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Separation of statistical poly[(N-vinyl pyrrolidone)-co-(vinyl acetate)]s by reversed-phase gradient liquid chromatography

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ABSTRACT

Although size exclusion chromatography (SEC) has been used successfully to determine the molecular weight distribution (MWD) of statistical poly[(N-vinyl pyrrolidone)-co-(vinyl acetate)]s [PVPVAs], SEC cannot separate the copolymers according to their chemical composition. In this article, the separation of commercial PVPVAs with varying chemical compositions is reported, by aqueous reversed-phase gradient liquid chromatography (RPLC) using polystyrene-divinylbenzene-based wide pore columns. RPLC–SEC cross-fractionation indicates the presence of molar mass dependant effects during RPLC separation due to broad MWD for the copolymer studied; therefore the width of the RPLC peak could not be associated entirely with chemical composition distribution of the copolymer. Coupling of RPLC with online FTIR spectroscopy reveals the increase of VA content with increasing THF gradient, an indication of interaction mechanism between VA repeating units and the stationary phase for water soluble PVPVAs. Separation of water insoluble PVPVAs and PVAs by the RPLC are possibly based on both interaction and precipitation/redissolution mechanisms.

1. Introduction

Copolymers of N-vinyl pyrrolidone-vinyl acetate or PVPVAs are commercially important products. Depending on their chemical composition and molecular weight (MW), these products can find wide applications in various fields such as cosmetic and pharmaceutical industries [1,2]. Size exclusion chromatography has been used successfully to characterize the molecular weight distribution of these products, but revealed no information on their chemical composition [3].

Chemical composition characterization of synthetic polymers by column HPLC was first reported in 1979 by Teramachi et al. for p(S-co-MA) [4]. Since then, a great variety of polymers, including polymer blends, statistical copolymers, and graft copolymers, have been characterized by HPLC techniques [5–16]. HPLC methods could provide not only average chemical composition like other conventional methods (e.g. NMR, FTIR, UV–vis, Titration, etc) do, but also chemical composition distribution (CCD), which is directly related to manufacturing process and product performance. To the best of our knowledge, separation of PVPVAs by eluent gradient reversed-phase HPLC has never been reported.

In the present work, separation of commercial PVPs, PVPVAs, and PVAs is studied by using aqueous gradient reversed-phase HPLC with wide pore polystyrene supports. The usefulness of the HPLC method is exemplified in quantifying (<1 wt%) homo-polymer contamination such as PVP in the PVPVAs.

2. Experimental part

2.1. Materials

Samples of commercial PVPVA copolymers were obtained from *International Specialty Products* (Wayne, NJ), and their molecular weight by SEC method [3] and composition data are summarized in Table 1. Fig. 1 also illustrates an overlay of SEC traces for PVPVAs and PVP homopolymers. The PVP K-30, K-60, and K-90 PVP homopolymers were provided by *International Specialty Products* (Wayne, NJ). The PVA homopolymers were obtained from *Acros Organics* (Fair Lawn, NJ) and *Polysciences Inc* (Warrington, MA). Molecular weights of PVP by SEC method [3] and PVA by providers are listed in Table 2. All HPLC solvents were used as received from *Thermo-Fisher Scientific* (Waltham, MA).

2.2. Measurements

HPLC separations were performed on Waters Alliance 2695 Module with a column heater at 35 °C. Photodiode array detector PDA 996 (Waters) and Waters 2424 evaporative light-scattering detector (ELSD) were coupled sequentially to the HPLC instrument. The ELSD nebulizer was heated at 75% power level, with drift tube at

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Table 1
Weight-average molecular weight, polydispersity (PD), and chemical composition of commercial VP–VAc copolymers.

PVP/VA	Lot #	% Solid (in ethanol)	Composition (VP/VA, w/w)	Mw (relative to PEO)	PD
E-335	05700182778	48.9	30/70	23,800	3.9
E-535	05700183001	48.6	50/50	36,200	4.3
E-635	05700193585	48.9	60/40	45,100	4.9
E-735	05800204923	51.4	70/30	39,800	4.1

SEC Conditions: 1.0 mg/ml, 50 μl injection, Shodex OHPak SB806MHQ (4.6 × 250 mm, 10 μm, 5 μm), 0.5 ml/min, run time 30 min, H_2O/MeOH 50/50 with 0.1 M LiNO3, RI detector (see Ref. [3] for other details).

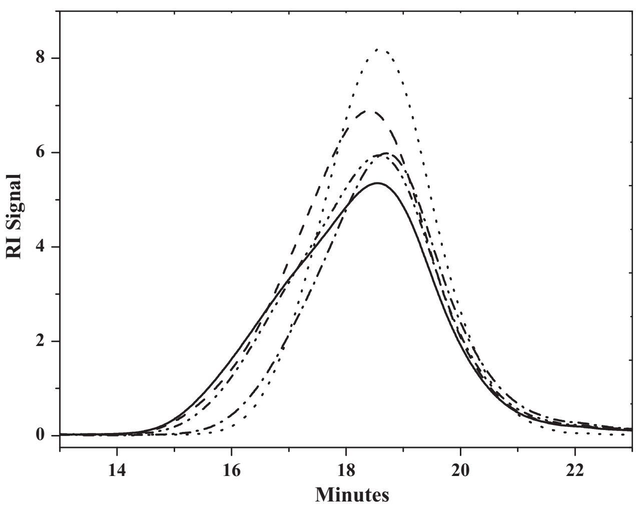

Fig. 1. Overlaid SEC chromatograms for PVP K30 (. . .), E-335 (– – –), E-535 (–··), E-635 (–), E-735 (–·–). SEC Conditions: Shodex OHPak SB806MHQ (8.0 × 300 mm, 13 μm), H_2O/MeOH 50/50 with 0.1 M $LiNO_3$, 0.5 ml/min, run time 30 min, 1.0 mg/ml, 50 μl injection, RI detector (see Ref. [3] for more details).

75 °C, and nitrogen pressure at 50 psi. Data acquisition and process were performed with *Empower* software. The HPLC column used was polystyrene-divinylbenzene-based PLRP-S columns (Polymer Laboratories, now a part of Agilent Technologies). Linear mobile phase gradient (5–75% THF in water over 5 min, 75% THF isocratic for 3 min, for a 50 × 4.6 mm column) with a flow rate of 1.0 ml/min was used for all gradient separations. The HPLC samples were prepared as 0.1 ∼ 0.2 wt% solution in HPLC grade water, except THF for PVA and 20 wt% THF aqueous solution for E-335. Full sample recovery was confirmed by absence of any ELSD peak from a blank injection of pure THF after each sample injection. HPLC with online FTIR detector was performed on a *DiscovIR-LC* system by *Spectra Analysis Inc* (Marlborough, MA). The nebulizer of *DiscovIR* was set at 15–18 W with carrier gas at 400 cc, disk speed at 3 mm/min, disk temperature at −5 °C, pressure chamber/cyclone at 3.2/160 torr, condenser (single) temperature at 0 °C, and cyclone temperature at 170 °C. The VA mol% of the samples was based on peak heights at 1740 cm^{-1} (for VA) and 1680 cm^{-1} (for VP), as well the VP/VA molar IR absorptivity ratio (1.22) determined from PVPVA standards with known compositions.

Table 2
Weight-average molecular weight and polydispersity (PD) of PVP and PVAc.

Sample	Provider	Lot #	Mw (relative to PEO)	PD
PVP K30	ISP	#05900219368	24,930	2.7
PVP K60		#03700177552	127,710	4.6
PVP K90		#03700186201	703,770	5.1
PVAc1	Acros Organics	#A0251821	170,000[a]	N.A.
PVAc2	Polysciences	#519165	90,000[a]	N.A.

[a] Relative to PS standards.

3. Results and discussion

PVPVA copolymers are amphiphilic due to hydrophilic VP repeating units and hydrophobic VA repeating units. The copolymers are water soluble except very hydrophobic copolymers with high VA content (e.g. E-335 with 70 wt% VA). These properties make PVPVAs excellent candidates for traditional aqueous gradient RPLC which utilizes mainly enthalpic interactions between small molecular solutes and stationary phases. Initial RPLC trials with C8/C18-based wide-pore silica columns were unsuccessful, possibly due to H-bond interactions between VP units in the copolymers and residual silanol groups in the stationary phase. Therefore we switched to silanol-free polystyrene (PS) based RPLC columns. Wide pore (1000 Å or 4000 Å) packing was chosen to minimize the SEC effects and maximize the contact between the VP–VA copolymers (hydrodynamic radius ∼10 nm) and packing surface. A water/THF gradient was used, since water is a weak RPLC solvent, while THF is a strong and displacing RPLC solvent, in addition to its good solubility for PVPs, VP–VA copolymers, and PVAs.

Fig. 2 presents an overlay of RPLC traces for PVP K30, E-735, E-635, E-535, E-335, and PVA homopolymers, using a polystyrene-based RPLC column (PLRP-S from Polymer Labs) and H_2O/THF gradient. Unlike their SEC traces with no separation (Fig. 1), the current RPLC method demonstrates separation between homopolymers and copolymers with varying chemical compositions (Fig. 2). PVP homopolymer without any VA content elutes at 2.2 min, indicating that there are weak interactions between VP repeating units of the polymer and PS stationary phase (V_0 = 0.8 min for the 50 × 4.6 mm column used). The retention increases to 3.2 min for 30 wt% VA (E-735), and to 3.8 min for 50 wt% VA (E-535). The increase of VA content in the copolymers increases interac-

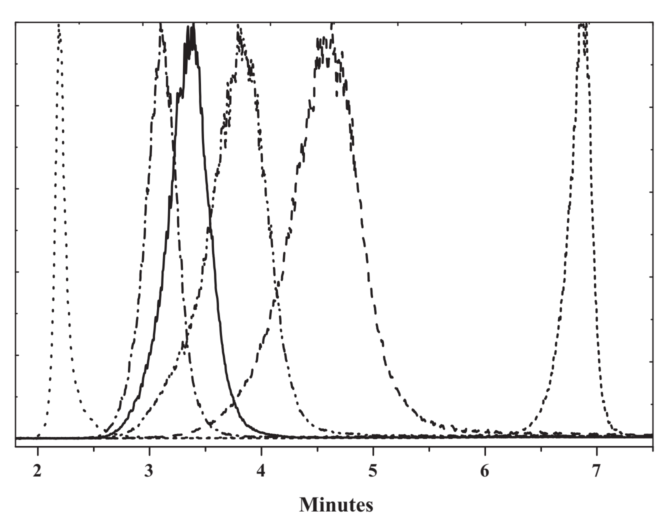

Fig. 2. Normalized overlaid RPLC chromatograms of PVP K30 (. . .), E-335 (– – –), E-535 (–··), E-635 (–), E-735 (–·–) and PVA (—, short dash). Column: PLRP-S; 1000 Å; 5 μm; 50 × 4.6 mm. Eluent: THF/H_2O, 1.0 mg/ml (sample concentration), 20 μl (injection volume), 1.0 ml/min, THF/H_2O gradient from 5/95 to 75/25 linearly in 5 min followed by 75/25 isocratic for 3 min.