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DETERMINATION OF STYRENE AND 2-VINYLPYRIDINE MONOMERS IN POLY(2-VINYLPYRIDINE–STYRENE)

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SUMMARY

Residual monomers such as styrene can be determined in polymers at microgram per kilogram concentrations by headspace techniques. However, such techniques often do not have adequate sensitivity for the determination of monomers less volatile than styrene. A method is described for the determination of trace concentrations of monomers that are less volatile than styrene and also monomers that are traditionally determined in polymers by headspace techniques. The method involves dissolution of the polymer, removal of the polymer by molecular ultrafiltration and determination of the monomer in the filtrate by gas chromatography–mass spectrometry. Concentrations of styrene and 2-vinylpyridine of less than 200 μg/kg were successfully determined in a copolymer used for the post-ruminal delivery of nutritional supplements and drugs.

INTRODUCTION

Eastman Chemicals has developed a post-ruminal delivery system for nutritional supplements and drugs based on a copolymer of styrene and 2-vinylpyridine[1–3]. Because vinyl monomers can be toxic to animals, an established manufacturing practice is to maintain the amount of residual monomer in polymers used for food applications well below levels that are considered harmful. The manufacturing specification for poly(2-vinylpyridine–styrene) requires that each monomer must not exceed a concentration of 200 μg/kg in the final polymer. Hence, a method is required for the determination of less than 200 μg/kg concentration of styrene and 2-vinylpyridine in this copolymer.

There have been several approaches to the determination of monomers in polymers[4]. The simplest approach is to dissolve the polymer in an appropriate solvent and analyze the solution by gas chromatography. This approach is not normally useful for determining low concentrations of monomers because the large amount of polymer deposited in the chromatographic system with repeated injections degrades the chromatographic separation and causes loss of sensitivity. With the present copolymer and some other vinyl polymers, the polymer that is deposited in the injection system can decompose to monomers which interfere with the analysis. For the determination

of styrene in polystyrene, a non-solvent such as methanol has been added to precipitate much of the polymer prior to analysis[5,6]. This approach has the potential disadvantage of further diluting the sample and raising the detection limit for monomers and also there is the possibility that the monomer can adsorb on the precipitated polymer. Styrene and other volatile monomers are commonly determined by headspace techniques[7–9]. This approach eliminates the disadvantages of the direct injection techniques. Detection limits of 1 mg/kg of polymer have been reported for styrene using flame ionization detection[7]. For monomers less volatile than styrene (b.p. 145°C) the detection limits increase rapidly with decreasing volatility. No methods for the determination of 2-vinylpyridine have been published.

This paper describes a method for the determination of trace amounts of monomers that have a boiling point too high to be determined with adequate detection limits by headspace techniques. This method is also applicable to the determination of volatile monomers such as styrene. The method consists in dissolving the polymer sample, removing the polymer by molecular ultrafiltration and determining the monomer in the filtrate by gas chromatography–mass spectrometry (GC–MS) using selected ion monitoring (SIM). The utility of this approach for residual monomer analysis is demonstrated by the successful development of a method for the determination of 2-vinylpyridine and styrene at the 200 μg/kg level in poly(2-vinylpyridine–styrene).

EXPERIMENTAL

Materials and equipment

Standards of styrene (99+% purity) and 2-vinylpyridine (97% purity) were obtained from Aldrich (Milwaukee, WI, U.S.A.). Acetone and methanol, obtained from Burdick and Jackson Labs. (Muskegon, MI, U.S.A.), were used without further treatment.

Polymer solutions were filtered with a Millipore (Bedford, MA, U.S.A.) molecular filtration apparatus equipped with a 62-mm Diaflo YM2 ultrafiltration membrane (Amicon, Danvers, MA, U.S.A.) with a molecular-weight cut-off of 1000. Air at a pressure of 380 kPa was used to force solutions through the membrane. The membranes were inspected visually for defects prior to use. Acceptable membranes were conditioned according to the manufacturer's instructions.

The analytical system consisted of a Hewlett-Packard (Avondale, PA, U.S.A.) Model 5890A gas chromatograph equipped with a Model 7673A autosampler and a Model 5970B mass-selective detector. Data were collected, integrated and reported with a Hewlett-Packard Model 59970C ChemStation, which also controlled the analytical instrumentation. The separation was performed on a 30 m × 0.25 mm I.D. fused-silica capillary column coated with a 0.25-μm film of DB-17 (J&W Scientific, Folsom, CA, U.S.A.). Ultra-high-purity helium (Matheson, Secaucus, NJ, U.S.A.) was used as the carrier gas at a head pressure of 70 kPa. Sample introduction was made with the Model 7673A autosampler into a split–splitless capillary inlet operated in the splitless mode. The glass insert in the splitless injector was routinely cleaned and resilylated. Silylation was performed using a 10% solution of dimethyldichlorosilane (Pierce, Rockford, IL, U.S.A.) in toluene (Burdick and Jackson), followed by immersion in methanol and toluene. The insert was then dried before installation. The

TABLE I
INSTRUMENT CONDITIONS

Parameter	*Condition*	*Parameter*	*Condition*
Initial temperature	30°C	Injector temperature	250°C
Initial time	0.6 min	Transfer line	275°C
Programming rate	30°C/min	Splitless injection period	0.6 min
Oven temperature 1	85°C	Open split interface to MSD	Set to vent 1 ml/min
Hold Time	4.0 min	Electron multiplier	700 relative
Programming rate	30°C/min	Mode	Set to selected ion monitoring (SIM)
Oven temperature 2	200°C	Resolution	Set to low for greater sensitivity
Hold time	2.0 min	SIM mass	104.00
Equilibration time	0.5 min	Dwell time	400 ms
		SIM mass	105.00
		Dwell time	400 ms

volume of injection was 5 μl. Other operating conditions are summarized in Table I. Styrene was monitored at *m/z* 104 and 2-vinylpyridine at *m/z* 105. In some samples other ions may occasionally yield better signal-to-noise ratios. These ions are summarized with their relative abundance in Table II.

Calibration

A stock solution containing 10 mg/l of each monomer was prepared in acetone–methanol (85:15, w/w). Standards of 10, 20 and 30 μg/l were prepared from this stock solution by dilution with acetone–methanol (85:15, w/w). The 10 mg/l stock solution was prepared weekly; the 10, 20 and 30 μg/l standards were prepared daily. The neat monomers were kept at −15°C and the stock solutions at 5°C during storage.

Before samples were analysed, the analytical system was calibrated by running each standard three times and averaging the area count obtained. The data were fitted to a linear calibration graph. Examples of the calibration graphs are shown in Fig. 1. A calibration standard was analysed after every ten samples and at the end of each set of samples to check for drift in the mass spectrometer response.

Sample preparation

Polymer solutions of various concentrations and polymer powders were analysed. For all sample types a polymer solution of known concentration in the range

TABLE II
APPROXIMATE RELATIVE ABUNDANCES OF MASS FRAGMENTS

Monomer	*Ion (m/z)*	*Percent of most abundant fragment*
Styrene	104	100
	103	45
	78	32
2-Vinylpyridine	105	100
	79	93
	104	55

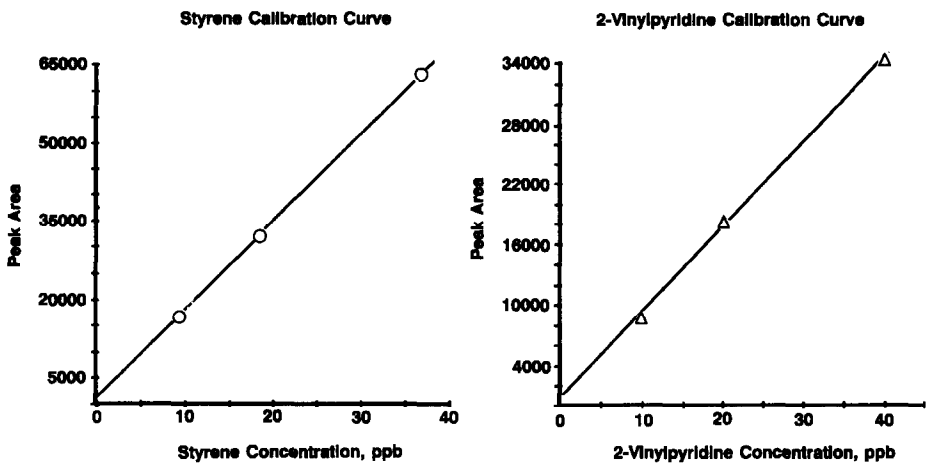

Fig. 1. Calibration graphs for the determination of styrene and 2-vinylpyridine in filtrates by SIM GC–MS. ppb = μg/l.

of 5 ± 0.5% was prepared in acetone–methanol (85:15, w/w). The filtration cell and membrane were washed by filtering 10 ml of methanol through the membrane. A 2-ml volume of the 5% polymer solution was added to the cell. The first 0.5 ml of filtrate was discarded, after which 0.5 ml of filtrate was collected in a sample vial for analysis. The vial was fitted against the filtration apparatus to avoid losses by evaporation.

RESULTS AND DISCUSSION

A method was required to ensure that polymer used to prepare rumen-protected formulations contained less than 200 μg/kg of each residual monomer. Polymer solutions more concentrated than 5% were too viscous to analyze. As the solution analyzed contains approximately 5% of polymer, the method must provide a reliable analysis of each monomer at the 10 μg/l level in the polymer solution. Preliminary work showed that the methods traditionally used for the determination of residual monomers in polymers did not provide adequate detection limits for 2-vinylpyridine. Direct injection of 5% polymer solutions was inadequate. If the polymer was precipitated prior to injection, some of the 2-vinylpyridine was absorbed by the precipitate. 2-Vinylpyridine (b.p. approximately 159°C) was not volatile enough to provide adequate detection limits by headspace techniques.

The method described provided acceptable detection limits, precision and recovery for both 2-vinylpyridine and styrene. The calibration is linear for both monomers up to a concentration of 2000 μg/l. Typical limits of detection, defined as three times the estimated standard deviation when the concentration approaches zero[10], are 1 μg/l for styrene and 2 μg/l for 2-vinylpyridine in the filtered polymer solution or 20 and 40 μg/kg, respectively, for the polymer. On several occasions the capability of the method was determined. A single polymer sample, a spiked polymer sample or a standard was analyzed 5–10 times during the course of a day by one person. At the 10 μg/l level the relative standard deviation was 5–10% for styrene and

8–13% for 2-vinylpyridine. This precision was essentially the same for monomer concentrations up to 40 μg/l. Recoveries ranged from 74 to 100% for both monomers at spiking levels of 10–40 μg/l in 5% polymer solutions.

Several steps are necessary to maximize the sensitivity and minimize interferences. As the levels of monomer detected are in the low micrograms per liter range, scrupulous care must be taken to avoid contamination of standards and solvents. Polystyrene is a ubiquitous material about the laboratory, and it typically contains significant concentrations of styrene monomer. It is essential to avoid any contact of samples with polystyrene. Bottles of solvents were analyzed before use to ensure the absence of interfering compounds. Trace levels of styrene were found in some batches of methanol and acetone. It was necessary to condition the column by repeated cycling through the temperature program to minimize the background associated with column bleeding. A non-linear response for 2-vinylpyridine indicates active sites in the system. Cleaning the injector or changing the column cured this problem. When detection limits could not be met, maintenance of the mass spectrometer source was performed, or a new column was installed.

A chromatogram for a typical sample is shown in Fig. 2. The main criteria for the choice of ions to monitor are their abundance and freedom from interferences. The molecular ions of styrene and 2-vinylpyridine are preferred. The other ions listed in Table II are of adequate intensity for this analysis, and on occasion they have been used when there were interferences. Interferences are detected by comparing the ratio of intensities given in Table II with those of the sample. Most often, the interference is an obvious broad peak in the single ion chromatogram.

For this type of analysis, three or more ions are usually monitored for each component. However, the number of ions monitored can depend on the objectives of the analysis and the kind of errors that are acceptable. For regulatory work the presence of an unacceptable concentration of some component must be confirmed with certainty. Hence, the regulatory agencies typically require three or more unique ions to be monitored in a GC–MS analysis. In production, the objective of the analysis is to ensure that the concentration of impurities in the product does not exceed the specification. The "risk" in only using one ion for analysis is that the product can be rejected if there is a positive interference for that ion. The improved sensitivity and convenience of using one ion for analysis outweighs the risk of a false positive result for this work. On the rare occasions where a positive interference was suspected the sample was analyzed again using the ions given in Table II. An analysis based on using three ions from Table II is suitable for regulatory analysis, but more effort is required to maintain adequate detection limits.

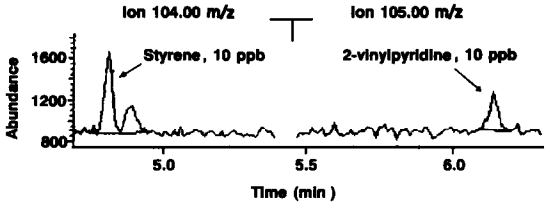

Fig. 2. Typical single-ion chromatogram obtained by SIM GC–MS analysis of the filtrate from molecular filtration of poly(2-vinylpyridine–styrene). ppb = μg/l.

The effectiveness of the filter in removing the polymer was investigated. The absorbance of the filtrate was measured at 263 nm, a wavelength suitable for measuring the aromatic components of the polymer. The absorbance measurement was calibrated against a solution of polymer of known concentration. A typical filtrate from a 5% polymer solution contained less than 20 mg/l of polymer. The effectiveness of this filtration enabled dozens of samples to be injected before the performance of the chromatographic separation was degraded.

The splitless injection mode can be the worst method for the analysis of thermally labile material owing to the high temperature needed to vaporize many samples and the relatively long residence time of the sample in the hot inlet. An investigation was made to determine if the small amount of polymer that passed through the filter could decompose in the inlet to form monomer that would interfere with the analysis. When a filtrate sample was analyzed at injection temperatures of 150, 250 and 350°C, a corresponding increase in the area of the monomer peaks was observed. However, when a 50 μg/l standard was analyzed at these injection temperatures, the area counts for styrene and 2-vinylpyridine increased in the same proportion as the area counts for the filtrate sample. This result supports the hypothesis that the observed increase in area counts is the result of physical transport processes in the injector. The increased variability of the areas at 150°C also supports this hypothesis. From these data, it is concluded that the recommended inlet temperature of 250°C did not cause detectable polymer decomposition.

CONCLUSIONS

Ultrafiltration of the polymer solution proved to be a convenient and effective means of separating monomers from the bulk of the polymer sample. We believe that this technique will prove to be generally applicable to the preparation of samples for the determination of residual monomers in polymers. The precision and accuracy of the method developed for 2-vinylpyridine and styrene meet the need for a method for monitoring polymer production.

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