# Fractional Turbidimetric Analysis of the Molar Substitution of Hydroxyethyl Cellulose

THOMAS E. MULLER and W. J. ALEXANDER,

Research Divisions, Rayonier Incorporated, Whippany, New Jersey

Synopsis

High quality packaging films from hydroxyethyl cellulose of low degree of substitution (DS) are being produced commercially in this country and abroad. Increasing demand for this and a variety of other applications requires a rapid and simple production control method for determining hydroxyethyl substitution of cellulose. None of the known analytical methods fulfills these requirements. The present paper describes a method which is based on the relationship between the solubility and the molar hydroxyethyl substitution of hydroxyethyl cellulose. A washed and dried sample of hydroxyethyl cellulose is dissolved in 7% aqueous sodium hydroxide. Methyl alcohol, a nonsolvent, is used to precipitate a fraction of the sample. The turbidity of the equilibrium system is determined and optical density readings are related to molar substitution. The method is most useful in low DS ranges of 2–8% EtO but is susceptible to broader application through adjustment of the composition of the solvent–nonsolvent mixture. Relatively large variations in DP can be tolerated. The molar substitution level of an hydroxyethyl cellulose sample can be obtained in 40 min. by this method, making it a practical production control technique.

Hydroxyethyl cellulose is prepared by reacting alkali cellulose with ethylene oxide:

$$\text{Cell—OH} + (\text{H}_2\text{C})_2\text{O} \xrightarrow{\ ^{-}\text{OH}\ } \text{Cell—OCH}_2\text{CH}_2\text{OH}$$
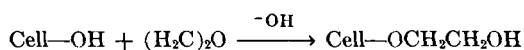
In practice a shredded, fluffy alkali cellulose crumb is reacted with gaseous ethylene oxide to yield a product which is soluble in aqueous sodium hydroxide. Such a solution may be used to form transparent filaments, films, and other products.

The molar substitution (MS) describes the extent of reaction in terms of the number of ethylene oxide moles combined with cellulose per anhydroglucose unit. Ethylene oxide may react with hydroxyethyl as well as with cellulose hydroxyls. Accordingly there is no theoretical upper limit for the MS. The degree of substitution (DS), the average number of cellulose hydroxyl groups substituted per anhydroglucose units, does have a theoretical maximum value of 3.

Side-chain polymerization takes place only after cellulose has been substituted at least partially, when the rate of direct substitution slows down. There is essentially no polymerization while the MS is low, in which case

it is substantially equal to the DS.   Croon and Lindberg[1] calculated the DS to be 0.4 for a 0.6 MS hydroxyethyl cellulose, while the MS is 0.154 at a DS of 0.145.

Several commercial applications are operating at low levels of DS.[2]

The relationship between MS and per cent ethylene oxide substitution was shown by Ott and Spurlin:[3]

$$MS = 162Y_w/[44(100 - Y_w)]$$

where Y_w is per cent ethylene oxide substitution.

There are two types of analytical methods to determine the extent of hydroxyethylation.

The first method employs ether cleavage to determine MS.   The Morgan modification of the Zeisel method[4,5] employs hydriodic acid.

$$Cell—OCH_2CH_2OH + 3HI \longrightarrow Cell—I + ICH_2CH_2I + 2H_2O$$
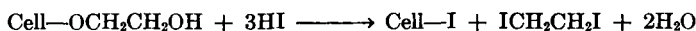
Ethylene iodide is converted partly to ethylene and partly to ethyl iodide; ethylene is taken up in bromine and ethyl iodide in silver nitrate. This method has a standard deviation of $\pm$ 0.1% ethylene oxide for an average substitution level of 4% (MS = 0.153), or an accuracy of $\pm$ 2.5%. The method requires a carefully trained operator and complex equipment, turning out only eight analyses per 8-hr. day, one of which must be a control.   A single determination requires 5 hr. to complete.   Other methods for the determination of the MS were reviewed by Morgan.

The second method determines DS by the selective reaction of polyoxy-ethylene hydroxyls.   Froment[6] reported such a method based on selective reaction with phthalic anhydride.   According to Senju,[7] phthalic anhydride is prevented by steric factors from reacting with hydroxyls other than those readily accessible at the end of long chains.   Quinchon reported a similar method.[8]
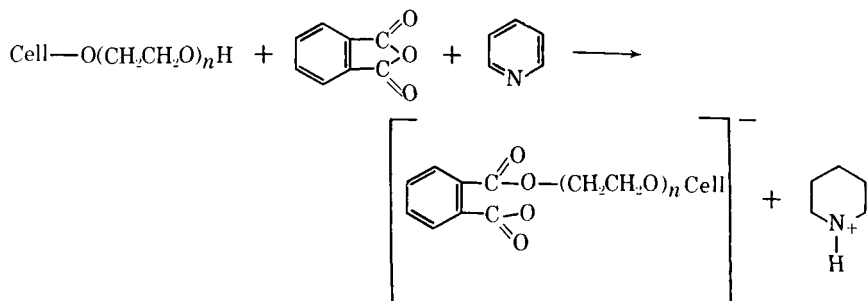
In this reaction, carried out at 40°C. for at least 5 hr., apparently no glycosidic hydroxyls reacted in a hydroxyethyl cellulose of 0.7 D.S.   The relative precision of the method at this DS level is of the order of 6%, decreasing with lower degrees of substitution (fewer long chains) to only about 12% for a DS of 0.3.

From the point of view of the material balance it is more significant to know the MS than the DS.   The location and substitution of the sub-

stituents in hydroxyethyl cellulose was studied by Brownell and Purves.[9] At an MS level of 1.33, the average polyoxyethylene chain length is 1.6 units.

For obvious reasons a production control method must be rapid and simple to carry out, as well as reasonably accurate and reproducible. None of the available analytical methods for hydroxyethyl cellulose fulfill these requirements. It is the purpose of this work to provide a method suitable as a guide in controlling MS in commercial operations.

The solubility of hydroxyethyl cellulose is a function of its MS. Solubility in dilute alkali is attained at an MS of about 0.08, water solubility at an MS of about 1.2, and solubility in organic solvents at an MS of >2.

The relationship between alkali solubility and MS was determined for a hydroxyethyl cellulose of 0.385 MS by Ward,[10] using aqueous sodium hydroxide of a concentration close to maximum solubility. The fractionated sample was analyzed by x-ray.

Fractionation of a polymer based on solubility differences can be carried out by either differential solution or differential precipitation. Fractional precipitation, however, offers a closer approach to equilibrium. Fractionation must be followed by monitoring the fractions, preferably, to save time, without isolating the fractions, in a heterogeneous system.

There are several papers in the literature describing characterization of molecular weight distribution of synthetic polymers based on differential solubility fractionation.[11-13] Some of these works propose turbidimetric methods as the means of analysis.[14,15] Polymers studied by this technique include ethylene–propylene copolymer, polypropylene, and polyethylene. Thermal gradient methods are based on solubility–temperature relationship. The principles of turbidimetric and nephelometric titration were reviewed by Meehan and Chiu.[16] Beattie determined the solubility and molecular weight distribution of polystyrene by turbidimetric titration.[17] With such work as a background we have developed a relatively simple measure for MS as described in the following section.

EXPERIMENTAL

Sampling and Sample Preparation

In commercial operations a representative sample of reacted crumb is usually withdrawn from the process stream at exit from the reactor. When the crumb is in a completely defibered state no further shredding is required. Otherwise a representative 2–3 g. sample should be dispersed in a Waring Blendor for 5 seconds. The dispersed crumb is slowly sifted into 200 ml. of 2.5% hydrochloric acid and after standing for 1 min. the crumb is collected on a medium-porosity glass filter and washed with 300 ml. of hot water. The suction-dry sample is hand-shredded and dried in a Moisture Teller Drier (Harry W. Dietert Co., Detroit, Mich.) for 10 min. at 150°C. to obtain the oven-dry weight.

End-product samples, e.g., washed crumb, pellets, or film, are usually

neutral and air-dry. These are shredded in a Waring Blendor for 30 sec. and the oven-dry weight is obtained in the same manner. In the case of film, plasticizer must be removed prior to this test.

Analysis

An oven-dry, 0.500 ± 0.005 g. sample of hydroxyethyl cellulose is weighed into a 125-ml. Erlenmeyer flask equipped with a glass stopper, and 50.0 ml. of distilled water is added from an automatic pipet. The flask is stoppered, shaken vigorously by hand for 30 sec., and 50 ml. of 14.0% aqueous sodium hydroxide is added also from a pipet. The flask is stoppered and the suspension is stirred vigorously for 20 min. or until all of the sample goes into solution. A 10.0-ml. aliquot of this solution is transferred into a clean, scratch-free Lumetron sample tube and 3.00 ± 0.01 ml. of dry methyl alcohol is added. The tube is stoppered, shaken vigorously 25 times by hand, and placed in a water bath at $20 \pm 1°C$. The tube is removed from the bath momentarily exactly 2 min. after the addition of the methyl alcohol and is inverted four times, removed again after 5 min. and inverted twice, and again after 8 min. to be inverted twice. Gentle inverting prevents settling without introducing air bubbles. The suspension should be free of air bubbles or signs of settling when the optical density is measured. The tube is removed from the bath exactly 10 min. after the addition of the nonsolvent, is slowly inverted once, and the optical density of the suspension is recorded in a Lumetron Model 401 colorimeter (Schaar and Co., Chicago, Ill.) equipped with a 420 filter. The colorimeter is pre-set to an optical density value of zero with a blank solution containing 5.0 ml. of distilled water, 5.0 ml. of 14.0% sodium hydroxide solution, and 5.0 ml. of methyl alcohol. Conditioning and periodic inverting is omitted for the blank, which should have an optical density of < 0.005 when measured against distilled water. Other turbidimeters are equally suitable.

RESULTS

Calibration

A calibration curve is required relating optical density to the molar substitution of hydroxyethyl cellulose. Such a calibration was obtained with the aid of the Zeisel-Morgan method[4,5] as shown in Figure 1. Neutralized and dry hydroxyethyl cellulose is stable, allowing standards to be kept. Once the MS of these standards is determined by the Zeisel-Morgan method, they can be used periodically to calibrate and check the equip- ment. Fractional turbidimetric analysis is primarily a convenient control method developed for routine use. Generally even visual examination of the suspension is sufficient if the process is drastically out of control.

Reproducibility

The method is capable of yielding turbidity measurements reproducible within ± 0.01 optical density. This corresponds to approximately $\pm$
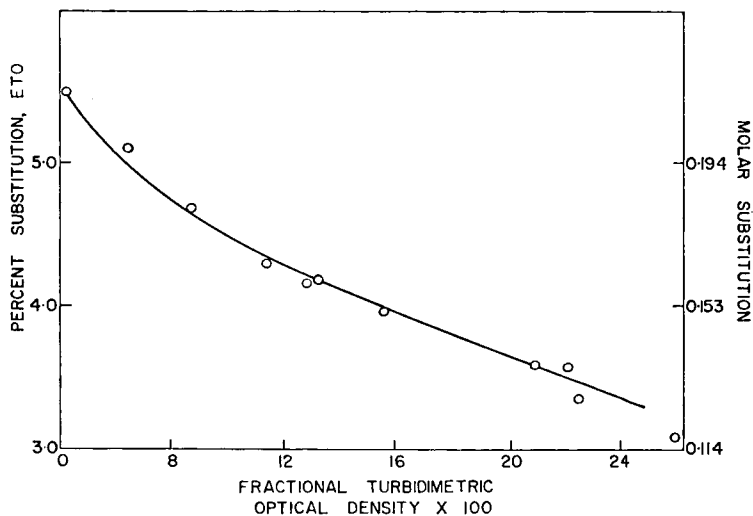
Fig. 1. Typical conversion curve.

0.1% ethylene oxide substitution or to an MS of ± 0.004. The reproducibility is increased if the optical density reading falls close to the center of the calibration curve for the range covered. The reproducibility is shown in Table I for four levels of substitution.

The method is sensitive to small variations in the amount of methyl alcohol nonsolvent added, so this has to be carefully controlled. In fact the amount of nonsolvent used is a means of varying the range of the method, when calibration is required. An addition of 3.00 ml. approximates the midpoint of the turbidity range with a 4.0% ethylene oxide, 0.1534 MS hydroxyethyl cellulose. The relationship between optical

TABLE I
Reproducibility of Fractional Turbidimetric Analysis at
Various Hydroxyethyl Cellulose Substitution Levels

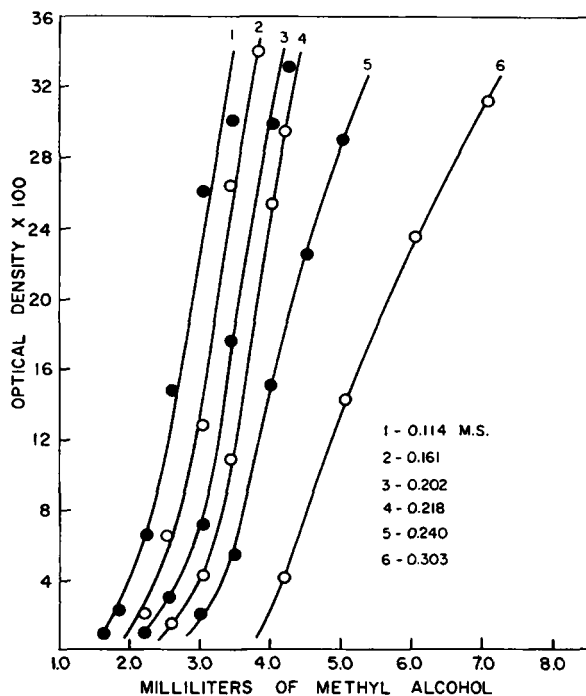| Test no. | Optical density ($\times$100) at various MS levels | | | |
	0.2024	0.1626	0.1162	0.1002
1	7.2	12.4	28.3	27.6
2	5.5	11.9	28.6	25.9
3	6.6	13.5	28.0	27.2
4	7.2	12.9	26.5	27.0
5	7.4	12.9	27.3	25.8
6	6.9	13.9	28.8	29.5
7	6.6	12.4	28.0	29.0
8	6.5	12.5	29.1	27.0
9	7.6	14.2	29.7	26.5
10	6.5	12.8	28.8	26.8
Average	6.8	12.9	28.3	27.2
Std. deviation	0.6	0.6	0.9	1.2

Fig. 2. Effect of varying the amount of nonsolvent for several MS levels.

density and amount of nonsolvent employed is shown in Figure 2 at five substitution levels.

The effect of the concentration of the hydroxyethyl cellulose in solution is not very critical, although not less than 20% of the sample should be either in solution or precipitated. To determine what fraction of a sample was precipitated by 3.00 ml. of methyl alcohol, solutions were centrifuged and the precipitates were isolated after equilibrium was reached. The data indicated that a substantial fraction of the sample defined the test level, as shown in Table II. A set of five samples could be reasonably well dupli-cated by a second analyst, provided that the same colorimeter was used. Table III shows operator and colorimeter as the variables.

TABLE II
Per Cent Hydroxyethyl Cellulose Precipitated
by 3.00 ml. Methyl Alcohol

MS	Ethylene oxide, %	Optical density ($\times 100$)	Solids precipitated, %
0.1614	4.2	12.0	32
0.1178	3.1	27.0	63

TABLE III
Effect of Various Colorimeters and Analysts on Reproducibility

| | Optical density ($\times 100$) | | |
| | Colorimeter I | | Colorimeter II |
Sample	Analyst A	Analyst B	Analyst B
1	31.4	33.0	22.3
2	29.4	30.2	20.8
3	28.2	26.2	15.5
4	26.1	24.6	12.9
5	20.3	20.2	11.2

Although fractional precipitation is allowed to reach equilibrium in a constant temperature bath, it was found that results were virtually unaffected by small variations in temperature within the range 15–25°C., as shown in Figure 3.

Figure 4 shows the influence of variations in the sample size.

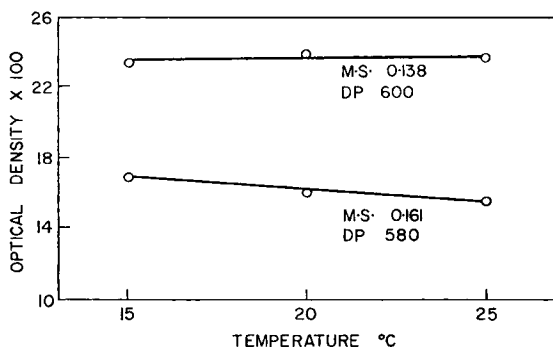Variations of up to 200 in DP are easily tolerated.   A 602 DP hydroxy-

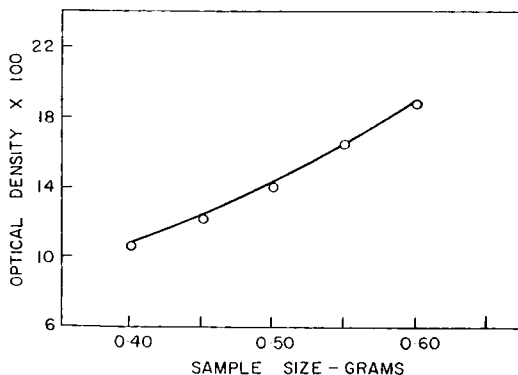Fig. 3. Effect of equilibrium temperature.

Fig. 4. Influence of sample size.

ethyl cellulose had an optical density of 20.9 as compared to the optical density value of 21.1 for a 335 DP sample, both at the same substitution level.

DISCUSSION

Fractional turbidimetric analysis to determine the molar substitution of hydroxyethyl cellulose fulfills the prime requirements of a practical method for process control analysis. It is quite impossible to wait for the result of any control test for 5 hr., the time required for the Zeisel-Morgan method. In routine use, fractional turbidimetric analysis yields results in less than 1 hr. from sampling of the alkaline hydroxyethyl cellulose crumb, and usually within 40 min. A small sample is adequate, though larger samples are more representative. The accuracy of the method is comparable to that of the slower and more intricate Zeisel-Morgan method and it is fully reproducible.

Limitations in range are limitations only in the sense that major changes in specifications may call for a changeover to a different range. The test was found applicable within wide limits of substitution. While the upper substitution limit was not established, samples studied had an ethylene oxide substitution of 2.6–7.6% corresponding to an MS range of 0.0983–0.3028. It is best to operate as close to the mid-point of the S-shaped calibration plot as possible. Should recalibration be required the amount of nonsolvent should be adjusted. Lower ranges of substitution call for less and higher ranges of substitution for more nonsolvent, in accordance with the respective degrees of solubility.

For obvious reasons one of the first objectives was to determine the influence of DP variations on reproducibility, since known fractionation methods are influenced or even based on differences in molecular size. It is erroneous, however, to assume that such fractionations must necessarily be influenced by molecular weight if the unsubstituted polymer is completely insoluble in all combinations of solvent–nonsolvent, and when only substitution renders the polymer derivative soluble. Such a solubility-substitution relationship is the basis of this method and it may be applied to cellulose derivatives other than hydroxyethyl cellulose, and to other polymer or copolymer derivatives, e.g., grafts. It may be applied to study the substitution uniformity of cellulose xanthate, viscose.

The choice of solvent–nonsolvent system was influenced by several factors. Hydroxyethyl cellulose is soluble in aqueous alkali in the substitution range. studied. The nonsolvent was required to be a true nonsolvent in the same substitution range, to be miscible with the solvent, to be a poor swelling agent for hydroxyethyl cellulose, and finally to be inert. It was also necessary to select a nonsolvent with a refractive index as close to that of the solvent as possible. The refractive index of methyl alcohol is 1.3312 and that of 7.0% aqueous sodium hydroxide is 1.3506. There is a change in the refractive index of the medium unless the components have a close refractive index.

It is also important that the polymer should have a refractive index different from that of the medium.   The refractive index of hydroxyethyl cellulose ranges from a value of 1.553/1.532 for 0% substitution to a value of 1.528/1.516 for 8.8% substitution (cellulosics have two refractive indices).

The time between methyl alcohol addition and the recording of the optical density is specified to allow for the system to reach equilibrium.   This permits the precipitate to "age," i.e., to coagulate, swell, and agglomerate. Unless this requirement is satisfied, the turbidity of the system may change without the quantity of the precipitate varying.

References

1. I. Croon and B. Lindberg, *Svensk Papperstidn.*, **59**, 794 (1956).

2. R. L. Mitchell, A. R. Albohn, and S. G. Palmgren (to Rayonier Inc.), U. S. Pat. 3,045,007 (July 17, 1962).

3. E. Ott, H. M. Spurlin, and M. W. Grafflin, *Cellulose and Cellulose Derivatives*, Vol. III, Interscience, New York, 1955, p. 1419.

4. S. Zeisel, *Monatsh.*, **6**, 989 (1885); *ibid.*, **7**, 406 (1886).

5. P. W. Morgan, *Ind. Eng. Chem., Anal. Ed.*, **18**, 500 (1946).

6. G. Froment, *Ind. Chem. Belge*, **23**, 115 (1958).

7. J. Senju, *Agr. Chem. Soc. Japan*, **22**, 58 (1948).

8. J. Quinchon, *Compt. Rend.*, **248**, 225 (1959).

9. H. H. Brownell and C. B. Purves, *Can. J. Chem.*, **35**, 677 (1957).

10. R. H. Gillespie, M. Muller, H. Swenson, and K. Ward, Jr., *Tappi*, **44**, 662 (1961).

11. F. W. Billmeyer, Jr., in *Analysis and Fractionation of Polymers (J. Polymer Sci. C*, **8**). J. Mitchell, Jr., and F. W. Billmeyer, Jr., Eds., Interscience, New York, 1965, p. 161.

12. A. S. Kenyon, I. O. Salyer, J. E. Kurz, and D. R. Brown, in *Analysis and Fractionation of Polymers (J. Polymer Sci. C*, **8**), J. Mitchell, Jr. and F. W. Billmeyer, Jr., Eds., Interscience, New York, 1965, p. 205.

13. N. S. Schneider *(J. Polymer Sci. C*, **8**), J. Mitchell, Jr. and F. W. Billmeyer, Jr., Eds., in *Analysis and Fractionation of Polymers*, Interscience, New York, 1965, p. 179.

14. W. C. Taylor and J. P. Graham, *J. Polymer Sci. B*, **2**, 169 (1964).

15. L. W. Gamble, W. T. Wipke, and T. Lane, *J. Appl. Polymer Sci.*, **9**, 1503 (1965).

16. E. J. Meehan and G. Chiu, *Anal. Chem.*, **36**, 536 (1964).

17. W. H. Beattie, *J. Polymer Sci. A*, **3**, 527 (1965).

Résumé

Des films d'emballage de haute qualité, à base de cellulose hydroxyéthylée de faible degré de substitution, sont produits commercialement dans ce pays de même qu'à l'étranger.   La demande croissante pour ces films et pour une variété d'autres applications nécessite une méthode de contrôle de production rapide et simple en vue de déterminer la substitution hydroxy-éthylée de la cellulose.   Aucune des méthodes analytiques connues ne satisfait à ces exigences.   Le présent manuscrit décrit une méthode qui est basée sur le rapport entre la solubilité et le degré de substitution molaire hydroxyéthylée de la cellulose hydroxyéthylée.   Un échantillon lavé et séché de cellulose hydroxyéthylée est dissous dans la soude caustique aqueuse à 7%.   L'alcool méthylique, un non-solvant, est utilisé en vue de précipiter une fraction de l'échantillon.   La turbidité du système à l'équilibre est déterminée et des mesures de densité optique sont reliées à la substitution molaire.   La méthode est la plus utile dans le domaine des faibles degrés de substitution de 2 à 8% d'oxyéthyle mais est susceptible d'application plus large par adjustement de la composition du mélange solvant–non-solvant.   Des variations relativement importantes du degré de polymérisation peuvent être tolérées.

Le niveau de substitution molaire de l'échantillon de cellulose hydroxyéthylée peut être obtenu en 40 minutes par cette méthode, ce qui en fait une technique de contrôle pratique pour la production.

Zusammenfassung

Verpackungsfilme hoher Qualität aus Hydroxyäthylzellulose mit niedrigem D.S. werden in den USA und in anderen Länderen kommerziell erzeugt. Die zunehmend Nachfrage für diese und eine Vielfalt anderer Anwendungen erfordert eine rasche und einfache Methode der Produktionskontrolle zur Bestimmung der Hydroxyäthylsubstitution von Zellulose. Keine der bekannten analytischen Methoden erfüllt diese Voraussetzungen. In der vorliegenden Mitteilung wird eine auf der Beziehung zwischen der Löslichkeit und der molaren Hydroxyäthylsubstitution von Hydroxyäthylzellulose beruhende Methode beschrieben. Eine gewaschene und getrocknete Probe von Hydroxyäthylzellulose wird in 7% wässrigem Natriumhydroxyd aufgelöst. Eine Fraktion der Probe wird mit Methylalkohol ausgefällt. Die Trübigkeit des Gleichgewichtssystems wird bestimmt und die optische Dichte zur molaren Substitution in Beziehung gesetzt. Die Methode ist am wertvollsten in niedrigen D.S.-Bereichen von 2–8% EtO, kann jedoch durch Einstellung der Zusammensetzung des Lösungsmittel–Fällungsmittelgemisches in einem breiteren Bereich angewendet werden. Verhältnismässig grosse Änderungen in D.P. können toleriert werden. Der molare Substitutionsgrad einer Hydroxyäthylzelluloseprobe kann nach dieser Methode in 40 Minuten erhalten werden, womit praktisch ein Produktionskontollverfahren gegeben ist.