RESEARCH ARTICLE

Macromolecular Symposia

www.ms-journal.de

Co-Crystalline Phases of Syndiotactic Polystyrene with Azelaic Acid Molecules of Pharmaceutical Interest

Verdiana Covelli, Antonietta Cozzolino, Manuela Rodriquez, Christophe Daniel, and Paola Rizzo**

Sorption of dicarboxylic acid molecules of pharmaceutical interest such as azelaic acid (AzA), in syndiotactic polystyrene (sPS) films presenting δ and ϵ nanoporous crystalline structure, is reported. Fourier Transform Infrared (FTIR), Polarized FTIR and Wide-Angle X-ray diffraction (WAXD) patterns on axially oriented sPS films has been performed to verify their sorption in crystalline lattices resulting in the formation of co-crystalline (CC) phases. Experimental evidence provides that AzA molecules can be included in the crystalline nanochannels of ϵ phase both as isolated and hydrogen-bonded molecules whereas they are only dissolved in the amorphous phase of δ samples.

1. Introduction

Azelaic acid (AzA) is a well-known dicarboxylic acid containing 9 C atoms (**Figure 1**), found in grain cereals and animal products.[1]

Thanks to its antimicrobial and anticomedonal properties, in 2002 it was approved by the US Food and Drug Administration (FDA) for rosacea and acne, either in monotherapy or in combination therapy.[2] Acne vulgaris has a multifactorial pathogenesis characterized by inflammatory papules and pustules, hyperkeratosis, and trapped sebum and comedones that are growth sites of skin bacteria. In this respect, AzA shows great versatility in dermatology since it has been proven to target multiple pathogenic factors involved in acne condition;[3] indeed, it exerts noteworthy antibacterial effects against *Propionibacterium acnes*, *Staphylococcus epidermidis*,[4] and other bacteria that populate the intrafollicular microflora of acne lesions, by inhibiting microbial DNA and protein synthesis.[3,5] Moreover, AzA is endowed with anti-inflammatory and antioxidant properties: it acts as a "free radical scavenger" attenuating the toxic effect of reactive oxygen species (ROS), known as chemical mediators of inflammation, and inhibits hydroxy and superoxide radical production by neutrophils.[5] In addition, it shows anti keratinizing and depigmenting effects with a reduction in the size and number of keratohyalin granules and tonofilament bundles, making it even more attractive from pharmaceutical and cosmeceutical perspectives.[6,7]

Syndiotactic polystyrene (sPS) is a commercial thermoplastic polymer, able to form nanoporous crystalline (NC) structures, known as δ and ϵ,[8] characterized by isolated nanocavities and nanochannels, respectively. These NC structures can enclose different molecules inside their crystalline lattices leading to the formation of hundreds of co-crystalline (CC) phases.[9–23] Based on properties of active molecules that can be included inside cavities or channels of δ and ϵ NC phases, such as antimicrobial,[18,22] fluorescent,[13,15,24] photoreactive,[25] magnetic,[14] and thanks to the ease of realizing polymeric products in different morphologies such as films,[26–29] gels,[30–33] aerogels,[34–39] or staple fibers[40] many possible uses and fields of application for sPS materials can be developed.

Recently, studies on the formation of CC phases of sPS with molecules presenting antimicrobial properties have been performed.[22,41,42] In particular, we reported that δ and ϵ phases are able to include hexanoic[41] and benzoic[42] acid guest molecules as isolated or as hydrogen-bonded molecules, in their nanocavities or nanochannels, respectively. Moreover, empty crystalline channels of ϵ phase are also able to host long aliphatic carboxylic acid molecules as well as dicarboxylic acid molecules, such as adipic acid.[43]

In the present work, we have turned our attention to molecules of dicarboxylic acids such as azelaic acid, a small molecule of pharmaceutical interest, to evaluate its possible incorporation into NC δ and ϵ phases to obtain AzA/sPS CC phases. Our analysis is based on axially stretched sPS films, which have been characterized by Polarized Fourier Transform Infrared (FTIR) and Wide-Angle X-ray diffraction (WAXD) analyses. The understanding of possible interactions between guest molecules and host polymeric phases is crucial to design AzA/sPS loaded systems, which may be considered for the manufacturing of transdermal patches useful for medical applications.

V. Covelli, A. Cozzolino, C. Daniel, P. Rizzo
Dipartimento di Chimica e Biologia "A. Zambelli" and INSTM Research Unit
Università degli Studi di Salerno
Via Giovanni Paolo II, 132, Fisciano 84084, Italy
E-mail: acozzolino@unisa.it; prizzo@unisa.it
V. Covelli
Dipartimento di Farmacia
Università degli Studi di Salerno
Via Giovanni Paolo II, 132, Fisciano 84084, Italy
M. Rodriquez
Dipartimento di Farmacia
Università degli Studi di Napoli
Via Domenico Montesano, 49, Napoli 80131, Italy

The ORCID identification number(s) for the author(s) of this article can be found under https://doi.org/10.1002/masy.202300069

DOI: 10.1002/masy.202300069

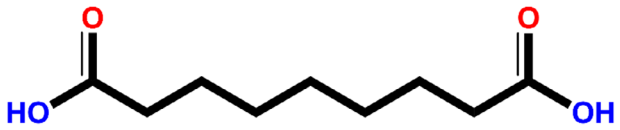

Figure 1. Chemical structure of azelaic acid (nonanedioic acid).

2. Results and Discussion

Axially stretched sPS films, with a thickness of 80–120 μm, presenting γ, NC δ and ϵ phases have been prepared, as described in the experimental section, and characterized by WAXD patterns and FTIR measurements. WAXD patterns and related equatorial profiles of sPS films showing γ, δ and ϵ crystalline phases, are shown in **Figure** 2A, B, C and in Figure 2A′, B′, C′, respectively. In particular, WAXD patterns presenting equatorial peaks at $2\theta = 9.3°$ and 10.4° indicate the presence of the dense crystalline γ phase (Figure 2A and A′); patterns showing equatorial peaks at $2\theta = 8.7°$ and at $2\theta \approx 10°$ indicate the presence of the triclinic NC δ phase[44] (Figure 2B and B′), whereas patterns presenting equatorial peaks at $2\theta = 6.9°$ and 8.2° indicate the existence of the orthorhombic NC ϵ phase[8] (Figure 2C and C′).

Sorption experiments on these films in AzA/ethanol solutions using different concentrations, soaking times, and temperatures have been performed. FTIR spectra of sPS films presenting γ, δ, and ϵ phases, before (black curves) and after immersion in a 30 wt% AzA/ethanol solution at 60°C (colored curves) are reported in **Figure** 3. The presence of AzA molecules in sPS films is clearly evidenced by peaks in the carbonyl stretching region (1750–1680 cm^{-1}) as well as by the broad band in the OH region (3200–2400 cm^{-1}). As apparent in Figure 3B, sorption of AzA molecules in sPS films exhibiting dense crystalline γ phase is negligible (< 0.3 wt%).

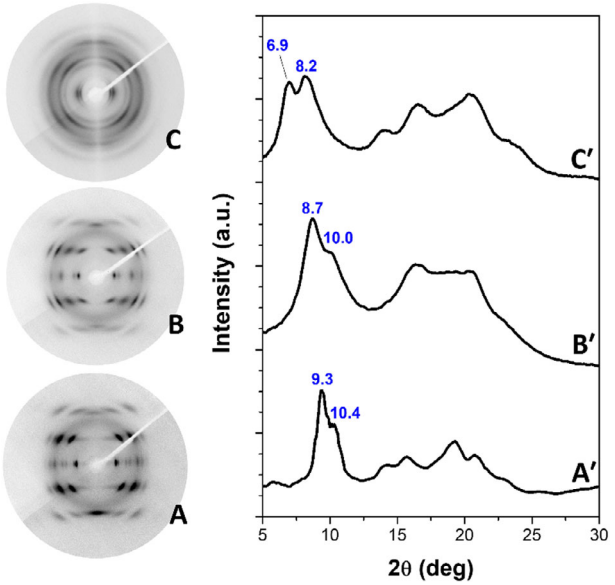

Figure 2. WAXD patterns of axially stretched sPS films exhibiting γ (A, A′), δ (B, B′) and ϵ (C, C′) crystalline phases: (A–C) 2D patterns; (A′–C′) equatorial profiles of the 2D patterns.

Even in the case of δ form films, AzA sorption in the same condition has been ineffective, only increasing the soaking time up to ≈60 h, an AzA uptake of ∼0.6 wt%, evaluated by thermogravimetric analysis (TGA), has been obtained (Figure 3C). AzA sorption in NC ϵ film, on the contrary, leads to an AzA uptake close to 1 wt% after 8 h of soaking (pink line, Figure 3D) and this value increases up to 3 wt% after 60 h (red line, Figure 3D). FTIR spectrum of AzA powder is also reported as a reference in Figure 3A. The faster and selective uptake of dicarboxylic acids in the crystalline channels of ϵ sPS films clearly indicates that AzA molecules can be hosted in the empty crystalline channels of the ϵ phase whereas they are instead absorbed much more slowly and only in the amorphous phase of sPS films presenting dense γ or NC δ phases.

In detail, looking at the FTIR spectra (Figure 3), it is apparent that AzA molecules present a broad band in the carbonyl region at 1693 cm^{-1} of the powder spectrum (Figure 3A) that is shifted at 1709 cm^{-1} if AzA molecules are absorbed into γ, δ and ϵ films. Moreover, an extra narrow peak appeared at 1739 cm^{-1} in the FTIR spectrum of ϵ film (Figure 3D), which was not present in the AzA FTIR spectrum (Figure 3A). The latter carbonyl peak might be associated to isolated AzA molecules enclosed inside ϵ CC phase, whereas the carbonyl peak at 1709 cm^{-1} could be related to hydrogen-bonded AzA molecules, respectively. A broad hydroxyl band at 3200–2400 cm^{-1} is also clearly shown.[45]

The ratio evaluated between the FTIR intensity of the aggregated guest peak (I_{1709}) and of the isolated guest peak (I_{1739}) was close to 2.0, meaning that, despite the low amount of AzA molecules absorbed in sPS ϵ film, most of them are aggregated species.

Polarized FTIR spectra of axially oriented sPS γ, δ and ϵ films, after AzA sorption, have been performed (**Figure** 4).

It is evident that for ϵ form film (FTIR spectrum C, Figure 4) the peaks at 1739 cm^{-1} and 1709 cm^{-1} as well as the broad band at 3200–2400 cm^{-1} are dichroic, indicating the presence of either isolated or aggregated AzA molecules inside the ϵ channels. On the contrary, the absence of dichroism for the FTIR peak at 1709 cm^{-1} as well as the broad not dichroic band at 3200–2400 cm^{-1} (labeled as n.d.) in the axially stretched δ form film (FTIR spectrum B, Figure 4) proves that aggregated AzA molecules are simply dissolved in the amorphous phase of δ form film. This is probably due to the large molecular volume of AzA molecules ∼217 $Å^3$, which is too big to be enclosed in crystalline δ nanocavities. The same AzA peaks are not dichroic also in the γ form film (FTIR spectrum A, Figure 4), due to the distribution of the molecules only in the amorphous phase.

The orientation factor of the host polymer has been evaluated on the peak at 572 cm^{-1} (Figure 4), it is positive and close to $S_h \approx 0.8$, indicating an orientation of polymer chain axes of the crystallites being preferentially parallel to the stretching direction. Dichroism measurements of the carbonyl stretching vibrational peaks at 1709 and 1739 cm^{-1} have been also evaluated, the negative values ($S_{g,1709} = -0.07$; $S_{g,1739} = -0.14$) indicate a preferential perpendicular orientation of C = O bonds of AzA molecules with respect to the crystalline polymer chain axis. It is certainly worthy of remark that the orientation factor can be equal to zero for random crystallite orientation, while it is equal to +1 and −0.5 for orientation of all polymer chain axes of the crystallites being parallel and perpendicular to the stretching direction, respectively.

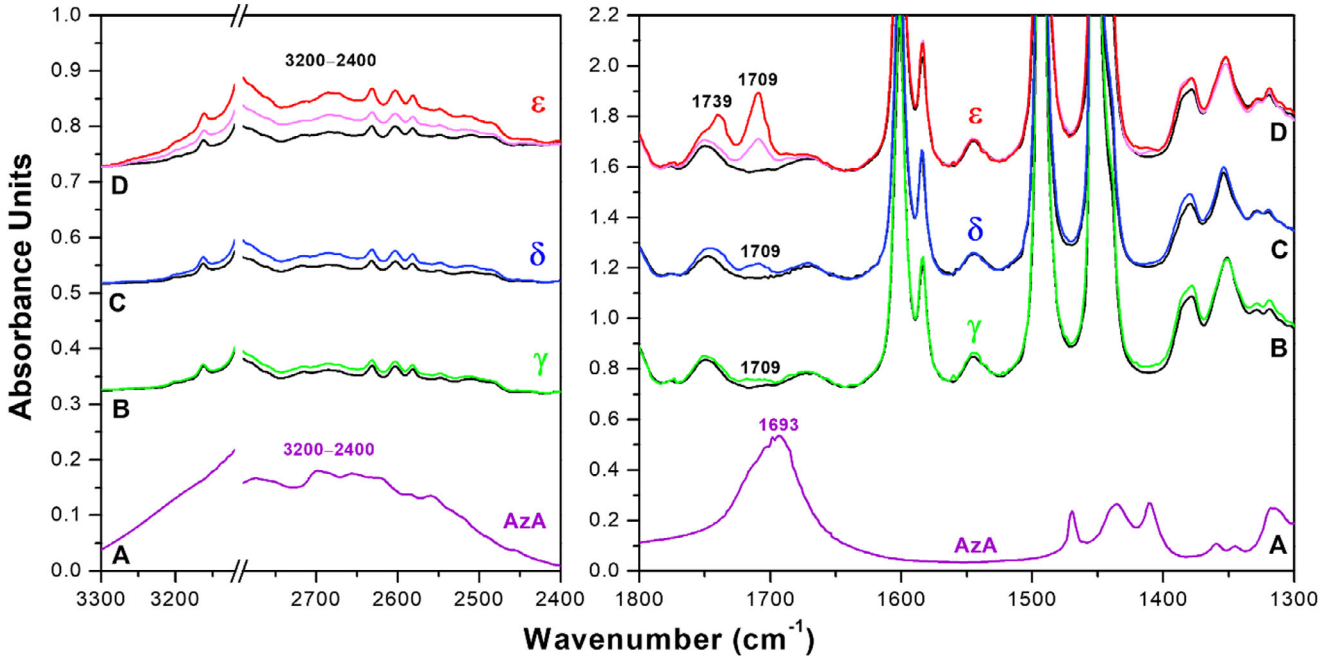

Figure 3. FTIR spectra in the ranges 1300–1800 and 2400–3300 cm^{-1} of sPS films, before (black lines) and after (colored lines) immersion in a 30 wt% AzA solution in ethanol at 60°C for 60h: B) γ form (60 h); C) δ form (60 h); D) ϵ form (8 h, 60 h). An FTIR spectrum of solid AzA as a reference is reported in (A).

As for the hydroxyl stretching region, the dichroism value of the vibrational broad band at 3200–2400 cm^{-1} is positive ($S_{g,2514}$ = +0.10), indicating in this case a preferential orientation of O–H bonds parallel to the crystalline polymer chain axis. The orientations of the double-bonded carbonyl and the hydroxyl groups might be attributed to the parallelism of the aliphatic chains (in their transplanar conformation) of AzA molecules, with respect to the chain axes of the ϵ crystalline phase, that brings O–H and C = O groups preferentially parallel and perpendicular to the polymer chain axis, respectively.

Finally, WAXD patterns of the axially oriented ϵ form films before and after AzA sorption are shown in **Figure 5**. It is noticeable that, after AzA molecule sorption, the intensities of lower angle (110) and (020) diffraction peaks at $2\theta = 6.9°$ and 8.2° have been reduced with respect to the intensity of the first-layer line reflections (mainly that one at $2\theta \approx 20.2°$), as usually observed when the inclusion of guest molecules in the NC ϵ phase occurs.[46] Hence, WAXD pattern (Figure 5) confirms the inclusion of AzA molecules in the sPS ϵ channels, leading to the formation of the corresponding CC phase; whereas, as expected WAXD analysis

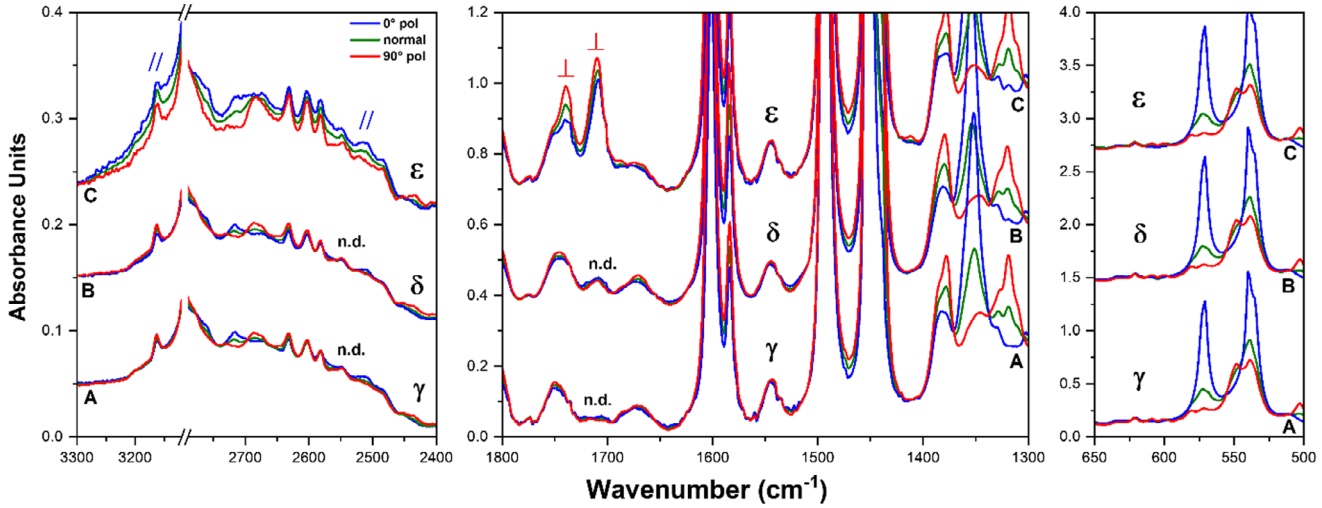

Figure 4. Unpolarized (green lines) and polarized FTIR spectra as taken with polarization plane parallel (blue lines) and perpendicular (red lines) to the film stretching direction, in the spectral ranges 650–500, 1300–1800 and 2400–3300 cm^{-1}, of axially oriented sPS films exhibiting γ phase (A), δ (B) phase and ϵ (C) CC phase after immersion in 30 wt% AzA/ethanol solution for 60 h at 60°C. (n.d. = not dichroic).

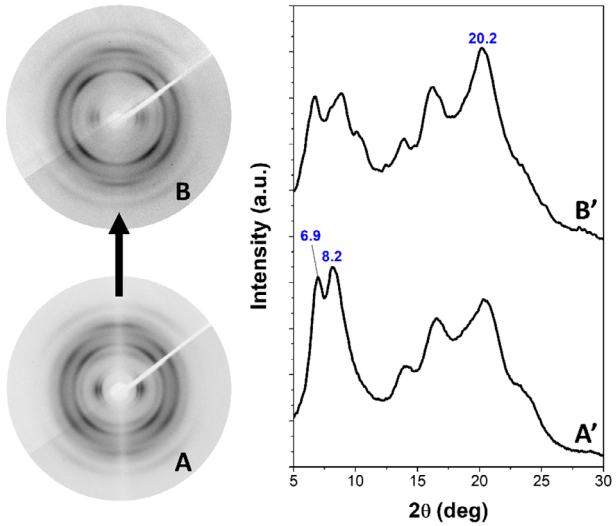

Figure 5. WAXD patterns of axially oriented sPS film exhibiting ϵ form, before (A) and after (B) AzA uptake from 30 wt% AzA/ethanol solution for 60 h at 60 C. (A, B) Equatorial intensity profiles of both 2D patterns are shown on the right part of the Figure.

of the axially oriented sPS films in δ and γ form before and after AzA uptake (not shown here) is unaffected.

In conclusion, a schematic representation of isolated as well as hydrogen-bonded AzA molecules hosted in the crystalline sPS ϵ channels is shown in **Figure** 6A and B, respectively. Here it is well visible the orientation of O–H and C = O groups preferentially parallel and perpendicular to the polymer chain crystalline axes, respectively, as suggested by polarized FTIR measurements.

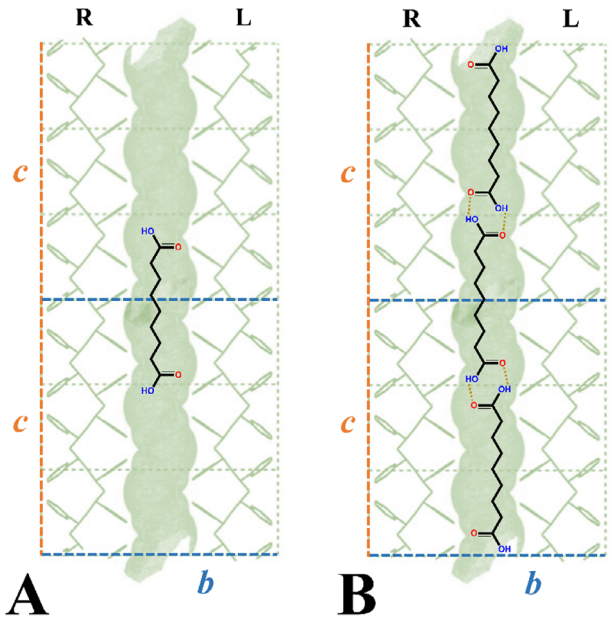

Figure 6. Schematic representation of isolated (A) and H-bonded (B) AzA molecules in the crystalline channels of the sPS ϵ form. The orientation of O–H and C = O groups are preferentially parallel and perpendicular to the polymer chain crystalline axes, respectively, as established by polarized FTIR measurements.

3. Conclusion

Sorption studies of AzA molecules in axially oriented sPS films have shown that only nanochannels present in ϵ NC phase are able to host AzA molecules leading to CC phases. AzA molecules are accommodated in these channels both as isolated and aggregated species, whereas they are simply dissolved in the amorphous phase of the NC δ or of dense γ phases. Due to the presence of two carboxylic groups at the end of the aliphatic chain, the aggregation of AzA molecules hosted in the crystalline sPS ϵ phase leads to the formation of hydrogen-bonded species in the channels, where O–H and C = O groups are preferentially parallel and perpendicular to the polymer chain axis, respectively.

AzA claims a well-established role in the treatment of acne and other cutaneous hyperpigmentary disorders, thanks to its anti-inflammatory, antimicrobial, anticomedonal, antikeratinizing, antioxidant, and depigmenting properties. Therefore, it is reasonable to consider and perform further investigations on AzA sorption and release from sPS fibers, which might be thought of as a part of transdermal patches useful for medical and cosmeceutical topical applications.

4. Experimental Section

Materials: Azelaic acid, solvents, and reagents were purchased from Merck KGaA (Darmstadt, Germany) and used without further purification. Syndiotactic polystyrene (Xarec 90ZC) was supplied by Idemitsu (Tokyo, Japan) and is characterized by a content of syndiotactic triads higher than 98%. The average molecular weight is M_w = 140 kg mol^{-1}, with polydispersity M_w/M_n = 2.0.

Amorphous sPS films were obtained by a blown extrusion process using a melt temperature of 290°C. Axially oriented amorphous films were obtained by stretching amorphous films with a dynamometer INSTRON 4301 (Norwood, MA, USA) at 105°C, up to a draw ratio of 4.0. Axially oriented films showing NC δ phase were obtained by immersion of axially stretched amorphous films in dichloromethane at room temperature for 3 h and subsequent guest removal by acetonitrile sorption for 3 h. Axially oriented films with the dense γ form were obtained from axially oriented NC δ films by treatment at 170°C for 1 h. Axially oriented films presenting NC ϵ phase were obtained by immersion of the axially oriented γ film for 1 h in chloroform followed by immersion in acetonitrile for 3 h.

Thickness of all δ, γ, and ϵ sPS films was in the range of about 80–120 μm.

Methods: FTIR spectra of axially oriented films were collected at 2.0 cm^{-1} resolution and 32 scans in the wavenumber range 4000–400 cm^{-1} by a Vertex 70 Bruker spectrometer (Billerica, MA, USA), equipped with deuterated triglycine sulfate (DTGS) detector and a Ge/KBr beam splitter. Polarized infrared spectra were recorded by using a SPECAC 12000 wire grid polarizer. The solid AzA was incorporated into KBr (spectroscopic grade) and pressed into a pellet with 2 wt% acid content for FTIR analysis.

Sorption of AzA in δ, γ, and ϵ sPS films was performed using 30 wt% AzA/ethanol solution at 60°C for 8 h and 60 h (ϵ), and 60 h (γ and δ).

TGA scans were performed with a TG 209 F1 *Netzsch* (Oberfranken, Bavaria, Germany) at a rate of 10°C min^{-1} in the temperature range of 25–350°C.

WAXD patterns of the axially oriented films were collected by an automatic Bruker diffractometer (Billerica, MA, USA), by using nickel filtered CuKα radiation. WAXD patterns combined with polarized FTIR spectra of axially oriented films provide relevant information about guest inclusion in CC phases and mutual orientation between polymer and guest molecules.

Evaluation of the degree of crystallinity (X_c) of the films was calculated by an FTIR spectral subtraction procedure according to the following formula $K = (I/I')(1–Xc)$,[42] where K is the subtraction coefficient, I and I' are

the thickness of the sample and of an amorphous reference film, considering the conformationally insensitive peak (at 1601 cm^{-1}).

The degree of crystallinity of all sPS semicrystalline films of this paper is in the range of 25–35%.

The order parameters of the guest molecules (S_g) as well as of the host crystalline polymer chains (S_h) were calculated by the formula:

$$S_{g/h} = (R - 1) / (R + 2) \quad (1)$$

where $R = A_{//}/A_{\perp}$ is the dichroic ratio and $A_{//}$ and $A_{\perp}$ are absorbances of a peak of guest molecules in polarized FTIR spectra, for polarization plane being parallel and perpendicular to the film stretching direction, respectively.

The molecular volume of the guest molecules was evaluated by the following equation:

$$V_{guest} = M/\rho NA \quad (2)$$

where M is molecular mass, ρ is density and NA is the Avogadro's number (6.02×10^{23} molecules/mol).

Acknowledgements

Financial support of "Ministero dell'Università e della Ricerca" (MUR) is gratefully acknowledged. Prin2020 (2020EZ8EPB) are gratefully acknowledged.

Conflict of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Keywords

azelaic acid molecules, co-crystalline polymer phases, FTIR spectra, WAXD patterns

Received: March 21, 2023
Revised: November 22, 2023

[1] A. Panyosak, J. Manosroi, Y. Rojanasakul, A. Manosroi, *Hum. Exp. Toxicol.* **2009**, *28*, 387
[2] H. Liu, H. Yu, J. Xia, L. Liu, G. J. Liu, H. Sang, F. Peinemann, *Cochrane Database of Syst. Rev.* **2020**, https://doi.org/10.1002/14651858.CD011368.pub2
[3] M. A. Sieber, J. K. E. Hegel, *Skin Pharmacol. Physiol.* **2014**, *27*, 9
[4] W.-H. Hung, P.-K. Chen, C.-W. Fang, Y.-C. Lin, P.-C. Wu, *Pharmaceutics* **2021**, *13*, 410
[5] A. Todea, C. Deganutti, M. Spennato, F. Asaro, G. Zingone, T. Milizia, L. Gardossi, *Polymers* **2021**, *13*, 4091
[6] S. Jacobus Berlitz, D. De Villa, L. A. Maschmann Inácio, S. Davies, K. C. Zatta, S. S. Guterres, I. C. Külkamp-Guerreiro, *Drug Dev. Ind. Pharm.* **2019**, *45*, 642
[7] T. Searle, F. R. Ali, F. Al-Niaimi, *J. Dermatolog. Treat.* **2022**, *33*, 722
[8] G. Guerra, C. Daniel, P. Rizzo, O. Tarallo, *J. Polym. Sci. B Polym. Phys.* **2012**, *50*, 305
[9] P. Musto, P. Rizzo, G. Guerra, *Macromolecules* **2005**, *38*, 6079
[10] S. Malik, C. Rochas, M. Schmutz, J. M. Guenet, *Macromolecules* **2005**, *38*, 6024
[11] S. Malik, C. Rochas, J. M. Guenet, *Macromolecules* **2006**, *39*, 1000
[12] C. Daniel, A. Avallone, P. Rizzo, G. Guerra, *Macromolecules* **2006**, *39*, 4820
[13] H. Itagaki, T. Sago, M. Uematsu, G. Yoshioka, A. Correa, V. Venditto, G. Guerra, *Macromolecules* **2008**, *41*, 9156
[14] A. R. Albunia, C. D'Aniello, G. Guerra, D. Gatteschi, M. Mannini, L. Sorace, *Chem. Mater.* **2009**, *21*, 4750
[15] P. Rizzo, T. Montefusco, G. Guerra, *J. Am. Chem. Soc.* **2011**, *133*, 9872
[16] K. Furukawa, T. Nakaoki, *Soft Materials* **2011**, *9*, 141
[17] R. C. Jose, P. Shaiju, B. Nagendra, E. B. Gowd, *Polymer* **2013**, *54*, 6617
[18] A. R. Albunia, P. Rizzo, G. Ianniello, C. Rufolo, G. Guerra, *J. Polym. Sci. Part B: Polym. Phys.* **2014**, *52*, 657
[19] P. Shaiju, E. B. Gowd, *Polymer* **2015**, *56*, 581
[20] S. Sato, T. Kawaguchi, F. Kaneko, *Macromol. Symp.* **2016**, *369*, 114
[21] H. Kobayashi, S. Akazawa, O. Urakawa, F. Kaneko, T. Inoue, *Macromolecules* **2018**, *51*, 8611
[22] P. Rizzo, A. Cozzolino, G. Guerra, *Macromolecules* **2019**, *52*, 2255
[23] T. Sano, H. Ebihara, S. Sano, T. Okabe, H. Itagaki, *Eur. Polym. J.* **2020**, *138*, 109975
[24] T. Sano, A. Uchiyama, T. Sago, H. Itagaki, *Eur. Polym. J.* **2017**, *90*, 114
[25] A. R. Albunia, P. Rizzo, M. Coppola, M. De Pascale, G. Guerra, *Polymer* **2012**, *53*, 2727
[26] P. Rizzo, A. R. Albunia, G. Milano, V. Venditto, G. Guerra, G. Mensitieri, L. Di Maio, *Macromol. Symp.* **2002**, *185*, 65
[27] C. D'Aniello, P. Rizzo, G. Guerra, *Polymer* **2005**, *46*, 11435
[28] P. Rizzo, E. Lepera, G. Ianniello, G. Guerra, *Macromolecules* **2014**, *47*, 2616
[29] P. Rizzo, A. Cozzolino, A. R. Albunia, A. M. Giuffrè, V. Sicari, L. Di Maio, C. Daniel, V. Venditto, M. Galimberti, G. Mensitieri, G. Guerra, *J. Appl. Polym. Sci.* **2018**, *135*, 46256
[30] S. Malik, C. Rochas, J. M. Guenet, *Macromolecules* **2005**, *38*, 4888
[31] A. N. Khan, M. Schmutz, J. Lacava, A. Al Ouahabi, T.-T.-T. Nguyen, P. J. Mesini, J.-M. Guenet, *Langmuir* **2015**, *31*, 7666
[32] P. Raut, W. Liang, Y.-M. Chen, Y. Zhu, S. C. Jana, *ACS Appl. Mater. Interfaces* **2017**, *9*, 30933
[33] P. S. Gotad, N. Kafle, T. Miyoshi, S. C. Jana, *Langmuir* **2022**, *38*, 13558
[34] C. Daniel, D. Alfano, V. Venditto, S. Cardea, E. Reverchon, D. Larobina, G. Mensitieri, G. Guerra, *Adv. Mater.* **2005**, *17*, 1515
[35] C. Daniel, S. Longo, R. Ricciardi, E. Reverchon, G. Guerra, *Macromol. Rapid Commun.* **2013**, *34*, 1194
[36] S. J. Kim, S. C. Jana, *Polymer* **2017**, *126*, 432
[37] S. J. Kim, P. Raut, S. C. Jana, G. Chase, *ACS Appl. Mater. Interfaces* **2017**, *9*, 6401
[38] V. G. Krishnan, A. M. Joseph, S. Kuzhichalil Peethambharan, E. B. Gowd, *Macromolecules* **2021**, *54*, 10605
[39] A. Kulkarni, S. C. Jana, *Polymer* **2021**, *212*, 123125
[40] A. Cozzolino, P. Rizzo, C. Gallo, R. Bianchi, C. Daniel, G. Guerra, *Polymer* **2021**, *228*, 123908
[41] A. Cozzolino, G. Monaco, C. Daniel, P. Rizzo, G. Guerra, *Polymers* **2021**, *13*, 3330
[42] A. Cozzolino, G. Monaco, P. Rizzo, G. Guerra, *Polymers* **2022**, *15*, 177
[43] A. Cozzolino, S. Pappalardo, P. Rizzo, G. Guerra, *Polymer* **2022**, *262*, 125484
[44] M. R. Acocella, P. Rizzo, C. Daniel, O. Tarallo, G. Guerra, *Polymer* **2015**, *63*, 230
[45] A. Nattkemper, T. Schleiden, J. M. Migliavacca, T. Melin, *Chem. Eng. Technol.* **2003**, *26*, 881
[46] O. Tarallo, M. M. Schiavone, V. Petraccone, C. Daniel, P. Rizzo, G. Guerra, *Macromolecules* **2010**, *43*, 1455