Journal of Industrial and Engineering Chemistry xxx (2017) xxx–xxx

Contents lists available at ScienceDirect

Journal of Industrial and Engineering Chemistry

journal homepage: www.elsevier.com/locate/jiec

Effect of various shaped magnesium hydroxide particles on mechanical and biological properties of poly(lactic-*co*-glycolic acid) composites

Hye Jung Jang[a,b,1], Sung-Bin Park[a,1], Tarek M. Bedair[a,c], Min-Kyu Oh[b], Dong-June Ahn[b], Wooram Park[d], Yoon Ki Joung[a,e,**], Dong Keun Han[d,*]

[a] Center for Biomaterials, Korea Institute of Science and Technology, Hwarangno 14-gil 5, Seongbuk-gu, Seoul 02792, Republic of Korea
[b] Department of Chemical and Biological Engineering, Korea University, 145 Anam-ro, Seongbuk-gu, Seoul 02841, Republic of Korea
[c] Chemistry Department, Faculty of Science, Minia University, El-Minia 61519, Egypt
[d] Department of Biomedical Science, College of Life Sciences, CHA University, 335 Pangyo-ro, Bundang-gu, Seongnam-si, Gyeonggi 13488, Republic of Korea
[e] Department of Biomedical Engineering, Korea University of Science and Technology, Gajeong-ro 217, Yuseong-gu, Daejeon 34113, Republic of Korea

ARTICLE INFO

Article history:
Received 30 September 2017
Received in revised form 16 October 2017
Accepted 21 October 2017
Available online xxx

Keywords:
Magnesium hydroxide
Poly(lactic-*co*-glycolic acid) composites
Mechanical property
Anti-inflammation effect
Anti-bacterial activity

ABSTRACT

Five different shapes of magnesium hydroxide ($Mg(OH)_2$) particles (Plate-S, Plate-N, Disk, Whisker, and Fiber) were synthesized and added to biopolymer (i.e., Poly(lactic-co-glycolic acid) (PLGA)) composite to improve their mechanical and biological properties. The PLGA composite films including $Mg(OH)_2$ particles were prepared by a solvent casting method. Their mechanical and biological properties were compared according to the composites containing different shapes of $Mg(OH)_2$ particles. Among them, the fiber shape of $Mg(OH)_2$ provided the highest mechanical strength, and anti-inflammation and anti-bacterial activity to PLGA films among other forms. This study demonstrated a new strategy for the design of biomaterials by controlling the form of inorganic additives.

Introduction

Many types of biodegradable synthetic polymer have been widely used in the biomedical field. Especially, biodegradable polymers based implants play an important role to replace or recover the damaged parts within human body due to their long-term biocompatibility. Generally, biodegradable polymers with polyester structures can be degraded by hydrolysis and the degradation products are metabolized in the body through Krebs cycle [1–4]. Among aliphatic polyesters, poly(lactic-*co*-glycolic acid) (PLGA) has attracted considerable interest use in stent and drug delivery due to its biodegradability and biocompatibility [4–8]. However, PLGA limits its use as stent backbone because of their relatively low mechanical properties compared to synthetic polymers. Also, it is known to trigger chronic inflammation and cell death due to foreign body reaction composed of macrophages and foreign body giant cells [9,10]. The nonspecific hydrolytic decompositions of PLGA produce acidic environment that may cause non-infectious inflammatory response in human body [10–12]. Therefore, several studies have been attempted to improve the mechanical properties and reduce the inflammatory responses of aliphatic biodegradable polymers [11–15].

Magnesium hydroxide ($Mg(OH)_2$) is an excellent biocompatible inorganic material with anti-bacterial activity [16]. These $Mg(OH)_2$ particles are degraded in the body and become magnesium which is an essential mineral for human metabolism (the adult human body contains from 21 to 28 g of magnesium) and linked to various pathological conditions [17]. Moreover, these $Mg(OH)_2$ are also well known as pH neutralization agents. The acidic environments produced by PLGA degradation i.e., lactic and glycolic acid, can be neutralized by adding $Mg(OH)_2$ [12–14]. In the case of adding inorganic particles without surface modification to the polymer matrix, the mechanical strength of the polymer composites decreased due to their low interfacial strength between matrix and inorganic particles which increase defects. Thus, the surface modification of $Mg(OH)_2$ with size control has been actively researched in the past few years [12,13,15]. However, the morphological comparison of $Mg(OH)_2$ particles when used as an additive to polymer composites is still insufficient.

* Corresponding author at: Department of Biomedical Science, College of Life Sciences, CHA University, 335 Pangyo-ro, Bundang-gu, Seongnam-si, Gyeonggi 13488, Republic of Korea.
** Corresponding author at: Center for Biomaterials, Korea Institute of Science and Technology, Hwarangno 14-gil 5, Seongbuk-gu, Seoul 02792, Republic of Korea.
E-mail addresses: ykjoung@kist.re.kr (Y.K. Joung), dkhan@cha.ac.kr (D.K. Han).
[1] These authors contributed equally to this work.

https://doi.org/10.1016/j.jiec.2017.10.032
1226-086X/

In this study, in order to improve both mechanical and biological functions of PLGA matrix, various shapes of $Mg(OH)_2$ particles (Plate-S, Plate-N, Disk, Whisker, and Fiber) were used as an additive (Scheme 1). The degradation behavior, mechanical properties, and anti-bacterial function of the PLGA composites were investigated with respect to the shapes of incorporated particles. In addition, anti-inflammatory behavior during the degradation of PLGA composite films was evaluated with IL-6 and IL-8 expressions.

Materials and methods

Materials

PLGA (Mw = 300,000 g/mol, copolymer ratio = 82:18) was obtained from Samyang Biopharm Inc. (Korea). Magnesium chloride ($MgCl_2$), magnesium chloride hexahydrate ($MgCl_2{\cdot}6H_2O$), magnesium sulfate heptahydrate ($MgSO_4{\cdot}7H_2O$), ethylene diamine, triethanolamine, sodium carbonate (Na_2CO_3), and poly (ethylene glycol) (Mw = 4,600 g/mol PEG4,600) were purchased from Sigma-Aldrich (USA). Ammonia solution (NH_4OH) and sodium hydroxide (NaOH) were obtained from Samchun Chemical Co. (Korea) and Daejung Chemical Co. (Korea), respectively. Luria–Bertani broth and agar were obtained from Difco™ (USA). *Escherichia coli* (*E. coli*; 25922) and *Staphylococcus aureus* (*S. aureus*; 25923) were purchased from Korean Culture Center of Microorganisms (Korea). All the chemical reagents were of analytical grade and used as received without further purification.

Synthesis of various shapes of $Mg(OH)_2$ particles

For the preparation of plate shape of $Mg(OH)_2$, PEG4,600 was used as a dispersant for wet precipitation method. $MgCl_2{\cdot}6H_2O$ (0.025 mol) and 0.1 g of PEG4,600 were dissolved in 50 mL of deionized water followed by dropwise addition of 15 wt% NH_4OH solution within 30 min under stirring. The mixture was maintained at room temperature for 24 h. After centrifugation, the precipitated products were washed with deionized water and ethanol to remove the remained impurities. Then, it was dried under vacuum at 25 °C for 24 h, stored in a desiccator and named as Plate-S.

The Plate-N shape of $Mg(OH)_2$ was synthesized following modified procedure for the Plate-S. Except for the addition of PEG 4,600, all the procedures accomplished in the same manner as the synthesis for Plate-S. The product was named Plate-N.

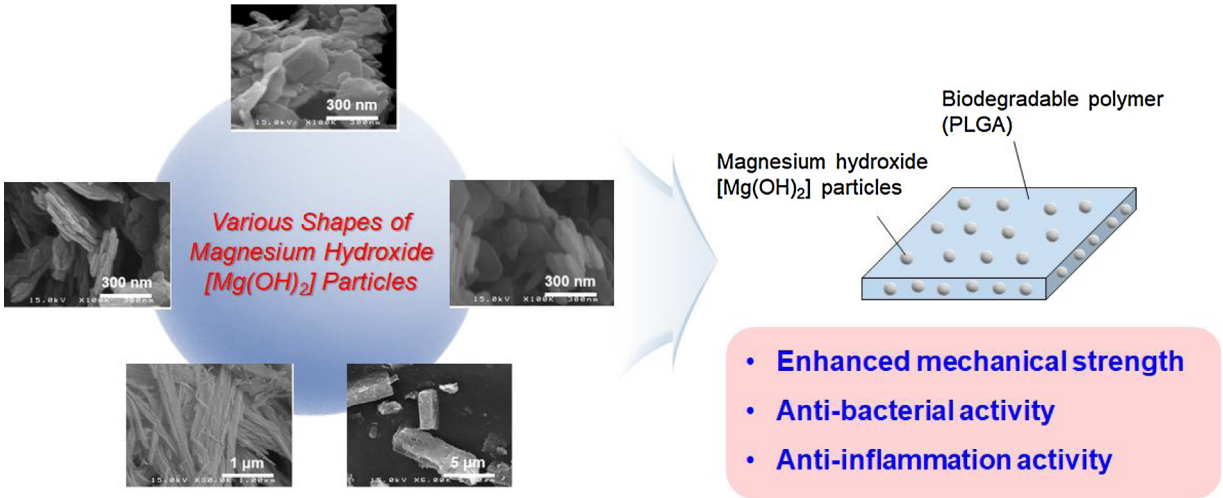
Hydrothermal method was used to prepare Disk shape of $Mg(OH)_2$ particles. In brief, 36 g of ethylene diamine dissolved in 10 mL of deionized water was poured to 0.02 mol of $MgCl_2$ dissolved in 10 mL of deionized water under stirring. Then, the mixture was refluxed at 180 °C for 24 h. The suspension was cooled down to room temperature followed by centrifugation at 10,000 rpm for 5 min. After washing with deionized water for at least ten times, the powder was dried under vacuum. This final white powder was named as Disk.

The whisker shape of $Mg(OH)_2$ was synthesized following a previous report [18]. In brief, 50 mL of 1 M Na_2CO_3 solution was dropped into 50 ml of 1 M $MgCl_2{\cdot}6H_2O$ solution within 30 min under stirring. The mixture was aged at room temperature for 24 h. Thereafter, it was washed with deionized water and acetone several times followed by centrifugation. The obtained magnesium carbonate was dried at 60 °C for 12 h, and followed by thermal treatment in muffle furnace at 750 °C (the heating was 5 °C/min) and maintained at this temperature for 2 h. After cooling to 150 °C, the product was moved from the furnace to vacuum oven. The obtained MgO whiskers were hydrated with deionized water for 2 h at room temperature. After hydration, the final product of $Mg(OH)_2$ particles was named as Whisker.

To prepare fibrous shape of $Mg(OH)_2$, 12 mL of triethanolamine was dropped into 2 M $MgSO_4{\cdot}7H_2O$ solution within 30 min under stirring. The mixture was heated at 80 °C for 24 h under vigorous stirring. Thereafter, the resulted suspension was cooled, centrifuged, and washed several times with deionized water. The resulting product was dried under vacuum at 25 °C for 24 h which represents fibrous magnesium oxysulfate (MOS, $5Mg(OH)_2{\cdot}MgSO_4{\cdot}3H_2O$) [19]. To convert fibrous MOS to fibrous $Mg(OH)_2$, 0.3 g of fibrous MOS suspended in 15 mL of absolute ethanol was treated with 0.24 g of NaOH dissolved in 50 mL of 90% ethanol solution at 180 °C. After 6 h reaction, the mixture was allowed to cool gradually to room temperature and the product was collected by centrifugation. After washing with deionized water and drying steps, the final product of $Mg(OH)_2$ particles was named as Fiber.

Preparation of PLGA/$Mg(OH)_2$ composite films

The composite films were prepared by solvent casting method. Simply, 0.15 g of $Mg(OH)_2$ was suspended in 70 mL of chloroform using a bath sonicator for 1 h. After dispersion, 2.85 g of PLGA was fully dissolved in the mixture at room temperature. The $Mg(OH)_2$ and PLGA mixture was poured into a Teflon mold and the



Scheme 1. Schematic illustration of an addition of various shapes of magnesium hydroxide ($Mg(OH)_2$) particles to biodegradable polymer matrix and the resulting improvements in the mechanical and biological properties.

Please cite this article in press as: H.J. Jang, et al., Effect of various shaped magnesium hydroxide particles on mechanical and biological properties of poly(lactic-*co*-glycolic acid) composites, J. Ind. Eng. Chem. (2017), https://doi.org/10.1016/j.jiec.2017.10.032