

# Poly(aspartic acid) in interpolymer complex with biomedical applications

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The study investigates the interactions in interpolymer complex based on poly(aspartic acid) known as a nontoxic, biocompatible and biodegradable polymer and a film-forming synthetic polymer, doped with silver nanoparticles with a wide antibacterial spectrum. There is a great potential in utilizing these blends in many domains such as biopharmaceutical preparations (drug delivery systems, percipients in tablets). The intervened interactions between the different components of the system are evaluated through dynamic rheology and FTIR spectroscopy.

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## 1. Introduction

Polymer-polymer complexation has attracted extensive attention in the past 2 decades. Interactions between two polymers may lead to the formation of an interpolymer complex (IPC), which essentially possesses properties entirely different from the component polymers. A large number of systems that form interpolymer complexes are known and they have already found wide applications in technology and medicine [1-4]. Except for stereocomplexes formed due to the van der Waals force and spatial fitting of chain conformations of the components, interpolymer complexes can be formed by intermolecular secondary binding forces, such as Coulombic interaction and hydrogen bonding, etc. Tsuchida et al. [5] reviewed the formation, structure, and properties of the intermacromolecular complexes, especially the polyelectrolyte complexes. The appeared interactions contribute to the stabilization of IPC. Very often they act in concert, and it is difficult to ascertain the true mechanism of the interactions and to assess the relative contribution of each force. Most of the hydrogen bonding complexes reported in the literature is composed of water-soluble polymers in aqueous media [5-10].

In our laboratory, it is of particular interest to study interpolymer complexes via hydrogen bonding as an extension of studies on the synthesis of new polymeric materials with biomedical applications. Our previous works reported the interpolymer complexation realized in the system poly(aspartic acid) / poly(acrylic acid) or poly(aspartic acid) / poly(vinyl alcohol) as polymeric matrices [11] and poly(aspartic acid) / poly(acrylic acid) subsequently doped with silver nanoparticles [12]. This kind of complexation in solution was clearly explored and confirmed by the dynamic rheology technique, FTIR and DSC studies.

In the present study, the methods we used in the previous papers are extended to the system poly(aspartic acid) / poly(vinyl alcohol) / silver with a wide antibacterial spectrum. This approach may be outlined because of our

interest in identification the specific interactions of low molecular weight silver nanoparticles with synthetic water – soluble polymers in aqueous solutions, in an interpolymer complex with potential biomedical applications.

## 2. Experimental

### Materials and IPC preparation

Poly(aspartic acid) (PAs) is synthesized by thermal polymerization of aspartic acid, at the temperature between 160 and 260 °C, time 1–4.5 h, with phosphoric acid as catalyst. It has  $M_w = 15,110$  and polydispersity  $= 1.317$ . Poly(vinyl alcohol) (PVA) of  $M_w = 120,000$  Da is purchased from Oriental Chemical Ind. Korea and is used as received.

The complex PAs / PVA is prepared by direct mixing for 60 min of the stock solutions of the same concentrations – 1 g/dL - in different ratios (% vol). The PAs / PVA % vol ratios of 1 g/dL solution are: 0/100; 25/75; 50/50; 75/25 and 100/0. Thus, the total polymer concentration in the mixture was maintained constant during each experiment.

The IPC PAs / PVA: 50 / 50 % vol is silver doped in two concentrations: Ag1-  $0.98 \times 10^{-3}$  % and Ag2-  $2.49 \times 10^{-3}$  % against polymer, by mixing for 60 min. All the measurements are done 5 min after the mixing, to allow IPC realization and thermal equilibrium to be reached.

### Rheological testing

The dilute aqueous solutions of the components and their mixtures in different ratios were tested with a Bohlin CVO rheometer equipped with a Peltier device for temperature control.

The measurements were performed by using parallel-plate geometry. Both plates are from stainless steel, with a gap of 0.5 mm, the upper plate having the radius of 30 mm. 2 ml of the mentioned solutions were poured on the

lower plate of rheometer, for each determination. The experiments as a function of composition are realized at physiological temperature  $37 \pm 0.1^\circ \text{C}$  for small amplitude rheological tests, at a frequency ( $\omega$ ) of 0.1 rad/sec and shear stress ( $\sigma$ ) of 1 Pa. Previous frequency sweep tests established the correctness of the all experiments within the linear viscoelastic range of oscillatory deformation.

### FTIR spectroscopy

The polymer films are characterized using Fourier Transform Infrared Spectroscopy (FTIR) experiment [31] on a spectrophotometer DIGILAB Scimitar Series-USA, with  $4 \text{ cm}^{-1}$  resolution; it was kept constant the amount of polymer (5 mg) in the KBr tablet (500 mg).

### 3. Results and discussion

Poly(aspartic acid) as biodegradable water-soluble alternative to poly(acrylic acid) currently in use, has been sought by scientists trying to improve the environmental acceptability of water-soluble scale controlling agents, sequestrants and dispersants that ultimately reach the environment (generally via the surface water). At the same time, in biomedical applications attention has been paid to polyaspartic acid's potential as a useful clinical nephroprotectant [13]. Thus, it is reported the effect of poly-L-aspartic acid on the pharmacokinetics of gentamicin, by reducing clinical, histopathological, and in vitro indices of aminoglycoside-induced cytotoxicity.

Poly(vinyl alcohol) is water soluble, nontoxic, highly hydrophilic with a wide industrial applications, and most importantly good film forming. It was studied as a material for biomedical applications [14], too.

Silver is well known for bactericidal activity [15-17] based on the inactivation of the bacterial proteins. Silver-doped materials are chemically durable and release silver ions for a long period of time [18].

Conformational characteristics and mobility of PAs macromolecules allow to form intermolecular hydrogen-bonds with both water and poly(vinyl alcohol) (PVA) [19]. The intermolecular hydrogen-bonding is formed at the side-chains of poly(aspartic acid) and affects no main-chain conformation, but it strongly affects the dynamics of PAs macromolecules. The carboxylic groups of the side-chains play an important role for the formation of intermolecular hydrogen-bonding between PAs and PVA. This implies that the mobility of the side-chain carbons is obviously changed from the slow motion region to the extreme motion region over a wide range of temperatures. The interactions established in the system PAs / PVA at 50 / 50 % vol doped with silver at the two concentrations are evidenced by dynamic rheology.

The elastic  $G'$  and viscous  $G''$  moduli, complex viscosity  $\eta^*$  and loss tangent  $\tan \delta$  are represented in Fig 1a,b,c,d, for polymers as well as of their mixtures doped with silver.

In these figures, the difference between the experimental viscosity of the mixture and an "ideal value" is the criterion for the compatibility or association of the

three components in aqueous solution [20, 21]. The ideal value (dashed lines in Fig. 1) is designed to the system in the absence of specific interactions between the components.

Any deviation from the ideal value indicates interactions between components; a negative deviation points up the formation of an interpolymer association with a compact structure while a positive deviation is representative for a gel-like association [22].

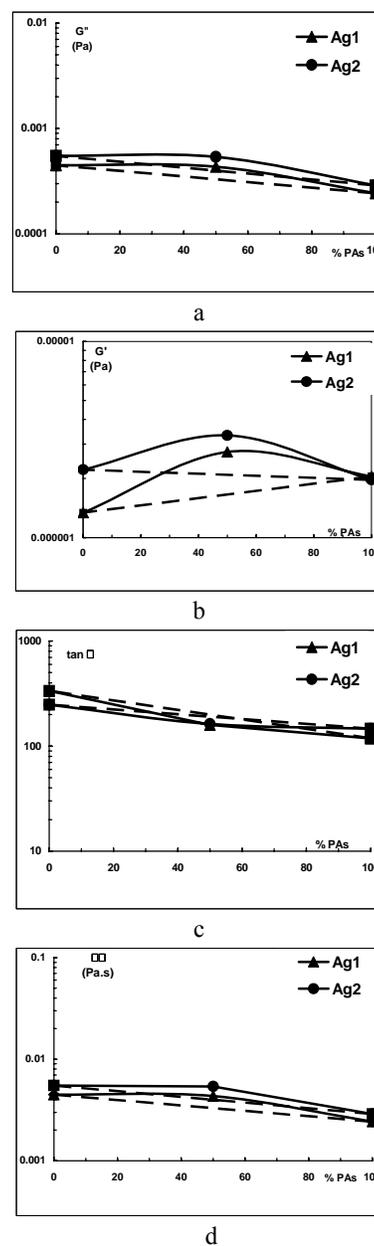


Fig. 1. PAs / PVA / silver interpolymer complex dynamic rheological data: a - Elastic modulus  $G'$ ; b - Viscous modulus  $G''$ ; c - Complex viscosity  $\eta^*$ ; d - Loss tangent  $\tan \delta$ . The dashed lines are for the corresponding additive dependencies. Ag1-  $0.98 \times 10^{-3} \%$  and Ag2-  $2.49 \times 10^{-3} \%$  against polymer.

The curves  $G'$ ,  $G''$  and  $\eta^*$  indicate slight positive deviations from the ideal additive. For both concentrations of silver,  $G'$  has too small values and the samples displayed no elastic response (Fig. 1a), while the viscous behaviour represented by  $G''$  is slight dominant (Fig. 1b).

$\tan \delta$  as ratio  $G''/G'$  (Fig. 1d), underlines these differences from the ideal, through small negative deviation.  $\eta^*$  (Fig. 1c) shows positive deviation of the experimental values from the additive dependence, as a measure of the formation of IPC's.

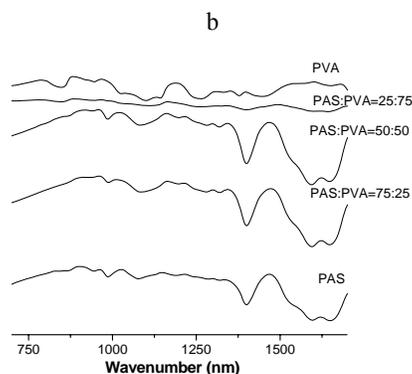
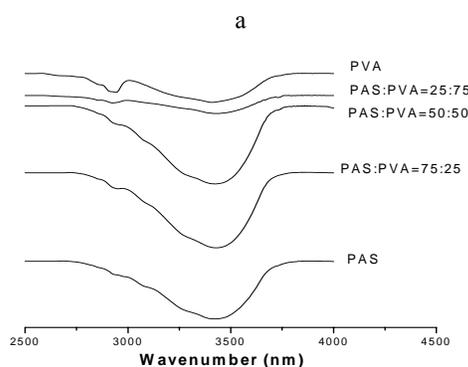
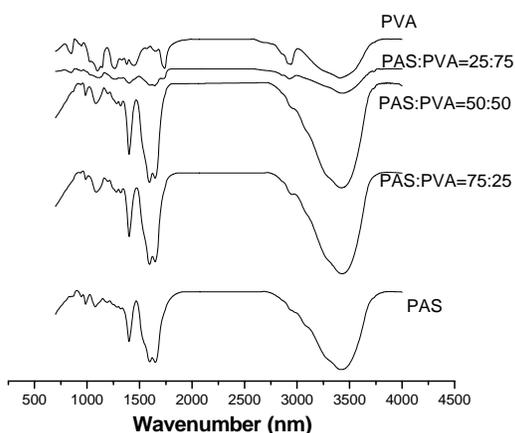


Fig. 2. FTIR spectra of: a- interpolymer complex with different Pas/PVA ratio; b-2500 - 4500  $\text{cm}^{-1}$  region for -OH stretching; c - 1500  $\text{cm}^{-1}$  region for carbonyl shifts.

In order to perform spectral characterization, the interpolymer complex is dried under vacuum. The FTIR spectra of films prepared from mixtures of Pas and PVA solutions with different ratio of Pas / PVA are shown in Fig. 2a. The spectrum of the polycomplex is characterized by the presence of the bands typical for both components confirming their complexation within one compound. The characteristic absorption bands of PAs are located at frequencies 3300, 3080  $\text{cm}^{-1}$  (peptidic link), 1710  $\text{cm}^{-1}$  (CO from carboxylic group), 1550  $\text{cm}^{-1}$  (in succinimide), while those of PVA are located at 3348, 1144  $\text{cm}^{-1}$  (-OH groups of PVA), 2940 (asymmetric stretching of -CH<sub>2</sub>) and 2909  $\text{cm}^{-1}$  (symmetric stretching of -CH<sub>2</sub> groups). The spectra evidenced a shifting of characteristic bands because of two competitive phenomena appeared between the two partners in interpolymer complex. Thus, FTIR spectra in the 2500 - 4500  $\text{cm}^{-1}$  region (O-H stretching) (Fig. 2b) show the shifting of nonassociated hydroxyl group from 3640  $\text{cm}^{-1}$  to 3437  $\text{cm}^{-1}$  assigned to associated -OH. Characteristic band for carbonyl shifts from 1730  $\text{cm}^{-1}$  to 1716  $\text{cm}^{-1}$  in FTIR spectra in 1500  $\text{cm}^{-1}$  region (Fig. 2c), because of their implication in H-bonds. This phenomenon is evidenced in connection with complexation by other authors, too [23-25].

#### 4. Conclusions

PAs/PVA interpolymer complexes (IPC) doped with silver were prepared through the established hydrogen bonds by mixing their aqueous solutions. Dynamic rheology and FTIR spectroscopy underline the interaction between the components into the IPC and their miscibility. These complexes are investigated as structures with microbial resiliency by doping with silver, with the aim of biomedical applications.

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