounds

The IR spectra of polymeric compounds were recorded in the 400-3600 cm^{-1} region. The essential absorption bands were shown in table (1).

Table (1) Shows the distinguish IR spectra bands of copolymers.

	Absorption bands (cm^{-1})				
	O-H	C=O	C-H bendin g	C-C	C-H
blend (PEG-PLA)(2)	3400	-	1470	600-1300	2800-2850
blend (PEG-AA)(3)	3400 weak	1850	1350	1100-1200	2700-2800
Polyurethane(6)	3300 weak	1770	1400	1000-1100	2750-2800
Polyurethane(7)	3400 weak	1760	1390	1200-1010	2750-2800

Hydro gel study

Table (2) was showed the pH dependent swelling behavior with change in pH of a buffer solution of polymers. Also loss of weigh

was estimated after different times of treatment as shows in table (3).

Table (2) The time effect of EWC% swelling of polyurethane

		EWC % after time of treatment (hrs)			
		4	24	48	72
Polyurethane (6)	6.5	73.0	77.0	76.0	78.6
	7.0	76.0	78.5	77.0	77.5
	7.4	74.3	76.0	76.6	77.0
Polyurethane (7)	6.5	70.0	71.8	96.6	97.0
	7.0	94.0	96.0	96.0	96.1
	7.4	68.0	68.5	70.0	71.0

Table (3) The weight loss of polyurethane after different time

		Loss of weight (gm) after (hrs)				
		24	48	72	96	120
Polyurethane (6)	6.5	0.02	0.02	0.03	0.03	0.03
	7.0	0.02	0.02	0.03	0.03	0.03
	7.4	0.02	0.02	0.03	0.03	0.04
Polyurethane (7)	6.5	0.06	0.09	0.11	0.15	0.20
	7.0	0.10	0.15	0.15	0.20	0.25
	7.4	0.11	0.15	0.19	0.250	0.30

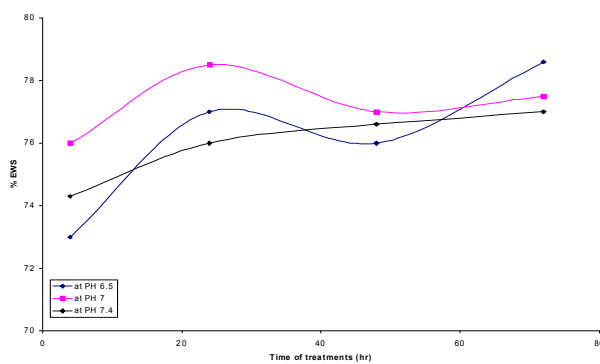


Figure (1): Shows the pH-dependant of polyurethane (6) of EWS.

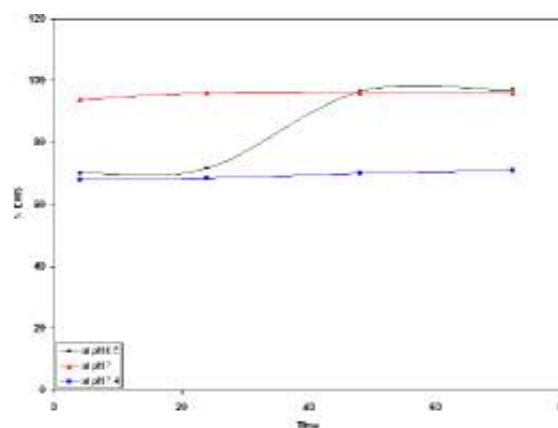


Figure (2): Shows the pH- dependant of polyurethane (7) of EWS.

Discussion

The IR spectra were characterized peaks of polymeric blends and polyurethane foams as shows in table (1). The hydroxyl groups are located at 3400 cm^{-1} . Hydroxyl peaks of PEG-AA blends and polyurethanes, was very weak due to esterfication between PEG and AA also isocyanat group with hydroxyl group in polymeric blends respectively (Kada, 1989). Time-dependent swelling behavior of polyurethane foam was observed with changes in pH of buffer solution. Swelling kinetics of hydrogels in pH (6.5, 7 and 7.4) buffer solution, at 35°C are plotted in figures (1 and 2) as average of three trials (Disa *et al.*,2001). The polyurethanes (6 and 7) swelled and reached equilibrium within 24 hrs. The pH dependent swelling behavior was observed with change in pH buffer solution. The EWC increases at pH 6.5 and 7, polyurethane exists as ammonium ions, due to the dissociation of intermolecular ammonium salt. At pH above 7, however, polyurethane form of $-\text{NH}_2$, resulting in even lower EWC than at lower pH. Because the blend (PEG – PAA) posses more hydroxyl and carboxyl groups in its structure, the swelling degree at pH7, were highest, with the highest total water contentment at all conditions of the experiments. The time dependent change of the mass of polyurethanes (6 and 7) disc in vitro was observed with changes in pH (6.5, 7 and 7.4) buffer solutions. The study indicating that the degradation of polyurethane (6 and 7) proceeds via non-enzymatic hydrolysis. Generally, the loss of weight increase within increase pH as the sequence of efficiency: $6.5 > 7 > 7.4$ as shown in table (3). The polyurethane (7) foam was highest degree of degradation of

pH profile. The highest degree of degradation in polyurethane (7) due to highest in polarity for hydroxyl and carboxyl groups in alginic acid molecules. The hydrogel polymers give advantages in wound dressing. The most significant advancement in wound care came with winters (Winter and Scales 1963) study in 60 patients, which showed that occluded wounds healed much faster than dry wounds and moist wound healing environment optimized the healing rates. He demonstrated that when wounds on pigs are kept moist, epithelialisation is twice as rapid as on wounds allowed to dry by exposure to air. Moist healing prevents the formation of scab as the dressing absorbs wound, exudates secreted from the ulcer (Willi and Sharma 2004). The high water vapor permeability polyurethane top layer can be used as a semi-permanent skin substitute on full thickness wounds until sufficient autografts are available. This layer provides a barrier against infection and optimal vapor permeability (JMFH, 1993).

Conclusion

Polyethylene glycol polylactic acid, polyether glycol-alginic acid and polyurethanes were synthesized and characterized. All hydrogels exhibited a high EWC in the rang (68-97). The pH sensitive characteristics were studied by a swelling test under various pH conditions at 35 C and conclude:

- 1- Polyurethanes (6,7) samples appeared highest swelling ratio in pH (6.5 and 7).
- 2- Polyurethanes (6,7) appeared time – dependent swelling behaviors.
- 3- Polyurethane (7) was a high degree in degradation.
- 4- Polyurethane (7) was pH and time - dependent of hydrolysis in buffer systems.

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تحضير وتشخيص بوليمرات متحللة احيائيا جديدة ودراسة بعض خواصها في

محلول الفوسفات المنظم

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فرع الكيمياء الصيدلانية / كلية الصيدلة / جامعة البصرة

الخلاصة

تم تحضير بوليمرات مشتركة بولي ايثيلين كلايكول مع بولي حامض اللاكتك وكذلك بولي ايثيلين كلايكول مع حامض الالجينك وكذلك حضرت الرغوة الاسفنجية للبوليمرين مع المثيلين داي ايزوسيانيت .درس تأثير الدالة الحامضية والزمن للمحاليل المنظمة على كفاءة الرغوة في سحب الماء وكذلك على استقرارية الرغوة .