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Intrinsic viscosity and chemical composition of the polyanhydridepoly(Sebacic acid-co-Azelaic acid) synthesized by microwave irradiation

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Abstract : Poly(Sebacicanhydride:azelaic anhydride) poly(SA:AA) was synthesized by microwave irradiation at three molar rations (25:75, 50:50 and 75:25) and irradiation times of 3 to 5 minutes. The intrinsic viscosity of poly (SA:AA) at molar ratio of 50:50 at 5 minutes was higher according with equations of Huggins, Kraemer, solomon-Ciutaand Martin. The chemical composition and morphology of this polymer was analyzed by infrared spectroscopy FTIR, nuclear magnetic resonance (NMR) and scanning electron microscopy (SEM). Anhydride bond was found in two absorption bands at 1742 and 1812 cm^{-1}. Acetyl groups was corroborated at 2.4 ppm by ^{1}H NMR spectrum. In addition, the SEM images showed the formation of a compact material without presence of porosities or microcanalson its surface, suggesting the formation of a homogeneous copolymer.

Keywords : polyahydride, sebacic acid, azelaic acid, Microwave, irradiation, intrinsic viscosity.

Introduction

Polyanhydrides have become an important group of biodegradable polymers used for biomedical, such as controlled drug delivery systems and biomaterials for tissue engineering applications[1-3]. This is due largely to their biocompatibility characteristics, so side effects, such as inflammation, have not been reported. Moreover, its degradation mechanism by the effect of pH or temperature of the suspending medium, causes monomers nontoxic diacids which can be metabolized and eliminated by the body easily[4-5].

Several synthesis techniques for polyanhydrides have been used with the aim at obtaining a polymer with high molecular weight, viz. ring opening polymerization, melt polycondensation, interfacial polymerization, dehydro-chlorination and dehydrative coupling agents. Solution polymerization limits the macromolecular size. Microwave irradiation allows the polymers synthesis (Microwave-assisted polymer synthesis (MAPS)) with high molecular weight at lower polydispersity, low power and time of reaction[6] in comparing with conventional thermal heatingallowing areductionin the solvent content andfavoring the green chemistry[7]as detailed Frediani et al. and Nakamura et al in the bulk ring opening polymerization and polycondensation of lactide and lactic acid, respectively, to produce poly(lactic acid)[8-9].

The main advantages of MAPS are that reaction times are reduced from hours to minutes[10-11] and higher molecular weights are attainable[12-13], which can be determined by several techniques. However, viscometric methods offer a simple and inexpensive alternative. The intrinsic viscosity [η] provides information about the interactions between a solute (polymer) with a solvent and thehydrodynamic volume occupied by a macromolecule that is associated with the size and structure of the macromolecular, being useful for applications in biopolymers pharmaceuticals, cosmetics, and emulsions processing[14]. The high affinity of polymer with the solvent increases the hydrodynamic volume, but the use of poor solvent causes aggregation between the macromolecules[15-16].

This report presents the synthesis of poly(sebacicanhydride: azelaic anhydride) poly(SA:AA) at different molar ratios using microwave irradiation. In addition, a study of the intrinsic viscosity was realized to the selection of the better combination according with higher molecular. The poly(sebacicanhydride: azelaic anhydride) poly(SA:AA) was characterized by ^{1}H-NMR, FTIR and SEM.

Experimental

Materials

All the reagents were purchased commercially with high purity. Sebacic acid (98%) and azelaic acid (98%) were obtained from MERCK. Other solvents suchas acetic anhydride (98%) and chloroform (99.8%) were manufactured by PANREAC.

Synthesis of poly(sebacicanhydride:azelaic anhydride) poly(SA:AA)

Microwave-assisted polymer synthesis (MAPS) was carried out in two stages: (1) pre-polymerization and (2) copolymerization. For the first stage, the oligomers of sebacic acid (SA) and Azelaic Acid (AA) wereobtained for 3 or 5 minutes in a Whirlpool Microwave Oven(WMCSG141XD model, 1500 W, 80% power), in a solution of acetic anhydride with each monomer at a relation of 1:3 w/w, respectively. Excess acetic anhydride was removed under evaporation in hot using a vacuum pump with a thermostat at 40°C[10]. The pre-polymerization of each monomer was conducted maintaining a limit of 1g per sample of oligomer formed, this small amount of sample prevents the dielectric heating mechanism, ensuring a uniform irradiation that is observed by the absence of layers with different heat content in the material[17-18].

For the copolymerization step, poly(sebacic anhydride:azelaic anhydride) poly(SA:AA) was formed by the reaction of the prepolymers of sebacic acid (SA) and azelaic acid (AA) also using MAPS, for which the polymers were of molar composition 75:25, 50:50, 25:75at 3 and 5 minutes of synthesis reaction.

Viscosity measurements

The intrinsic viscosities [η] of poly(sebacic anhydride:azelaic anhydride) poly(SA:AA) were determined in chloroform solutions ($CHCl_3$) in a Ubbelohde type viscometer (PHYME) at 25 ± 0.2 °C. Theexperiment consisted of the measurements of efflux time of the pure solvent and four dilutions of 0.0025, 0.005, 0.0075 and 0.01 g/cm3. The intrinsic viscosity was obtained by extrapolating of reduced viscosity (η_{sp}/c) and inherent viscosity (lnη_{sp}/c) to infinite solution, according the relations of Huggins, Kraemer, Solomon-Ciuta and Martin. These equations are as follow

Huggins $\frac{\eta_{sp}}{c} = [\eta] + K_H[\eta]^2 c$ (1)
Kramer $\frac{Ln(\eta_r)}{c} = [\eta] + K_K[\eta]^2 c$ (2)
Solomon-Ciuta $[\eta] = \frac{1}{c}\sqrt{2\eta_{sp} - 2Ln(\eta_r)}$ (3)
Martin $\frac{Ln(\eta_{sp})}{c} = [\eta] + K_M[\eta]c$ (4)

Where
η_r: relative viscosity or ratio of viscosity (ratio of efflux time of the pure solvent and dilutions of polymer)
η_{sp}: Specific viscosity ($\eta_{sp} = n_r - 1$)
$\frac{\eta_{sp}}{c} = \eta_{red}$: Reduced viscosity
$\frac{Ln(\eta_r)}{c} = \eta_{inh}$: Inherent viscosity
K_H, K_K: Constantsof Huggins and Kramer

Characterization of poly(sebacic anhydride: azelaic anhydride) poly(SA:AA)

The structural chemistry poly(sebacic anhydride:azelaic anhydride) poly(SA:AA) of greater intrinsic viscosity was determined by infrared spectroscopy (FTIR), nuclear magnetic resonance spectrometry (NMR) and scanning electron microscopy (SEM).

IR spectrum were recorded using a IR Affinity-Shimadzu, A213749 SN with an operating range of 400 to 4000 cm-1. The 1H NMR spectra were recorded with FOURIER300 -300 MHz instrument in CDCl3 solvent. SEM images were obtained using a Quanta FEG equipment 650. For this analysis, a sample of the polymer powder was dispersed in ethanol in an ultrasonic bath for 15 minutes with H2O. A drop of polymer solution was placed on a black metal microscope slide. The acquisition of the images was performed in low vacuum mode using the secondary electron detector "large field detector" (LFD for imaging in Low Vacuum mode).

Results and Discussion

Intrinsic viscosity measurements

Figure 1 presents the linear relationship of η_{sp}/c versus c of Huggins plot, a significant effect of polymer solution concentrations about intrinsic viscosity was observed. The intrinsic viscosity estimated from Huggins equation and the intercept of plot was found to be 79.09mL/g while the K_H value was -0.99 at composition 50:50, negative values of this constant are unusual but other studies have reported similar values of Huggins constant for viscosity measurements of polymer solutions of *Eucalyptus citriodora (EC) Gum*[19] and polyacrylamide[20]. Values of K_H above 0.5 and 1.0 are related withpoor solvents and theta solvents; values larger than 1 predict strong interactions polymer-polymer, that causes aggregation[21], due to the use of poor solvent and the existence of ionic charges in polymer chain[22]. As shown in Table 1, values of $K_H$less than 0.25were observed in all solutions, mainlyin the compositions of 75:25 and 25:75 (poly (SA:AA)). The range for 0.25 to 0.5 in theHuggins coefficient (K_H)is assigned to good solvation[23-24].Moreover,negative values of $K_K$are attributed to goodsolvents[25].The low affinity between polymer and solvent, chloroform, avoidsthe expansion of polymer chains[15-16].

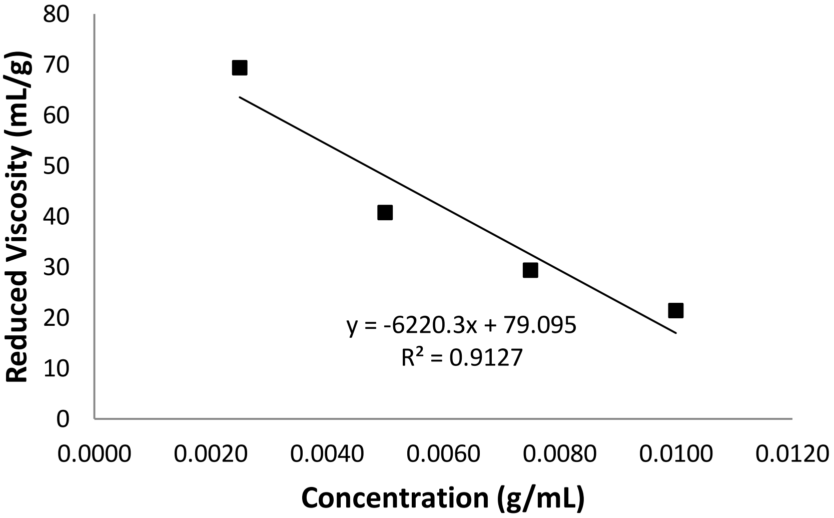

Figure 1. Huggins plot for poly (SA:AA) 50:50 at 5 minutes of microwave synthesis.

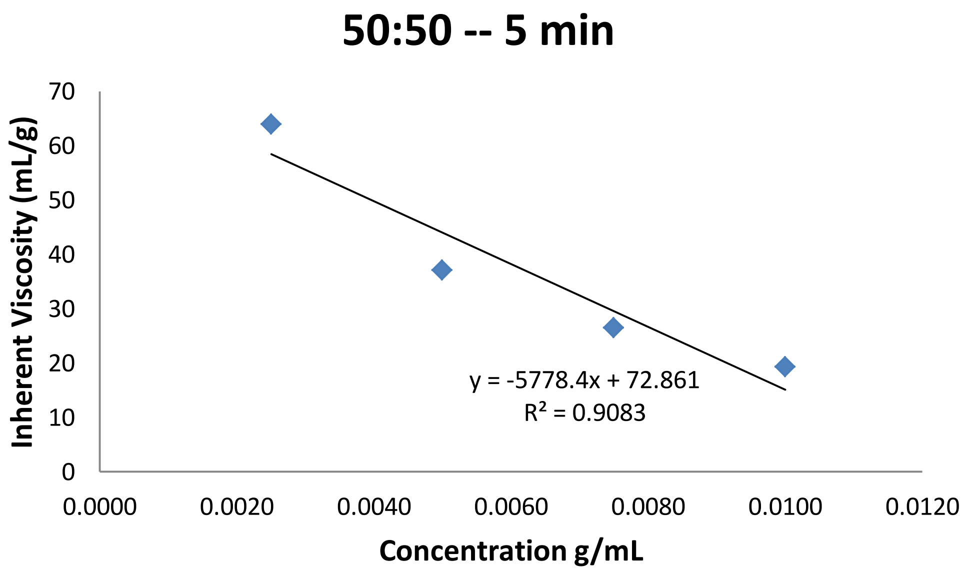

Figure 2. Kraemer plot for poly (SA:AA) at 50:50 with 5 minutes of microwave synthesis

The degree of linearity decreased proportionally with the composition of sebacic acid (See Table 1). Other studies have reported that the curvature in Huggin'splots[26-27]corroborated the presence of aggregates[28]. The intrinsic viscosity was not determined by extrapolation of experimental data for infinite dilution i.e. C = 0. Initial slopes[26,28-32] of plots of Huggins and Kraemer were used to calculate the intrinsic viscosity, K_H and K_K[33](See Table 1). The methods used to determine the intrinsic viscosity from slopes of plots have larger correlation coefficients and smaller standard errors than those based on intercepts of plots[21].Moreover, the slope model of Martin equation was applied(See Table 2).Although, the relation $K_H + K_K = 0.5$ was not found for all samples, the values of intrinsic viscosity were close in all the applied models, including values obtained through the Solomon-Ciuta equation by single point determination.

Table 1.Viscometric constants calculated and Intrinsic viscosity values

time (min)	Composition	K_H	K_K	η Solomon-Ciuta (cm^3/g)	η Huggins (cm^3/g)	η Kraemer (cm^3/g)	r^{2*}
3	75-25	-1.484	-1.580	44.55	51.24	48.56	0.86
	50-50	-1.071	-1.166	65.24	73.30	67.92	0.89
	25-75	-17.055	-17.192	4.29	4.22	4.2	0.5
5	75-25	-1.388	-1.482	50.17	58.14	54.69	0.85
	50-50	-0.994	-1.088	68.71	79.09	72.86	0.91
	25-75	-9.891	-10.073	5.38	5.05	5.03	0.36

* Correlational factor of Huggins and Kraemer equations, these had similar values.

Table 2. Intrinsic viscosity values

Time (min)	Composition	η Martin(cm^3/g)	r^2
3	75-25	58.89	0.94
3	50-50	87.46	0.97
3	25-75	3.14	0.4
5	75-25	68.94	0.94
5	50-50	95.88	0.98
5	25-75	4.80	0.29

The intrinsic viscosity observed in composition of polyahydride with 50:50 of composition at 5 minutes of reaction was higher with larger correlation coefficient in applied methods of initial slopes from the equations of Huggins, Kraemer and Martin.

The measurement of intrinsic viscosity, [η], provides information about viscosity average molecular weight of a polymer $(\overline{\mathrm{M_v}})$ according semi-empirical Mark-Houwink-Sakurada equation:

$$[\eta] = \mathrm{KM}_{\mathrm{v}}^{\alpha}$$

Where K and α are constants related to system of polymer-solvent and temperature. According with configurations of a polymer chain[34], the values of α are between 0.5 and 0.8 for flexible random coils in a good solvent, polymer macromolecules of stiff chain exhibit α values between 0.8 and 1.0 and α values are found between 1.0 and 1.7 for extended chains polymers, Regardless the quality of solvent, and the values of Mark-Houwink-Sakurada constants, the intrinsic viscosity of linear polymers (random coil configuration or not) is directly dependent to the molecular weight (MW), high intrinsic viscosity of solution of polymer is related with high molecular weight, as can be corroborated with viscometric studies of solutions with different polymers as cis-polyisoprene[35], high-cis polybutadiene[36] and poly(octadecanoic anhydride)[37]. Higher molecular weight polymers have better mechanical properties and more chemical resistance, due to this the poly(sebacicanhydride:azelaic anhydride) poly(SA:AA) of composition 50:50 at 5 minutes of microwave synthesis was selected, similar results were reached with copolymer synthesized with a ratio of 50:50 (azelaicacid:dodecanedioic acid) at 3minutes of microwave irradiation[38]. The copolymer with composition 25:75 (SA:AA) present lower correlation coefficient, high content of azelaic acid interferedthe chain length of polymer.

The weight average molecular of polyanhydrides based in sebacic acid was determined by Determanand Balaji[39]. Copolymers as poly(fumaric-co-sebacic anhydride) (poly(FA:SA))and poly(sebacic acid) with poly l,6-bis(p-carboxyphenoxy)hexane (poly(CPH)) (poly(CPH:SA))and poly(l,3-bis(pcarboxyphenoxy) propane) (poly(CPP)) (poly(CPP:SA))were characterized with gel permeation chromatography (GPC) and viscosity measurements to stablish a relation between molecular weight (Mw) of polyanhydrides with their intrinsic viscosities (in chloroform). Ranges of intrinsic viscosity (in chloroform) between 0.13 to 1.25 dL/g were attributed to Mw values from 2000 to 300000. The poly(sebacicanhydride:azelaic anhydride) poly(SA:AA) of molar composition 50:50 exhibited intrinsic viscosity (in chloroform) from 0.6 to 0.9 dL/g (See Table 1 and 2) according with the equations of Huggins, Kraemer and Martin The Mw values of poly(SA:AA) could be between this range (2000 to 300000) due to the relations found by Determan and Balaji for intrinsic viscosity using a universal calibration curve with GPC, where the Mark-Houwink relationship (Equation 5) for poly(CPP:SA) was applied to all the experimental Mw of obtained polyanhydrides (poly(FA:SA), poly(CPH:SA) and poly(CPP:SA)) with fit complete.

$$[\eta]_{CHCl_3}^{23°C} = 3.88 \times 10^{-7} M_W^{0.658} \qquad (5)$$

Characterization of poly(sebacic anhydride:azelaic anhydride) poly(SA:AA)

Figure 3 shows theFTIR spectrum of poly(sebacic anhydride:azelaic anhydride) poly(SA:AA) with composition 50:50 at five minutes of reaction.The carboxylic group (R-COOH) wasidentified at 2930 $\mathrm{cm^{-1}}$ due to the elongation of –OH and (-C-), at 1709 $\mathrm{cm^{-1}}$due to the carbonyl stretching (-C=O) and at 1308 $\mathrm{cm^{-1}}$due to the stretching of bond –C-O-[40]. The anhydride group was detected in twoabsorption bands at 1742 and 1812 $\mathrm{cm^{-1}}$ (-C=O stretching) and 1206.53 $\mathrm{cm^{-1}}$ (C-O bending)[40-41].These anhydride doublet (1742 and 1812 $\mathrm{cm^{-1}}$) indicatesthat the poly(SA:AA) did not undergone hydrolysis[42].

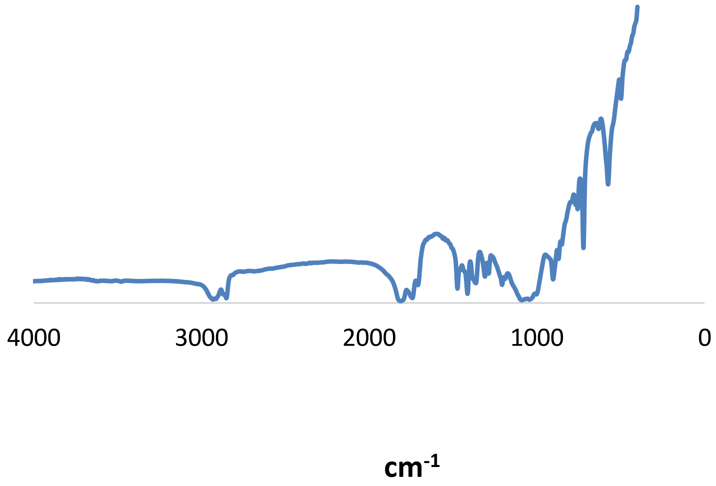

Figure 3. FTIR spectrum for of poly(sebacic anhydride:azelaic anhydride) poly(SA:AA) at 50:50 molar composition and 5 minutes of microwave irradiation

^{1}H-NMR spectroscopy supported the presence of the poly(sebacic anhydride:azelaic anhydride) poly(SA:AA) (Figure 4). The spectrum presents proton signals at $\delta = 2.4$ ppm which is characteristic of acetyl groups (See Table 3). Moreover, methyl group (the protonnextto the anhydridegroup**)** was detected at $\delta = 2.17$ ppm. The signals are reported as following:

^{1}H NMR ($CDCl_3$, ppm) δ: 10.13 (d, -C(O)OH), 2.4 (m, -CH_2-CO-), 2.17 (t, —CH_2—COOR), 1.63 (q, -CH_2-), 1.32 (d, -CH_2-)

Table 3. Chemical shift and assignment of proton signal showed in ^{1}H NMR

Structural Unit	**Characteristic**	**Chemical Shift (ppm)**
-C(O)OH (proton of hydroxy group)	Carboxylic acid in oligomers	10.131 10.136
$CDCl_3$	7.31 (solvent, $CDCl_3$),	7.306
-CH_2-CO-	Methyl protons bound to ketone group of polyahnydride	2.309 2.334 2.358 2.412 2.418 2.437 2.443 2.461 2.467
—**CH_2**—COOR	Methyl protons bound to anhydride group	2.082 2.207 2.213
—**CH_2**—**CH_2**—COOR	Methyl protons bound to group —**CH_2**—COOR	1.599 1.620 1.642 1.664
—(**CH_2**)—	Aliphatic side-chain protons	1.313 1.331

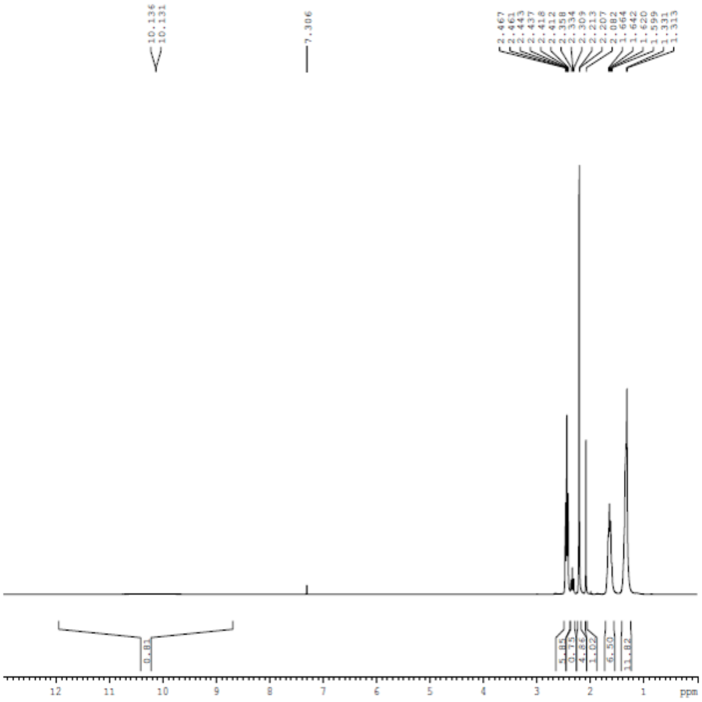

Figure 4. 1H NMR spectrum of the poly(sebacicanhydride:azelaic anhydride) poly(SA:AA)

The Figure 5shows the SEM images of poly(sebacicanhydride:azelaic anhydride) poly(SA:AA) with 50:50 molar composition at 5 minutes of reaction time. A compact material was observed without porosities o microcanals in the surface.

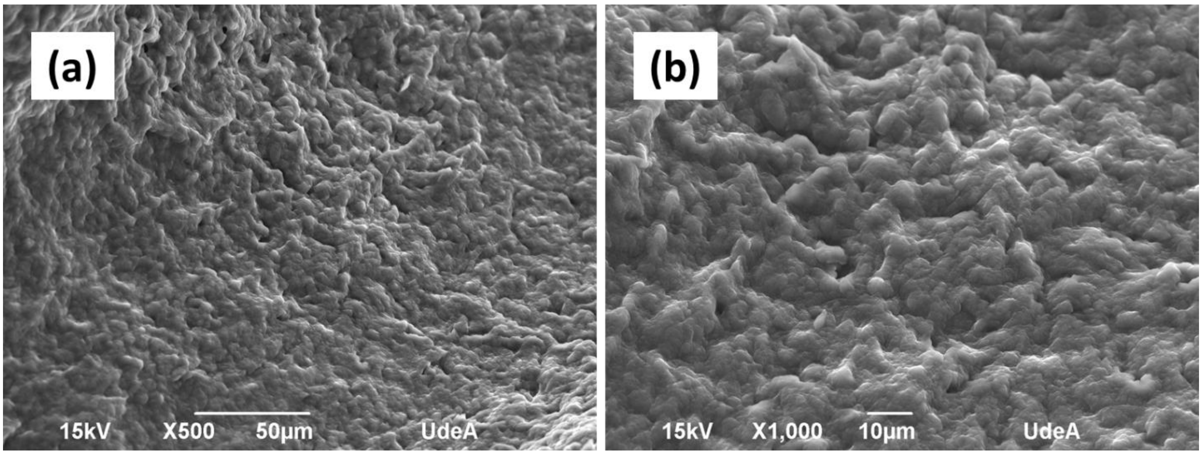

Figura 5. SEM images for the poly(sebacicanhydride:azelaic anhydride) poly(SA:AA. (a) magnificación a 50 µm y (b) magnificación a 10 µ m

Conclusions

Microwave-assisted polymer synthesis (MAPS)provides accessible alternatives for the obtaining of polyanhydrides based in sebacic acid due to that the reported intrinsic viscosity values were found between the achieved ranges with other polymerization techniques as melt polycondensation, in solution, and ring opening reactions[39]. The synthesis of poly(SA:AA) was corroborated using FTIR and NMR, the presence of anhydride bond was detected in two absorption bands at 1742 and 1812 cm^{-1}, besides the protons next to the acetyl groups and anhydride groups were observed at 2.4 ppm and 2.17 ppm, respectively. The viscosity measurements were useful to the identification of change in the molecular weight of polyanhydrides according with reaction time and molar composition of dicarboxilic acid. This technique has low cost with an application very simple and it offered a high correlation coefficient at poly(SA:AA) of 50:50 molar composition using the equations of Huggins, Kraemer and Martin. High content of comonomer of azelaic acid affects the molecular mass of polyanhydride,

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