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Thermomechanical properties of PEGDA and its co-polymers

Abstract: Current research activities focus on personalized, comfortable and safe products for systemic or local drug application in patients. Poly(ethylene glycol) diacrylate is in particular interest as a drug delivery material, as it shows appropriate biological properties such as hydrophilicity and low toxicity. Additionally, as an easily photopolymerizable compound it can be also utilized for the production of scaffolds with the use of different techniques such as stereolithography. Even though it is often used as a biomaterial or as a copolymer in many photopolymer systems for drug delivery, thermomechanical analysis and basic understanding are rare.

Therefore, we investigated the tensile stress and the glass transition temperature of pure PEGDA and of its copolymers with 1,3-butanediol diacrylate or pentaerythritol triacrylate, as a function of the photoinitiator (PI) or acrylate concentration. Additionally, we demonstrated that the washing procedure decreases the tensile stress values. We showed, that by the means of composing PEGDA with these, it is possible to influence thermomechanical properties of the sample. Our outcomes have revealed, that there is no clear influence of the PI concentration on the thermomechanical properties. However there is an influence of the monomer concentration. Therefore, it should be possible to modify drug release profiles in future experiments.

Keywords: Drug delivery system, Poly(ethylene glycol) diacrylate (PEGDA), 1,3-butanediol diacrylate, pentaerythritol triacrylate, photopolymerisation, glass transition temperature, mechanical properties

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1 Introduction

Drug delivery systems (DDS) are recently intensively developed and investigated among scientific groups all over the world [1]. This kind of drug application offers controlled release manner and may be employed in a local therapy to obtain therapeutic, topical drug concentrations or for a systemic treatment as an alternative for oral or parenteral administration.

Poly(ethylene glycol) diacrylate (PEGDA) is particularly interesting as a material for the fabrication of DDS. This photopolymerizable substance is considered to be hydrophilic, non-toxic and biocompatible [2]. Furthermore, it can be easily shaped into the desired 3-dimensional constructs with the use of numerous techniques, such as microstereolithography [3, 4]. In the presence of UV radiation and a corresponding photoinitiator (PI), here Irgacure 2959, it rapidly undergoes a polymerisation under formation of stable, covalent bonds [5].

We believe, that the combination of PEGDA and other acrylates, such as 1,3-butanediol diacrylate or pentaerythritol triacrylate enables to influence and to adjust the thermomechanical properties, such as tensile stress and glass transition temperature (T_g) to their medical applications [6]. Therefore, it should be possible to manufacture a DDS with an immobilized drug which release is highly controllable and adjustable to the specific medical needs [7].

In this study the results of the recognition of the basic PEGDA system and some copolymers for the creation of a potential DDS are presented. We have produced dumbbell-shaped samples consisting of PEGDA and its copolymers of di- or triacrylate with different photoinitiator concentrations. Additionally, we analysed the influence of a washing procedure, for removing unreacted monomers and photoinitiator residuals, to the thermomechanical properties and performed mechanical tests to determine and compare the physical properties of the samples with different composition.

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2 Materials and methods

2.1 Chemicals

All of the chemicals: poly(ethyleneglycol) diacrylate $M_n=250$ g/mol (PEGDA), 1,3-butanediol diacrylate, pentaerythritol triacrylate and the PI: 2-Hydroxy-4'-(2-hydroxyethoxy)-2-methylpropiophenone (Irgacure 2959) were purchased from Merck KGaA (Darmstadt, Germany).

2.2 Sample preparation

The following solutions were prepared:

- PEGDA containing 0.50%; 0.75%; 1.00% and 1.25% (w/v) PI
- PEGDA with 1%; 5% and 10% 1,3-butanediol diacrylate (v/v) and each with 0.50%; 0.75%; 1.00% and 1.25% (w/v) PI
- PEGDA with 1%; 5% and 10% pentaerythritol triacrylate (v/v) each with 0.50%; 0.75%; 1.00% and 1.25% (w/v) PI

625 μ L of each solution was transferred to a handmade silicone holder to form dumbbell samples (design according to the ISO 527-2). The samples were polymerized in the UV Chamber (CL-1000L, UVP, USA) with $\lambda = 365$ nm for 10 minutes. Afterwards, the samples were washed six times for 30 minutes with acetonitrile and three times for 30 minutes with distilled water. Throughout the washing process the samples were shaken at 100 rpm at 37 °C. Afterwards they were dried for 2 hours at 40 °C in the vacuum chamber.

2.3 Mechanical properties analysis

Tensile stress measurements were performed with the use of uniaxial testing system Zwicki ZN 2.5 (Zwick GmbH & Co.KG, Ulm, Germany). The tests were performed with a 500 N load cell and a crosshead speed of 25 mm/min.

2.4. Differential scanning calorimetry

Differential scanning calorimetry (DSC) measurements were carried out under a nitrogen purge with a DSC1 (Mettler Toledo GmbH, Greifensee, Switzerland). Calibration of the heat of fusion (ΔH) was performed with an indium standard. The sample weights were in the range of

10 – 20 mg. Preliminary detections of the glass transition temperature (T_g) was performed at a heating rate of 10 K/min ($n = 1$), the values were determined from the second heating curves.

3 Results

3.1 Mechanical properties

The results of the tensile stress measurements of unwashed and washed pure PEGDA as a function of the PI concentration are presented in Figure 1. No clear influence of the PI concentration on the tensile stress values is noticed. The washed samples show averagely 71% lower values in comparison to the unwashed ones.

For the copolymers PEGDA - 1,3-butanediol diacrylate and PEGDA - pentaerythritol triacrylate the tensile stress results for unwashed and washed samples as a function of the acrylate and PI concentration are presented in Figure 2.

Here the same trend as in the case of the pure PEGDA samples is observed – the tensile stress for the washed samples is on average 64% lower than in case of the unwashed samples. For the PEGDA-triacrylate unwashed ones a relationship between the PI and the tensile stress is recognized. The stress values increase with increasing concentration of the PI. However, due to high standard deviations, more data to confirm this presumption is needed. The content of di- and triacrylate seems not to affect the tensile stress values in PEGDA co-polymer samples.

Figure 1: Tensile stress for the unwashed (red) and washed (blue) PEGDA samples prepared with different photoinitiator concentrations ($n=5$)

Figure 2: Tensile stress diagrams for the unwashed (red) and washed (blue) samples prepared with PEGDA and different PI and 1,3-butanediol concentrations(A) or pentaerithritol triacrylate (B) (n=5)

3.2 Glass transition temperatures

The results of the DSC measurements are presented in Table 1. Glass temperature rises with the increasing concentration of PEGDA copolymers. PI concentration and the washing process seem not to influence the T_g .

4 Discussion

The mechanical studies described here, reveal, that the washing procedure highly decreases the tensile stress values. This substantial difference between washed and unwashed samples occurs likely due to removal of unpolymerized monomers and the PI residues. For the unwashed pure

PEGDA samples, PI concentration seems to influence only negligibly the tensile stress values. The unwashed samples, especially ones containing triacrylate, seem to have higher stress values with the increasing concentration of the PI. The concentration of both acrylates appears not to exhibit any influence on the mechanical properties of the samples. Nevertheless, further experiments are needed to reduce the standard deviations.

In all of the experiments the T_g values of unwashed and washed samples were similar. Thus, it seems that PI concentrations also demonstrated no unambiguous influence on thermal properties of the samples. Surprisingly, the alteration of the coacrylate content in the sample highly influences the T_g , which increases with the increasing concentration of both di- and triacrylate. Therefore, the composition of PEGDA copolymers is most probably a core factor in future drug release tests to modify the drug release rates.

Table 1: Glass transition temperatures (°C) for unwashed (uw) and washed (w) samples of PEGDA containing different photoinitiator, 1,3-butanediol diacrylate and pentaerithritol triacrylate concentrations (conc.) (n=1).

PI conc. %	PEGDA (uw/w)		
	0.50	0.75	1.00
0.50	27.4/26.8		
0.75		27.5/27.6	
1.00			26.6/27.1
1.25			26.3/26.8

PI conc. %	Diacrylate conc. % (uw/w)		
	1	5	10
0.50	31.0/29.8	34.3/33.5	37.2/44.8
0.75	29.9/27.4	33.7/37.8	43.1/46.0
1.00	27.7/29.7	39.2/39.0	45.2/47.8
1.25	32.4/30.1	37.4/34.7	51.0/46.8

PI conc. %	Triacrylate conc. %		
	1	5	10
0.50	32.0/32.7	38.5/39.0	40.2/46.1
0.75	28.9/33.8	30.4/39.6	42.5/51.2
1.00	27.4/32.8	34.7/37.5	40.6/43.4
1.25	30.6/32.7	39.5/39.9	44.8/47.8

5 Conclusion

In summary, these preliminary results confirm, that the addition of the di- and triacrylates to PEGDA enable taking control over T_g and therefore even to design a thermoresponsive drug release system. The described outcomes give us also information about the influence of the washing process, as this procedure causes clear changes in the mechanical properties. Samples after washing out the non-polymerized residues are much more fragile. Nevertheless, the presented results are promising and enable a creation of a new, possibly thermosensitive DDS. In order to determine the full potential and suitability of PEGDA and its copolymers as DDS, especially with drugs incorporated, thermomechanical and biocompatibility tests will be investigated.

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