Polymer Bulletin 5, 413–416 (1981)

Polymer Bulletin

Physico-Chemical Studies of Polymeric Carriers
1. Hydrolysis and Fractionation of Copolymer of N-Vinylpyrrolidone and Maleic Anhydride

Éva Csákvári, Mária Azori and Ferenc Tüdős[1]

Central Research Institute for Chemistry of the Hungarian Academy of Sciences,
P.O.Box 17, 1525 Budapest, Hungary

[1] Eötvös Lóránd University, Department of Chemical Technology, Muzeum krt. 6–8,
1088 Budapest, Hungary and

Central Research Institute for Chemistry of the Hungarian Academy of Sciences,
P.O. Box 17, 1525 Budapest, Budapest, Hungary

SUMMARY

Fractionation procedure on copolymer of N-vinylpyrrolidone and maleic anhydride has been elaborated using water/acetone solvent/nonsolvent system. Viscosity and molecular weight measurements of the fractions were carried out in acidic aqueous medium at 25 °C. The relationship between the intrinsic viscosity and the molecular mass $[\eta]_c = K \cdot M^{\alpha}$ was obtained at pH = 2.1.

INTRODUCTION

The aim of our present work was to prepare and characterize a polymeric carrier for drugs and other biologically active compounds. As a model system an alternating copolymer of N-vinylpyrrolidone (NVP) and maleic anhydride (MA) was chosen. It was prepared by heterogeneous copolymerization initiated by AIBN. Reaction conditions and kinetical measurements will be published elsewhere.

Copolymers of NVP are usually characterized by viscometry and apparent molecular mass values estimated adopting the Mark-Houwink equation determined only for the homopolymer (KOTENKO et al. 1972, GEORGIEV et al. 1979). However there is a considerable demand for the expression of real molecular mass figures particularly from the pharmacological profession. In addition fractionation of the polymer is for itself very important since there are serious contradictions for the very large as well as for very small molecules in medical applications. The molecular mass determination of polymeric acids encounters numerous experimental difficulties (KATCHALSKY and EISENBERG, 1951; OTH and DOTY 1952; NAGASAWA and TAKAHASHI 1972; KITANO et al. 1979). In this paper we wish to report our experimental results obtained in this field.

HYDROLYSIS

Prior to fractionation samples of P(NVP-co-MA) were purified by extraction (in a Soxhlet for 24 hrs) in dry benzene to remove monomers and oligomers. IR spectra of the copolymer evidenced that partial hydrolysis of anhydride groups by air moisture is unavoidable. In order to bring the sample to definite and homogeneous chemical composition it was converted to poly-acid by hydrolysis. For complete conversion of anhydride groups but to prevent the opening of lactam rings alkaline medium under mild conditions was applied. An example of hydrolysis procedure

0170-0839/81/0005/0413/$01.00

was as follows. Equimolar amounts of copolymer (17.1 g) and $NaHCO_3$ (13.9 g) were mixed in 240 cm^3 water at room temperature. After stirring for 3 hrs the clear solution was poured into 1200 cm^3 acetone. The precipitate was redissolved and the excess of $NaHCO_3$ was eliminated by diluted acetic acid (10%). The resulted sodium salt P(NVP-co-MA Na_2) was ion-exchanged on an Amberlite IR 120 column, then freeze dried.

FRACTIONATION

Fractionation of the polymer was performed in water/acetone solvent/nonsolvent system. The course of fractionation was the following. 18.5 g ion-exchanged poly-acid was dissolved in 250 cm^3 water. The first fraction (Fr.I) was obtained by slow addition of the solution into 870 cm^3 acetone. The second fraction (Fr.II) was precipitated by the addition of further 380 cm^3 acetone. The residue was the third fraction (Fr.III), recovered by rotary evaporation. Fr.I and Fr.III were subjected to further fractionation steps (Fig.1, Fig.2). The initial concentrations of the solutions were 7.5% in each case.

Characterization of the fractions has been carried out by molecular light scattering and viscometry, both in dilute solutions at pH = 2.1, at 25 °C.

DETERMINATION OF MOLECULAR WEIGHT

Detailes of light scattering measurements will be described in the next paper of the series. The measurements were performed on a Brice-Phoenix Series 2000 instrument. The optical clarification of solvent and solutions was accomplished by pressure filtration through ultrafine glass-sinters G5 and G4 respectively. The intensities of scattered light were measured at $\lambda = 546$ nm. The numerical value of the refractive index increment was 0.146, determined on a Phoenix Precision Instrument 60 Type Differential Refractometer. Results obtained are summarized in Table I together with viscometric data.

DETERMINATION OF INTRINSIC VISCOSITY (limiting viscosity number)

The intrinsic viscosities of the polymer solutions were determined in an Ubelhode viscometer which had a flow time for the solvent of 26 s at 25 ± 0.01 °C. The values of relative viscosities were between 1.1 and 1.5. The starting concentrations of the solutions were of about 0.02 $g \cdot cm^{-3}$. In all cases the solutions were dilute enough to show no curvature on graphs of η_{rel} vs. $\underline{c}$. Plotting η_{sp}/c vs. $\underline{c}$ straight lines were obtained (from 5 - 7 points). Values determined are listed in Table I.

MARK-HOUWING EQUATION AND DISCUSSION

From the data above the relation between limiting viscosity number and molecular mass was calculated using the least-squares method:

$$[\eta]_c = 3.25 \cdot 10^{-4} \cdot M^{0.62}$$

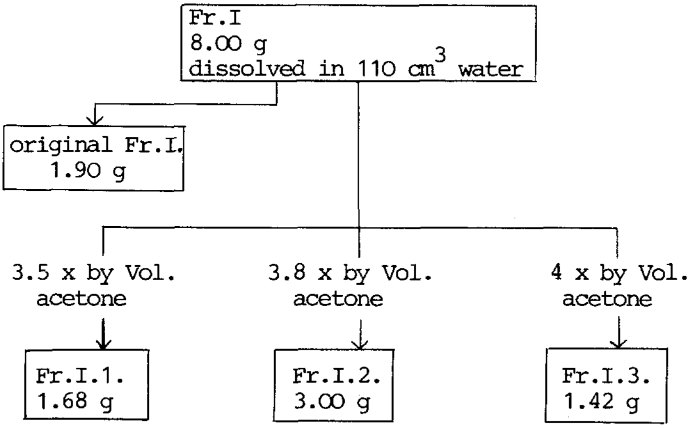

Figure 1. Scheme of repeated fractionation of Fr.I

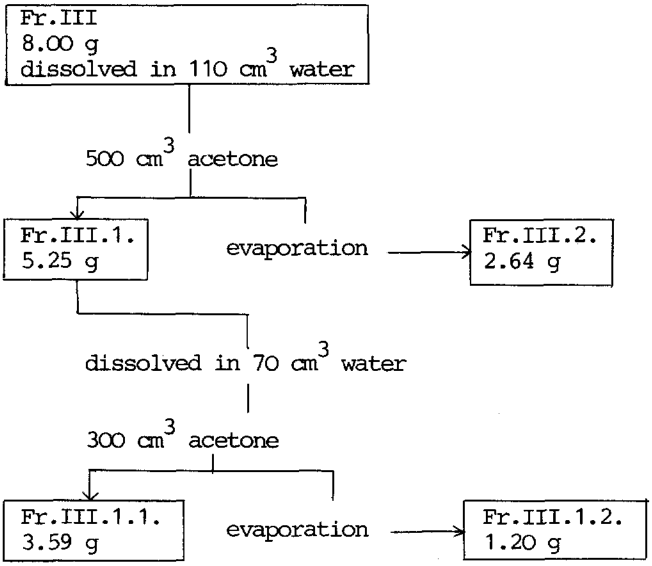

Figure 2. Scheme of repeated fractionation of Fr.III

Table I

Sample	$[\eta]_c$ $cm^3 \cdot g^{-1}$	$10^{-3} \cdot M_w$
I.	0.20	30.8
I.1.	0.22	35.0
I.2.	0.18	29.0
I.3.	0.17	25.0
II.	0.10	10.2
III.1.1.	0.11	10.5
III.1.2.	0.09	10.0

On the basis of the data above it can be concluded, that the copolymer prepared, relieved from low molecular mass compounds by extraction, consists of two main fractions of about 50 - 50 per cent. The second fractionation of Fr.I resulted in three distinct fractions (see Table I) while Fr.II and Fr.III are of the same molecular mass. Consequently the molecular mass distribution of the copolymer studied is quite narrow.

REFERENCES

GEORGIEV,G.G., ILIEV,D.V., POPOV,D.V., GEORGIEVA,M.P. and KABAIVANOV,V.S.: Preprints Macro Mainz, Vol.III. 1506 (1979)

KATCHALSKY,A. and EISENBERG,H.: J.Polym.Sci., 6, 145 (1951)

KITANO,T., TAGUCHI,A., NODA,I. and NAGASAWA,M.: Macromolecules 13, 57 (1980)

KOTENKO,S.I., LISUNKIN,Yu.I. and POCHINOK,V.Ya.: Pharm.Zh., 1, 19 (1972)

NAGASAWA,M. and TAKAHASHI,A.: Light Scattering from Polymer Solutions, Ed. Huglin,M.B., Academic Press, London and New York, 1972

OTH,A. and DOTY,P.M.: J.Phs.Chem., 56, 43 (1952)

Received and accepted September 7, 1981