International Journal of Bio-Science and Bio-Technology
Vol. 8, No.3 (2016), pp. 315-322
http://dx.doi.org/10.14257/ijbsbt.2016.8.3.32

Studies on the Effect of Molecular Weight on Biodegradable Polymer Membrane

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Abstract

PLA and PLGA have been extensively used for controlled drug delivery and used to fabricate device for tissue engineering. The objective of the present study was to know the effect of different molecular weight of PLLA and PLLGA. PLLA and PLLGA membrane was prepared using a solvent-casting method. In vitro degradation of the blank membrane was characterized by techniques including NMR, SEM, BET. And examined the degradation of PLA-PGA copolymer at different temperature range. The lower molecular weight, the more porosity and the smaller pore size. The degradation ratio of membrane increased with increasing test temperature.

Keywords: *Degradation, Molecular Weight, Phase inversion, PLGA membrane, Porosity*

1. Introduction

Poly lactide (PLA) and poly (lactide-co-glycolide) copolymers (PLGA) have been extensively utilized for controlled drug delivery systems and used to fabricate devices for tissue engineering over the past decades. These biodegradable polymers are safe in vivo to produce biocompatible, toxicologically safe by-products by the normal metabolic pathways [2-3, 7]. And they are physically strong and highly biocompatible and have long clinical experience, favorable degradation characteristics [1, 4-5]. These materials have been approved by the USA Food and Drug Administration [8]. It has been shown that the degradation rate is affected by physical and chemical factors, such as medium pH, temperature of medium, molecular weight, and pore size [6, 9-10]. However, until now the degradation process has not been completely understood [11]. The polymer molecular weight is very important because influences the particles size and the drug or therapeutic agent encapsulation, adsorption or physicochemical interaction and release rate [12-14].

The degradation of PLA and PLGA displayed as two stages. In the first stage, the molecular weight of PLA and PLGA decreased continuously with degradation time, whereas little weight loss occurred. But in the second stage, the molecular weight of PLGA had decreased to a low value and was almost unchanged with time, while the sample experienced significant weight loss [8].

In this study, different molecular weight of PLLA and PLLGA membrane were prepared using a solvent-casting method and subjected to degradation in phosphate-buffered saline at the different test temperatures for different periods of time. And degradation of membranes was characterized by different scanning calorimetry (DSC), scanning electron microscopy (SEM) and Brunauer Emmett Teller equation (BET). In vitro degradation studies of membrane from PLLA and PLGA are usually performed at the physiologic 37°C and often take long periods of time to complete.

ISSN: 2233-7849 IJBSBT

The objective of the present study was to examine the degradation of PLLA and PLLGA at higher temperature [15].

2. Materials and Methods

2.1. Materials

Different molecular weight PLLA (Poly (L-lactic acid)) and PLLGA (Poly (L-lactic-co-glycolic acid, 85/15) was purchased from Purac co. (Netherland) as listed in table 1. Chloroform (GR grade), ethanol (GR grade) were purchased from Daijung chem, (Korea). Phosphate buffered saline (PBS, pH 7.4) was purchased from Biosesang Lnc, (Korea).

Table 1. The Inherent Viscosity (IV) and Molecular Weight (Mw) of PLLA and PLLGA.

No. Sample	IV(dl/g)	Mw(g/mol)
Poly(L-lactide)18	1.8	221,000
Poly(L -lactide)24	2.4	339,000
Poly(L -lactide)32	3.2	521,000
Poly(L -lactide)38	3.8	647,000
Poly(L -lactide)49	4.9	954,000
85/15L-lactide/Glycolide copolymer23	2.3	363,000
85/15L-lactide/Glycolide copolymer31	3.1	560,000

2.2 Preparation of Membranes

All membranes were prepared by a solvent-casting method. PLLA and PLLGA was dissolved at room temperature in a chloroform. The PLLA and PLLGA solutions (3w/v) were casted into the mold, and then it was placed in ethanol. After complete of phase inversion, the membranes were dried in a fume hood overnight, followed by a vacuum oven for 24 hours at room temperature. The resulting membranes had a thickness of about 150-300μm and were cut into a square shape with dimensions of 10mm×30mm.

2.3. In vitro Degradation of Membranes

The membranes were each weighed and then immersed in 10ml of phosphate buffered saline (PBS, pH 7.4) in individual vials. Then the samples were incubated at test temperatures of 45°C, 55°C and 65°C. At different time intervals, 4 parallel samples were tested for each type of membrane. The membranes were removed, washed three-fold with water, and weighed after removal of surface water. The samples were then dried in a vacuum for 48 h, and analyzed for changes in mass. The pH of the degradation media was also measured at each time point. And then used for DSC, SEM and BET studies.

2.4. Differential Scanning Calorimeter (DSC)

Measurement of glass transition temperature (Tg) was performed using a differential scanning calorimeter (DSC 821, Mettler Toledo, Greifensee, Switzerland). All the samples were heated twice under nitrogen atmosphere. Thermograms covering a range from -10 to 200°C were recorded at a heating or cooling rate of 10 K/min. And all the DSC thermograms were obtained from the first heating cycle.

2.5. Scanning Electron Microscopy (SEM)

The membranes were fractured in liquid nitrogen. All the samples were sputter-coated with gold and observed under a scanning electron microscope (SEM S-4800, Hitch, Japan). And SEM was used to inspect the morphology change of membranes with degradation.

2.6. Brunauer Emmett Teller (BET)

Pore diameter and porosity was performed by surface area and pore characterization system (BET, ASAP2020, AutoChem, Micromeritics). Interaction with adsorption data is direct.

3. Results

3.1 The Glass Transition Temperature of Membranes

Figure. 1 is the glass transition temperature of different molecular weight PLLA and PLLGA membrane. A is the glass transition temperature of PLG23, PLG31 and PLG60 membrane. B is the glass transition temperature of PL10, PL18, PL32, PL49 membrane. A and B shows that the glass transition temperature is higher when the molecular weight is higher.

3.2 Morphological of Blank Membranes

Figure 2 is SEM image of the membrane prepared from different PLLA and PLLGA. (A) PL18, (B) PL32, (C)PL49, (D)PLG23, (E) PLG31, (F) PLG60. SEM image shows the morphology of blank membranes before in vitro degradation. The higher molecular weight, the smaller pore size.

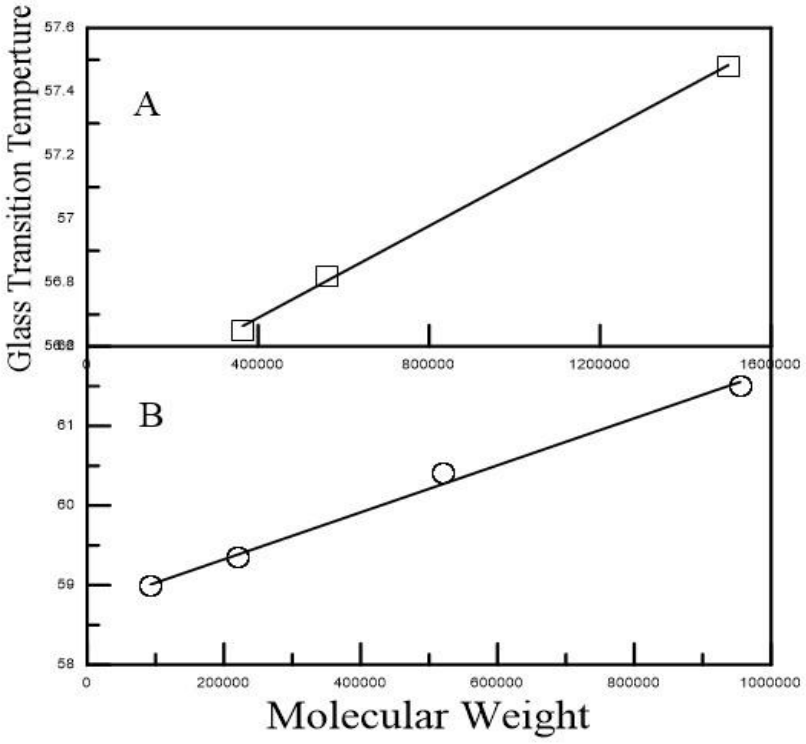

Figure 1. The Glass Transition Temperature of Different Molecular Weight PLLA Membrane (A) and PLLGA Membrane (B)

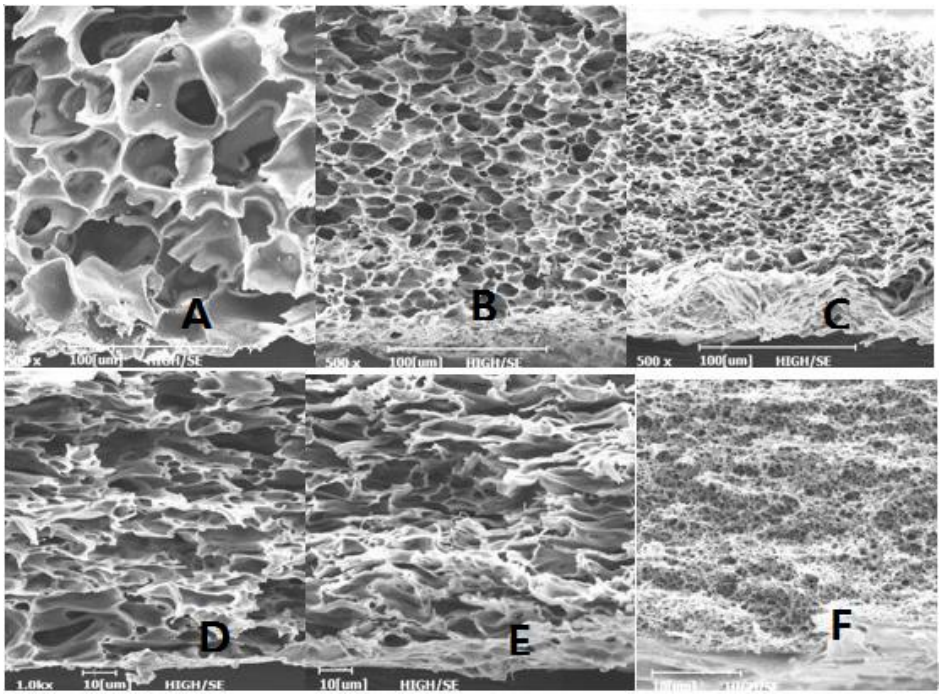

Figure 2. SEM Image of the Membrane prepared from Different PLLA and PLLGA. (A) PL18, (B) PL32, (C)PL49, (D)PLG23, (E) PLG31, (F) PLG60

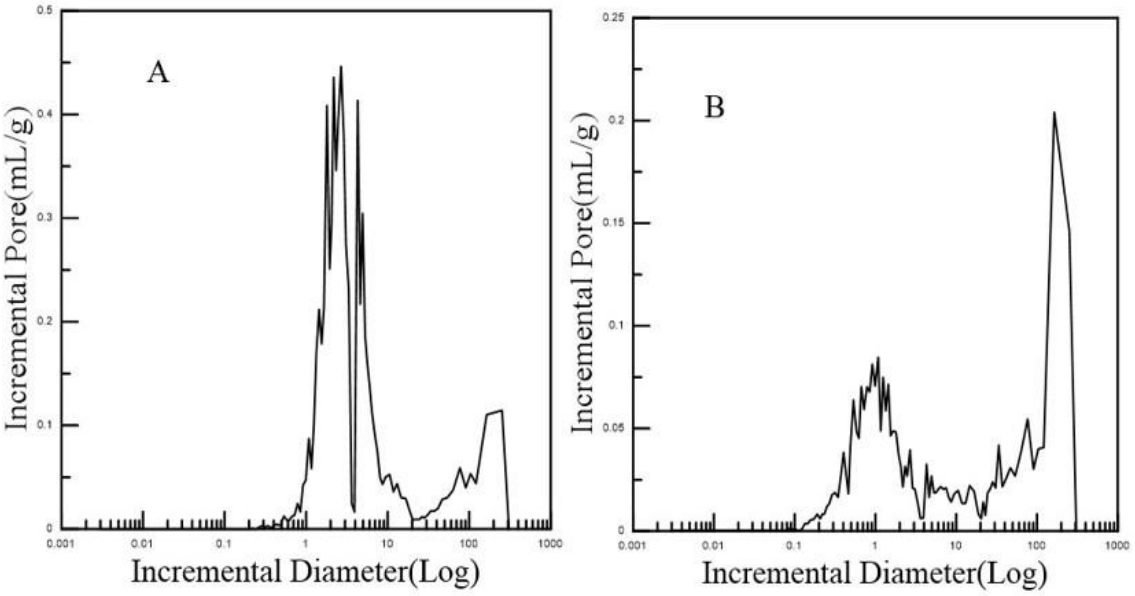

Figure 3. The Distribution on Pore Size of PL24 (A, Mw=339,000) Membrane and PLG8523 (B, Mw=363,000) Membrane

3.3 Pore Size and Porosity of PLLA and PLLGA Membranes

Figure 3 is the distribution of pore size of PL24 (A, Mw=339,000) membrane and PLG8523 (B, Mw=363,000) membrane. Figure 3 shows that as the same molecular weight, the amount of Microscopic pores of PLLA membrane is more than these of PLLGA membranes. In addition, the pores of PLLA membrane and PLLGA membrane have a different kinds of distributions.

Figure 4 is the average pore diameter of PLLA and PLLGA membrane as a function of molecular weight. Figure 5. The porosity of PLLA and PLLGA membrane as a function

of molecular weight. Figure 4 shows that the higher molecular weight, the smaller average pore diameter of PLLA and PLLGA membrane. As it is shown in figure 5, the higher molecular weight, the smaller porosity. These results are consistent with SEM image of in figure 2.

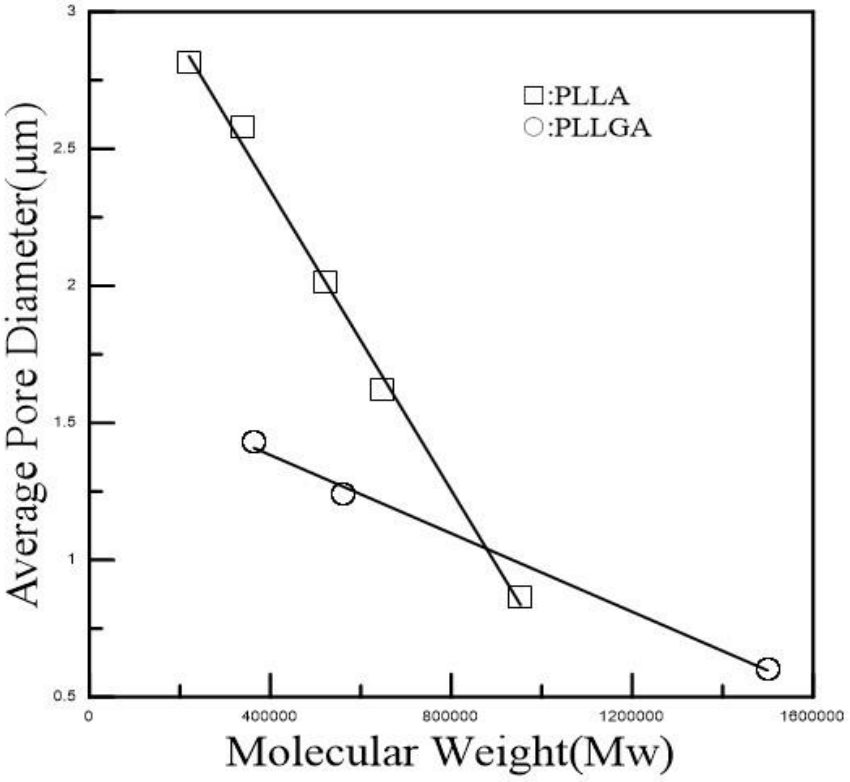

Figure 4. The Average Pore Diameter of PLLA and PLGA Membrane as a Function of Molecular Weight

3.4 Weight loss of PLLGA membranes

Figure. 6 shows that the degradation ratio of PLG23 membrane and PLG31 membrane with degradation time at 45℃, 55℃, 65℃. The weight loss of PLG23 membrane was faster than the weight loss of PLG31 in the same temperature. And it could be observed that the first stage of the degradation of all the PLG membrane was shorter than those of their corresponding hydrolytic degradation. And the weight loss at 65℃ more rapidly than the weight loss at 55℃. The results indicated that the degradation ratio of membrane increased with increasing test temperature.

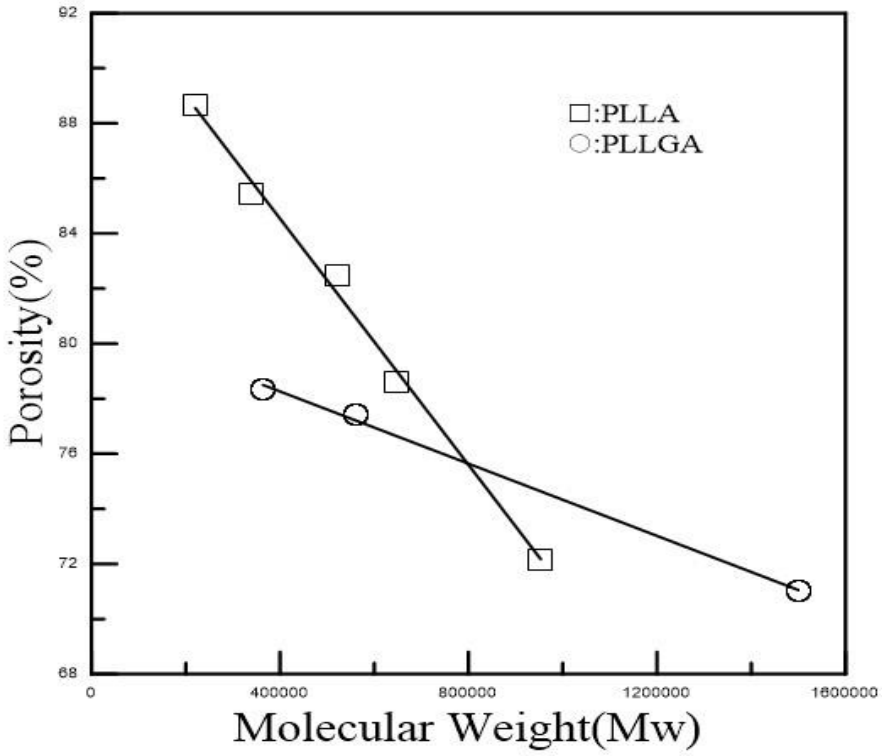

Figure 5. The Porosity of PLLA and PLLGA Membrane as a Function of Molecular Weight

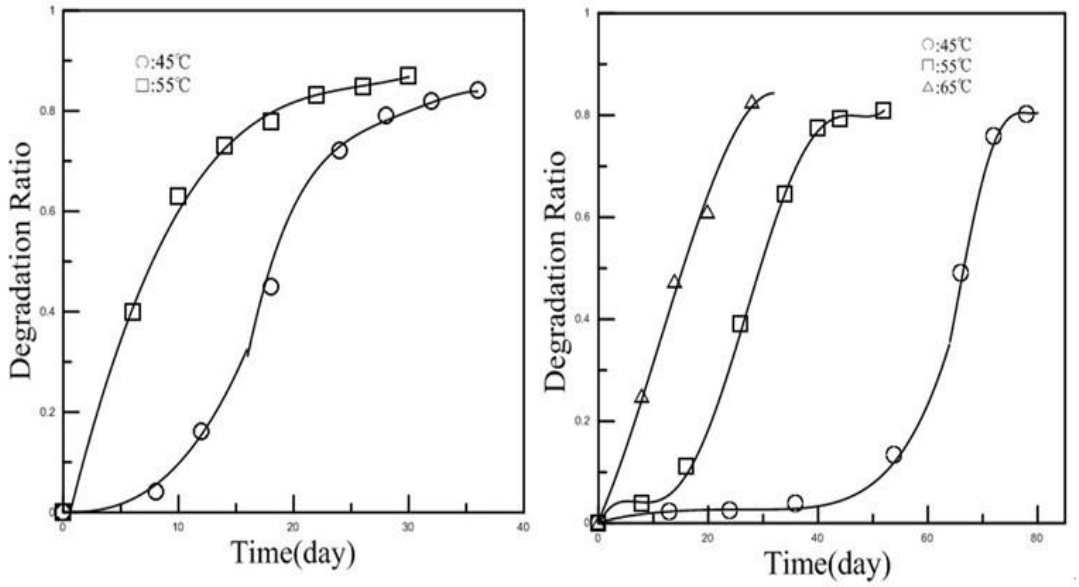

Figure 6. The Degradation Ratio of PLG23 Membrane and PLG31 Membrane at 45℃, 55℃, 65℃

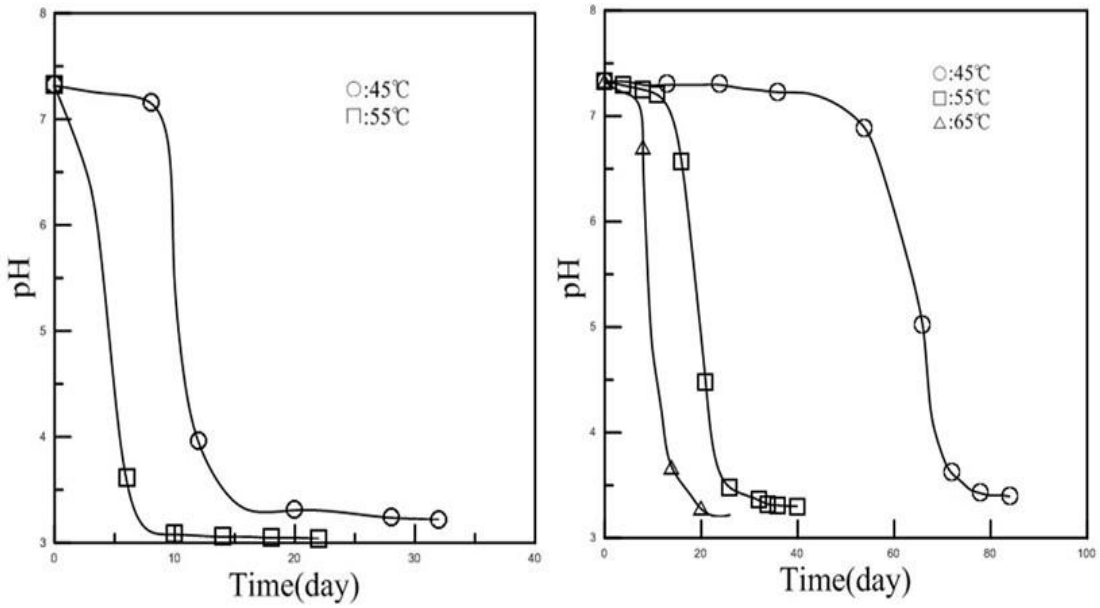

Figure 7. The pH value change of media during the degradation of PLG23 membrane, PLG31 membrane

3.5 Media pH Measurements

Figure 7 showed that the pH of the degradation media decreased degradation time. The rate of pH change increased with increasing temperature, and this rate was the lowest at 45℃. The pH of the degradation media surrounding PLG23 membrane was faster than the pH of the degradation media surrounding PLG31 membrane in the same temperature.

4. Conclusions

- The glass transition temperature is higher when the molecular weight is higher.
- The pores of PLLA membrane and PLLGA membrane have a different kinds of distributions. In addition, the amount of Microscopic pores of PLLA membrane is more than these of PLLGA membranes.
- The higher molecular weight, the smaller average pore diameter of PLLA and PLLGA membrane, and the smaller porosity.
- Faster degradation of the membranes, at higher temperatures, and when acidic degradation products were allowed to accumulate in the media.
- The higher molecular weight, the higher glass transition temperature and the smaller pore size.
- The degradation ratio of membrane increased with increasing test temperature. And as the molecular weight increase, hydrolysis rate was decrease in geometrical progression. And the first stage of the degradation of all the membrane was shorter than those of their corresponding hydrolytic degradation.

References

[1] R. Barbucci, "Integrated biomaterial science", New York: Kluwer Academic/Plenum Publishers, **(2002)**.
[2] D. D. Lewis, "Controlled release of bioactive agents from lactide/glycolide polymers", Chasin M, Langer R, Biodegradable Polymers as Drug Delivery Systems, New York: Marcel Dekker, **(1991)**, pp. 1-41.
[3] A. C. Albertsson and I. K. Varma, "Recent developments in ring opening polymerization of lactones for biomedical applications", Biomacromolecules, vol. 4, **(2003)**, pp. 1466-1486.
[4] L. S. Nair and C. T. Laurencin, "Biodegradable polymers as biomaterials", Prog. Polym. Science, vol. 32, **(2007)**, pp. 762-798.

[5] H. K. Makadia and S. J. Sieqel, "Poly Lactic-co-Glycolic Acid (PLGA) as Biodegradable Controlled Drug Delivery Carrier", Polymers, vol. 3, **(2001)**, pp. 137-1397.
[6] I. Grizzi, H. Garreau, S. Li, S and M. Vert, "Hydrolytic degradation of devices based on poly (DL-lactic acid) size-dependence", Biomaterials, vol. 16, **(1995)**, 305-311.
[7] T. Ouchi and Y. Ohya, "Design of lactide copolymers as biomaterials", Journal Polymer Science, Polym. Chem. Ed., vol. 42, **(2004)**, pp. 453-462.
[8] Y. Y. Xie, J. S. Park and S. K. Kang, "Study on the degradation rate and pH change of PLGA membrane with a biodegradation", Journal of Korea Academia-Industrial Cooperation Society, vol. 16, no. 9, **(2015)**, pp. 6403-6410.
[9] K. Makino, H. Ohshim and T. Kondo, "Mechanism of hydrolytic degradation of poly (L-lactide) microcapsules: effect of pH, ionic strength and buffer concentration, Journal Microencapsul, vol. 3, **(1986)**, pp. 203-212.
[10] M. Miyajima, A. Koshika, J. Okada, M. Ikeda and K. Nishimura, "Effect of polymer crystallinity on papaverine release from poly (lactic caid) matrix", Journal Control Release, vol. 49, **(1997)**, pp. 207-215.
[11] S. Gnsine, S. Carsten, F. Stefan and W. Ralf, "Thomas Kissel. Hydrolytic degradation of poly (lactide-co-glycolide) films: effect of oligomers on degradation rate and crystallinity", International Journal of Pharmaceutics, vol. 266, **(2003)**, pp. 39-49.
[12] H. C. Yang and M. H. Hon, "The effect of the molecular weight of chitosan nanoparticles and its application on drug delivery", Microchem Journal., vol. 92, **(2009)**, pp. 87-91.
[13] A. Kumari, S. K. Yadav and S. C. Yadav, "Development of biodegradable nanoparticles for delivery of quercetin", Colloids and Surfaces B: Biointerfaces, vol. 80, iss. 2, **(2010)**, pp. 184-192.
[14] P. Juliana, V. H. Orozco and L. L. Betty, "Effect of the Molecular Weight on the Physicochemical Properties of Poly(lactic acid) Nanoparticles and on the Amount of Ovalbumin Adsorption", Journal Braz. Chem. Soc., vol. 22, no. 12, **(2011)**, pp. 2304-2311.
[15] Y. Y. Xie, J. S. Park and S. K. Kang, "Study on the characteristics and biodegradable of synthetic PLGA membrane from lactic acid and glycolic acid", Journal of Korea Academia-Industrial Cooperation Society, vol. 16, no. 4, **(2015)**, pp. 2958-2965.

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