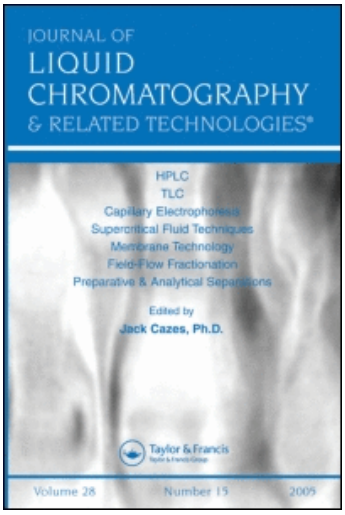

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[a] International Specialty Products, Wayne, New Jersey

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Analysis of Residual Vinyl Pyrrolidone Monomer in Polyvinylpyrrolidone with a Mixed Mode Separation, using a Fast Gel Permeation Chromatography Column

Laurence Senak, James Cullen, Paul Suszczynski, Adriene Malsbury, Lawrence Feeley, Chi-san Wu, Michael Tallon, and Edward Malawer

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Abstract: The technique of high throughput or fast gel permeation chromatography was used to separate and quantify residual vinyl pyrrolidone monomer present in polyvinyl pyrrolidone polymer (PVP) and in a copolymer of vinyl pyrrolidone and vinyl caprolactam [P(VP/VCL)]. The chromatography exploits both size-exclusion and adsorption modes of separation. This methodology offers a single step analysis for residual vinyl pyrrolidone monomer as compared to multistep and time-consuming reverse-phase chromatography measurements, yielding similar results. Fast GPC and reverse-phase analyses are quantitatively compared and reported using both typical industrial and European Pharmacopeia methodologies for HPLC. The results of this study demonstrate that fast gel permeation chromatography presents a viable option to traditional reverse- phase chromatography in the quantitative analysis of residual vinyl pyrrolidone monomer.

Keywords: Fast gel permeation chromatography, Gel permeation chromatography, Polyvinyl pyrrolidone Residual monomer, Reverse phase liquid chromatography, Size exclusion chromatography, Vinyl pyrrolidone

Correspondence: Dr. Laurence Senak, International Specialty Products, 1361 Alps Road, Wayne, NJ 07470, USA. E-mail: lsenak@ispcorp.com

INTRODUCTION

The use of a mixed mode or multi-modal separation approach in chromatography is growing in acceptance, particularly in the areas of biological metabolite and peptide separations. Among the most common mechanism combinations are reverse phase and ionic in nature. Typical examples of separations across a broad span of applications include the separation and purification of a peptide (*N*-acetyl-Ile-Glu-Gly-Arg-*p*-nitroanilide) from its side products by reverse phase and weak anion exchange chromatography,[1] the isolation of uridine diphosphoglucuronosyltransferase by C_{18} and anion exchange chromatography,[2] and the purification of plant hormones auxin and abscisic acid with a mixed mode reverse phase, anion exchange solid phase extraction coupled to two dimensional chromatography.[3] Additionally, amphipathic alpha helical peptides had been separated with mixed hydrophilic interaction, cation exchange chromatography,[4] while a C_8, cation exchange mixed mode solid phase extraction has been used for the isolation of the cycloxygenase II (COX II) inhibitor.[5] While reverse phase ion exchange combination techniques grow in acceptance, mechanisms such as size exclusion chromatography, however, would unlikely be thought of as a promising candidate for mixed mode methodology for instance in monomer, polymer separations.

In recent years the advent of fast size exclusion chromatography (SEC) or gel permeation chromatography (GPC) has been introduced as a high throughput method for the fast and efficient separation of macromolecules. Fast GPC, as applied to biological separations, has been practiced for many years in the technique of FPLC (Fast Protein Chromatography). Unlike microbore HPLC, fast GPC is limited by the size of the pores available in the chromatographic stationary phase, and therefore is differentiated only from analytical GPC by the dimensions of the chromatographic column. Examples of fast GPC in the literature for polymer analysis are growing. This technique has been used to characterize polyolefins for the prediction of flow properties.[6] It has also been utilized for at-line determination of the conversion of polystyrene polymerization reactions.[7]

While the above studies focused on the traditional use of GPC, namely the determination and quantitative analysis of a molecular weight distribution of a polydisperse polymer, they typically ignored the elution of low molecular weight species such as unreacted monomer at or after the chromatographic total permeation point in the chromatography. In the course of experimental work intended to support the development of an aqueous size exclusion chromatography method for the determination of the molecular weight distribution of poly(vinylpyrrolidone),[8,9] it was noticed in our laboratory that a peak continued to appear at a retention time beyond the total permeation point in the separation.

This was unexpected since in a true SEC separation, which is governed strictly by entropic effects, there should be no impurity that elutes beyond this point unless a mixed mode separation is involved. It was suspected that the unknown peak was due to residual vinyl pyrrolidone monomer. This was, in fact, confirmed by standard addition. Therefore, under appropriate stationary phase conditions, GPC has the potential to separate vinyl pyrrolidone monomer from the polymer and solvent regions of the chromatogram and determine its concentration quantitatively in the sample. In fact, fast GPC represents an elegant means of separating and analyzing residual monomer (and other small non-polymer molecules) from the principal polymeric species. This is an extremely important measurement, since assurance that the residual monomer is reduced to a de minimis and safe level is essential to the use of polymers produced by the free radical route, particularly in personal care and pharmaceutical applications.

The analysis of residual vinyl pyrrolidone monomer (VP) in polyvinyl pyrrolidone (PVP) by reverse phase HPLC is well established and documented in the U.S., European, and Japanese Pharmacopoeias.[10–12] While reverse phase HPLC is both a specific and sensitive tool in the quantification of VP, this methodology requires either the use of molecular weight cut-off filters to separate the polymer from low molecular weight species such as residual monomer, or a back-flush technique to avoid exposing the analytical column to the polymer (as recommended in the United States, Japanese (JP), and European Pharmacopoeias (EP)), and therefore requires a relatively long overall analysis time. In fact, either approach typically requires nominally two hours of total analysis time. (It should be noted that gas chromatography (GC) is not considered an optimal methodology for trace levels of monomer due to the possibility of polymer degradation to the monomer in the instrument injector port, as well as the relative insensitivity of the GC's flame ionization detector versus that of the LC's UV detector.)

The use of high speed GPC eliminates the need for either molecular weight cut-off filters or column back-flushing. It significantly reduces analysis time from traditional GPC by virtue of a reduced column dimension without a significant loss of column resolution for the monomeric species. The high speed GPC size separation excludes the polymeric portion of the sample by the expected entropic size exclusion mechanism while retaining the residual VP monomer by an enthalpic mechanism (i.e., adsorption), ensuring that the monomer elutes well after the chromatographic total permeation point in the chromatograph. The residual monomer is then well resolved from the polymer matrix, as well as other low molecular weight species, and readily quantified. This method is elegant in its simplicity and reduces sample preparation and/or analysis time significantly.

The present study demonstrates the utility of high speed GPC in the quantification of residual vinyl pyrrolidone monomer in industrial grade polyvinyl pyrrolidone (K-90 and K-30 grades), and provides a quantitative comparison between the method of fast GPC and the method of the European Pharmacopoeia for the trace analysis of residual vinyl pyrrolidone in pharmaceutical grade polyvinyl pyrrolidone (Povidone K-90 and K-29/32 grades). The HPLC approach in the industrial grade comparison utilizes molecular weight cut-off filters, while the HPLC method in the pharmaceutical grade fast GPC to HPLC comparison uses the back-flush HPLC methodology as specified in the EP.

Finally, the method of fast GPC is also studied for a copolymer of vinyl pyrrolidone/vinyl caprolactam [P(VP/VCL)] in the range of 1 to 1,000 ppm.

EXPERIMENTAL

Materials

HPLC grade water and methanol, as well as sodium phosphate, dibasic monohydrate (99+%) were purchased from Aldrich (Milwaukee, Wisconsin). Solvents were further purified using a Kontes filter degassing apparatus 0.45 μm filters. Vinyl pyrrolidone polymer (PVP K-90 and K-30) and vinyl pyrrolidone/vinyl caprolactam copolymers (technical grade), as well as high purity vinyl pyrrolidone and vinyl caprolactam monomers, were provided by International Specialty Products (Wayne, NJ). Millex-HQ, 0.45 μm syringe filters used with disposable filters and Centricon SR-3 molecular weight cut-off centrifuge filters were purchased from Millipore (Bedford, MA).

Fast GPC and Reverse Phase HPLC Quantitative Analysis

For fast GPC analysis, the LC system was composed of a Waters 2695 Separation Module equipped with a column heater box and Waters 484 Tunable Absorbance Detector set at 235 nm. The fast GPC column employed for PVP homopolymer was a Shodex Asahipak GF-310 GPC column of 8 mm ID × 150 mm length (note that this is a custom column), with a mobile phase of Water/Methanol (80/20, v/v) with 0.1 M sodium hydrogen phosphate (dibasic). For the VP/VCL copolymer a Shodex SB802.5 HQ-8D column of 8 mm ID × 150 mm length was employed. The mobile phase in this case was composed of 0.1 M sodium hydrogen phosphate (dibasic) in a mixture of 90% water and 10% methanol. The flow rate utilized in both analyses was 1.0 mL/minute. The injection

volume was 100 μL and the polymer solution concentration was typically prepared to be 0.2% (w/v) in the chromatographic mobile phase using 25 mL volumetric flasks. The temperature of the experiment was maintained at 30°C using a Waters column heater box, and data was captured and processed using Waters Millenium software. All samples were filtered before injection with a Millipore 0.45 μm Millex-HQ syringe filter and a 5 mL syringe. Retention volumes for pure vinyl pyrrolidone or vinyl caprolactam monomers were measured by injecting 1.0 ppm of monomer standard solutions onto the GPC column. Standard solutions ranging from 0.01 ppm to 1.0 ppm were injected onto the system to determine both linear range and detection limits of the experiment. System pressure should not exceed 1200 psi. Typical analysis time was twenty minutes.

The reverse phase HPLC analysis was also performed with a Waters 2695 Separation Module equipped with a column heater box, and Waters 484 Tunable Absorbance Detector set at 235 nm. The HPLC column employed was a HP LiChroCART Superspher 60 RP-Select B, 250 mm × 2 mm, with a Superspher 60 RP Select B, 10 mm × 2 mm guard column. The mobile phase was 80% methanol to 20% water, v/v. The mobile phase flow rate was 0.25 mL/minute and column temperature set at 40°C. The injection volume was 5 μL, and analysis time for each injection was nominally 15 minutes. Sample preparation for the reverse phase HPLC method was accomplished by pipetting a solution made from 0.2 grams of polymer (weighed to the nearest 0.1 mg), dissolved in methanol, and brought to volume in a 10 mL volumetric flask, then transferred into a Millipore Centricon-3 molecular weight cut-off filter. The samples were centrifuged in a 45 degree fixed angle rotor running at 2,500 G-forces and refrigerated at 10°C. The samples were centrifuged until a minimum of 0.3 mL was collected. As in the case of fast GPC, data was collected and processed using Waters Millenium software.

Reference Solution Preparation

Reference solutions for both chromatographic methods were produced the same way with the exception that the reverse phase HPLC solutions were prepared in pure methanol, whereas the fast GPC method reference solutions were prepared using the chromatographic mobile phase. Preparations of 1000 ppm stock solutions of vinyl pyrrolidone and vinyl caprolactam monomers were made by weighing 0.1 gram of monomer into 100 mL volumetric flasks and diluting to volume. A set of serial dilutions was then performed using 10 and 50 mL volumetric pipettes with 100 mL volumetric flasks. Resulting standard reference monomer concentrations produced were 1.0, 0.5, 0.1, 0.05, and 0.01 ppm. After incorporating to the dilution factor resulting from the sample

preparation, this reference standard range would correlate to a 0.5 to 100 ppm range in a diluted sample.

European Pharmacopeia Methodology

HPLC analyses that were performed by the European Pharmacopeia monograph require a backwash as described in the Version 5.2 update.[11] The analyses were performed on the above mentioned HPLC system. The methodology employed both a Phenomenex Luna guard column (30×4 mm) and analysis column (250×4 mm) packed with 100Å C_{-18} stationary phase. The mobile phase was acetonitrile/water, 10/90, v/v. The flow rate was 1.4 mL/minute (or adjusted to provide approximately 10 mL of elution time for VP). Sample preparation was the same as the preceding HPLC experiment. After injecting 50 μL of sample solution onto the system and waiting 2 minutes, the precolumn was back flushed with the mobile phase at the same flow rate applied to the analysis for 30 minutes. The UV detector setting was 235 nm.

RESULTS AND DISCUSSION

As in any form of HPLC quantitative analysis, one must establish the linearity of the analyte, in this case the measurable residual monomer in the fast GPC chromatographic experiment. Standard solutions containing from 0.01 ppm through 1.0 ppm of VP were analyzed. As described above, this correlated to 0.5 ppm to 100 ppm VP in a sample based on a 0.2% concentration sample preparation. A multipoint external standard calibration not forced through the origin, plotting the peak area versus concentration, resulted in a linear correlation coefficient of 0.9999. The multipoint calibration curve and the equation are displayed in Figure 1. The response factor is linear only from 0.01 to 1.0 ppm, which corresponds to 1 through

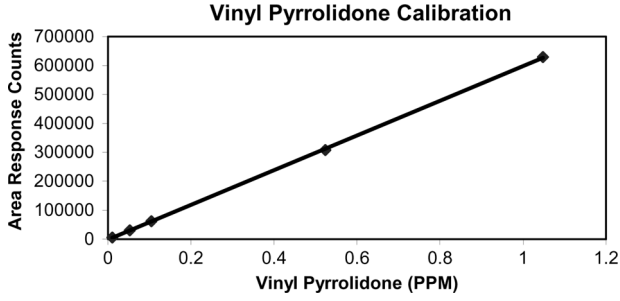

Figure 1. Calibration of vinyl pyrrolidone monomer using UV detection.

100 ppm in a sample. If a sample contains up to 200 ppm of VP it must be diluted to 0.1 wt.% and reanalyzed to provide a linear result. Higher VP containing samples would have to be similarly diluted.

The chromatogram for the elution of residual vinyl pyrrolidone for the polyvinyl pyrrolidone (K-90) polymer by fast GPC is displayed in Figure 2. (An example of a reverse phase HPLC chromatogram for the quantification of VP in PVP K-90 is provided as Figure 3.) The elution volume of the residual VP peak in the fast GPC chromatogram displayed in Figure 2 was 14.5 minutes, leaving the residual VP peak separated from the polymeric species by over 6 minutes, and the total permeation peak or system peak in the chromatogram appears normally. The chromatography is consistent over the range of VP based polymers. Since a UV detector set at 235 nm (λ_{max} for VP versus 205 nm for PVP) is employed in this study, both polymer and system peaks are also minimized. The theoretical instrumental detection limit for VP in the PVP sample was determined

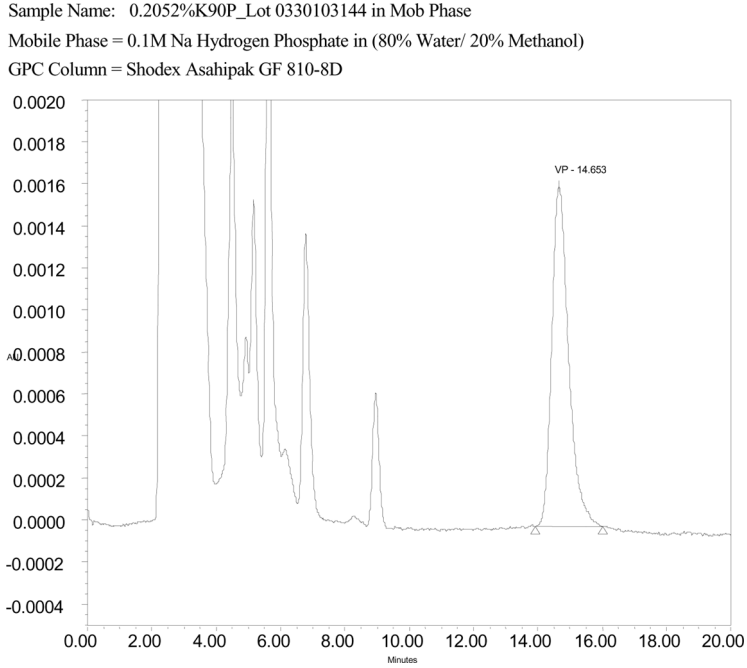

Figure 2. The chromatographic profile of residual vinyl pyrrolidone (14.5 minutes elution time) in polyvinyl pyrrolidone as separated on a Shodex Asahipak GF-310 GPC column of 8 mm ID × 150 mm length with a mobile phase of Water/Methanol (80/20, v/v) with 0.1 M sodium phosphate dibasic. The flow rate was 1.0 mL/minute.

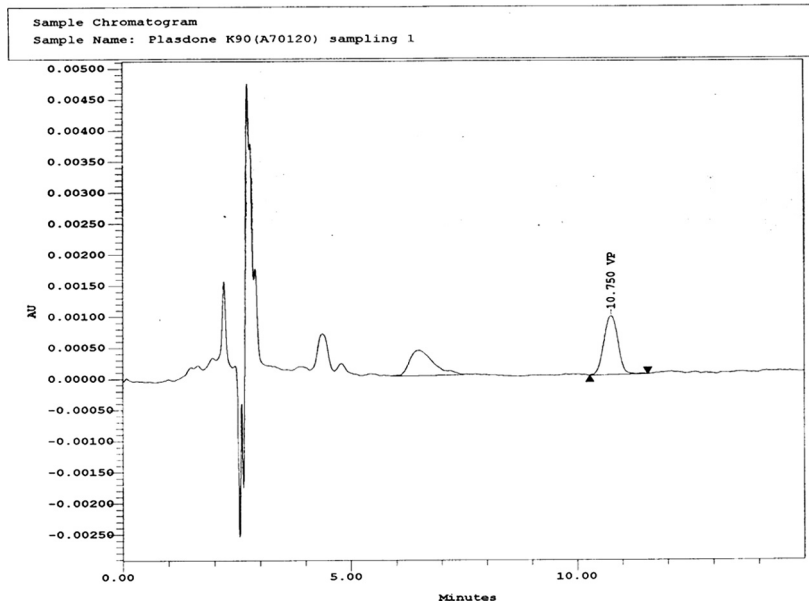

Figure 3. The reverse phase HPLC chromatographic profile of vinyl pyrrolidone in polyvinyl pyrrolidone as separated on a HP LiChroCART Superspher 60 RP-Select B, 250 mm × 2 mm, with a Superspher 60 RP Select B, 10 mm × 2 mm guard column. The mobile phase was 80% methanol to 20% water. The mobile phase flow rate was 0.25 mL/minute and column temperature set at 40°C.

to be 0.22 ppm with S/N = 3, whereas the minimum quantifiable level (S/N = 10) was determined to be 0.74 ppm using an unspiked sample.

Two important factors have been considered for system suitability in this method. They are the tailing factor (t), and the resolution (R). The first of these performance descriptions or tailing factor is easily calculated from the chromatograms using equation 1.

$$Tailing\ Factor = t = \left(\frac{peak\ width_{5\%\ peak\ height}}{2\,t_w}\right) \tag{1}$$

Where t_w is equal to the distance between the peak front and the peak apex at 5% of the peak height. From this measurement, the tailing factor of the residual vinyl pyrrolidone in Figure 2 was found to be 1.6. The second of these factors, the resolution, (R) of the fast GPC column was evaluated from the relationship:

$$Resolution = R = \frac{1.18(t_2 - t_1)}{W_{0.5,1} + W_{0.5,2}} \tag{2}$$

Table 1. Comparison of tailing and resolution characteristics for vinyl pyrrolidone monomer separations using fast GPC and traditional reverse phase HPLC

Technique	*t*	R
Fast GPC	1.2	8.9
RP HPLC	1.1	8.7

Where $W_{0.5,1}=$ the first peak width at 50% of peak height, $W_{0.5,2}=$ the second peak width at 50% peak height. Here t_1 and t_2 correspond to the retention time of two peaks of interest. An overview of these column performance descriptors is presented in Table 1. It is remarkable to observe that fast GPC and pure reverse phase chromatography are so comparable in resolution and tailing performance, since only the reverse phase column is designed expressly for small molecule separation.

A quantitative comparison for the performance of both chromatographic techniques in the analysis of vinyl pyrrolidone is presented in Table 2. This data is broken into three categories: the system precision, the sampling precision, and the spiked sample recovery. Both system and sampling precision are based upon six replicate measurements. System precision is the result of six replicate injections of the same solution in the chromatography system, while sampling precision entails six separate sample preparations and subsequent single injections of each sample solution upon the chromatographic system. Not surprisingly, system precision is slightly better than sampling precision regardless of the type of analysis. From this table, the standard deviation and relative standard deviation are quite consistent for the system precision, not presenting any clear advantage of one technique over the other in terms of their relative standard deviation. The sampling precision, does however, seem to favor the GPC technique. This is most likely due to the increased number of sample preparation steps as mentioned in the sample preparation

Table 2. Comparisons of system precision, sampling precision, and % recovery for vinyl pyrrolidone monomer in PVP K-90 and K-30 polymers using fast GPC and traditional reverse phase HPLC methodologies

Technique	System Precision			Sampling Precision			Recovery (%)	
For K-90	PPM	Std dev	% RSD	PPM	Std Dev	% RSD	% Rec.	% RSD
Fast GPC	39.7	0.20	0.50	38.9	0.26	0.66	96.6	0.48
RP HPLC	46.8	0.36	0.77	46.8	0.61	1.30	96.6	3.60
For K-30								
Fast GPC	98.9	0.53	0.54	99.04	0.83	0.84	97.5	0.79
RP HPLC	112.0	0.15	0.17	111.8	1.21	1.36	97.6	1.20

Table 3. Fast GPC vs. HPLC (European Pharmacopoeia) for residual vinyl pyrrolidone in pharmaceutical grade polyvinyl pyrrolidone (K-90 Grade)

Analysis of 5 commercial lots (PPM VP)				
Lot	EP	Fast GPC	Difference	Fast GPC 5 ppm spike
A	4.39	3.41	0.98	8.60
B	2.56	2.25	0.31	7.00
C	2.55	1.78	0.77	5.95
D	1.91	2.12	−0.21	6.40
E	2.54	1.67	0.87	6.40
Std. Dev. for Differences			0.49	
Mean of Differences			0.54	
95% Confidence Limit			1.09	

section above. (The variances for the individual steps are expected to be additive.) There appears to be equivalence in recovery between the GPC and the HPLC techniques.

An analytical data comparison between fast GPC and the European Pharmacopeia monograph chromatographic approaches for determining residual VP content in pharmaceutical grade PVP is presented for the K-90 and K-29/32 grades in Tables 3 & 4 and 5 & 6, respectively. K-90 grade data (Table 3) is presented for single samplings of five different lots of material (Labeled A–E), as well as five samplings for a single lot (A). The five lots ranged nominally from 2 to 4.5 ppm in residual VP content. The standard deviation of difference between the EP and fast GPC methodologies for the five lots was 0.49 ppm, and the mean of

Table 4. Fast GPC vs. HPLC (European Pharmacopoeia) for residual vinyl pyrrolidone in pharmaceutical grade polyvinyl pyrrolidone (K-90 Grade)

Intra-lot sampling for lot A (PPM VP)			
Sample	EP	Fast GPC	GPC-5 ppm Spike
1	4.15	3.83	8.5
2	4.11	4.00	8.5
3	3.97	3.95	8.3
4	3.90	4.28	8.4
5	2.54	3.99	8.6
Average	3.73	4.01	8.46
Std. deviation	0.68	0.17	0.11
95% CL	0.84	0.21	0.14

Table 5. Fast GPC vs. HPLC (European Pharmacopoeia) for residual vinyl pyrrolidone in pharmaceutical grade polyvinyl pyrrolidone (K-29/32 Grade) spiked with 5 PPM VP

Analysis of 5 commercial lots (PPM VP)			
Lot	EP	Fast GPC	Difference
A	4.82	4.89	0.07
B	4.85	4.87	0.02
C	4.89	4.80	−0.09
D	4.88	4.79	−0.09
E	4.66	4.93	0.27
Standard deviation for difference			0.15
Mean of difference			0.04
95% Confidence level			0.18

the difference between methods was 0.54 ppm. Intra-sampling analysis for K-90 lot A, for five replicate measurements as presented in Table 4, demonstrates a near identical VP measurement of about 4.0 ppm. Standard deviation for the EP method was 0.68 ppm while fast GPC was 0.17 ppm. A 5 ppm spike was also introduced for inter- and intra-sample statistics displaying 4–5.2 ppm recovery.

The same kind of equivalence between methodologies is displayed in Tables 5 & 6 for the K-29/32 pharmaceutical grade PVP (povidone) samples. In this case the samples studied (again labeled A–E) did not display a measurable amount of VP, so that the samples needed to be spiked with 5 ppm of VP for the sake of the experiment. For the five lots studied, the

Table 6. Fast GPC vs. HPLC (European Pharmacopoeia) for residual vinyl pyrrolidone in pharmaceutical grade polyvinyl pyrrolidone (K-29/32 Grade)

Intra-lot sampling for lot A (spiked with 5 PPM VP)		
Sample	EP	Fast GPC
1	4.34	4.81
2	4.21	4.92
3	4.33	4.91
4	4.24	4.85
5	4.21	4.87
Average	4.27	4.87
Standard deviation	0.07	0.04
95% CL	0.08	0.11

Table 7. Fast GPC vs. HPLC (European Pharmacopoeia) for residual vinyl pyrrolidone in pharmaceutical grade polyvinyl pyrrolidone (K-15 Grade)

Intra-lot sampling		
Sample	EP	Fast GPC
1	1.98	1.50
2	1.93	1.63
3	1.95	1.64
4	1.91	1.57
5	1.99	1.68
Average	1.95	1.60
Standard deviation	0.03	0.07
95% CL	0.04	0.09

standard deviation of the difference between EP and fast GPC methodologies was less than 0.15 ppm. Again, there is not a bias or trend for this difference. The statistical analysis for the single lot (A) studied with 5 replicate injections is displayed in Table 6. Here the amount of residual VP determined from the fast GPC measurement is slightly higher than the EP monograph method (although the sampling for this lot obtained with the other lots was nearly identical for both methods). Standard deviation for the replicate analyses was less than 0.1 ppm in both cases. Furthermore, Table 7 demonstrates that this technique may be extended to low molecular weight K-15 pharmaceutical grade samples. In the case of the unspiked K-15 sample displayed, the VP sample contained less than 2 ppm residual VP. While there would appear to be a slight high bias in the fast GPC data, in practical terms this amounts to less than 0.4 ppm ppm VP. From the chromatographic results of both industrial and pharmaceutical grades of PVP, which includes that of the European Pharmacopeia, comparable capability between the fast GPC and C_{-18} HPLC methods is, therefore, demonstrated.

Although the principal topic of this paper is the quantitative analysis of residual VP monomer in PVP by fast GPC, it should be noted that a peak due to the residual vinyl caprolactam monomer is visible in the fast GPC chromatogram of the VP/VCL copolymer presented in Figure 4, using the Shodex SB802.5 HQ-8D column of 8 mm ID $\times$ 150 mm length and mobile phase composed of 0.1 molar sodium hydrogen phosphate (dibasic), in a mixture of 90% water and 10% methanol (as described in the Experimental section). The resolution of the monomers is really quite remarkable when considering the similarity in molecular structure and polarity between the two monomers (see Figure 5). From the

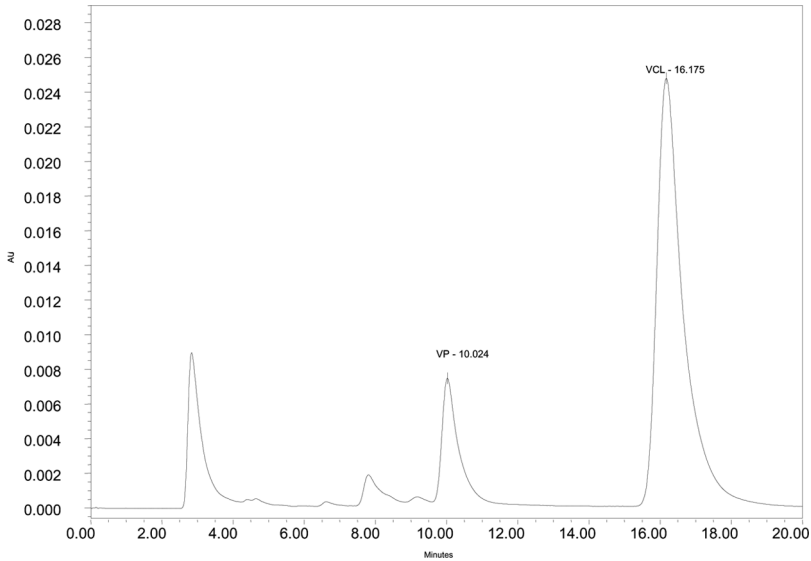

Figure 4. The chromatographic profile of residual vinyl pyrrolidone (nominally 10 minutes retention time) and residual vinyl caprolactam (nominally 16.2 minutes retention time) in a copolymer of vinyl pyrrolidone/vinyl caprolactam (as separated on a Shodex SB802.5 HQ-8D column of 8 mm ID × 150 mm length. The mobile phase used was 0.1 molar sodium hydrogen phosphate (dibasic), in a mixture of 90% water and 10% methanol, and flowed at 1.0 mL/minute.

chromatographic definitions stated above, the tailing factor (t) and resolution (R) are 1.5 and 6.9, respectively, for the vinyl caprolactam peak. For the sample examined, the system and sampling precisions are 18.1 ppm (0.9% RSD) and 48.5 ppm (2.2% RSD), respectively. The spiked sample recovery was 94% with respect to the vinyl caprolactam monomer. As this study is centered on the analysis of vinyl pyrrolidone monomer, the analysis of vinyl caprolactam was not pursued by reverse phase HPLC technique. It is demonstrated here, however, that fast GPC is also a viable option in the analysis of vinyl caprolactam, as well as vinyl pyrrolidone monomer in polymers or copolymers based upon these chemistries.

The molecular weight characterization of PVP and its copolymers has been well established and described in the literature extensively.[13] In these studies, as in any typical GPC analysis, the point of total permeation of the GPC or (size exclusion) column has traditionally been the point beyond which no additional analytical information would be derived. In fact, a typical GPC polymeric matrix designed for aqueous GPC also lends itself well to a reverse phase interaction by which the residual monomer, vinyl pyrrolidone, may be separated and quantified.

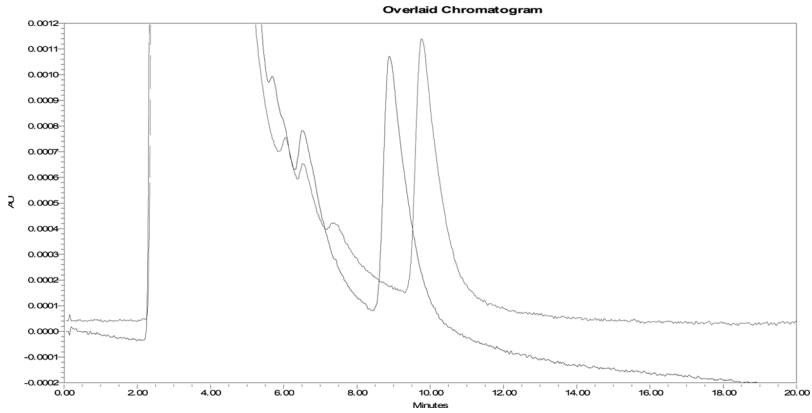

Figure 5. This figure displays the effect of mobile phase composition upon the retention volume of residual vinyl pyrrolidone. VP elutes at nominally 9 minutes (black line) in a mobile phase of 80/20, water/methanol, v/v made 0.1 molar sodium hydrogen phosphate, and at a nominal 10 minutes retention time using a mobile phase of, 90/10, water/methanol, v/v made 0.1 molar sodium hydrogen phosphate. The column was a Shodex SB802.5 HQ-8D column of 8 mm ID × 150 mm length and the flow rate was 1.0 mL/minute.

Typical reverse phase behavior is demonstrated in the overlay presented in Figure 6, wherein the polarity of the mobile phase has been altered to affect the elution time of the vinyl pyrrolidone peak. The figure displays results from the typical chromatographic solvent ratio of 90/10, water/methanol, v/v (blue line) and 80/20, water/methanol, v/v (black line) separated with the same column. As expected, the vinyl pyrrolidone elutes significantly earlier in the less polar mobile phase.

While this paper describes a study involving a Shodex Asahipak GF-310 HD 150 × 8 mm column and a Shodex SB802.5 HQ-8D 150 × 8 mm column, encouraging results have also been obtained with other columns, such as the Polymer Standards Services Suprema Linear High Speed XL column.

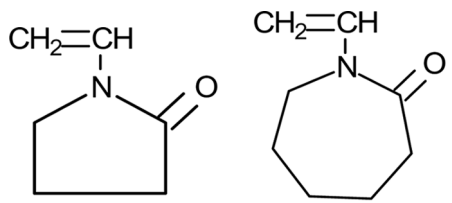

Figure 6. Molecular structures for vinyl pyrrolidone and vinyl caprolactam monomers.

CONCLUSIONS

This study demonstrates that the use of a fast GPC column presents a viable alternative to reverse phase HPLC methodology as described in monographs such as the European Pharmacopoeia, with respect to the quantitative analysis of residual vinyl pyrrolidone. Furthermore, we have shown that it provides comparable analytical results with both a significant gain in analysis time and savings in material costs for PVP manufacturers or testing laboratories, since neither a high molecular weight cut-off filter pre-column step nor a column back flushing postcolumn step are required in this method. The value of this technique becomes particularly apparent when considering the need for timely in-process analyses for residual monomer in polymer manufacturing. Since we believe that it is extendable to other vinyl monomer/polymer systems, this mixed mode chromatographic technique should often be considered as an efficient technique to separate residual vinyl monomers from macromolecular matrices for quantification.

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