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Controlled synthesis and properties of degradable 3D porous lactic acid-based poly(ester–amide)

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Abstract

A novel 3D porous lactic acid-based Poly(ester–amide) (PLPEA) was synthesized via condensation polymerization of toluene diisocyanate (TDI) and dicarboxylic-terminated oligoester ELDA. Pores were generated in situ and the porous structure could be controlled with the feed ratio of reagents, which was examined with scanning electron microscopy (SEM). FTIR verified the structures of intermediate and PLPEA. It was found that the mechanical properties of the PLPEA were related well to the porous structure. The tensile strength and bend strength of PLPEA obtained with NCO/COOH of 1.5:1 could be 16.59 and 70.44 MPa, respectively. On the other hand, the thermal of PLPEA was mainly dominated with the chemical compositions. The glass transition temperature and thermal decomposition temperature of PLPEA were 3 and 427 °C (80 wt%), respectively. The weight loss percentage of PLPEA could be 8.5% after 124-days immersing in phosphate-buffer saline at 37 °C, suggested that PLPEA was degradable.

Keywords: Porous; Lactic acid-based; Poly(ester–amide)

1. Introduction

Owing to the degradable and non-toxic character, lactic acid-based polymers had received growing interest [1]. The homopolymer of lactic acid and its copolymers were readily biodegradable and extensively used in drug delivery systems, tissue engineering and environmentally friendly applications [2–4]. Thus, lactic acid moiety was commonly incorporated in polymer backbone to act as degradable points [5].

Poly(ester–amide)s (PEA) were regarded as promising biodegradable materials which combined good mechanical, thermal and processing properties of polyamides and the biodegradability of polyesters [6]. Among them, PEA derived from naturally occurring α-aminoacids, α-hydroxyacids and carbohydrate had attracted great attention [7–10].

Three-dimensional biodegradable porous scaffolds were essential for tissue engineering [11] and could be used as drug delivery matrices either [12,13]. Both naturally occurring and synthetic biodegradable polymers were widely explored as porous scaffolds. Alginate, chitosan, and poly(ether–ester–amide) derived from poly(ethylene glycol), especially the copolymers of lactic acid or blends of polylactide were the good candidates [14–19].

Considering the aforementioned, we developed a new approach for preparing 3D porous lactic acid-based PEA (PLPEA). It was anticipated that the properties of the PLPEA would be tailored by incorporating flexible oxyethylene groups and a large number of singular hydrolabil lactic acid unit into the backbone. Herein, the relationships among the reaction conditions, porous structure, chemical compositions and properties were investigated and presented.

2. Experimental

2.1. Materials

The dicarboxylic-terminated oligoester ELDA, with the number average molecular weight of 2008 and 4056 g/mol, was prepared according to the literature [20] by using lactic acid and ethylene glycol as starting materials. Succinic anhydride, toluene 2,4-diisocyanate (TDI), methanol, 95% ethanol and *N*,*N*-dimethylformamide (DMF) were all analytical reagent grade (Shanghai chemical agents Ltd Co., China) and used as received.

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2.2. Preparation of PLPEA

PLPEA was synthesized via melt-polycondensation of TDI and ELDA by two-steps. With vigorous stirring, TDI was added into 15 g melt ELDA in the molar ratio of 1.5:1, 1.75:1, 2.0:1, 2.25:1, and 2.5:1 (TDI/ELDA). The mixture was allowed to react at 140 °C for 30 min. Then it was poured into a mold and kept in an air oven at 140 °C for another 2 h. Porous lactic acid-based PEA derived from ELDA of 2008 and 4056 g/mol was denoted as PLPEA2008 and PLPEA4056, respectively.

2.3. Porosity measurement

The porosity of PLPEA was evaluated by the non-solvent displacement method [21].

Two 10 mm × 10 mm × 3 mm samples were submerged in a known volume (V_1) of 95% ethanol at ambient temperature (25 ± 2 °C) for 15 min, respectively. The total volume of ethanol and the ethanol-impregnated sample was recorded as V_2. Then the ethanol-impregnated sample was removed and the remaining ethanol volume was V_3. The porosity of the PLPEA was given as $P(\%) = (V_1 - V_3)/(V_2 - V_3) \times 100$ and took the average value.

The pore structure of PLPEA was also examined with a Hitachi S-3500N scanning electron microscope.

2.4. FTIR analysis

Powdered ELDA was mixed with dry KBr and compressed into disk. The intermediate polymer and PLPEA was cast to prepare film samples. Then, FTIR spectra of the samples were recorded using a Nexus 470 FTIR spectrometer.

2.5. Mechanical properties testing [22]

Both the tensile and bend test were performed at room temperature on a SANS GTM6104 Universal instrument. The tensile strength was measured at a crosshead speed of 15 mm/min and the initial distance between grips was 60 mm. The specimens were dumbbell-shaped with an overall length of 75 mm and the width of the ends was 10 mm. The length, width and thickness of narrow parallel portion were 60, 6 and 3 mm, respectively. To obtain the bend strength, the rectangular specimens (40 mm × 3 mm × 2 mm with the initial effective length of 40 mm) were used and the crosshead speed was 1.47 mm/min. The data reported were averaged from five measurements.

2.6. Thermal analysis

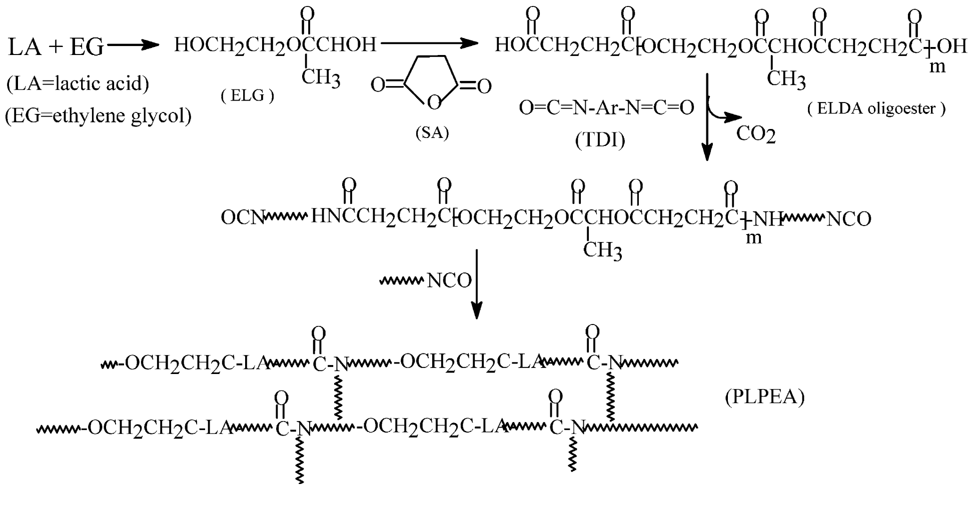
The different scanning calorimeter (DSC) and thermogravimetric analysis (TGA) were carried out with a Universal V2.4F TA Instruments DSC–TGA analyzer. The samples were heated from −50 to 150 °C at a heating rate of 10 °C/min to record DSC curves and from 0 to 900 °C at 20 °C/min to obtain thermogravimetric profiles under nitrogen atmosphere.

2.7. Hydrophilic evaluation

The hydrophilic or hydrophobic property of PLPEA was examined with water contact angle, which was measured with a JC2000A digital contact angle analyzer and an average of five measurements was taken.

2.8. In vitro degradation

The weighed 6 mm × 5 mm × 2 mm tabular samples were placed in vials that contained 3 mL phosphate-buffer saline (PBS) (0.1 M, pH 7.4) and maintained at 37 °C. At timed intervals, the samples were removed, dried under vacuum at ambient temperature and weighed. The weight loss percentage of the samples was calculated from the initial weight of sample (W_i) and the weight of dried sample (W_d): $WL\% = (W_i - W_d)/W_i \times 100$. An average of triplicate measurements was taken.



Scheme 1. The synthesis of PLEPA.

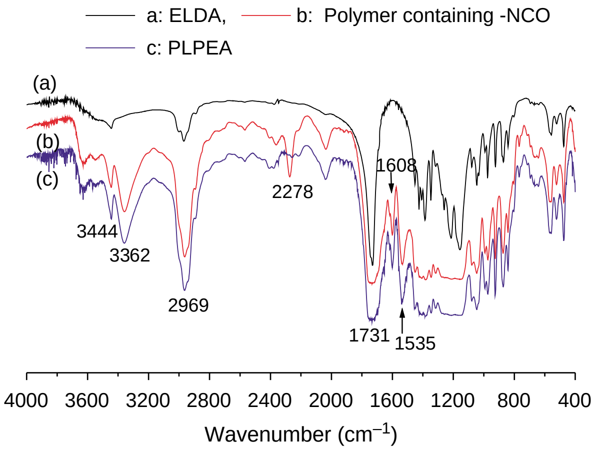


Fig. 1. The FTIR spectra of ELDA, intermediate polymer and porous lactic acid-based poly(ester–amide).

3. Result and discussion

3.1. Preparation of PLPEA

By means of the reaction between diisocyanate and dicarboxylic acid [23], PLPEA was synthesized (Scheme 1). Under vigorous stirring, excess TDI and melt ELDA were allowed to react homogeneously and the obtained polymer contained –NCO end groups. Then in an air oven, the active –NCO would react gradually with –NH– group in the chain and form the cross-linked structure. The by-product CO$_2$ of the reaction between –NCO and –COOH was released to generate pores.

The reaction procedure was verified with FTIR (Fig. 1). A band was observed at 2278 cm^{-1}, indicated that the intermediate polymer contained –NCO groups. The absorption hands of benzyl and –NH– groups appeared at 1608 and 3362 cm^{-1}, respectively, which suggested that the reaction between ELDA and TDI was carried out. The characteristic peaks exhibited at 1731 (widened evidently) and 1535 cm^{-1}, which was attributed to the amide group [24], further confirmed the structure of PLPEA.

The more TDI added, the more –NCO groups the intermediate contained and the more CO$_2$ would be released. Thus, as the molar ratio of TDI/ELDA increased, more pores formed. When NCO/COOH was greater than 1.75, several pores connected together and formed continuous big pore (Fig. 2). To further understand the pore structure, the porosity of PLPEA was determined with non-solvent displacement method. The procedure invoked adsorption and deadsorption of ethanol, which would affected with the number of pores and pore sizes. As the molar ratio of TDI/ELDA increased, more pores formed and the porosity of PLPEA increased at first. When NCO/COOH was greater than 1.75, pore became bigger and made the retention of ethanol more difficult. As a result, the porosity of PLPEA decreased (Fig. 3). It was evident that the porous structure of PLPEA could be controlled with the feed ratio of reagents.

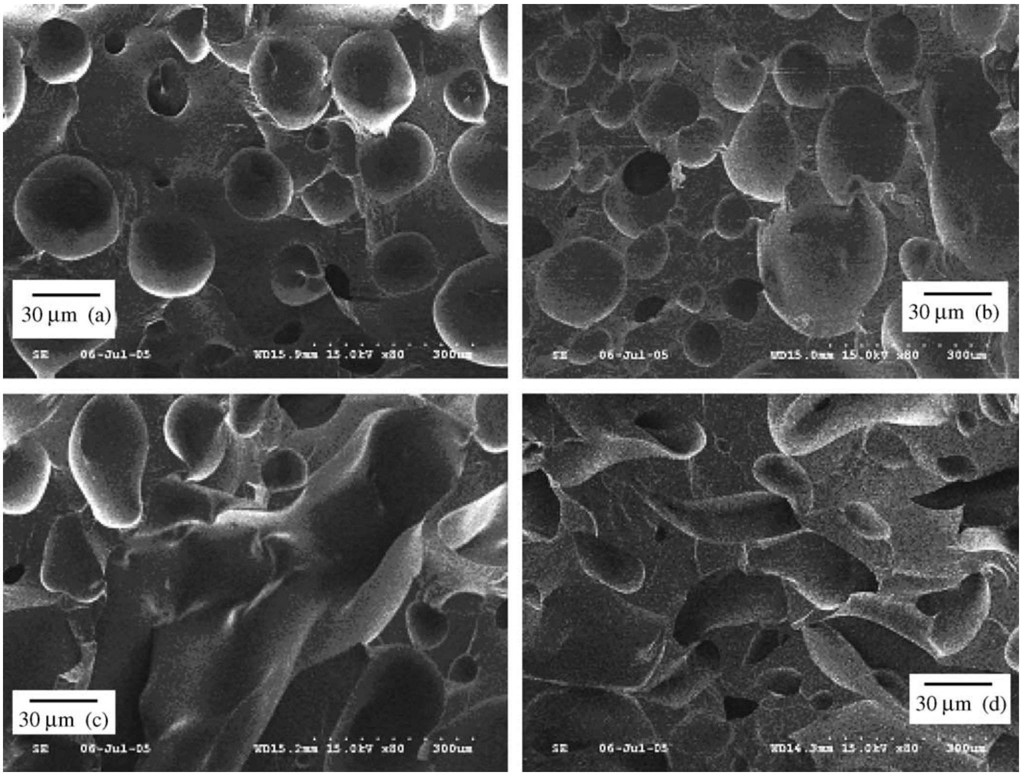


Fig. 2. The scanning electron microscope photographs of cross-sections of porous lactic acid-based poly(ester–amide)s: (a) TDI/ELDA = 1.5:1; (b) TDI/ELDA = 1.75/1; (c) TDI/ELDA = 2.0:1; (d) TDI/ELDA = 2.25:l.

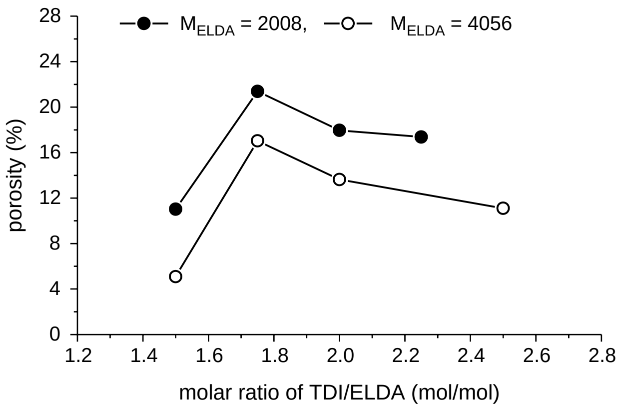


Fig. 3. The effect of feed ratio of reagents on the porosity of porous lactic acid-based poly(ester–amide)s.

3.2. Properties of PLPEA

The mechanical properties of PLPEA were related to its porous structure. The less the pore size was, the more compact the PLPEA was and the better the mechanical properties would be. As mentioned above, the porous structure of PLPEA would be ready to form with the increase of the molar ratio of NCO/COOH. Thus, the tensile strength and bend strength decreased with the increase of the TDI/ELDA ratio (Figs. 4 and 5). In addition, the mechanical properties of PLPEA were also related to the number molecular weight (M_n) of ELDA. It might be assumed that the intermediate derived from ELDA of 2008 g/mol would contain much –NH– groups in the chain than that from 4056 g/mol. The –NH– groups would react with –NCO subsequently and they were the potential pore-forming points. Consequently, much –NH– groups would result in PLPEA more fragile. Actually, when TDI/ELDA was 1.5:1, the tensile strength of PLPEA2008 and PLPEA4056 was 6.61 and 16.59 MPa, respectively. The bend strength of the corresponding samples was 22.65 and 70.44 MPa, respectively.

A glass transition exhibited on the DSC thermograms of PLPEA and the glass transition temperature (T_g) was around 3 °C (Fig. 6). As seen, the glass transition was mainly dominated with the chemical compositions of the polymer. The effect of porous structure, controlled with the TDI/ELDA ratio, on the Tg could be neglected. As PLPEA derived from ELDA, a large number of flexible oxyethylene (–OCH_2CH_2–) groups were incorporated into the backbone of PLPEA. Thus, T_g of PLPEA was much lower than that of polylactide (ca. 60 °C) [25]. PLPEA could resist the temperature as high as 270 °C due to the amide groups incorporated. As shown in

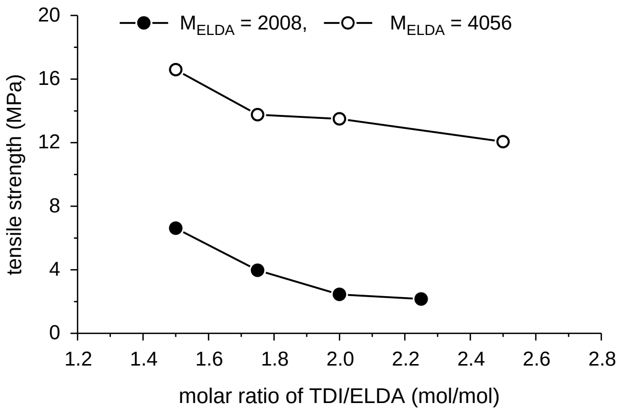


Fig. 4. The effect of feed ratio of reagents on the tensile strength of porous lactic acid-based poly(ester–amide)s.

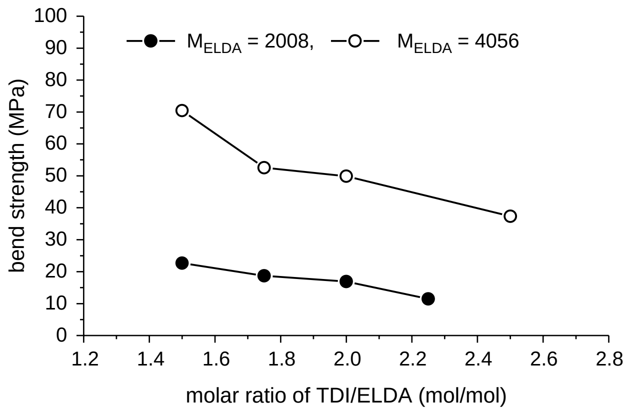


Fig. 5. The effect of feed ratio of reagents on the bend strength of porous lactic acid-based poly(ester–amide)s.

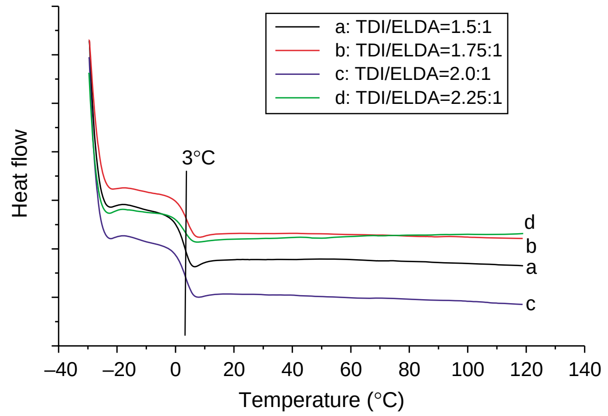


Fig. 6. Differential scanning calorimetry curves of porous lactic acid-based poly(ester–amide)s.

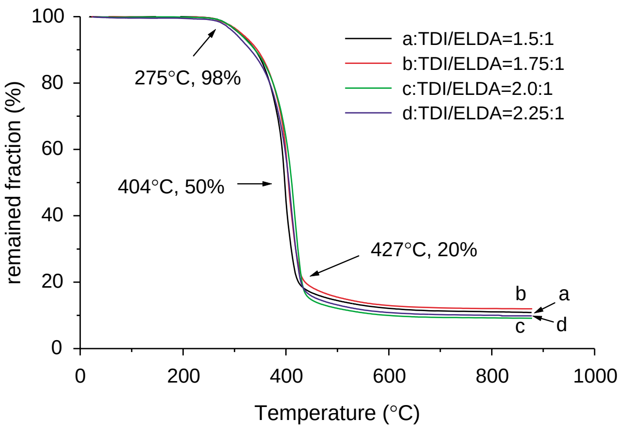


Fig. 7. Thermogravimetric analysis profiles of porous lactic acid-based poly(ester–amide)s.

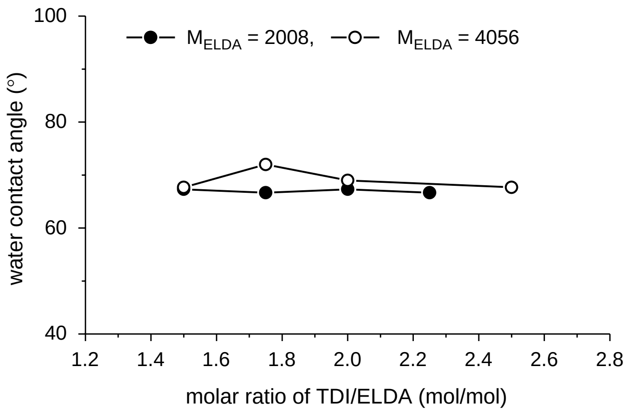


Fig. 8. The effect of feed ratio of reagents on the water contact angle of porous lactic acid-based poly(ester–amide) films.

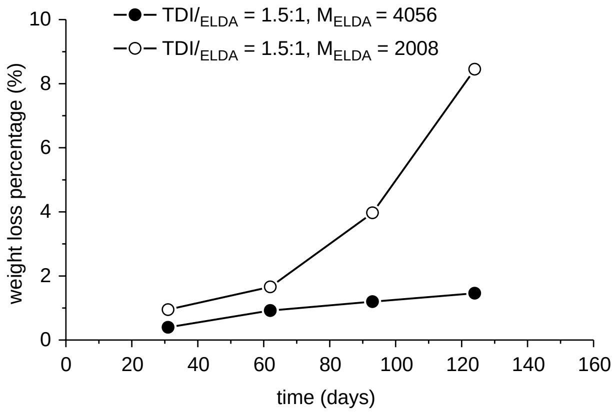


Fig. 10. The in vitro degradation behavior of porous lactic acid-based poly(ester–amide) in phosphate-buffer saline (0.1 M, pH 7.4) at 37 °C.

Fig. 7, the thermal decomposition temperatures of PLPEA were 275 (2 wt%), 404 (50 wt%) and 427 °C (80 wt%), respectively. The thermal decomposition temperature of PLPEA was also unaffected by the ratio TDI/ELDA.

It was found that the water contact angle of PLPEA was 68 ° (Fig. 8), which nearly was not changed with the molecular weight of ELDA or the TDI/ELDA ratio. Though the inner of PLPEA was porous, its surface was compact (Fig. 9). As a consequence, the hydrophilic property of PLPEA was mainly determined with the chemical compositions. Owing to –NH– groups incorporated, the water contact angle of PLPEA was lower than that of polylactide (79 and 76 ° for PDLLA and PLLA, respectively) [26], indicated that PLPEA was more hydrophilic than polylactide.

Attributed to the labile lactic acid unit incorporated, PLPEA showed degradable (Fig. 10). The weight loss percentage of PLPEA2008 could be 8.5% after 124-days immersing in PBS at 37 °C. The apparent porosity of PLPEA2008 was higher than that of PLPEA4056. Thus, PLPEA2008 was more easily to be attacked by water. In addition, shorter ELDA segments would be easier to degrade and diffuse into the solution. As a consequence, the degradation rate and the weight loss percentage of PLPEA2008 were higher than that of PLPEA4056.

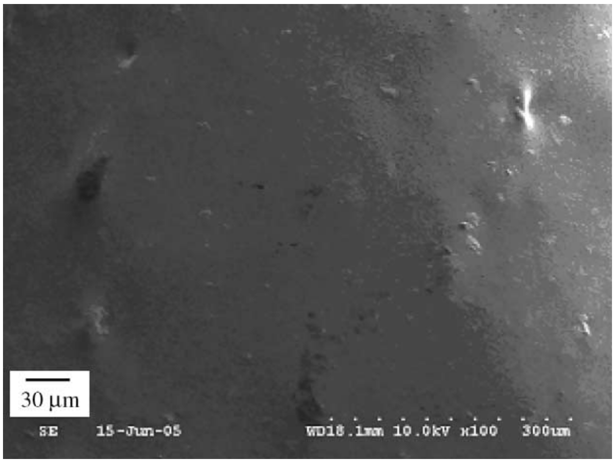


Fig. 9. The scanning electron microscope photograph of porous lactic acid-based poly(ester–amide) surface.

4. Conclusions

A novel 3D porous lactic acid-based poly(ester–amide) (PLPEA) was synthesized. The mechanical properties of PLPEA were related to the porous structure, which could be controlled with the feed ratio of reagents. On the other hand, the thermal and hydrophilic properties of PLPEA were dominated with the chemical compositions. Both the porous structure and the chemical compositions affected in vitro degradation behavior of PLPEA.

By varying the porous structure, chemical compositions and the length of dicarboxylic-terminated oligoester, the PLPEA might be tailored to meet the requirements of scaffold for tissue engineering, drug delivery carrier or environment friendly materials.

Acknowledgements

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