S511146

Test of Schematic Flow for Safety Evaluation of Polymers

[redacted]

TORAY RESEARCH CENTER, INC.

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Abstract

1. Contents of Test

The test was carried out based on "SCHEMATIC FLOW FOR SAFTY EVALUATION OF POLYMERS". The abbreviated name of the sample is [redacted]

2. Test Method

The test is composed of the stability tests, the solubility tests in water and the organic solvents, the molecular weight distribution measurements to estimate the values of average molecular weight and the content of low molecular weight components(<MW 1000). The detail is described in the document of "SCHEMATIC FLOW FOR SAFETY EVALUATION OF POLYMERS".

3. Test Condition

3.1 Stability test

Test solutions	:	pH 1.2, pH 4.0, pH 7.0, pH 9.0
Concentration	:	1000 mg/L
Temperature	:	40 ± 2℃
Light	:	fluorescent light, 24 hours/day
Duration	:	2 weeks(24 hours for pH 1.2)
Test numbers	:	n = 2

3.2 Solubility test

Test solvents	:	Water, n-Heptane and Tetrahydrofuran
Concentrations	:	2000 mg/L and 200 mg/L
Temperature	:	35 - 40℃ for 1 hour and 25 ± 2℃ for 24 hours
Test numbers	:	n = 2

3.3 Molecular weight distribution measurement

Apparatus : GPC-LALLS

4. Results

4.1 Stability test

No difference is observed between the weights of the samples before and after the stability tests under pH 1.2, pH 4.0, pH 7.0 and pH 9.0 test solutions. The IR spectra of the tested samples are the same as the spectrum of the original sample. The average molecular weights and the molecular weight distribution curves of the tested samples are almost same as those of the original sample. DOC values of the pH 1.2, pH 7.0 and pH 9.0 tested solutions are less than 5.0 mg/L.

4.2 Solubility test

The sample is insoluble in water and fat-soluble solvent such as n-heptane. The sample is soluble in typical organic solvent such as tetrahydrofuran. The solubilies in water as total carbon are less than 0.1% (sample concentration 2000 mg/L) and 0.3% (sample concentration 200 mg/L).

4.3 Molecular weight, molecular weight distribution, and content of the components having MW less than 1000

[redacted]

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REPORT

1. Sponsor

[redacted]

2. Test Laboratory

Name Toray Research Center, Inc.
Address 3-3-7 Sonoyama, Otsu, Shiga 520-8567, Japan

3. Objective

The objective of this measurement is to obtain the safety data of the organic polymer material.

4. Test Method

The test is composed of the stability tests, the solubility tests in water and the organic solvents, the molecular weight distribution measurements to estimate the values of average molecular weight and the content of low molecular weight components(<MW 1000). The detail is described in the document of "SCHEMATIC FLOW FOR SAFETY EVALUATION OF POLYMERS".

5. Duration

June 23, 1999 – September 16,1999

6. Sample

6.1 Sample name

[redacted]

6.2 Chemical structure

[redacted]

6.3 Physical property

White powder at room temperature

7. Stability Test

7.1 Test procedure

The sample (200 mg) and the buffer solution (200 mL) were placed in a flask. The flask was slowly shaken in a water bath at 40℃ for 24 hours (pH 1.2) or 2 weeks (pH 4.0, pH 7.0 and pH 9.0).

7.2 Test condition

(1) Concentration	:	1000 mg/L
(2) Temperature	:	40 ± 2℃
(3) Light	:	fluorescent light, 24 hours / day
(4) Duration	:	2 weeks (24 hours for pH 1.2)
(5) Test numbers	:	n = 2

7.3 Preparation of buffer solutions

pH 1.2 The mixture of 161 mL of 0.2N-HCl and 125 mL of 0.2M-KCl was prepared, and filled up water up to 500 mL.

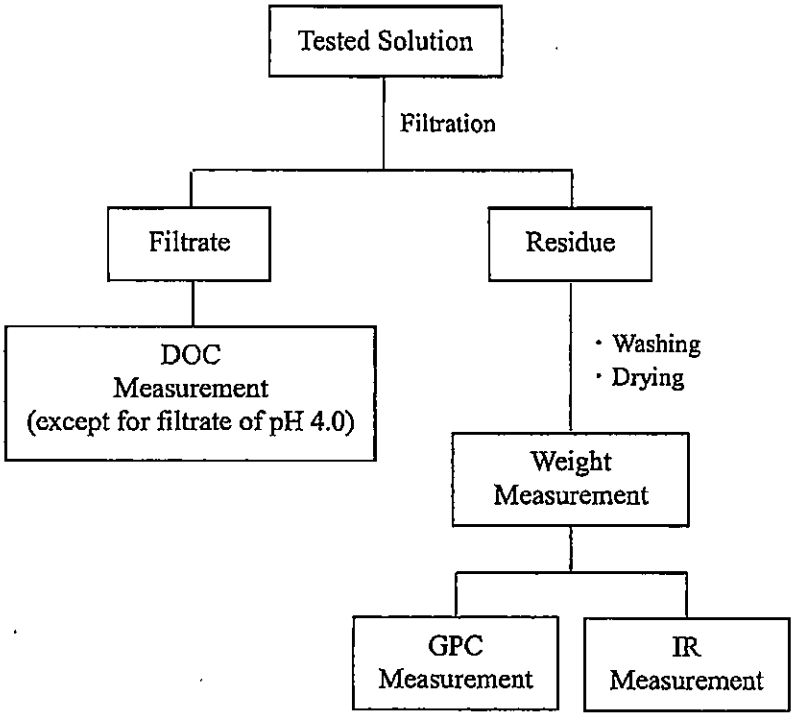
pH 4.0 The mixture of 2.0 mL of 0.1N-NaOH and 250 mL of 0.1M-potassium hydrogen phthalate was prepared, and filled up water up to 500 mL.

pH 7.0 The mixture of 148 mL of 0.1N-NaOH and 250 mL of 0.1M-potassium dihydrogenphosphate was prepared, and filled up water up to 500 mL.

pH 9.0 The mixture of 106 mL of 0.1N-NaOH and 250 mL of 0.1N-KCl / 0.1M-boric acid was prepared, and filled up water up to 500 mL.

7.4 Condition and results of measurements for the solutions subjected to the stability tests

7.4.1 Schematic diagram



7.4.2 Change of weight

The test solution was filtered (using a 0.45 μm membrane filter), and the residue was washed with water and dried at 40℃ in vacuum. The comparison with the weights of the original sample and the residue was performed. The results are summarized in Table 1.

7.4.3 Change of chemical structure

The IR spectra of the original and the tested samples were obtained to compare the chemical structure. The IR spectra of the original sample and the tested samples are shown in Figs.1 to 5.

7.4.4 Change of molecular weight distribution and average molecular weights

The GPC measurements of the original sample and the tested samples were performed. The GPC conditions are as follows.

Apparatus	:	Gel permeation chromatograph (Waters)
Columns	:	Column set of TSKgel GMH_{XL}(2) and $G2500H_{HR}$(1) (TOSOH)
Mobile phase	:	Tetrahydrofuran
Flow rate	:	1.0 mL/min
Concentration	:	0.20% (wt/vol)
Filter	:	0.5 μm- MAISHORIDISK (TOSOH)
Injection volume	:	300 μL
Temperature	:	23℃
Calibration curve	:	The calibration curve (Fig.11) is shifted, so that the weight average molecular weight (M_W) of the sample can coincide with the absolute weight average molecular weight obtained with GPC-LALLS.

The elution curves (Gel Permeation Chromatogram) are shown in Figs.6 to 10. The molecular weight distribution curves are shown in Figs.12 to 16. And the average molecular weights are summarized in Table 2.

7.4.5 DOC

The DOC measurements of the filtrate were carried out except the tested solution of pH 4.0. The results are summarized in Table 3.

8. Solubility Test

8.1 Test procedure

The sample (400 mg and 40 mg) and the solvent (200 mL) were placed in a flask,

respectively. After these flasks were slowly shaken in a water bath at 35 - 40℃ for 1 hour. They were placed at 25±2℃ for 24 hours.

8.2 Test condition

Concentrations	:	2000 mg/L and 200 mg/L
Temperature	:	35 - 40℃ for 1 hour and 25±2℃ for 24 hours
Test period	:	24 hours
Test numbers	:	n = 2

8.3 Solvents

(1) Water
(2) n-Heptane
(3) Tetrahydrofuran

8.4 Procedure and results of measurements for the samples subjected to the solubility tests

After the insoluble components were separated from the solution by filtration with the membrane filter (0.45 μm), these were washed with the solvents, and dried. The insoluble components were weighed. The results are summarized in Table 4. The results of the DOC measurements of the water solution are summarized in Table 5.

9. Molecular Weight, Molecular Weight Distribution, and Content of the Components less than MW 1000

9.1 Method

The measurements of molecular weights, a molecular weight distribution, and a content of components less than MW 1000 were attempted using GPC-LALLS. The GPC-LALLS conditions are as follows.

[GPC]

Apparatus	:	Gel permeation chromatograph (Waters)
Columns	:	Column set of TSKgel GMH_{XL}(2) and $G2500H_{HR}$(1) (TOSOH)
Mobile phase	:	Tetrahydrofuran

Flow rate	:	1.0 mL/min
Concentration	:	0.207% (wt/vol)
Filter	:	0.5 μm- MAISHORIDISK (TOSOH)
Injection volume	:	300 μL
Temperature	:	23℃
Detector	:	Differential refractive index detector R-401 (Waters)

[LALLS]

Apparatus	:	Model KMX-6 Low Angle Laser Light Scattering Detector (Chromatix)
Wave Length	:	633 nm (He-Ne)
d*n*/d*c*	:	0.086 mL/g
Gain	:	800 mV
Temperature	:	23℃
Filter	:	0.30 μm-Fluoro pore FP-030 (SUMITOMO DENKO)

[Data analysis]

Data Processing system : GPC-LALLS Data Processing System (Toray Research Center)

9.2 Results

9.2.1 GPC-LALLS curves

GPC-LALLS curves of the sample are shown in Fig.17 and Fig.18. The signals from the sample are detected from about 19 to 29 minute in the RI curves. The peaks detected after about 29 minute of the elution time are attributable to the solvent-composition-change, solvent-impurity and/or the system peak (It is confirmed from the GPC-LALLS measurement of the solvent; See Fig.19).

9.2.2 Calculation of absolute molecular weight

The absolute molecular weight (M_W) of the original sample can be calculated on the Eqs. (1) and (2).

$$\frac{K \cdot c_i}{R_{\theta i}} = \frac{1}{M_i} + 2A_2 \cdot c_i \qquad (1)$$

$$M_W = \sum c_i M_i / \sum c_i \qquad (2)$$

where, M_W : Absolute weight average molecular weight

Mi : Weight average molecular weight of each elution time

K : Constant =
instrument constant × (refractive index of the solvent)^2 ×
(specific refractive index increment)^2

$R_{\theta i}$: Excess Rayleigh ratio of each elution time

A_2 : Second virial coefficient

c_i : Concentration of each elution time

As the second term is much smaller than the first term in the right side of Eq.(1), the second term can be neglected. The absolute molecular weight of the original sample is estimated to be 71100.

9.2.3 Determination of specific refractive index increment (d*n*/d*c*)

1) Conditions of d*n*/dc measurements

Apparatus	:	Laser light differential refractometer (Chromatix model KMX-16)
Wave length	:	633nm(He-Ne laser)
Solvent	:	Tetrahydrofuran
Temperature	:	23℃

2) Results

The relationship between the concentration(c) and Δn/c are shown in the following table and Fig.23. d*n*/dc is determined from the intercept. The value of d*n*/dc is 0.086 mL/g.

The relationship between concentration(c) and the difference in refractive index of the solvent and the polymer solution (Δn/c)

$c/10^{-3}$ (g/mL)	Δn/c (mL/g)
0.98	0.086
2.01	0.084
2.99	0.086
4.00	0.086
5.01	0.086

9.2.4 Construction of calibration curve

Calibration curve is shown in Fig.20. It is approximated by the linear equation using the data of elution time (t_i) and molecular weight (M_i). The dots in the center of the calibration curve are observational points. Poly methyl methacrylate (MW=1950, elution time = 27.50 minute) is used as a low molecular weight standard compound.

$$\log M = A_0 + A_1 t$$

where, M : Molecular weight
t : Elution time
A_i : Coefficients

9.2.5 Calculation of MWD and average molecular weights

The MWD is originated from the RI curves of the sample (Fig.17 and Fig.18) and the calibration curve (Fig.20) using GPC data processing system. The MWD curves are shown in Fig.21 and Fig.22. and the average molecular weights are summarized in Table 6.

The notations of the symbols in the Table 6 are as follows:

M_n : Number average molecular weight
M_w : Weight average molecular weight
M_z : Z average molecular weight
M_w / M_n : Polydispersity
M_z / M_w : Polydispersity

9.2.6 Estimation of content of the components having MW less than 1000

The MWD data is listed in Table 7 and Table 8. The content of the components having the molecular weight of less than MW 1000 is 0.05% (average of 0.04% and 0.06%). Taking account of the experimental error 0.30%, it is less than 0.35%

10. Summary

10.1 Stability test

10.1.1 Change of weight

No difference is observed between the weight of the samples before and after the stability tests.

10.1.2 Change of chemical structure

The IR spectra of the tested samples are same as the spectrum of the original sample.

10.1.3 Change of molecular weight and molecular weight distribution

The average molecular weights and the molecular weight distribution curves of the tested samples are almost same as those of the original sample.

10.1.4 Dissolved Organic Carbon

The DOC values of the tested solutions are less than 5.0 mg/L.

10.2 Solubility test

The sample is insoluble in water and fat-soluble solvent such as n-heptane. The sample is soluble in typical organic solvent such as tetrahydrofuran. The solubilies in water as total carbon are less than 0.1% (sample concentration 2000 mg/L) and 0.3% (sample concentration 200 mg/L).

10.3 Molecular weight, molecular weight distribution, and content of the components having MW less than 1000

[redacted]

11. Instruments and reagents

11.1 Instruments

Instrument	Maker (Type)
Gel permeation chromatograph - Low Angle Laser light Scattering Detector	Chromatix (KMX-6)
Gel permeation chromatograph	Waters (201D)
Fourier Transform Infrared Spectrometer	Perkin Elmer (1720X)
Total Organic Carbon Analyzer	Shimadzu (TOC-5000A)

11.2 Reagents

Reagent	Producer
Water	Katayama Chemical
Hydrogen chloride	Katayama Chemical
Potassium chloride	Wako Pure Chemical
Sodium hydroxide	Katayama Chemical
Potassium hydrogen phthalate	Wako Pure Chemical
Potassium dihydrogenphosphate	Wako Pure Chemical
Boric acid	Wako Pure Chemical
n-Heptane	Wako Pure Chemical
Tetrahydrofuran	Ishizu Pharmaceutical

This work was carried out by Senior Research Chemist Tomohiro Yoshida and Manager Hideaki Takahashi at 1st Materials Characterization laboratory, Toray Research Center, Inc.

Manager : Hideaki Takahashi

Signature : Hideaki Takahashi Date : 11. Sep. 2015

Study Director : Tomohiro Yoshida

Signature : Tomohiro Yoshida Date : 11. Sep. 2015

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Table 3 Results of Stability Test (Change of DOC and Change of IR Spectra)

Test solution	Concentration (mg/L)	Change of DOC				Change of IR Spectra	
		DOC (mg/L)					
		C_0 *a	C *b	ΔDOC *c	Average		
pH 1.2	1000	0.4	0.8 0.5	0.4 0.1	0.3	Fig.2	The IR spectra of the tested samples were the same as the spectrum of the original sample.
pH 4.0	1000	- -	- -	- -	-	Fig.3	
pH 7.0	1000	0.4	0.4 0.9	0.0 0.5	0.3	Fig.4	
pH 9.0	1000	0.4	0.4 0.7	0.0 0.3	0.2	Fig.5	
Original						Fig.1	

*a : DOC concentration of original buffer solution
*b : DOC concentration of tested solution
*c : ΔDOC(mg/L)=C(mg/L)- C_0(mg/L)

Table 4 Results of Solubility Test (Change of weight)

Concent-ration (mg/L)	Test solution	Weight (mg)			$\Delta W / W_0 \times 100$ (%)	
		W_0 *a	W *b	ΔW *c		Average
200	Water	40.0	39.8	0.2	0.5	0.8
		40.5	40.1	0.4	1.0	
	n-Heptane	40.0	39.9	0.1	0.3	0.4
		39.8	39.6	0.2	0.5	
	Tetrahydro-furan	40.7	0.1	40.6	99.8	99.9
		40.4	0.0	40.4	100.0	
2000	Water	399.7	396.0	3.7	0.9	1.0
		400.9	396.6	4.3	1.1	
	n-Heptane	399.9	398.8	1.1	0.3	0.2
		400.4	400.1	0.3	0.1	
	Tetrahydro-furan	400.2	0.5	399.7	99.9	100.0
		400.3	0.2	400.1	100.0	

*a : Weight of original sample
*b : Weight of tested sample
*c : ΔW (mg) = W_0 (mg) - W (mg)

Table 5 Results of Solubility Test (Change of DOC)

Test solution	Concentration (mg/L)	DOC(mg/L)				Solubility as Organic Carbon (%)	
		Before test	After test	ΔDOC	Theoretical Value *a		Average
Water	1998.5	0.4	0.7	0.3	853.4	< 0.1	< 0.1
	2004.5		0.7	0.3	855.9	< 0.1	
	200.0	0.4	0.7	0.3	85.4	0.4	0.3
	202.5		0.6	0.2	86.5	0.2	

*a : Carbon content calculated from structural formula(Stoichiometric values) : 42.7%

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Table 7 Molecular Weight Data

[redacted]

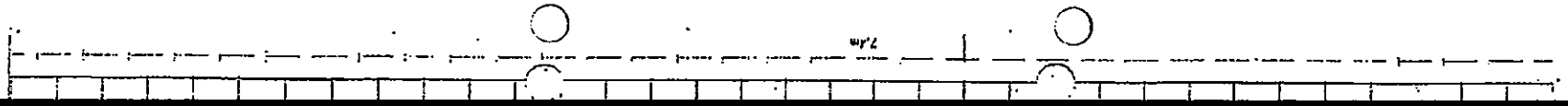
Table 8 Molecular Weight Data

[redacted]

4.0m

3.8m

[redacted]



7.2m

7.0m

[redacted]