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Doubly degradable dynamers: dynamic covalent polymers based on reversible imine connections and biodegradable polyester units

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We report the preparation and features of environmentally friendly "Green Dynamers" (GDs), dynamic polymers presenting sequential double-degradation features, chemical and biological. They were obtained by connecting biodegradable oligomers (such as small units of polybutylene adipate, PBA, and polybutylene succinate, PBS) through chemically degradable reversible imine bonds. The GDs possess water disintegratability, mendability and biodegradability. Their degradation rate may be modulated through and increases with the number of imine groups in the polymeric chain. The GDs were thermodynamically stable and maintained their molecular weight and their mechanical strength in air. However, when they were contacted with water, the imine bonds easily hydrolyzed, breaking up the polymer chains into oligomers. After such water disintegration, the residual oligomers were biodegraded into CO_2 and water. In addition, the imine bonds were restored by evaporation of the water, leading to recovery of the molecular weight and of the mechanical properties of the GDs. The present GDs may be considered to represent a class of doubly-degradable polymers, combining chemical and biological degradability features, that operate in mild environmental conditions. This concept may contribute to solve the problem of waste elimination associated with the use of non-degradable polymeric materials.

Introduction

Dynamic polymers (dynamers) are reversible polymeric entities of either a molecular/covalent or supramolecular/non-covalent nature.^{1,2} Covalent dynamers result from the polycondensation of monomers *via* reversible chemical reactions generating labile chemical bonds whose formation and dissociation can be controlled through the physical and chemical conditions of their environment. Therefore, such dynamers have an adaptive ability under the effect of external physical stimuli or chemical effectors.^{3–10} They provide the possibility of developing new functional materials with water disintegrative,¹¹ self-healing^{12–15} and drug-release^{16–19} properties.

Currently, thermoplastic polymers are widely used as raw materials in various industrial fields, largely because of their moldability and good mechanical properties.²⁰ If the distinctive abilities of dynamers, such as disintegration or self-repairing, were introduced to thermoplastic polymers by linking their oligomers through reversible bonds, it could open the door to new applications in flushable, construction, agricultural and medical materials. Biodegradability is also a highly desirable property for such applications, because the persistent, non-biodegradable polymeric materials present high environmental load and cause

very serious waste problems.²⁰ In addition, biodegradability is also required for therapeutic and medical applications. It presents great merits such as easing the damage to tissues and organs from surgical processes, whilst also reducing costs. Drug delivery and implant systems from dynamers would offer the possibility of controlling and prolonging the effective period of therapeutic agents, whereas non-biodegradable ones require a removal process from the body at the end of their activity period.^{16,21}

Herein we report on the development of such degradable dynamic polymers, "green dynamers", based on biodegradable polyesters and polyethers, presenting the desirable properties mentioned above and eliminating many of the problems associated with the use of the usual "static", persistent polymers. Scheme 1 presents the concept of green dynamers (GDs). They can be obtained by connecting biodegradable oligomers, such as small units of poly(butylene adipate) (PBA), poly(butylene succinate) (PBS), poly(lactic acid) (PLA), polyethylene glycol, PEG, and other biodegradable polymers, through dynamic, reversible imine bonds. The imine bonds are thermodynamically stable and maintain the molecular weight and the mechanical strength of ordinary polymers. However, they readily undergo hydrolysis²² and cleave to aldehydes and amines even at room temperature. One may thus expect that, after disintegration by water, the residual oligomers are gradually biodegraded to CO2 and water. The rate of water disintegration is much faster than that of biodegradation. In addition, GDs possess self-healing properties because the imine bonds can be restored by evaporation of the water.

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Scheme 1 Schematic representation of water-disintegration, selfhealing and biodegradation processes of a green dynamer.

Experimental

Materials

All reagents and solvents were purchased at the highest commercial quality and were used without further purification.

Measurements

¹H NMR spectra were recorded on Bruker Avance 400 spectrometers. The spectra were internally referenced to the residual proton solvent signal. The molecular weight of polymers was determined by gel permeation chromatography (GPC). Polystyrene was used as a standard substance. A water solubility test of the film was carried out by weighing the film immersed in distilled water at 35 °C for 24 h and dried. Water disintegratability of a film was tested in distilled water (around pH 7). The tensile strength and tensile modulus were measured by a tensile tester (Instron1123) at a pull rate of 50 mm min⁻¹. The differential scanning calorimetry measurement were carried out using DSC system (SII DSC7020). The glass transition temperature (T_g) was obtained from the second heating at a heating rate of 10 °C min⁻¹. Thermogravimetric analysis (TGA) was performed on a thermal analyzer system (Shimadzu TA-60) at a heating rate of 10 °C min⁻¹ under nitrogen atmosphere. A biodegradability test of a film was carried out according to ISO14855.

Synthesis of the bis-imine component

N,N'-(1,4-Phenylenedimethlyidene)-bis(2-(2-aminoethoxy) ethanol). To a 300 ml separable flask equipped with a Dean-Stark trap with a condenser, a thermometer, a glass agitation blade and a dropping funnel, were added 13.40 g (0.10 mol) of terephthalaldehyde (Sigma-Aldrich) and 120 ml of toluene. The mixture was stirred and chilled below 5 °C in an ice water bath. Then, 21.46 g (0.20 mol) of 2-(2-aminoethoxy)ethanol (Tokyo Chemical Industry: TCI) was added dropwise to the flask over 30 min. Thereafter, the mixture was refluxed until water formation stopped. The mixture was cooled to room temperature and then filtered to collect the precipitate which was washed with 120 ml of toluene. The crystalline solid obtained was dried under a nitrogen atmosphere at 50 °C overnight to yield 28.3 g

of *N*,*N*^{*}-(1,4-phenylenedimethlyidene)-bis(2-(2-aminoethoxy)ethanol) as a pale yellow solid. mp. 44–46 °C; ¹H NMR (400 MHz, DMSO): δ = 3.44 (m, 8H), 3.68 (m, 8H), 4.58 (t, 2H), 7.79 (s, 4H), 8.37 (s, 2H); elemental analysis calcd (%) for C₁₆H₂₄N₂O₄: C 62.3, H 7.8, N 9.1; found: C 62.3, H 8.1, N 9.1.

Preparation of biodegradable oligomers

Poly(butylene succinate) (PBS). To a 1 L separable flask equipped with a water quantification receiver with a condenser, a thermometer, a bent tube and an agitation blade, were added 320.40 g (2.70 mol) of succinic acid (Wako Pure Chemical Industries) and 303.5 g (3.30 mol) of 1,4-butanediol (Wako Pure Chemical Industries) and the mixture was heated progressively under a nitrogen atmosphere to 180 °C. When water formation at 180 °C was hardly observed, 1.32 g of a 1% tin(II) 2-ethylhexylhexanoate toluene solution (Wako Pure Chemical Industries) was added to the reaction mixture and the reaction was continued until Mn measured by titration increased to 1950. The PBS with different M_n and PBA were also synthesized by similar methods.

Preparation of green dynamers. To a 200 ml separable flask equipped with a condenser, a thermometer and an agitation blade, were added 100.00 g (hydroxyl group 0.103 mol) of PBS $(M_n \ 1950)$ and 15.80 g (hydroxyl group 0.103 mol) of bis-imine compound. After the mixture was melted at 130 °C under nitrogen atmosphere, 0.89 g of 1% dibutyltin(IV) dilaurate toluene solution (Wako Pure Chemical Industries) was added. Thereafter, 16.45 g (isocyanate group: 0.195 mol) of hexamethylenediisocyanate (HDI) (Mitsui Chemicals) was added dropwise over 10 min and then HDI that remained in the dropping funnel was rinsed with 1.30 g of toluene. After continuing the reaction at 130 °C under nitrogen for 3 h, the corresponding polymeric material, of green dynamer type, was obtained. The green dynamers based on other oligomers such as PBA and PEG were also synthesized by similar methods.

Calculation of the number average molecular weight, M_n , of GDs in water disintegration

The number average molecular weight, M_n , of GDs in the course of disintegration in water was calculated from NMR data using the following eqn (1).

$$M_{\rm n} = M_{\rm n,initial} / (1 + n \cdots \alpha / 100) \tag{1}$$

where $M_{n,initial}$ is the initial and theoretical M_n calculated as:

$$M_{n,\text{initial}} = M_{n,\text{HDI}} \cdots n + M_{n,\text{OH}} \cdots (n+1)$$
(2)

in which $M_{n,HDI}$ is the molecular weight of HDI, $M_{n,OH}$ is the average of molecular weight of bis-imine component and biodegradable oligomer, *n* is the number of repeating unit [n = R/(1 - R)] which is determined by the ratio between the number of isocyanate groups and hydroxy groups of the starting materials (R = NCO/OH), and α is the mol% of aldehyde (new end groups formed by water disintegration) which is calculated from the NMR data as:

$$\alpha = (2I_{\rm A} + I_{\rm B}) \cdots 100 / (2I_{\rm A} + 2I_{\rm B} + 2I_{\rm C}) \tag{3}$$

where I_A , I_B , and I_C stand for the integral of the aromatic proton of units A, B, and, C in Fig. 3, respectively.

Results and discussions

Preparation, mechanical properties, and thermal properties of green dynamers

Scheme 2 lines out the preparation of the green dynamers. They were obtained by connecting a PBS oligomer presenting two hydroxyl groups and a diol compound incorporating imine bonds through hexamethylene diisocyanate (HDI). GDs based on other oligomers were also prepared using similar methods, only exchanging PBS for the desired oligomers. Films were obtained by heat pressing the material at 130 °C for 5 min and the mechanical properties of these films were evaluated.

Table 1 shows the mechanical properties of GDs films with respect to low density polyethylene (LDPE) films. They had excellent tensile strengths comparable to those of LDPE. Furthermore, the mechanical properties of the GDs were controllable by simply changing the type of oligomers, as these determine the mechanical properties. GDs based on PBS (75 wt%) and PEG (25 wt%) oligomers had almost half the tensile modulus compared to those made of only PBS. The introduction of PEG into the GD based on PBS decreased the tensile modulus. This preparation method gives easy control of the mechanical properties, a notable subject in material science, as they play a crucial role in applications.^{3b} These GDs also showed thermoplasticity, a feature of much importance for making roll films, laminated films, or nonwoven fabrics (Fig. 1).

Thermal characterization of the GD based on PBS was accomplished by DSC and TGA. The T_g of GD based on PBS was -36 °C, which is almost the same as the T_g of PBS. The weight losses (under nitrogen atmosphere) were 1, 5, and 50% at



Scheme 2 Preparation of green dynamers by connecting a PBS oligomer with a diol compound, containing imine bonds, through condensation with hexamethylene-1,6-bisisocyanate.

Table 1 Mechanical properties of green dynamers and LDPE

Based polymer	"Green" dynamers			
	PBS	PBA	PBS (75 wt%) PEG (25 wt%)	LDPE
Melting point (°C) Tensile strength (MPa) Tensile modulus (MPa)	105 24 490	107 27 600	105 20 210	110 20 150



Fig. 1 Pictures of a roll film (20 cm \times 60 m \times 30 μ m) and of a nonwoven fabric made of GD based on PBS ($M_n = 2500$).



Fig. 2 Pictures of the water disintegration tests at 23 °C after 80 h for PBS film (a) and green dynamer films (thickness 15 mm) based on PBS of $M_n = 6300$ (b) and $M_n = 2500$ (c).

temperatures of 278, 319, 384 °C, respectively. The GD also possessed a good thermal stability.

Water disintegratability and self-healing properties of green dynamers

First, a water solubility test was performed with a film (thickness 100 μ m) of GD ($M_n = 18000$ by GPC) based on PBS ($M_n = 2500$). When the film was immersed in distilled water at 35 °C for 24 h and dried, the weight retention rate of the film was 98.8 wt%, which confirms that this film was not water soluble.

Water disintegratability of films (size: 11 cm²; thickness: 15 µm) having a different number of imine bonds was evaluated in distilled water (around pH 7). Fig. 2 shows the photos of the water disintegration test at 23 °C after 80 h for (a) a PBS film without imine bonds and GD films based on PBS of (b) $M_{\rm n}$ = 6300 and (c) $M_{\rm n}$ = 2500. The conventional PBS film (a) did not change shape even over 7 d. On the other hand, marked changes in shape were observed in the GD films (b) and (c). The film (c) based on PBS ($M_n = 2500$) disintegrated from an area of 11 cm² into $1-2 \text{ cm}^2$ fragments and the M_n measured by GPC decreased from 18 000 to 8500. The film (b) (PBS, $M_n = 6300$) had a small crack after 80 h. It disintegrated to small pieces like film (c) after 185 h. The slower rate of water disintegration of film (b) compared to (c) may be attributed to a lower number of imine bonds. Thus, the disintegration rate depends on and may be modulated by the number of imine bonds in the dynamer, the rate increasing with the number of imine bonds.

NMR studies were carried out to elucidate the mechanism of disintegration by water. Fig. 3 shows the NMR spectra of GD films (thickness 15 μ m) before (a) and after immersing in distilled water at 50 °C for 24 (b) and 240 h (c). Before immersion, the NMR spectrum showed very small peaks of aldehyde derived from unit B (one imine and one aldehyde group). These aldehydes were formed in the film preparation process at high



Fig. 3 NMR spectra of green dynamer films before (a) and after soaking in distilled water at 50 $^{\circ}$ C for 24 (b) and 240 h (c).

temperature. As the immersion time in water became longer, the peaks of unit B and unit C increased with respect to those of unit A, containing the fully formed two imine groups. This means that the imine bonds dissociate to aldehyde and amine through hydrolysis, thus causing the water disintegration of the GD film. The proton NMR data also indicate that the deformation of the shape of the film did not need a large amount of dissociation of imine bonds. The amount of aldehyde calculated from NMR was only 19% after 240 h which is enough for the deformation of the shape of GD films, as illustrated in Fig. 2(c).

Fig. 4 shows the changes of M_n calculated from the NMR spectra of GD films immersed in water at different temperatures. As may be expected, disintegration was accelerated at higher temperatures. Thus, GDs are stable for use, without decomposition on contact with moisture in the air or a small amount of water, due to their insolubility, but disintegrate on contact with a large amount of water. In addition, the time it takes for disintegration can be controlled from 1 h to a few days simply by changing the number of imine bonds (with respect to the length of the polymeric chain) in the polymer molecule.

The self-healing properties of dynamers are also of much interest for numerous applications.^{12–15} To investigate the self-healing properties of GDs, NMR measurements were carried out on films as just prepared, after immersing in water at 50 °C for 14 h, and after subsequent drying at 80 °C for 240 h. After immersing in water, the M_n calculated from NMR data decreased from 13 000 to 7000. When the film was dried at 80 °C for 240 h, the M_n of the film recovered to 13 000, which is comparable to the M_n before immersion in water, thus demonstrating that the GDs possess self-healing properties.

Biodegradatability of green dynamers

A biodegradability test was performed using films of GDs based on PBS ($M_n = 1950$). The film with a 30 µm thickness was well mixed in activated compost²³ and transferred to a reaction vessel. The vessel was kept at 58 ± 2 °C and the amounts of CO₂ produced were measured by periodical titration using an



Fig. 4 Changes in mean molecular weight, M_n , of green dynamers soaked in water at different temperatures of 23, 35, and 50 °C.

automatic potentiometric titrator. The degree of biodegradation of the films was calculated from the amounts of CO_2 and the theoretical amount of CO_2 of the samples. It was found to be 16.0 and 66.2% after 10 and 38 d, respectively. Thus GDs indeed possess biodegradation properties, which reduce the environmental load.

Conclusions

In conclusion, green dynamers presenting moldability and good mechanical properties, also demonstrate excellent water disintegratability, mendability and biodegradability. The films do not deteriorate in shape or disintegrate with moisture in the air because the GDs investigated here do not have water solubility. They lose their shape only when they come into contact with a large amount of water. Therefore, the GD films can be stored in a normal atmosphere, but the imine bonds tend to dissociate at higher temperatures in the presence of a small amount of water. Products made of green dynamers can be discharged into toilet bowls or kitchen sinks without any clogging of pipes because of their water disintegratability.¹¹ After being discharged into the environment, they are biodegraded by microorganisms, in a sewage disposal treatment center or in the countryside, thus preserving the natural environment from contamination.²⁰ GDs can be used in domestic and personal care, in hygienic products, in agricultural and horticultural materials, in civil engineering, in construction materials, as well as in pharmaceutical preparations and medical devices.^{16,21} A vast range of specialized as well as consumer products can take advantage of the remarkable properties displayed by dynamers^{1,2} in general, and green dynamers in particular.

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- 23 The controlled compost, which was cultivated from municipal waste, was fermented for 2 months before use. The properties of this compost are as follows: The total dry solids was 50% as calculated from the amount of solids after drying at 105 °C for 10 h. Volatile solids amounted to 40% as calculated from the amount of solids after incineration at about 550 °C. C/N ratio and pH of compost were 12 and 8.7, respectively.