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Thermomechanical properties of PEGDA in combination with different photo-curable comonomers

Abstract: The technology of pharmaceutical drug delivery systems (DDS) as an individual and adjustable tool for drug administration has been intensively developed in the last years. Additive manufacturing (AM) techniques, such as stereolithography, are a promising approach towards DDS scaffold manufacturing. Stereolithography, by using layer-by-photo-polymerisation, creates DDS scaffolds with highly controlled 3D geometry. Combined with inkjet printing it allows a very precise positioning of the drug depot in the basic scaffold and therefore also a better control of the drug release. Furthermore, this hybrid AM technique also allows for the creation of a multi-drug DDS with a several drug depots localized in desired positions within the scaffold. Determination of the scaffold and drug depot material properties is one of the initial steps for such novel DDS development. Basic characteristics, such as stiffness, elasticity or glass transition temperature (T_g), are important for designing and adapting the material for biomedical application. The photosensitive poly(ethylene glycol) diacrylate (PEGDA) can be easily formed into a desired biocompatible scaffold geometry via stereolithography. In this study we have focused on the evaluation of PEGDA ($M_n=700$ g/mol) as a pure and copolymer system in combination with other acrylates (butanediol diacrylate, pentaerythritol triacrylate) as possible materials for DDS using this novel hybrid AM technique. Irgacure 2959, a biocompatible photoinitiator (PI), was used as a radical starter for photopolymerisation. Samples varying in PI and coacrylate concentration were prepared by conventional photopolymerisation. Physico-chemical analyses of the samples were performed and several parameters, such as

stiffness, elongation at break and glass transition temperatures, were determined.

Keywords: Drug delivery system (DDS), Poly(ethylene glycol) diacrylate (PEGDA), 1,3-butanediol diacrylate, pentaerythritol triacrylate, photopolymerisation, glass transition temperature, stiffness, elongation at break
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1 Introduction

Preparation of DDS via AM techniques is a rapidly growing area of research. It aims at the development of medical products, which should assure desired therapeutic effects according to the individual needs of the patients, which is often difficult with the use of traditional routes of drug administration [1, 2]. An essential step in the process of designing such novel therapeutic systems is the selection of a polymer material, showing desired biological and mechanical properties, but also offering a possibility to attain a sustained, highly controlled and reproducible drug release profile.

PEGDA can be easily photocured in the presence of a radical photoinitiator, for instance Irgacure 2959 (PI), via an AM technique, such as stereolithography [3, 4]. In our previous study traditionally photocured PEGDA samples ($M_n=250$ g/mol) were investigated in order to determine thermal and mechanical properties of this material as a potential scaffold and drug depot base component [4]. Here, the T_g and physical parameters of unwashed PEGDA samples with $M_n=700$ g/mol were specified. Apart from analysing the pure PEGDA material with different PI concentrations, also variously composed samples with the addition of different amounts of butanediol diacrylate (diacrylate) and pentaerythritol triacrylate (triacrylate) were investigated. It is shown, how the differences in the number and positioning of acrylate groups influence the crosslinking, reflecting in the presented results.

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2 Materials and methods

2.1 Chemicals

Poly(ethyleneglycol) diacrylate $M_n=700$ g/mol (PEGDA), comonomers: 1,3-butanediol diacrylate (diacrylate) and pentaerythritol triacrylate (triacylate), the photoinitiator 2-Hydroxy-4'-(2-hydroxyethoxy)-2-methylpropiophenone (Irgacure 2959, PI) and the PI solvent DMSO were purchased from Merck KGaA (Darmstadt, Germany).

2.2 Sample preparation

Samples were prepared as specified in our previous work [5]. Briefly, PEGDA was mixed with diacrylate or triacrylate to obtain 1%, 5% and 10% (v/v) solutions for 0.50% and 1.25% PI (w/v) concentration. Reference samples without comonomers were used. A handmade silicone holder was applied for the generation of dumbbell samples (design according to the ISO 527-2). Samples were cured in the UV chamber at $\lambda = 365$ nm for 10 minutes.

2.3 Mechanical properties analysis

A strength 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, $n=5$.

2.4 Differential scanning calimetry

Differential scanning calorimetry (DSC) measurements were carried out under a nitrogen purge with a DSC1 (Mettler Toledo GmbH, Greifensee, Switzerland). Temperature calibration 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 ($n=1$). T_g values were determined from the second heating curves.

3 Results

3.1 Mechanical properties

The results of the tensile strength measurements as a function of the acrylate and PI concentration are presented in Figure 1. No clear influence of PI concentration on the tensile stress values is observed for all diacrylate containing samples. In case of triacrylate samples, the tensile strength values seem to decrease with increasing PI concentration. With increasing coacrylate content tensile strength of triacrylate samples increased: 4.4/5.85/7.57 MPa (1/5/10% triacrylate). Furthermore, the 10% triacrylate samples also show almost 2-fold higher tensile strength than the reference samples without crosslinker addition. This trend is not observed for the diacrylate samples.

Elongation at break values are shown in Figure 2. The PI concentration appears not to affect these values in diacrylate samples, whereas in triacrylate samples, the elongation appears to decrease with decreasing PI concentration. This is especially evident in samples containing 5% of the triacrylate. Here, 1.25% PI samples show 45% lower elongation value in comparison with 0.5% PI samples. Different concentrations of the coacrylate do not affect this parameter in neither di- nor triacrylate samples.

Figure 1: Tensile strength for the unwashed PEGDA₇₀₀ samples prepared with different PI and coacrylates concentrations. Red line relates to the average of pure PEGDA₇₀₀ samples without coacrylate addition ($n=5$).

Figure 2: Elongation at break for the unwashed PEGDA₇₀₀ samples prepared with different PI and coacrylates concentrations. Red line relates to the average of pure PEGDA₇₀₀ samples without coacrylate addition (n=5).

3.2 Glass transition temperatures

The results of the glass transition temperature measurements are presented in Table 1. All of the values are under 0°C. PI concentration does not appear to have any particular influence on T_g .

Table 1: Glass transition temperatures (°C) for the unwashed PEGDA₇₀₀ samples prepared with different PI and coacrylates concentrations (n=1).

PI conc. %	Diacrylate conc. %		
	1	5	10
0.50	-41.5	-39.7	-33.8
0.75	-44.1	-38.1	-34.0
1.00	-40.6	-38.5	-34.3
1.25	-39.2	-35.4	-33.6

PI conc. %	Triacrylate conc. %		
	1	5	10
0.50	-40.9	-37.1	-34.5
0.75	-40.6	-39.1	-34.1
1.00	-42.0	-39.2	-36.9
1.25	-43.1	-40.6	-34.3

Samples with the addition of acrylate appear to have increasing T_g with the higher concentration of the coacrylate. This can be particularly observed for both coacrylates samples, where the difference between samples containing 1% and 10% diacrylate is at least around 5°C.

4 Discussion

The mechanical studies in this paper reveal, that the samples with the addition of the triacrylate to the basic polymer PEGDA₇₀₀ increased tensile strength. This can probably be attributed to the fact, that the pentaerythritol triacrylate as a crosslinker with three functional acrylate groups increases the crosslinking density, promoting changes in mechanical properties of the material. This is not observed in case of samples copolymerised with the linear molecule butanediol diacrylate with two functional acrylate. It also appears that the increase of PI content in the triacrylate samples acts contrarily, inducing lower tensile strength. Probably, the higher amount of active free radicals increases the polymerisation efficacy but concurrently increasing the sample fragility. This may be explained by the fact, that after reaching the maximum conversion level, further increase of PI concentration leads to a loss of chain mobility and consequently to non-uniform curing, which makes the sample less mechanically resistant [6]. This observation appears to be confirmed in the results of the elongation at break measurements. Here, in particular 5% triacrylate samples with lower PI concentration elongate clearly more than samples with a higher PI. This is not noticed in case of diacrylate samples, where neither PI nor coacrylate concentration affect the results.

Thermal analyses show, that the addition of both coacrylates increases T_g . All of the values consequently are below 0°C. The material is already in its rubbery state at room temperature. Moreover, the modification of the coacrylate content will not change the mobility of the molecular chains by medical applications at 37°C. The photoinitiator concentration appears not to influence the T_g .

Only one T_g transition for each sample is observed. Therefore, we assume that during the photopolymerisation covalent bonds between the basic polymer PEGDA₇₀₀ and the additional acrylate are built up, forming a copolymer. For individually polymerized materials two T_g transition should be observable. Therefore, the composition modifications create the possibility to influence the properties of the material and their adaptation to the desired application.

5 Conclusion

The results presented in this paper enable the determination of basic thermomechanical properties of PEGDA₇₀₀ in combination with 1,3-butanediol diacrylate and pentaerythritol triacrylate as potential candidates for DDS

material. The tensile strength and elongation at break results of some samples can be modified by adding different amounts of the PI and triacrylate. Although T_g of all of the samples is under 0°C , which precludes influencing the drug release rate with the use of this parameter, it may still be modified according to different crosslinking density and mobility of the polymer chains, which should be investigated in further in vitro drug release studies.

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