

# Dissolution of Macromolecules I: Surface Phenomena Associated with Polymer Dissolution

ALLEN HEYD\*, DANE O. KILDSIG, and GILBERT S. BANKER

**Abstract** □ A series of polymer free acids, derived from ethylene maleic anhydride resins has been used to study solvent penetration into a polymer compressed disk and polymer swelling. The influence of polymer molecular weight and solvent pH on solvent penetration and polymer swelling was determined. The rate of disappearance of the hydrated layer, formed by simultaneous swelling and solvent penetration, was found to agree closely with the rate of solvent penetration.

**Keyphrases** □ Dissolution—macromolecules □ Polymer disk dissolution—surface phenomena □ Solvent penetration—polymer swelling □ Diagram—polymer dissolution test apparatus

When a solid polymer is placed in a liquid, a quantity of the liquid may be absorbed and result in swelling of the polymer. If the polymer is present in the form of a compressed disk, a swollen layer or gel forms around the disk, the degree of swelling being related to the extent of interaction between the polymer functional groups and the liquid. As would be expected, polymers containing polar functional groups swell to the greatest extent in polar solvents. Further, the formation of this swollen layer on the polymer surface may greatly influence the dissolution of the solid polymer.

In a linear polymer, such as used in this investigation, there are minimum molecular restrictions on the molecule and the extent of swelling is limited only by the quantity of solvent present and the dissolution properties of the polymer. If the polymer has a cross-linked structure it may be restricted in its molecular dimensions and hence an equilibrium-swelling condition is reached which is determined by the elasticity of the molecules. Flory (1) has presented an extensive theory for the swelling of cross-linked or network polymer structures.

The degree of crystallinity also influences the swelling of a polymer. Polymer swelling decreases with increasing crystallinity when the affinity of the solvent for the polymer is not strong enough to break the crystal forces. Many of the cellulosic and other polymers which are used pharmaceutically are partially crystalline at room temperature. Crystallization is seldom complete,

Table I—EMA Copolymers Studied

Polymer Designation	Number Av. Mol. Wt. <sup>a</sup>	Polymer Form
H11 <sup>b</sup>	2,000	Linear
H1103 <sup>b</sup>	8,000	Linear
22	20,000	Linear
H31 <sup>b</sup>	97,500	Linear

<sup>a</sup> R. T. Haynes, Monsanto Chemical Co., private communication, August, 1967. <sup>b</sup> Designation of free acid prepared by hydrolysis of the anhydride.

however, and the amorphous fraction of even substantially crystalline polymers may interact with solvent to swell and then dissolve.

Solvent penetration into a solid polymer has apparently not been investigated to any great extent. Ueberreiter and Asmussen (2) attempted a mathematical approach relating the velocity of dissolution to solvent penetration rate. The mathematical treatment was applied to data from polymer systems which had no reactive functional groups and nonaqueous solvents were used. Corbiere *et al.* (3) studied the depth of solvent penetration into polyvinylchloride in an effort to classify various solvents and solvent mixtures.

As the number of pharmaceutically important polymers containing polar substituents increases and the use of these materials as controlled-release coatings increases, it becomes important to understand the mechanism by which these polymers dissolve. The present investigation was therefore undertaken to study the surface factors which would be expected to influence polymer dissolution, namely solvent penetration into the polymer and polymer swelling.

## EXPERIMENTAL

**Materials**—The polymers used in this study were the free acid derivatives of ethylene maleic anhydride resins, EMA-11, -1103, and -31, and the free acid EMA-22.<sup>1</sup> The free acids were prepared

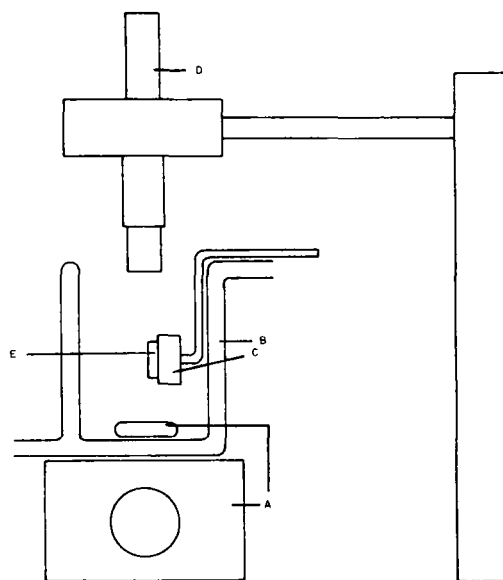


Figure 1—Instrumentation for determining polymer swelling, solvent penetration, and hydrated layer thickness. A, magnetic stirrer apparatus; B, hollow-walled cell; C, sample holder; D, optical micrometer; E, compressed disk.

<sup>1</sup> Monsanto Chemical Co., St. Louis, Mo.

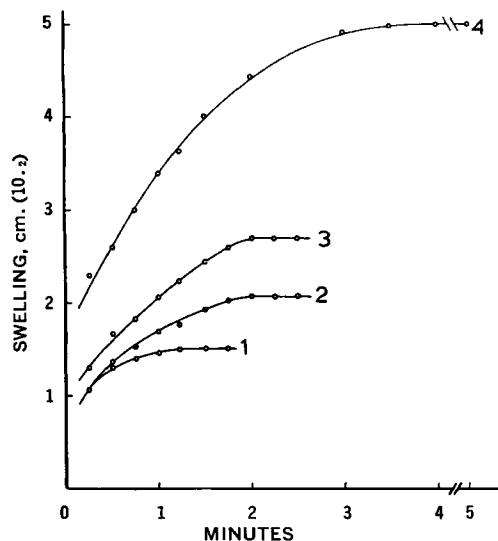


Figure 2—Swelling of EMA copolymers in pH 7.4 buffer. Key: 1, EMA-H11; 2, EMA-H1103; 3, EMA-22; 4, EMA-H31.

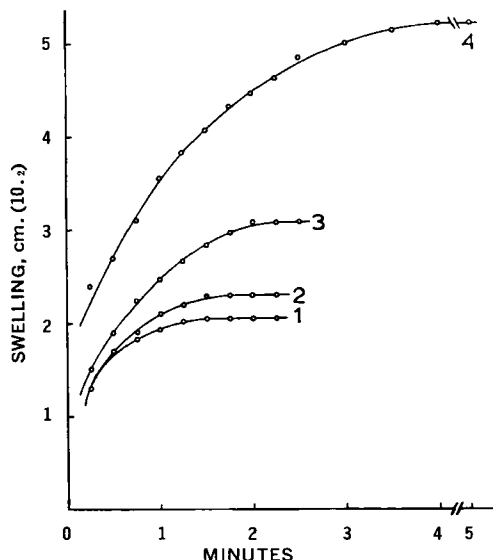


Figure 4—Swelling of EMA copolymer in distilled water. Key: 1, EMA-H11; 2, EMA-H1103; 3, EMA-22; 4, EMA-H31.

from EMA-11, -1103, and -31 by placing 20 g. of the anhydride on a shallow plate in a desiccator saturated with water vapor for a period of 1 week. The molecular weight data for these polymers are shown in Table I. Reagent grade materials were used to prepare the buffer solutions.

**Preparation of Compressed Disks**—The EMA free acid polymers were compressed into disks using a laboratory press<sup>2</sup> employing a 1.58-cm. (<sup>5</sup>/<sub>8</sub>-in.) flat-face punch and die set. One-gram disks were compressed under a force of 5,000 lb. There was no significant effect on swelling with an increase in compressional load, above 5,000 lb., employed in preparing sample disks.

**Swelling Measurements**—The swelling characteristics of the polymers were studied in distilled water and pH 1.2 and pH 7.4 buffer solutions at 30 ± 0.1°. Swelling of the polymer was measured in centimeters by following the formation of a swollen layer on the polymer disk with an optical micrometer<sup>3</sup> as shown in Fig. 1.

**Solvent Penetration Measurements**—The optical micrometer (Fig. 1) was used to follow the solvent penetration, in centimeters, into

the polymer disks in distilled water and pH 1.2 and 7.4 buffer solutions at 30 ± 0.1°.

**Hydrated Layer Thickness Measurements**—Maximum hydrated layer thickness in centimeters and the subsequent receding rate of the hydrated layer front were also measured with the optical micrometer as shown in Fig. 1. The measurements were made in distilled water and pH 1.2 and 7.4 buffer solutions at 30 ± 0.1°. The layer thickness of EMA-22 was also determined on 12 buffer solutions ranging in pH from 0.5 to 9.4.

## RESULTS AND DISCUSSION

**Swelling of EMA Free Acid Copolymers**—The swelling of the polymers with time is shown in Figs. 2-4. It can be seen that a plateau is reached for all polymer-solvent systems indicating apparent maximum swelling. The pH of the solvent and the polymer molecular weight influence the swelling as shown in Table II. The extent of swelling for all systems was greatest in pH 7.4 buffer solution and increased with increasing molecular weight.

Swelling of ionic polymers is related to ionization of the functional groups on the polymer chain, extension of the polymer molecules, and an increase in the spatial requirements for the polymer chains. The pH of the EMA polymer series studied has been reported as 4.9 (4). It is therefore not surprising that the greatest swelling was observed at pH 7.4. The transparent swollen layer which is formed on the polymer surface may be considered as a polymer solution which retains considerable order and structure with respect to the polymer. As such its properties would be expected to greatly influence the dissolution of the polymer.

**Solvent Penetration Measurements**—The penetration of solvent into the polymer compressed disks is shown in Figs. 5 and 6. An initial linear penetration rate was established in each polymer molecular weight fraction which appeared to change rapidly to a lower rate of penetration (Table III). The greatest change in rate was seen in pH 7.4 buffer solution. The decrease in the solvent

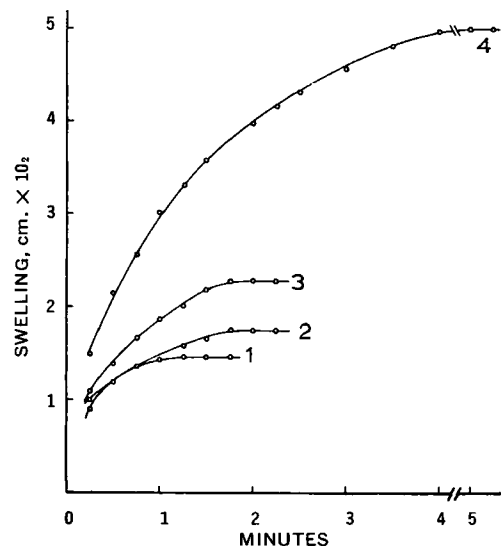


Figure 3—Swelling of EMA copolymers in pH 1.2 buffer. Key: 1, EMA-H11; 2, EMA-H1103; 3, EMA-H22; 4, EMA-H31.

Table II—Extent of Polymer Swelling as Related to Molecular Weight and pH

Polymer	—Maximum Swelling <sup>a</sup> cm. × 10 <sup>2</sup> —		
	pH 1.2	Water	pH 7.4
EMA-H11	1.47	1.49	2.08
EMA-H1103	1.70	1.85	2.00
EMA-H22	2.37	2.67	3.06
EMA-H31	5.03	5.08	5.88

<sup>a</sup> The experimental values were multiplied by 10<sup>2</sup> to obtain the values in the table.

<sup>2</sup> Carver Model B, Fred S. Carver Co., Summit, N. J.

<sup>3</sup> Gaertner Scientific Co., Chicago, Ill.

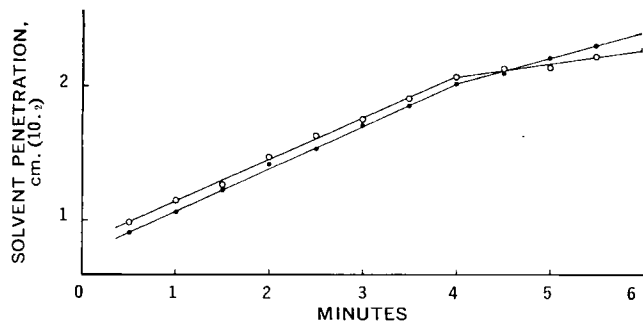


Figure 5—Solvent penetration into EMA-H22. Key: ●, Water and pH 1.2 buffer; ○, pH 7.4 buffer.

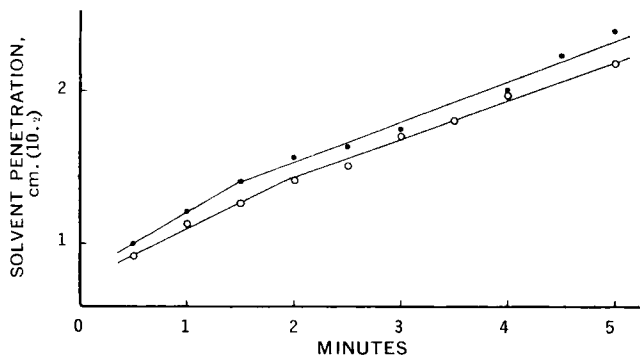


Figure 6—Solvent penetration into EMA-H11 and EMA-H1103 in distilled water. Key: ●, EMA-H11; ○, EMA-H1103.

penetration rate at the higher pH would appear to be due to an increase in overall polymer swelling which would be expected to restrict solvent movement into the polymer disk. Further evidence of restricted solvent penetration with increased swelling is indicated by the decrease in solvent penetration rate with increasing molecular weight (Table III), as the extent of polymer swelling was shown to increase with increasing molecular weight (Table II).

**Hydrated Layer Thickness Measurements**—The hydrated layer was defined in this study as that layer of the polymer disk which had interacted with or was capable of interacting with the solvent; it is therefore the sum total of polymer swelling and solvent penetration. A constant hydrated layer thickness was achieved within 3 to 4 min. following disk exposure to solvent. The maximum hydrated layer thickness increased with molecular weight (Fig. 7) and with pH between pH 2 and 7 (Fig. 8). As expected from swelling data, the hydrated layer thickness was related to the degree of dissociation of the hydrated polymer molecules in the layer.

The hydrated layer edge of EMA-22 receded at a rate of  $2.23 \times 10^{-5}$  cm./sec. in distilled water and pH 1.2 buffer solution. These rates were in close agreement with the final solvent penetration rates for EMA-22 (Table III). The rate at which polymer molecules

Table III—Initial and Final Solvent Penetration Rates for Various Molecular Weight Fractions of EMA Free Acid

	Rate, cm. $\times 10^5$ /sec.		
	Distilled Water	pH 1.2	pH 7.4
EMA-H22			
Initial	5.30	5.30	5.13
Final	2.17	2.17	1.10
EMA-H1103			
Initial	5.88	5.86	—
Final	2.83	2.79	1.67
EMA-H11			
Initial	6.50	6.48	—
Final	4.80	4.08	2.70

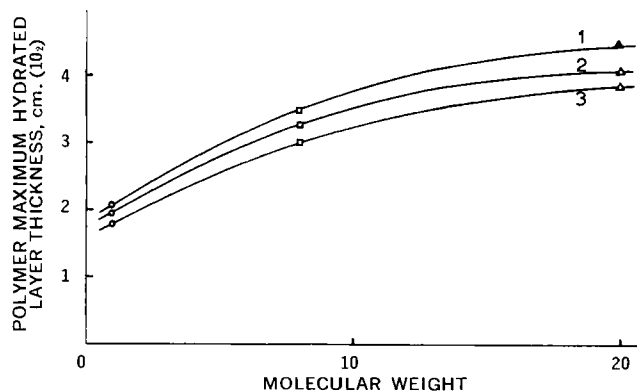


Figure 7—Polymer maximum hydrated layer thickness as related to molecular weight. Key: 1, pH 7.4 buffer; 2, distilled water; 3, pH 1.2; ○, EMA-H11; □, EMA-H1103; △, EMA-H22

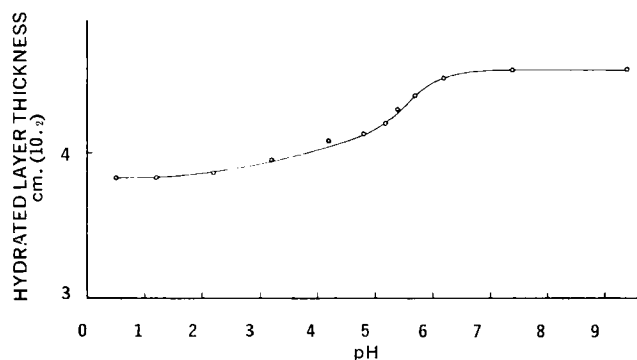


Figure 8—Maximum hydrated layer thickness of EMA-H22 as affected by pH.

left the hydrated layer surface or the rate of polymer dissolution appears therefore to correspond to the penetration rate of solvent into the polymer disk. Therefore, the extent of polymer swelling in the EMA copolymer series studied would appear to be a limiting factor in polymer dissolution due to its influence on solvent penetration rate.

## SUMMARY

Through the use of an optical method, the rate of solvent penetration into a compressed polymer disk and the extent of polymer swelling at the disk surface were determined in distilled water, pH 1.2 and 7.4 buffer solution. Maximum swelling occurred at pH 7.4 whereas the slowest rate of solvent penetration occurred at this pH. The disappearance of the hydrated layer edge was found to correspond to the rate of solvent penetration, indicating that the extent of polymer swelling may be a limiting factor in polymer dissolution.

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\* Present address: School of Pharmacy, University of Connecticut, Storrs, Conn.