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A Study on Surface, Thermal and Mechanical Properties of Absorbable PLGA Plate

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Abstract

In recent years, it has been become important to develop an effective material to be used as scaffolds for bone fixation in surgical field. PLA (Poly lactic acid), PGA (Poly glycolic acid), PLGA(Poly lactic-co-glycolic acid) and PLLA(Poly (L)-lactic acid) are well known to absorbable polymers that exhibit sufficiently low toxicity to useful for internal applications. So, we are study on the one of absorbable polymers as scaffolds (Plates and screws) consisting of PLGA (85/15). The aim of this study is to fabricate this plates and screws using an injection molding and to evaluate its surface, thermal and mechanical properties. The obtained plates and screws were observed with SEM, NMR, XRD, XPS, FTIR, DSC, TGA and mechanical moment (tensile and compressive strength). The glass temperature and molecular of PLGA were influenced by absorbed moisture. Therefore, obtained injection moldings were stored at 40°C and 20%, 50%, 80% relative humidity. Weight fraction absorbed free moisture was determined using a chemical balance.

Keywords: *PLGA, Plates and Screws, Injection molding, Physical properties*

1. Introduction

Biodegradable Poly (lactic-co-glycolic acid)-PLGA is a synthetic copolymer from lactic acid (α-hydroxy propionic acid) and glycolic acid (hydroxy acetic acid). Lactic acid has two optical isomers (L(+) lactic acid and D(-) lactic acid) because lactic acid contains an asymmetric carbon atom. Lactic acid exists present in nature as either an intermediate or an end product in carbohydrate metabolism. Lactic acid is widely distributed in all living creatures (man, animals, plants, and microorganisms). Also, glycolic acid is distributed in nature to a limited extent. PLGA degrades in vivo to relatively harmless products such as lactate (salt form of lactic acid) and glycolate (salt form of glycolic acid) [1].

Biodegradable Po1y(1actic-co-g1yco1ic acid) co-polymers have been extensively used as sutures, plates, and screws for repair of bone fractures, drug delivery systems and templates for surgical tissue engineering of medical uses [2-4]. The hydrolysis degradation of PLGA co-polymers produced into metabolic products (lactic and glycolic acid). The hydrolysis degradation of PLGA co-polymer was incorporated with metabolic pathways, therefore it was excreted as CO_2 and H_2O. The PLGA is biodegradable, biocompatible and FDA approved polymer material for surgical tissue engineering. The biodegradation level of PLGA can be

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regulated by choosing appropriate amount of co polymer molecular weight and moll ratio of PLA and PGA [5].

The orthopedic and cosmetic applications of metal plates and screws have produced good clinical results [6-7]. They are widely used because of easy handling and positive fixation, but they have some disadvantages and problems. Metal itself may limit the subsequent use of magnetic resonance imaging (MRI) and X-ray as a postoperative assessment tool. Therefore, to remove metal plates and screws would require a second operation. For these reasons, a biodegradable plates and screws of PLGA has been introduced for the orthopedic and cosmetic applications. Biodegradable polymers have been used for suture, vascular clips, and bone fixation implants [8-9]. There are positive benefits for the use of PLGA because they need not be removed because they are absorbed in vivo. The fixation properties of plates and screws geometry are adequate and maintenance of physical integrity is a sufficient duration. The inflammation by PLGA implant is minimal and the cost of PLGA implant is a little expensive with metal. Therefore, plates and screws of PLGA should be a suitable alternative [10-11].

Due to the hydrolysis of PLGA plates and screw with injection molding, typical parameters including the glass transition temperature, moisture content and polymer molecular weight were changed with exposed time. And the modification of PLGA properties during polymer biodegradation were influenced with the release and degradation rates due to water moisture degradation. The Gordon-Taylor equation has been used to relate glass transition temperature and water content in PLGA within narrow range of moisture content and limited polymer degradation [12-15]

The aim of this study was to evaluate this plates and screws with using a injection molding concerning its basic properties and biocompatibility. The obtained plates and screws were observed with scanning electron SEM, DSC, TGA, NMR, XRD, bending moment and tensile strengths. And physical properties (glass temperature, molecular weight, *etc*.) of PLGA were influenced by absorbed free moisture in plates and screw. And effects of water moisture adsorption on PLGA degradation were measured at 40°C and 20%, 50%, 80% relative humidity. Weight fraction absorbed free moisture was determined by using an electric chemical balance.

2. Materials and Methods

2.1. Materials

PLGA (2012D) in pellet form was purchased from Purac(Netherlands) is a semi-crystalline grade with approximately 85% Lactic acid monomer. The melting index of PLGA(85:15) is very low and so injection molding condition is a little difficult.

Table 1. The optimum condition of PLGA injection molding.

Conditions	Plates and screws
Nozzle temperature	180 ℃
Mold temperature	60℃
Injection speed	6 cc/sec
Cooling time (s)	8 sec
SCF injection pressure(MPa)	5 MPa

PLGA (85:15) plates and screws were injection molded using an 'Korea hydraulic system' equipped with injection molds. The Optimized processing conditions for both plates and screws of PLGA injection molding were listed in Table 1. The photographs of PLGA plates and screws were shown in a Figure 1.

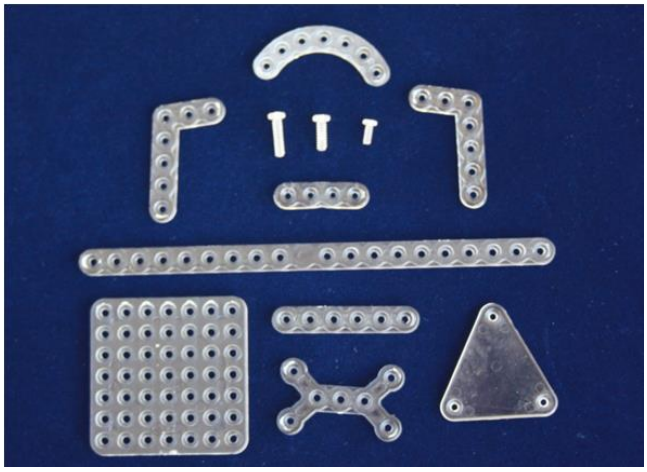

Figure 1. Photographs of biodegradable PLGA(85:15) plates and screws with injection molding.

2.2. Experimental Methods

XRD analyses were conducted using a high resolution X-ray diffractometer (Hitachi, japan). The plates of PLGA with injection molding were scanned at room temperature in reflection mode using incident CuKα radiation (A = 1.5405Å) at a step width of $0.04^{o}\,min^{-1}$ from $2\Theta = 1^{o}$ to 15^{o}. The basal spacing (d-spacing) of the plates of PLGA with injection molding was estimated from the (001) diffraction peak using Bragg's law, $\lambda = 2d\sin\Theta$. All diffraction patterns were normalized to the peak of highest intensity.

FTIR analyses were conducted MATRIX™-F duplex FT-NIR spectrometer (Bruker Optics Ltd., UK). The spectrometer was set to operate in the near-infrared region from 11,000 to 4000 cm^{-1}. Spectra were collected at a resolution of 4 cm^{-1} over 64 scans. The plates of PLGA with injection molding were injected into a de-mountable (open-end) optical glass cell with a path-length of 1 mm (Starna, UK). The cell was housed in a CUV-TLC-50F temperature regulated holder (Ocean Optics Inc., USA).

^{1}H NMR spectra analysis was conducted on a Bruker Avance400 MHz (Bruker Espanola S.A., Madrid, Spain). Solid-state NMR spectra were obtained with the cross-polarization /magic angle spinning (CP/MAS) technique. Magic angle spinning was earned out with 4-mm double bearing rotors of ZrO_2 and Spinning rate of 12,000 Hz at probe temperature of 295 K. The proton 90^{o} pulse length was 4.7 as with contact and delay times of 2ms and 4 s, respectively. A total of 10 K transients were accumulated at a time domain size of 2 K data point with an acquisition time of 40ms.

TGA analyses were conducted on a Thermogravimetric Analyzer Q200 (TA, USA). Samples of 20 mg were heated from room temperature to 500 ℃ at a rate of 10 ℃/min under a nitrogen atmosphere. All TGA results were the average of a minimum of three measurements and the temperatures were reproducible to ±1℃.

DSC analyses were conducted on a Diamond DSC (PerkinElmer Inc., UK). DSC was calibrated with pure indium and tin prior to use. The sample and reference compartments of

the calorimeter were purged with nitrogen gas at a flow of 30cm^3/min. The plates of PLGA with injection molding were prepared just prior to use, and approximately 30 mg was placed in an open pan. In the case of the dynamic scans, these were performed from 25 to 250 ℃ at a heating rate of 10 ℃/min.

The mechanical properties (tensile strength and compressive strength) of the plates of PLGA with injection molding were tested in a tensile testing machine (Testmetric M350-20KN) equipped with a 100-N load-cell. Samples were prepared with width 5 ~ 30 mm, length 35 ~ 100 mm and thickness 1.5mm. Each tensile strength and compressive strength tests were operated under a cross-head speed of 5 mm/min at room temperature (ASTM guide No. 12134). The calculation values of tensile strength and compressive strength were represented with the average results of five tests. Statistical analysis was carried out using an ANOVA. A correlation coefficient, R = 0.997 was showed, the tests were considered to be statistically significant.

Water moisture adsorption and degradation of PLGA were performed at 40 ± 2 ℃ using hermetic chambers containing saturated salt solutions with different relative humidity (RH) ($MgCl_2$: RH = 20%, KI: RH = 50%, K_2SO_4: RH = 80%). The granule type particles of PLGA about 200± 5mg were placed on open glass dish and incubated in the chambers until equilibration. Simultaneously, the samples of PLGA with injection molding about 1000± 5mg was placed in each chamber and the weights of plates and screws of PLGA with injection molding were monitored using an electric chemical balance with a expose running time at 20%, 50% and 80% RH.

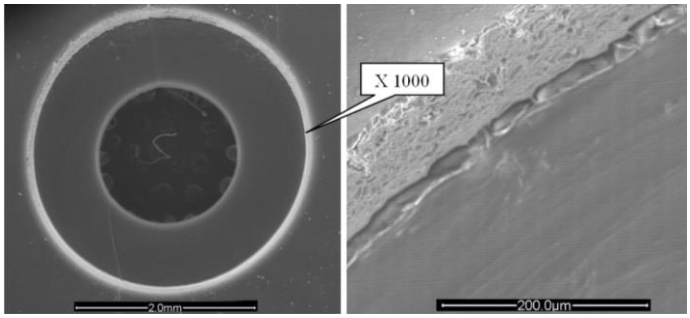

Figure 2. SEM images of plate hole [A] and hole edge [B] of PLGA plate with injection molding

3. Results and Discussions

3.1. Surface properties of absorbable PLGA plates

Figure 2[A] shows SEM image of hole located in PLGA plate with injection molding shown Fig. 1 and SEM image of hole edge(x 1000) is shown in Figure 2[B].

XRD spectra curves of PLGA raw sample [A] and PLGA plate with injection molding [B] were shown in Figure 3. As shown in Figure 3, the overall XRD curve pattern [B] of PLGA plate with injection molding was similar to that of PLGA raw material. In addition, the main peak of XRD spectra from 7 (2-theta) to 25 (2-theta) was assigned to amorphous hydrocarbon. As shown in Figure 3[B], another peak at 43 2-theta in XRD spectra of PLGA plate was assigned to crystalline hydrocarbon due to rearrangement of molecular orientation. Therefore the condition of injection molding slightly influences on the rearrangement of molecular orientation.

The surface chemical composition of PLGA plate with injection molding was investigated by X-ray Photo-electron Spectroscopy (XPS). XPS spectra of sample were measured at a residual pressure of 10^{-9} mbar, using a ESCALAB 250(VG Scientific) analyzer operating with an Al Kα a monochromatic source. The spectra of XPS allow the determination of the elements and average chemical composition of the PLGA plate at its surface in 5~10 nm depth by measuring the binding energy of electrons associated with atoms [16]. Concerning the chemical structure of PLGA plate, C1s signal at 288eV was assigned to C-C SP^2 and neighboring peaks(right peaks) were assigned to the C-C SP3, C-O and C=O. O1s signal at 534eV was assigned to C-O and neighboring peak(left peak) was assigned to the C=O as shown in a Figure 4.

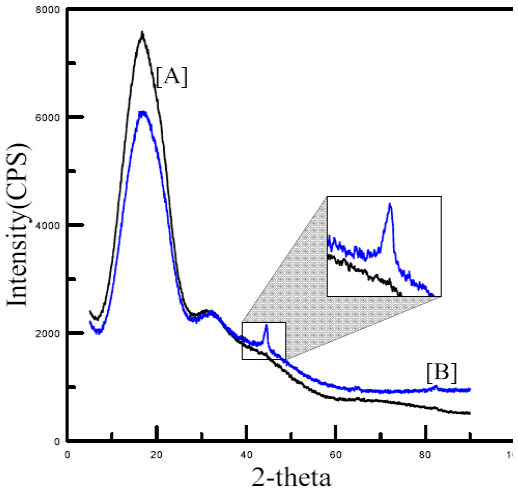

Figure 3. XRD curves of raw PLGA [A] and PLGA plate with injection molding [B]

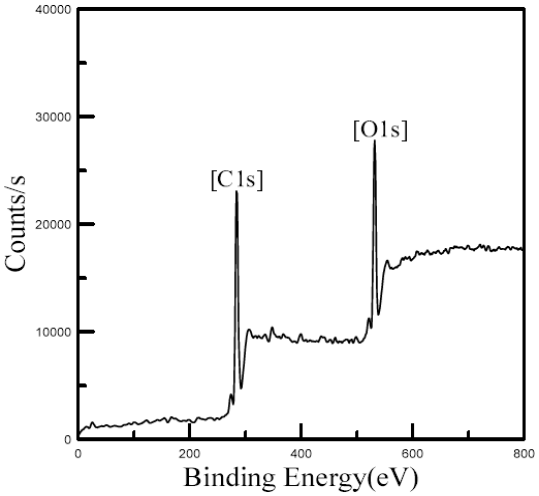

Figure 4. XPS spectra of PLGA plate with injection molding

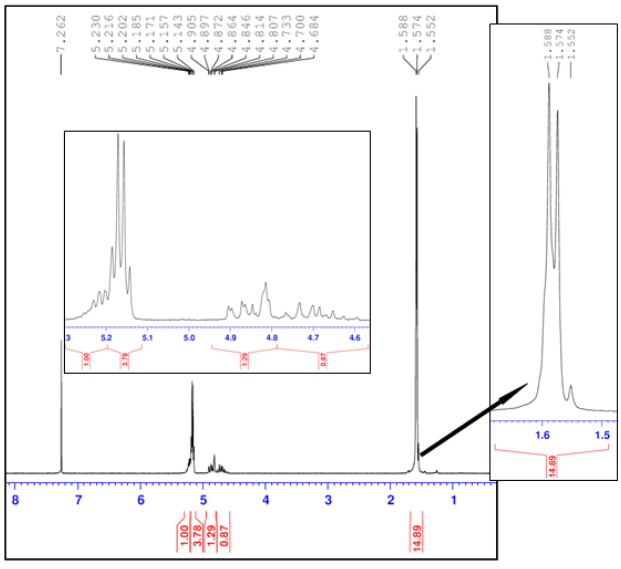

Figure 5. NMR spectra of PLGA plate with injection molding

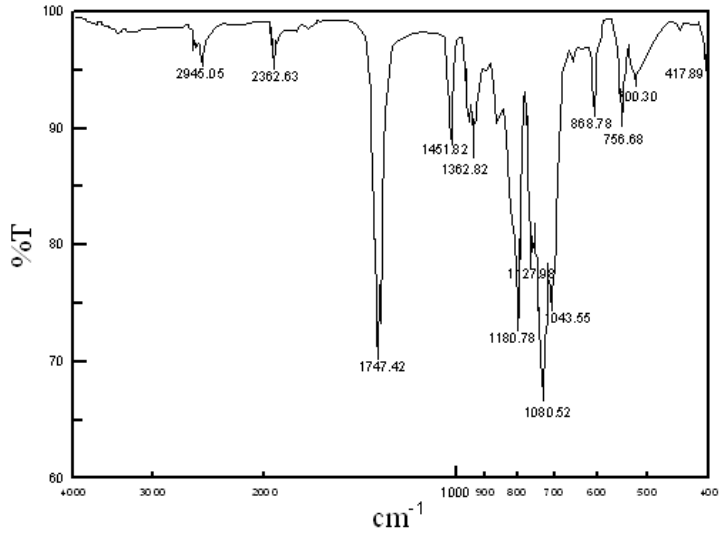

Figure 6. FTIR spectra of PLGA plate with injection molding

Nuclear magnetic resonance (NMR) is a non-destructive technique used to solve problems related to elucidation of Structures. Figure 5 showed ^{1}HNMR spectrum of PLGA plate with injection molding. As shown Figure 5, ^{1}HNMR analysis of PLGA revealed the presence of three sets of peaks: the first one corresponds to carboxylic and carbonyl bonds at 7.25ppm, the second one at 5.1 ppm corresponds to CH bonds in lactic acid and $(CH)_n$ in glycolic acid and the third one corresponds to methylen groups of the D, L-1actic acid repeated units at 1.520 ppm [17]. The proposed chemical structures had been re-confirmed with the ^{1}HNMR simulation software ChemDraw Ultra v8.0.3) and the simulated ppm values were close matches to the actual ^{1}HNMR peak ppm values.

FTIR analysis was performed for the surface characterization of PLGA plate with injection molding. Figure 6 showed the FTIR spectra of PLGA plate sample. It was observed in Fig. 6 that the carbonyl and C-O-C stretching bonding was appeared at respectively 1747 cm^{-1} peak and 1080 cm^{-1} peak, respectively. Another peak at 1451 cm^{-1} was due to C-H stretching in methyl groups, and 1043 cm^{-1} peak was assigned to the C-CH_3 stretching vibrations [18]. The methyl groups on the surface of PLGA plate preferentially were oriented at polymer/air interface and were free to vibrate as compared to methyl groups in PLGA plate [19]. Also, FTIR spectrum of PLGA plate was consistent with the expected structure of the copolymer showing a very weak band at in the region of 2860-2960 cm^{-1} assigned to C-H stretch of CH_2 and CH_3.

3.2. Thermal properties of absorbable PLGA plates

DSC analysis is a helpful technique for the investigation of the thermal properties, providing information about the physicochemical state of the PLGA [20]. DSC curves of raw PLGA [A] and PLGA plate with injection molding [B] are shown in Figure 7.

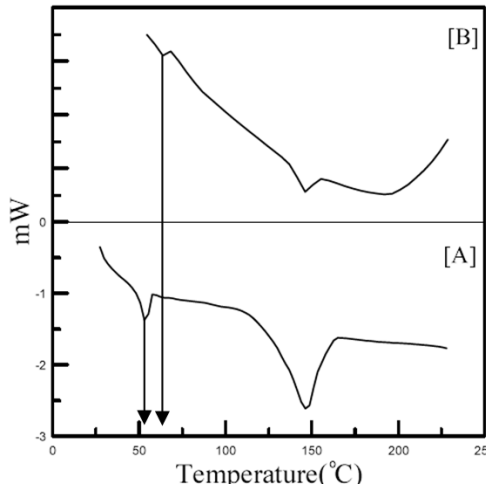

Figure 7. DSC curves of raw PLGA [A] and PLGA plate injection molding [B]

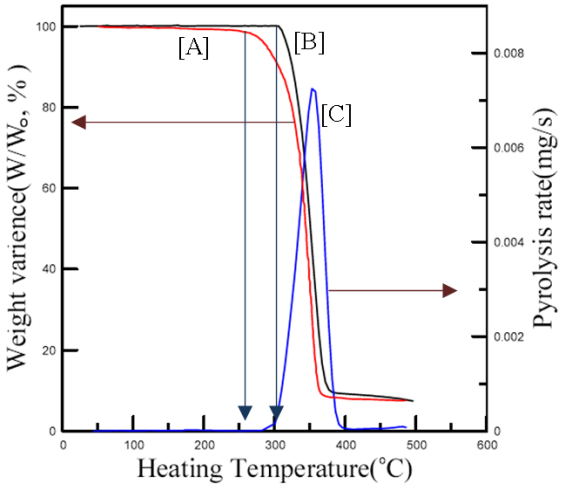

Figure 8. TGA curves of raw PLGA [A], PLGA plate injection molding [B] and pyrolysis rate of plate

DSC curve of raw PLGA showed an endothermic melting peak at 146℃ and an endothermic peak at 52℃ corresponding to its glass transition temperature (Tg). But Tg peak of PLGA plate with injection molding shifted from 52℃ to increasing temperature 63℃ as shown in Figure 7. This positive deviation in Tg between raw PLGA and PLGA plate with injection molding may be ascribed to the rearrangement of molecular orientation.

The thermal properties of raw PLGA and PLGA plate with injection molding were examined by TGA measurement. Figure 8 shows the TGA thermogram of raw PLGA [A] and PLGA plate with injection molding [B] over the temperature range from 25 ~ 500 ℃ at a heating rate of 10℃/min under a N_2. Compared to PLGA plate, raw PLGA has lower thermal degradation temperatures. The pyrolysis temperatures of raw PLGA and PLGA plate with injection molding is appeared at 255℃ and 302℃, respectively. Chain and branch bonding such as –OH, -CH, –C-O-O and C=O was thermally decomposed and vaporized with temperature ranging 300 ~ 400℃ [21], therefore the weight ratio of residual carbon is 7%.

3.3. Mechanical properties of absorbable PLGA plates

Figure 9 shows the tensile strength curve [A] and compressive strength curve [B] of PLGA plate with injection molding in dry state. PLGA plate exhibited higher tensile strength (34.9 ± 0.12 Kg_f) and compressive strength (48.1 ± 0.32 N). Generally, increased mechanical properties are in good agreement with the increased Tg and gel content values as reported previously [22]. The increased mechanical properties of PLGA plates with injection molding concurred with the fact that the amorphous morphology of PLGA encouraged more cross-linking, resulting in a stronger and more rigid network of chains [23].

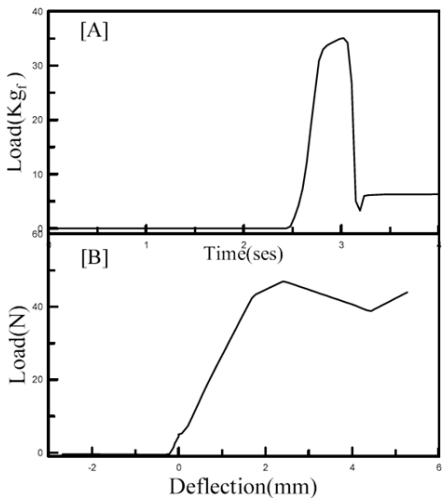

Figure 9 Tensile strength curve [A] and compressive strength curve [B] of PLGA plate with injection molding

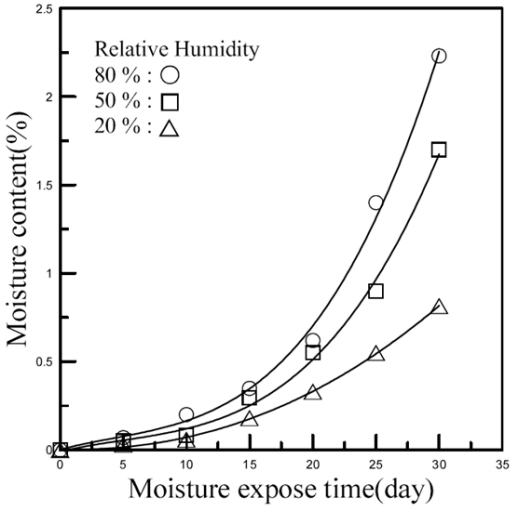

Figure 10 Moisture content absorbed by PLGA plate versus expose time at 40℃ and 20%, 50%, 80% RH

Since the water absorbed into the polymer at different RH was non-freezable, it should be retained in molecular state in the polymeric matrix. The water molecules could directly interact with the polymeric hydrophilic groups such as C=0 and COO^- by forming hydrogen bonds [24-25]. Fig. 10 shows the adsorbed moisture weight ratio (%) data of PLGA plate at 45°C with a relative humidity 20%, 50% and 80% over 30 days. The adsorbed moisture weight ratio (%) to sample of PLGA plate was calculated using the following equation:

$$\text{Absorbed moisture content (\%)} = \frac{W_s - W_o}{W_o} x100 \quad (1)$$

Where W_s [mg] is the modified weight of PLGA plate with injection molding, W_o[mg] the initial sample weight of PLGA plate. As shown Fig.10, the weight ratio (%) of the adsorbed moisture exponentially increased with increasing relative humidity (%) and exposed time (day). But amount of absorbed moisture for initial adsorption (<a 5 days) was small due to the high polymer hydrophobic hydration.

4. Conclusions

In order to better understand the influence of injection molding on physical properties such as surface, thermal and mechanical strength of PLGA plate, XRD, NMR, FTIR, XPS, DSC, TGA and tensile testing were performed. The overall XRD curve pattern of PLGA plate with injection molding was similar to that of PLGA raw material. Peak at 43 2-theta in XRD spectra of PLGA plate was assigned to crystalline hydrocarbon due to rearrangement of molecular orientation. ^{1}HNMR analysis of PLGA revealed the presence of three sets of peaks: the first one corresponds to carboxylic and carbonyl bonds at 7.25ppm, the second one at 5.1 ppm corresponds to CH bonds in

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