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DISCLAIMER

Buffer Effects on Aqueous Swelling Kinetics of Polyelectrolyte Gels

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SYNOPSIS

Electrolytes are often added to a gel-swelling medium under the assumption that the important conditions which characterize swelling rates are the solution pH and ionic strength, with little emphasis on the nature of the electrolyte. Previous research by Siegel et al (1,2) has indicated that the presence of the un-ionized acidic form of an electrolyte buffer is a primary rate-determinant for swelling of a polybase gel. A systematic swelling study on two separate gels, 2-hydroxyethyl methacrylate copolymerized with methacrylic acid (HEMA/MAA) and N,N dimethylaminoethyl methacrylate (HEMA/DMA) has been performed to investigate the influence of the concentration of the un-ionized buffer by three principal factors: 1) total buffer concentration, 2) solution pH, and 3) buffer pK_a. Swelling and deswelling kinetics were obtained.

In the presence of an electrolyte buffer, a dramatic swelling rate increase is observed for the HEMA gels, with substantial gains in rate obtained as total buffer concentration rises. Results also emphasize that to enhance swelling kinetics, the pH must be such that the buffer is essentially unionized.

INTRODUCTION

Although the effect of buffer rate-enhancement has been documented for various processes (reaction in immobilized enzyme systems (3), proton transport in muscle (4,5), drug dissolution (6-11)), the use of buffers in polyelectrolyte gels remains largely unexplored. Much of the work on polyelectrolyte-gel swelling kinetics stresses the importance of solution conditions such as pH and ionic strength in influencing the characteristics of gel behavior (10-16). Often, salts and other strong electrolytes are incorporated into the external solution to modulate swelling equilibria of the ionized gels. Electrolyte buffers, in the form of acids and bases, may also be added to stabilize

solution pH. These electrolytes are often added into the swelling medium under the assumption that the important conditions characterizing swelling behavior are primarily solution pH and ionic strength, with little emphasis on the nature of the electrolyte (15). Previous work has shown, however, that the electrolyte type in the external solution is a primary factor in determining the swelling rate of a copolymer gel. For a poly(methyl methacrylate-co-N,N-dimethylaminoethyl methacrylate) gel (MMA/DMA), swelling of a gel disk, (9 mm in diameter and 0.4 mm in thickness), in an unbuffered solution at relatively neutral pH normally takes on the order of several weeks or months to reach equilibrium; by incorporating an electrolyte buffer in solution (1,2) swelling equilibria are attained within hours.

A shuttle mechanism has been introduced to explain the rate enhancement of gel swelling due to buffer present in solution (1,2) For MMA/DMA polybasic gels, external hydrogen ions are carried through the swollen gel by the acidic form of the buffer to the fixed amine groups within the network; ionization of the amine groups in the gel subsequently occurs by proton transfer from the buffer to the amine. The deprotonated buffer then acts as a counterion which ultimately is exchanged with chloride from the salt present in the external solution. Hence, it was postulated that the acidic form of the buffer is the rate-determining species for swelling. The buffer can thus increase the rate of swelling by one of two different mechanisms: 1) the unionized, acidic form of the buffer enhances the number of total hydrogen ions available in solution to protonate the amine groups, and 2) the unionized, neutral form of the buffer facilitates the transport of hydrogen ions through the outer layer of swollen, charged gel. In the first mechanism, the carboxylic acid buffer acts as an extra source of protons in addition to those already present in solution as hydronium ions. The buffer protons are available for protonating the fixed-amine groups, provided the buffer pK_a is lower than the amine pK_a.

The second mechanism is based on the Donnan-exclusion principle. The swelling process in a gel disk is assumed to occur one-dimensionally; swelling proceeds from both faces of the disk and gradually works towards the center of the gel disk. As the swelling process occurs, an outer layer of charged gel, consisting of positively ionized amine groups, gradually forms on both faces of the gel disk. The positively charged gel layer sets up a Donnan potential, which acts as a barrier to the entrance of free protons in the solution by charge exclusion. On the other hand, protons that are attached to the neutral or negatively charged buffer can diffuse through the charged gel undisturbed by the Donnan potential.

Although the preceding interpretations apply to polybase gels, the buffer effect can be easily extended to include both polyacid and polybasic gels for a wide variety of gel types. Rather than free protons and carboxylic acid buffers protonating fixed amine groups, the same interpretation can apply to hydroxide ions and amine buffers which extract protons from fixed carboxylic-acid groups. Moreover, polyacid gels can also be made to swell using a carboxylic acid buffer with a pK_a higher than that of the gel. Therefore, a systematic swelling study on two separate gels, 2-hydroxyethylmethacrylate copolymerized with methacrylic acid (HEMA/MAA), and N,N dimethylaminoethyl methacrylate (HEMA/DMA), has been performed to investigate the influence of three different factors controlling the concentration of the unionized buffer: 1) the total buffer concentration, 2) the solution pH, and 3) the buffer pK_a (2). In addition, swelling studies on poly(methylmethacrylate-co-methacrylic acid) gels were performed to complement previous work (1,2). Swelling and deswelling experiments were conducted for the HEMA gels to obtain comprehensive results.

MATERIALS AND METHODS

Materials

High-purity monomers, 2-hydroxyethyl methacrylate (HEMA), methyl methacrylate (MMA), methacrylic acid (MAA), and 2-(dimethylamino)ethyl methacrylate (DMA), were from Polysciences, Inc. Crosslinking agents used for polyacid and polybasic gels were divinylbenzene (DVB), from Pfaltz and Bauer, Inc., and ethylene glycol dimethacrylate (EGDMA) from Polysciences, Inc. Vacuum distillation in the presence of polymerization inhibitor, 1,3,5-trimethyl-2,4,6-tris[3,5-di-tert-butyl-4-hydroxybenzyl] benzene (Ethyl Corp.), was performed on all commercial monomers and DVB to eliminate impurities. The free-radical initiator for polymerization, 2,2'-azobisisobutyronitrile (AIBN) (Polysciences, Inc.) was recrystallized from water-ethanol prior to use. Electrolyte buffers were obtained from Aldrich Chemical Company: 95-97% formic acid, 99+% dichloroacetic acid, and 99% ethanolamine. Additional buffers were grade-1, crystalline Imidazole (Sigma Chemical Company), and reagent A.C.S. grade, glacial acetic acid (Fisher Scientific). All buffer reagents were used as received. Dichlorodimethylsilane, (Eastman Kodak Company), and Ethanox 330, (1,3,5-trimethyl-2,4,6-tris [3,5-di-tertbutyl-4-hydroxybenzyl] benzene), (Ethyl Corporation) were also used as received. Certified A.C.S. toluene and methanol solvents, in addition to crystalline sodium chloride, were from Fisher Scientific. Water was double distilled and deionized to ultrafiltered, type-I reagent-grade water by the Barnstead Nanopure Series 550 system.

Polymerization

Copolymer gel sheets were synthesized by free-radical bulk polymerization (17) between two 10 x 10-cm silanized glass plates. Prior to synthesis the glass plates were silanized to prevent permanent adhesion of the gel to the plates, by submerging the plates in toluene containing 2% (v/v) dichlorodimethyl silane; the plates were subsequently rinsed with toluene and air-dried. Teflon spacers of 0.48 mm were inserted between the glass plates to form a uniform internal cavity for the monomer

solution and metal clamps were used to hold the cassette firmly in place. A mixture of 78/22 mole % HEMA or MMA and MAA or DMA monomer, respectively, 0.5% w/w initiator, and 0.1% w/w crosslinker was prepared, and then fitted with a manifold for degassing. After 5 minutes of constant stirring, the monomer solution was injected into the vertically-oriented cassette through a 24-gauge needle syringe and placed vertically in a vacuum oven at 60 °C under nitrogen for approximately 18 hours. After incubation, the cassette was allowed to equilibrate to room temperature before detaching the solid gel sheet from the glass plates with a razor edge; circular disks were punched with a 11-mm diameter metal borer. Gel disks were swollen in methanol for 4 hours to release any remaining reactants within the gel matrix and then collapsed in a 50% (v/v) solution of methanol and water for 1 hour to facilitate handling without damage. Lastly, the disks were dried at room temperature before transferrering to a vacuum oven for additional drying at 60 °C for 24 hours.

Measured disk dimensions were comparable to expected dimensions. Diameters ranged from 9-11 mm and thicknesses, measured with a micrometer, were slightly smaller than expected at 0.38-0.43 mm. Compositions of both MMA and HEMA gels were analyzed by elemental analysis and showed complete incorporation of the monomers into the gel.

Kinetic Measurements

Duplicate gel disks in perforated baskets were immersed in 2-liter flasks of either buffered or unbuffered solutions. Unless otherwise specified, buffered solutions contained 0.01M buffer, along with a precalculated amount of sodium chloride which brought the total ionic strength to 0.1M. Concentrated sodium hydroxide or hydrogen chloride were added to bring the solution to the desired pH. Experiments were performed at 25 °C with vigorous stirring. Gels were periodically removed from the solution, blotted with a kimwipe to eliminate excess solution from the surface, and

weighed; the gels were then returned to the solution within a 20-second period. Final pH values were measured after each experiment and in most cases, the pH change was only on the order of 0.05 pH units. However, a relatively large change in pH was observed for initially neutral pH unbuffered solutions. Measures were taken to maintain a constant solution pH for these runs by periodically adding small amounts of HCl or NaOH; intermittently, fresh solutions were made and the gel solution was subsequently exchanged to assure constant ionic strength. Identical procedures were employed in the deswelling experiments. However, prior to the deswelling measurements, gels were initially swollen to equilibrium in pH 12 unbuffered solutions.

Data Reduction

The extent of swelling was measured as a ratio of the weight of water absorbed into the gel divided by the weight of dry gel disk. The ratio is calculated as:

$$\frac{[W(t) - W(0)]}{W(0)}$$

where W(t) is the weight of the gel at time t, and W(0) is the initial dry weight of the gel. Normalized ratios were determined as:

$$\frac{[W(t) - W(0)]}{[W(e) - W(0)]}$$

where W(e) is the weight of the swollen gel at equilibrium.

Deswelling was measured similarly; however, ratios were also normalized to the equilibrium value of the deswollen gel as given in the following equation:

$$\frac{[W(t) - W(e2)]}{[W(e1) - W(e2)]}$$

where W(e1) and W(e2) are the equilibrium swollen and deswollen weights, respectively.

RESULTS AND DISCUSSION

In the following experiments, the relationship between the pK_a of the fixed, ionizable groups on the gel network and the buffer pK_a was an important factor in the selection of the various buffers, because, for buffer-enhanced swelling in polybasic gels such as MMA/DMA, the buffer pK_a must be below the pK_a of the gel amine. For carboxylic acid gels, the converse requirement applies that the buffer pK_a should be above that of the gel carboxylic acid, in order that the buffer can extract the proton from the gel. The pK_a of methacrylic acid is estimated to be 4.7, whereas the approximate pK_a of DMA is 7.7 (18). Hence, two amine buffers, imidazole and ethanolamine, were chosen for the polyacid gels with pK_a's of 6.95 and 9.50, respectively; carboxylic acid buffers -- dichloroacetic, formic, and acetic acids with respective pK_a's of 1.48, 3.75, and 4.75 -- were used in polybasic gel experiments. All pK_a values are specified at 25 °C.

Compositions of all gels were 78/22 mole % non-ionizable monomer (HEMA or MMA) to ionizable monomer (MAA or DMA), respectively, and all experiments were conducted at 25 °C and a final ionic strength of 0.1M.

Swelling Kinetics

Methyl methacrylate Gels

Prior to the swelling experiments conducted with MMA/MAA gels at a molar composition of 78/22 mole%, gels at various comonomer ratios were synthesized; however, at the lower limit of 70/30 mole% MMA/MAA the gels appeared cloudy and white in color, indicating phase separation (19-21). Gels synthesized at a higher concentration of MAA also showed similar turbidity.

The pH-dependence on the swelling kinetics of 78/22 mole% MMA/MAA gels was determined for several values in the pH range 8 - 13. Swelling curves resembled those for MMA/DMA gels in which swelling curves were characterized by a sigmoidal shape with relatively slow initial swelling followed by an acceleration in swelling rate; this sigmoidal behavior is explained by the "moving front mechanism" described in detail elsewhere (16,22-23). Prior to swelling, the dry gel is glassy and rigid in texture. During the swelling process, two solution fronts consisting of water and mobile ions propagate inwards from both surfaces of the disk, ionizing the fixed groups within the gel network immediately after hydration occurs; a rubbery consistency characterizes the swollen gel. The gel is confined to swelling in one direction since the glassy core present in the center of the gel prevents swelling in other directions. Once the two fronts meet, however, three-dimensional swelling can then proceed and an acceleration in rate results. The swelling diagram is thus characterized by an initial slow region in which swelling is constrained to one direction, followed by rapid, three-dimensional swelling. Finally, a slower swelling region occurs due to mechanical relaxation within the gel.

Buffer effects on MMA/MAA gels are shown in Figure 1, in which the amine buffer, imidazole, was employed at buffer concentrations of 0.01M and 0.02M. All experiments were performed at pH 9. In the unbuffered case, for neutral pH, swelling rates are extremely slow, on the order of several months, to reach equilibrium. However, the influence of buffer on swelling rate is demonstrated in Figure 1; at pH 9, the swelling rate with buffer is 9 times that without buffer. The effect of total buffer concentration is also shown in Figure 1 in which doubling the total buffer concentration from 0.01M to 0.02M produces a rate increase of 18%.

Recently, evidence for base-catalyzed hydrolysis of the MMA ester group has been documented (24). An essential problem with MMA gels concerns the hydrolysis of the methyl ester to methacrylic acid to form methanol in the alkaline pH region. The

overall result is the development of a more ionizable gel which would introduce considerable uncertainty in kinetic results. To minimize this hydrolysis effect, a different monomer with a bulkier ester group was used.

Hydroxyethyl methacrylate Gels

To conduct a comprehensive study on the effect of buffer, results were obtained for the swelling and deswelling kinetics for both polyacid and polybasic 2-hydroxyethyl methacrylate gels (HEMA).

Total Buffer Concentration

Figure 2 shows the influence of total buffer concentration at fixed pH = 9 and ionic strength of 0.1M on the swelling rate of HEMA/MAA gels. With reference to the buffer concentration curve of 0.01M, substantial gains in swelling rate are seen with buffer concentration increases to 0.02M and 0.05M. By increasing the total buffer concentration, the quantity of base is amplified without effectively increasing the pH of the solution.

Buffer effects are clearly observed in a comparison between Figures 3 and 4 which indicate a substantial difference in rate for pH 8 thru 11. HEMA/MAA gels in unbuffered solution of the latter pH range ordinarily reach equilibrium in a period of several days. However, the addition of imidazole buffer into the external solution at the same pH produces a dramatic increase in swelling rate; the time to reach equilibrium is reduced to only a few hours, as shown in Figure 4.

Solution pH

The swelling-rate dependence on solution pH is shown in Figures 3 through 5 for both the polyacid and polybasic, HEMA gels. HEMA/MAA curves in unbuffered solutions are shown in Figure 3; Figures 4 and 5 display buffered swelling curves for HEMA/MAA in imidazole, and HEMA/DMA in formic acid, respectively. In the unbuffered solution, the pH-dependence on swelling is influenced by the

concentration of protons and hydroxide ions. As the concentration of protons falls, the rate of swelling increases for acidic gels, but decreases for basic gels. The swelling curves in Figures 3 through 5 show several important features. First, sigmoidal swelling curves are observed for the HEMA gels, as seen in the MMA gels. However, a distinctive swelling acceleration is observed in the MMA gels, whereas only a slight sigmoid shape appears for the HEMA gels. Different mechanisms may possibly play a role for each gel type.

In the swelling kinetics of HEMA/MAA gels, all gels reached approximately the same equilibrium plateau. Swelling equilibrium ratios were in the range 6.0 to 6.5. Since the solution pH is well above the pKa of the polyacid gel, the gel can become fully charged; hence, swelling equilibria are constant throughout the swelling pH range. Monovalent buffers were also used exclusively and the ionic strength was maintained constant. Buffer effects dominate swelling kinetics but not swelling equilibria.

Finally, a comparison of the MMA and HEMA polyacid gels in Figures 1 thru 4 indicates a significant difference in buffer effect between the two gel types. Although similarities exist in which general trends for HEMA/MAA are similar to those observed for MMA/MAA gels, the difference in swelling rates for the 0.01M buffered and unbuffered cases between the MMA/MAA and the HEMA/MAA gel clearly shows a greater increase in rate for the more hydrophilic HEMA gel. A 9-fold increase in rate at pH 9 was observed for the MMA gel. A considerably larger increase of 75 times that of the unbuffered case was determined for HEMA at the same pH. The large discrepancy in buffer effect between the two types of gels may be attributed to differences in the glass transition temperature of each gel. Another possible explanation for the discrepancy could be ascribed to the hydrophobicity of the MMA monomer. Although the presence of the buffer may enhance the ionization of fixed groups, the hydrophobic character of MMA may dominate the hydration step of the

swelling process in which the influx of water into the gel can be retarded or even inhibited. Further evidence for the hydrophobic dominance is also apparent in the correlation between total buffer concentration and rate for both gel types from Figures 1 and 2.

Buffer pKa

A comparison between Figures 4 and 5 gives direct evidence for the effect of a pK_a-pH relationship on buffered swelling rates. Figure 4 for HEMA/MAA gels in imidazole reveals an important feature near the neutral pH values: swelling curves at pH 8 to 10 coincide to fit approximately a single curve, whereas curves separate into regular-spaced intervals as pH rises. However, this behavior is not apparent in Figure 5 for the HEMA/DMA gels in formic acid. Instead, swelling rates gradually increase at constant intervals, even in the low-pH range. The difference in low-pH swelling behavior for the two buffered solutions can be attributed to the relationship between the solution pH and pK_a of the buffer used in each case; these two factors mutually interact to alter the concentration of unionized buffer present in solution. For polyacid gels, the pK_a of the amine buffer must be lower than the solution pH for the buffer to be basic and hence available to extract a proton from the fixed groups. In Figure 4, all pH values shown for HEMA/MAA are above the imidazole pK_a of 6.95. In addition, the lowest pH of 8 is one pH unit above the pK_a of imidazole. Hence, the different rates observed at pH 8 to 13 are effectively due to the concentration of hydroxide ions rather than imidazole since the total imidazole concentration is the same in each case.

A possible simple interpretation can be made for the superimposed curves in Figure 4. At pH 8 to 10, hydroxide concentrations are relatively low and little difference in swelling rate can exist. However, as pH increases, the increase in hydroxide ion concentration become sufficient to influence swelling rates substantially. It is important to note that the buffer effect at high pH values is modest in comparison to those at lower pH values. Swelling rates in the presence or absence of buffer are comparable

at pH 13. Both buffered and unbuffered solutions contain a large concentration of hydroxide ions at pH 12 and 13, and the buffer is negligable. On the other hand, the hydroxide concentration for both buffered and unbuffered solutions at low pH are relatively small in comparison to the 0.01M concentration of buffer and the effect of buffer is apparent.

In contrast, to interpret the widely-spaced swelling curves in the acidic pH range in Figure 5, previous explanations regarding HEMA polyacid gels can apply inversely to polybasic gels. In general, the carboxylic-acid buffer pK_a for polybasic gels must be above the solution pH for the buffer to exist in the neutral form to enable the buffer to protonate the fixed, amine groups. Hence, at pH values of 4 and 5, the pH is greater than the formic-acid buffer pK_a of 3.75; the conjugate base of the buffer is consequently charged, rendering the buffer unable to donate protons. A small, yet significant increase in rate, however, is observed at pH 4 since the pK_a-pH difference is less than one pH unit; an appreciable fraction of neutral formic acid buffer is thus still present in solution.

The effect of the pK_a-pH relationship on swelling rate is further emphasized by results in Figures 6 and 7. Swelling curves are compared for various buffers at pH values encompassing the buffer pK_a's. In Figure 6, ethanolamine, imidazole, and unbuffered solutions are compared at pH 9 and 11 for HEMA/MAA gels. As expected, the unbuffered experiment indicates the slowest swelling rate in both pH cases. In addition, imidazole exhibits the fastest rate in comparison to ethanolamine. The difference in swelling rate between the two buffers, however, is much greater at pH 9 than at pH 11. In view of the ethanolamine and imidazole pK_a's of 9.5 and 6.95, respectively, the former buffer predictably induces a slower rate at pH 9 and the close proximity of the two buffered curves at pH 11 is due to the neutrality of both buffers. At pH 9, a fraction of the ethanolamine is positively charged and acidic, inhibiting the buffer from extracting protons from the carboxylic acids within the gel. On the other

hand, imidazole remains in its neutral, basic form. At pH 11, both buffers are neutral, thereby resulting in a substantial decrease in the difference between the two swelling rates.

Complementary results are noted in Figure 7 for HEMA/DMA gel with formic acid (pK_a 3.75), and acetic acid (pK_a 4.75) buffers. These results are in line with observations made in a previous study (2).

To test the buffer-effect hypothesis, HEMA polyacid gel was swollen in a solution buffered with acetic acid rather than an amine; results at pH 9 were compared to other cases in Figure 8. The conjugate base of acetic acid would predominate at pH 9 and would be a relatively weak base in comparison to hydroxide and other amine buffers. Thus, swelling by acetic acid would not be significant. In Figure 8, however, the swelling rate for acetic acid is somewhat greater than that for the unbuffered case, although less than that for amine buffers. This difference may be explained by comparing the acetic acid pK_a and the effective pK_a of the HEMA/MAA gel; both are very close in value, respectively 4.75 versus 4.7, so that the conjugate form of acetic acid acts as a stronger base for extracting MAA protons than originally expected. More importantly, the acetic acid concentration at 0.01M is greater than that of the hydroxide ion, 10^{-5}M at pH 9; hence, the rate of swelling for the acetic acid is larger than that for the unbuffered solution.

Deswelling Kinetics

Deswelling kinetics were determined using both HEMA/MAA and HEMA/DMA gels. Gels were initially swollen to equilibrium at pH 12 prior to deswelling. Swelling ratios are normalized to both the swollen and deswollen equilibria, as described above.

Typical pH-dependent deswelling curves for HEMA/MAA are shown in Figure 9. Although not shown, similar curves are observed for HEMA/DMA gels. Deswelling

kinetics were conducted under conditions opposite to those employed in the corresponding swelling experiments; carboxylic-acid buffers were used for polyacid gels. Where a decrease in pH from 8 to 13 produced a decrease in swelling rates, a pH decrease from 6 to 1 resulted in increased deswelling rates.

From Figure 9, the greatest change in rate due to formic acid buffer is at pH 3 to 4; rates are closer in proximity at pH 5 and 6 as well as for pH 1 and 2. As pH decreases, a greater concentration of protons is available in unbuffered solution for protonating the ionized carboxylic acids fixed in the gel network, thereby increasing the deswelling rate. With respect to large buffer effects observed at pH 3 and 4, varying fractions of available formic acid buffer for protonating fixed groups exist at these pH values since the formic acid pK_a is 3.75. The approximately 1 unit difference in pK_a between formic acid and methylacrylic acid makes the former an excellent delivery carrier of protons to the latter.

A distinctive sigmoidal shape is once again observed in the deswelling curve at pH 3. However, unlike those observed in swelling, the sigmoidal shape is not attributed to the moving-front mechanism. During the deswelling process, a rigid, glassy layer forms around the gel disk. As deswelling proceeds, pressure is generated within the gel, leading to a "bursting" of the gel. Evidence for "bursting" was clear: the gel disk appears to split into two individual disks in the deswollen state. Similar effects for other gel types has been documented (25-27). The effect is indiscernable in the curves for low pH extremes, perhaps due to the rapidity of the deswelling rate which conceals any evidence of a "bursted" gel.

Figures 10 and 11 show deswelling rates for HEMA/MAA and HEMA/DMA gels, respectively; these figures indicate how the relation between solution pH and buffer pK_a affects the rate of deswelling. In Figure 10, pH values were chosen near the pK_a's of formic and dichloroacetic acid. Formic acid curves show the greatest deswelling rate at all pH values, with the largest difference between formic and

dichloroacetic acid at pH 3. The smallest difference in buffer effect is observed at pH 1 since the pH is below both buffer pK_a's; most important, the proton concentration present in the solution dominates the buffer concentration at pH 1, overshadowing any buffer effects. The differences in rate observed at pH 1 can be ascribed to experimental error.

Figure 11 shows systematic results for HEMA/DMA gels.

The Donnan exclusion effect seen in swelling kinetics does not play a role in deswelling (28). Since the deswelling process consists of the formation of a neutral outer layer, protons are not required to overcome a Donnan potential. Hence, the effect of buffer on deswelling is described only as an enhancement of base or acid in the solution. The enhancement of deswelling rates by buffers is observed elsewhere (29).

In summary, the following rules apply to polyacid and polybasic gels for both swelling and deswelling in buffered solutions. To increase the rate of swelling in a polyacid gel, the basicity of the buffer must be maximized to allow for proton extraction of the gel acid groups. Two conditions must be met: the solution pH must be greater than the buffer pK_a and the buffer pK_a must be greater than the pK_a of the gel. In contrast, deswelling rates may be increased in a polyacid gel by increasing the acidity of the buffer to donate protons to the conjugate base groups of the gel. Hence, in this case, the solution pH must be less than the buffer pK_a and the buffer pK_a must be less than the pK_a of the gel. The opposite cases apply for polybasic gels. Solution pH must be less than the buffer pK_a which in turn must be less than the gel pK_a for proton exchange to occur rapidly during swelling. To facilitate deswelling, protons are readily extracted if the following conditions are met: the solution pH is greater than the buffer pK_a and the buffer pK_a is greater than that of the gel .

CONCLUSIONS

Evidence is provided that the presence of a neutral electrolyte buffer in the external medium significantly increases the rate of swelling; two possible explanations have been introduced: the buffer enhances the base or acid concentration in the solution without effectively changing the solution pH, and the neutrality of the buffer circumvents the Donnan potential generated in the swollen gel. Various swelling and deswelling experiments with polyacid and polybasic, 2-hydroxyethyl methacrylate gels and poly(methyl methacrylate-co-methacrylic acid) gel have shown that the concentration of the un-ionized buffer is influenced by solution pH, buffer pK_a, and total buffer concentration. Results indicate that the buffer effect is greater for the more hydrophilic gel. An important pH-pK_a relationship determines the degree to which swelling or deswelling is augmented. The Donnan exclusion effect is not apparent in the deswelling process.

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FIGURE CAPTIONS

Figure	Captions
1	Comparison of swelling kinetics for buffered and unbuffered solutions; variation of total buffer concentration78/22 mole % MMA/MAA gel; pH =9; Imidazole buffer used; Cb = total buffer concentration. Unbuffered (—◆—); Cb = 0.01M (—□—); Cb = 0.02M (—■—).
2	Variation of total buffer concentration for swelling kinetics; 78/22 mole % HEMA/MAA gel; pH=9; Imidazole buffer used; Cb = total buffer concentration. Cb = 0.01M (—◇—); Cb = 0.02M (—■—); Cb = 0.05M (—□—).
3	Swelling pH-dependency;78/22 mole % HEMA/MAA gel; Unbuffered. pH 8 (—□—); pH 9 (—◆—); pH 10 (—■—); pH 11 (—◇—); pH 12 (—■—); pH 13 (—□—).
4	Swelling pH-dependency;78/22 mole % HEMA/MAA gel; Imidazole buffer. pH 8 (—□—); pH 9 (—◆—); pH 10 (—■—); pH 11 (—◇—); pH 12 (—■—); pH 13 (—□—).
5	Swelling pH-dependency;78/22 mole % HEMA/DMA gel; Formic Acid buffer. pH 1 (—□—); pH 2 (—◆—); pH 3 (—■—); pH 4 (—◇—); pH 5 (—■—).
6	Comparison between swelling kinetics for unbuffered, ethanolamine, and imidazole at pH 9 and 11;78/22 mole % HEMA/MAA gel. Ethanolamine at pH 9 (—■—) and pH 11 (—□—); Imidazole at pH 9 (—●—) and pH 11 (—○—); Unbuffered at pH 9 (—▲—) and pH 11 (—△—).
7	Comparison between swelling kinetics for unbuffered, formic acid and acetic acid at pH 4 and 5; 78/22 mole % HEMA/DMA gel. Unbuffered at pH 4 (—■—) and pH 5 (—□—); Formic Acid at pH 4 (—●—) and pH 5 (—○—); Acetic Acid at pH 4 (—▲—) and pH 5 (—△—).
8	Comparison of swelling kinetics for amine versus carboxylic acid buffered solutions; 78/22 mole % HEMA/MAA gel; pH =9. Unbuffered (—□—); Imidazole (—◆—); Ethanolamine (—■—); Acetic Acid (—◇—).
9	Deswelling pH-dependency; 78/22 mole % HEMA/MAA gel; Formic Acid buffer. pH 1 (—□—); pH 2 (—◆—); pH 3 (—■—); pH 4 (—◇—); pH 5 (—■—); pH 6 (—□—).

10 Comparison of deswelling kinetics for unbuffered, dichloroacetic acid, and formic acid at pH 1, 3, and 5; 78/22 mole % HEMA/MAA gel. Formic Acid at pH 1 (—△—), pH 3 (—○—), and pH 5 (—□—); Unbuffered at pH 1 (—▲—), pH 3 (—o—), and pH 5 (—■—);Dichloroacetic Acid at pH 1 (—▲—), pH 3 (—o—), and pH 5 (—▫—).

11 Comparison of deswelling kinetics for unbuffered, imidazole, and ethanolamine at pH 9 and 11;78/22 mole % HEMA/DMA gel. Unbuffered at pH 9 (—○—) and pH 11 (—□—); Ethanolamine at pH 9 (—o—) and pH 11 (—▫—); Imidazole at pH 9 (—o—) and pH 11 (—▫—).

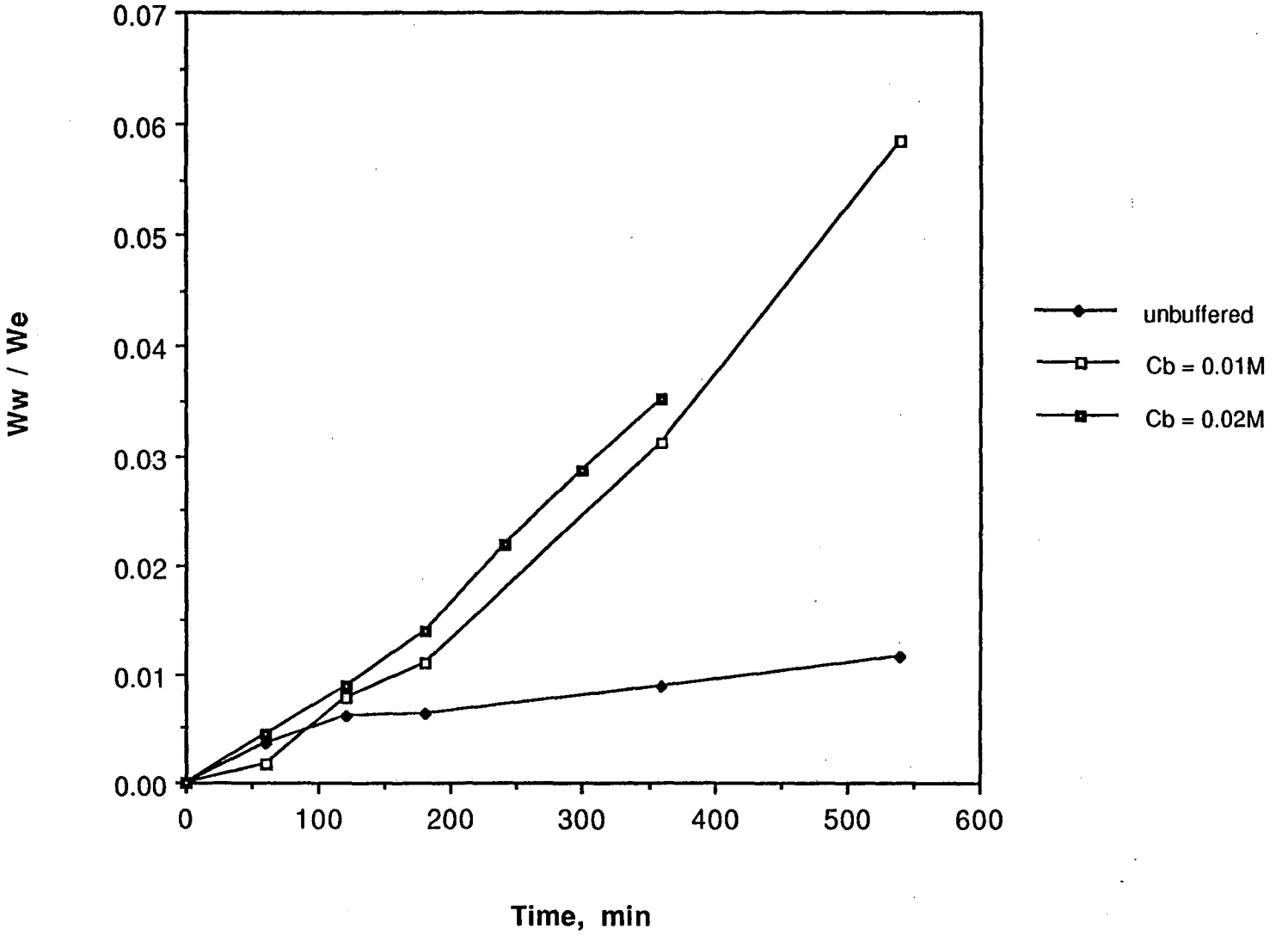

Figure 1: 78/22 mol% MMA/MAA gel; pH = 9; Imidazole buffer used; Cb is the total buffer concentration

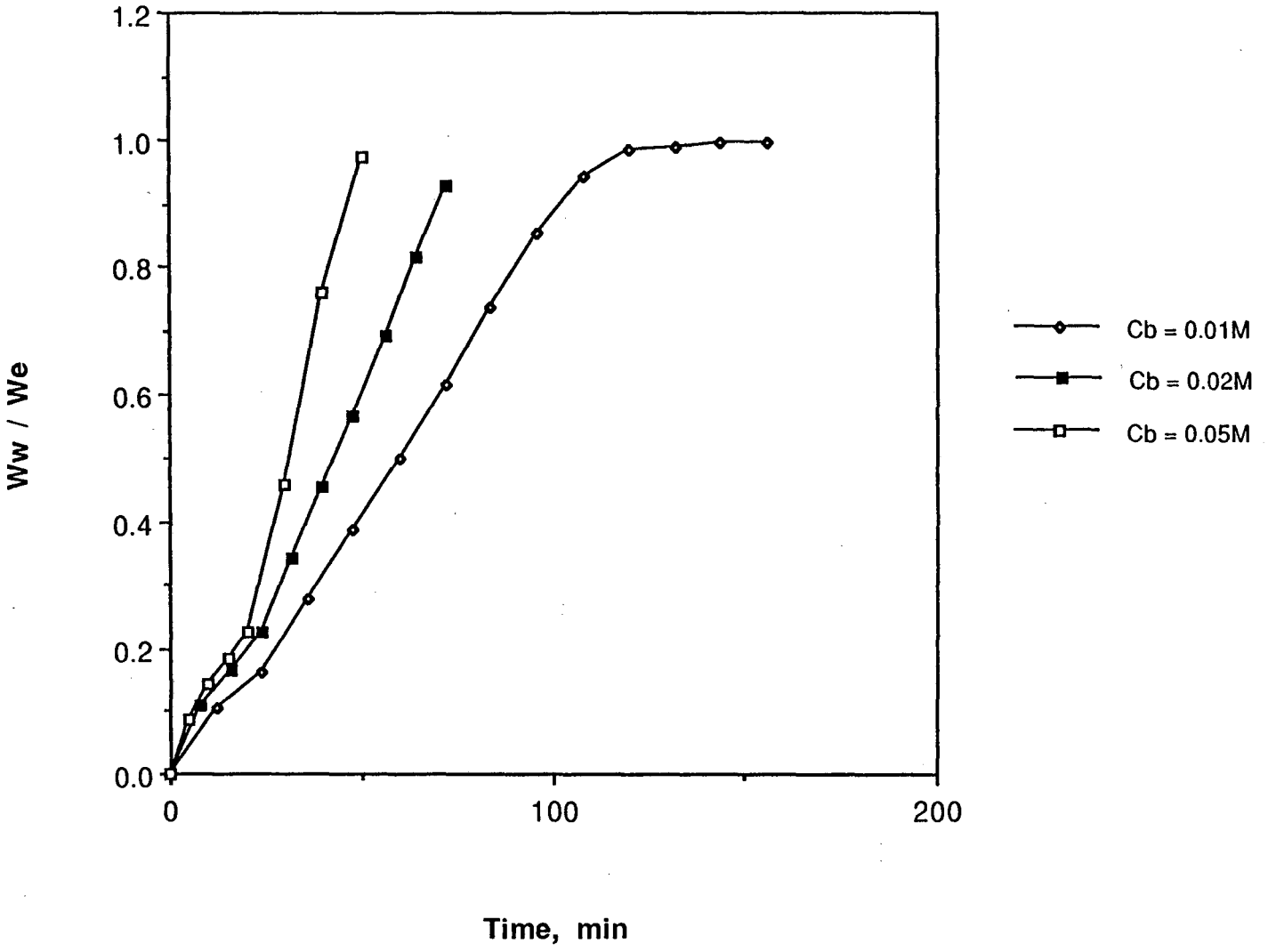

Figure 2: 78/22 mol % HEMA/MAA gel; pH = 9; Imidazole buffer used; Cb is the total buffer concentration

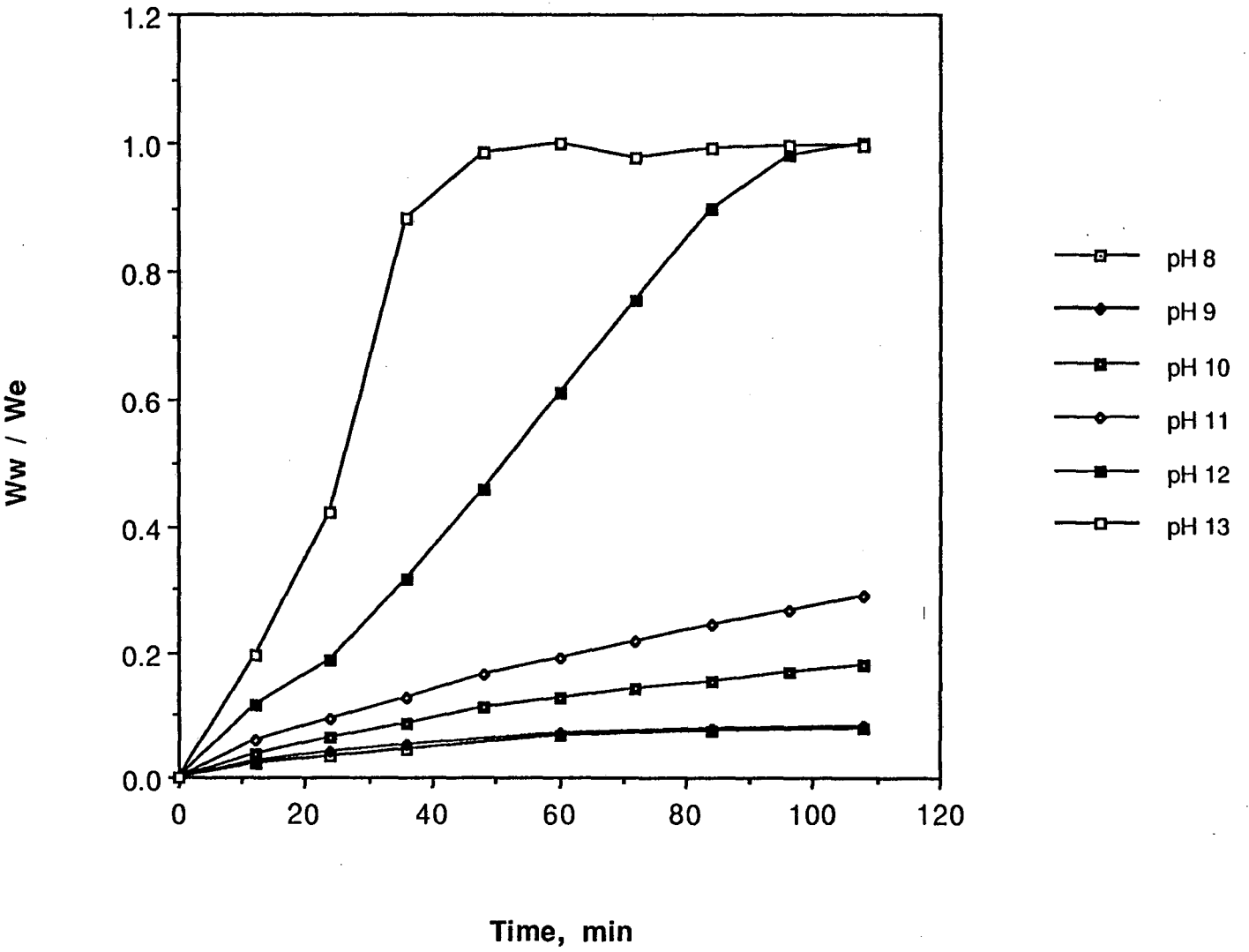

Figure 3: 78/22 mol % HEMA/MAA gel; Unbuffered

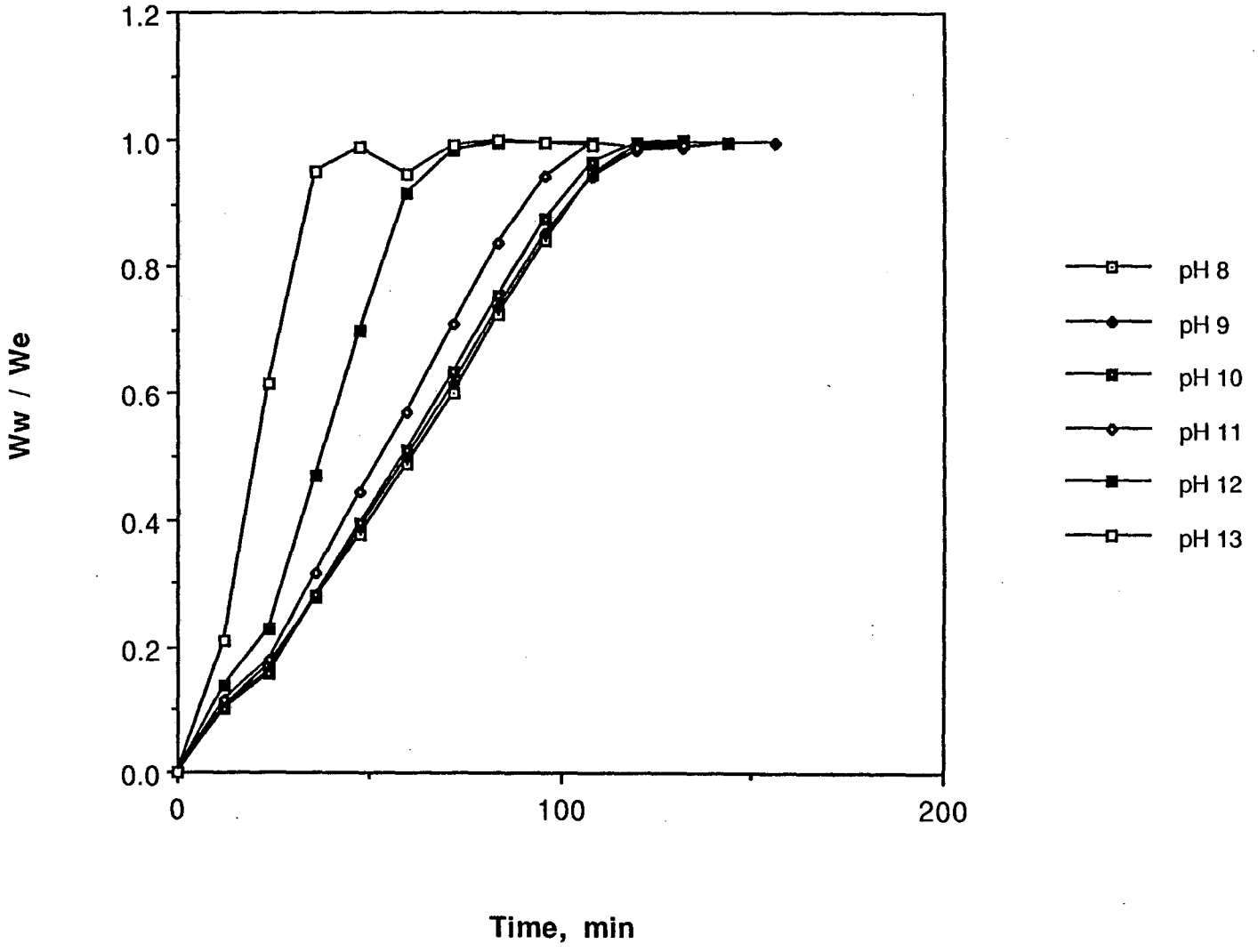

Figure 4: 78/22 mol % HEMA/MAA gel; Imidazole buffer

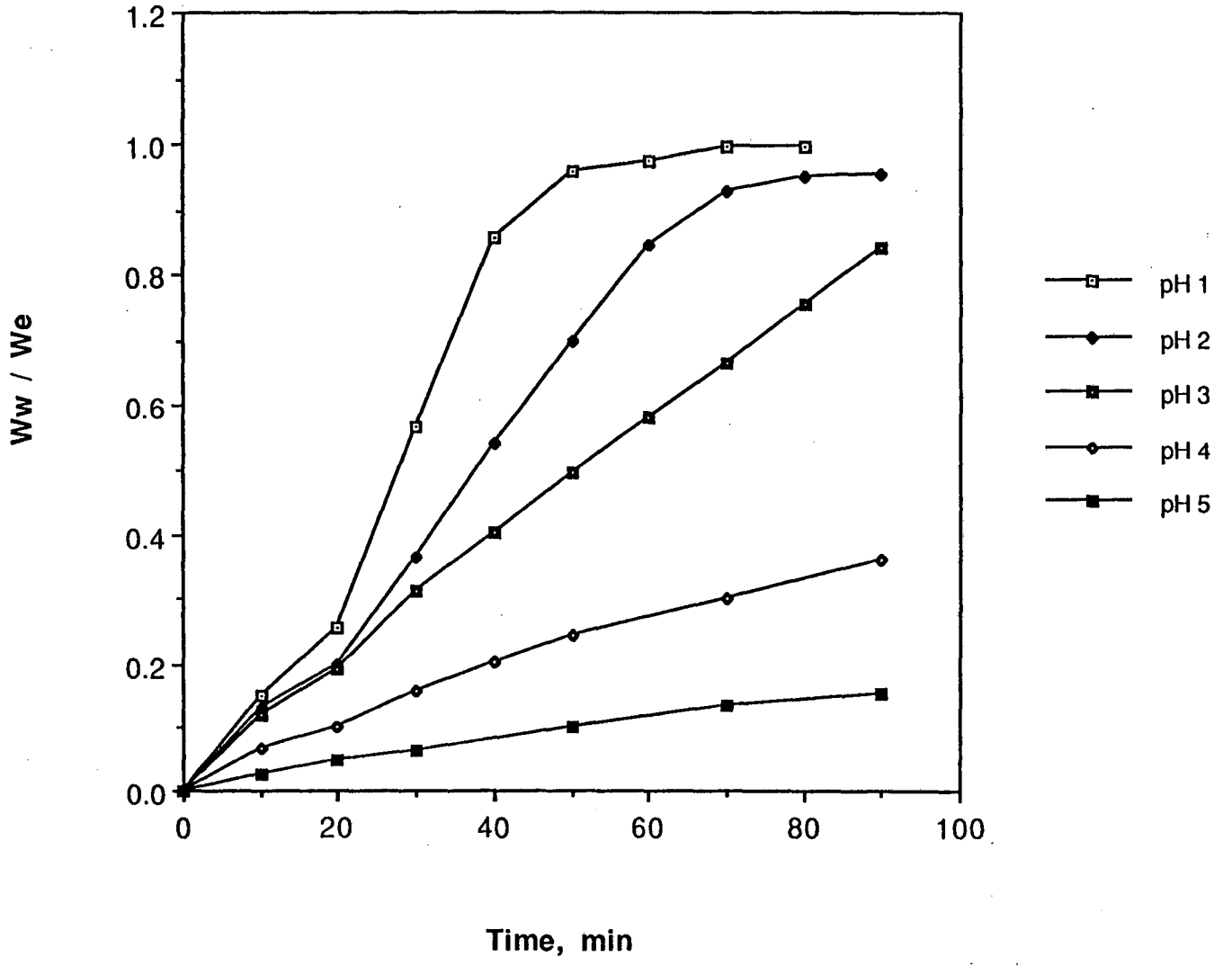

Figure 5: 78/22 mol % HEMA/DMA gel; Formic Acid buffer

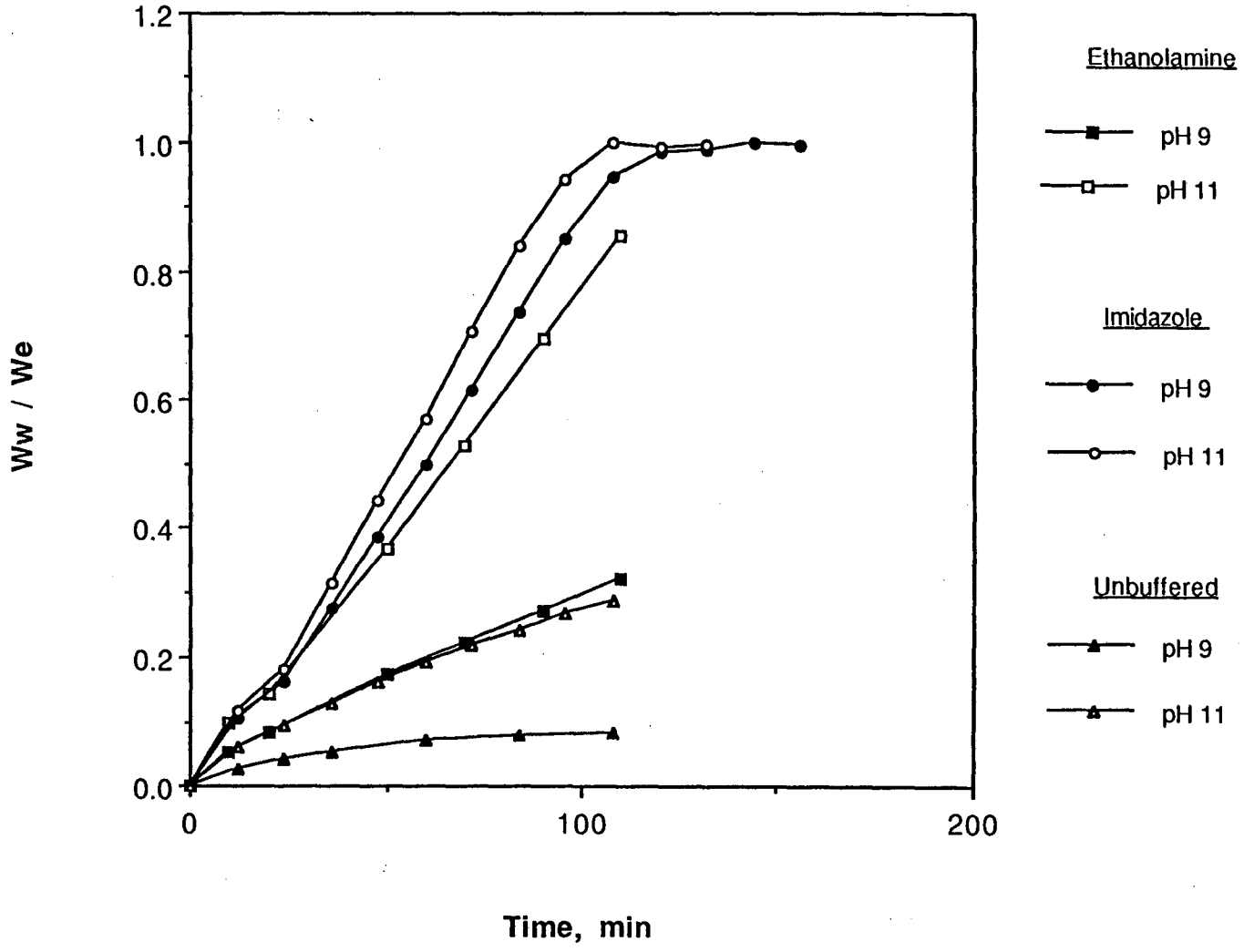

Figure 6: 78/22 mol % HEMA/MAA gel

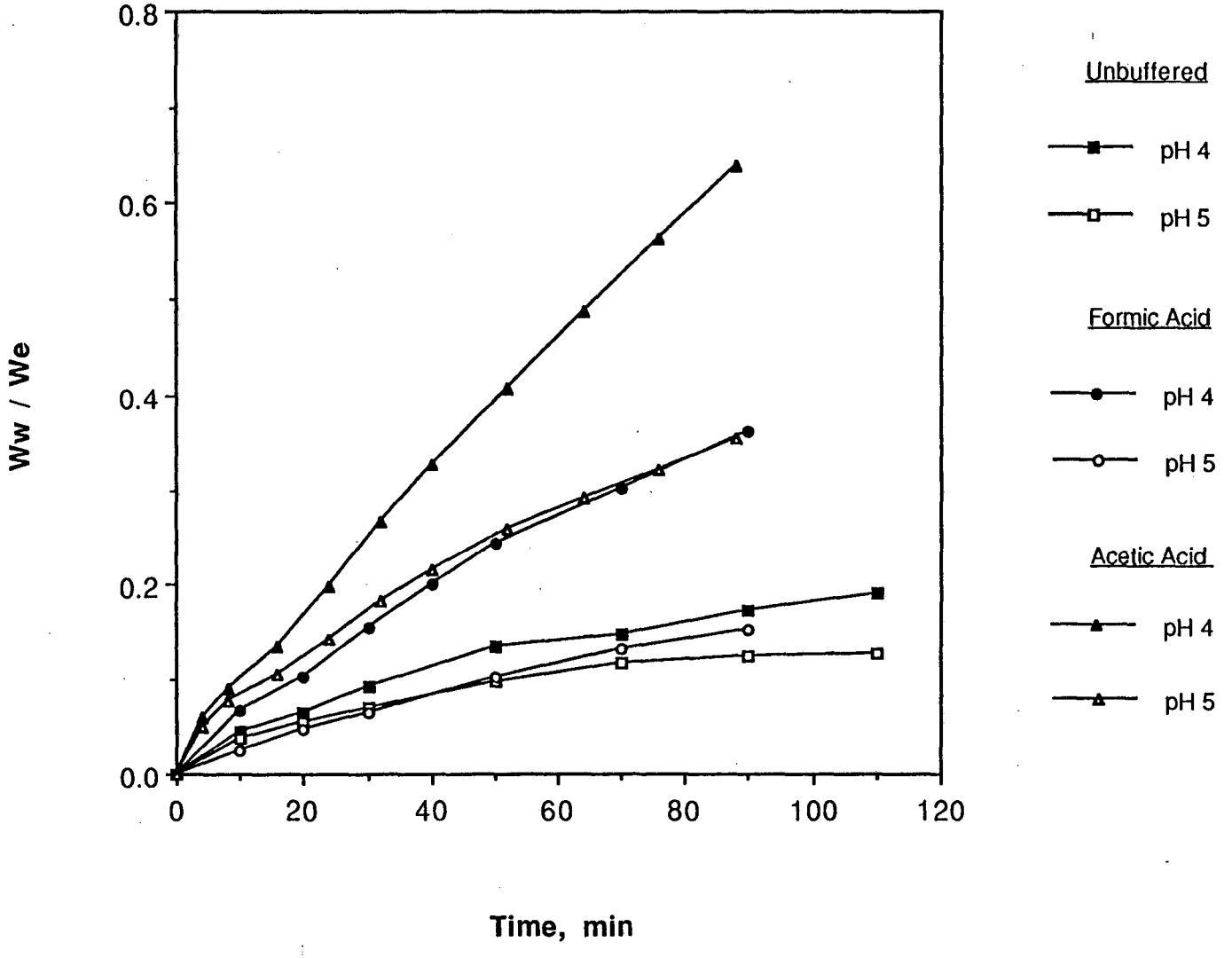

Figure 7: 78/22 mol % HEMA/DMA gel

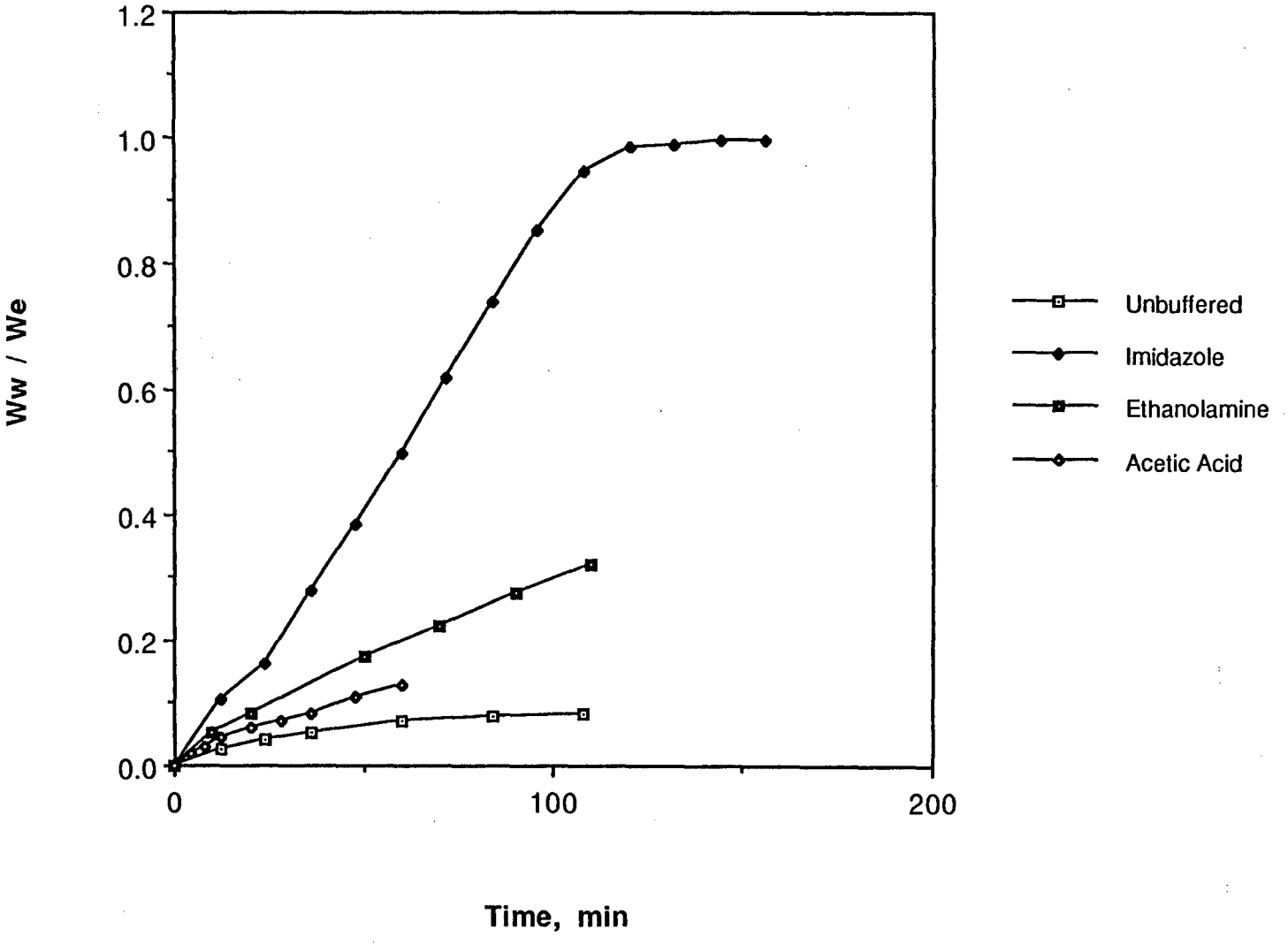

Figure 8: 78/22 mol% HEMA/MAA gel; pH = 9

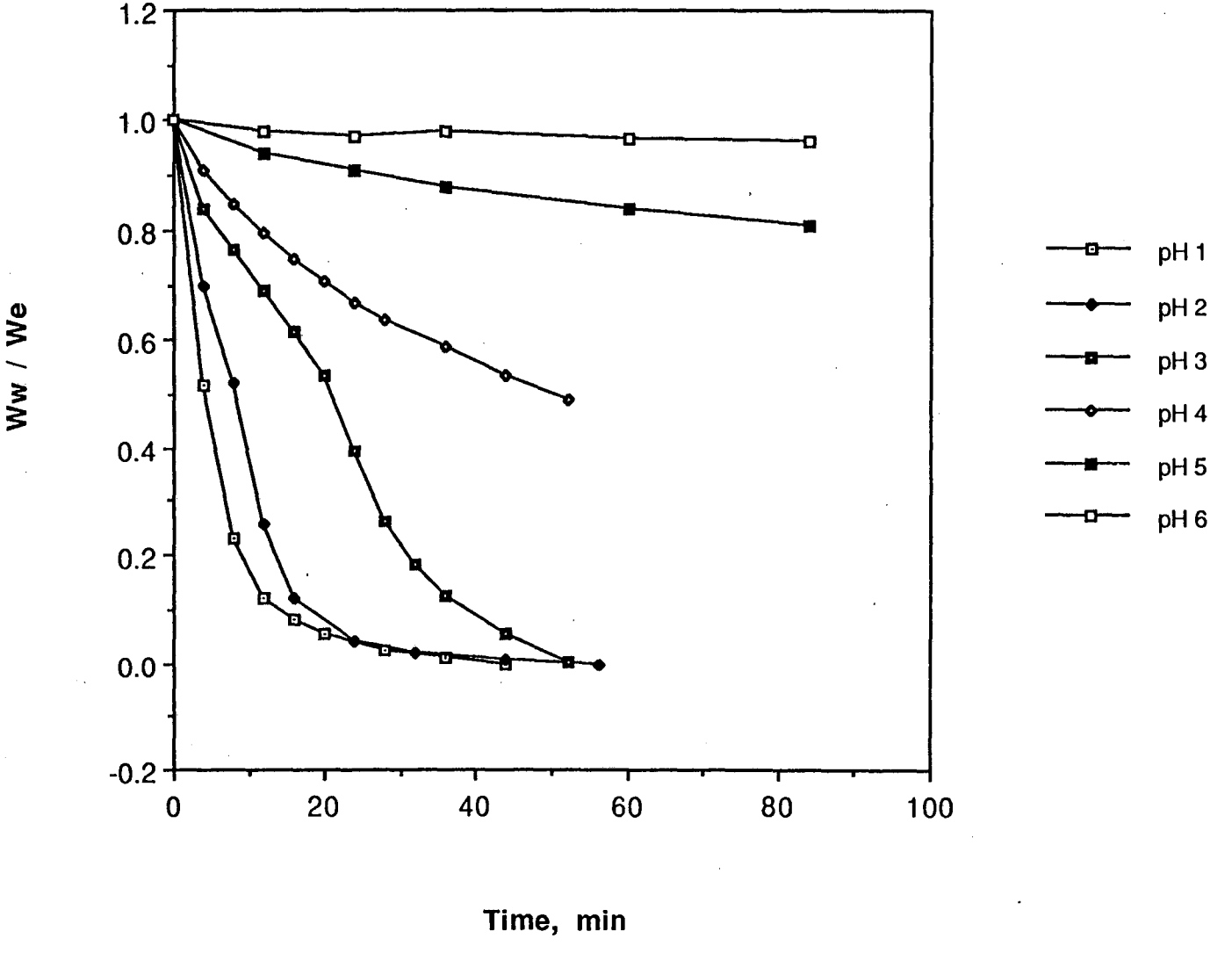

Figure 9: 78/22 mol % HEMA/MAA gel; Formic Acid buffer

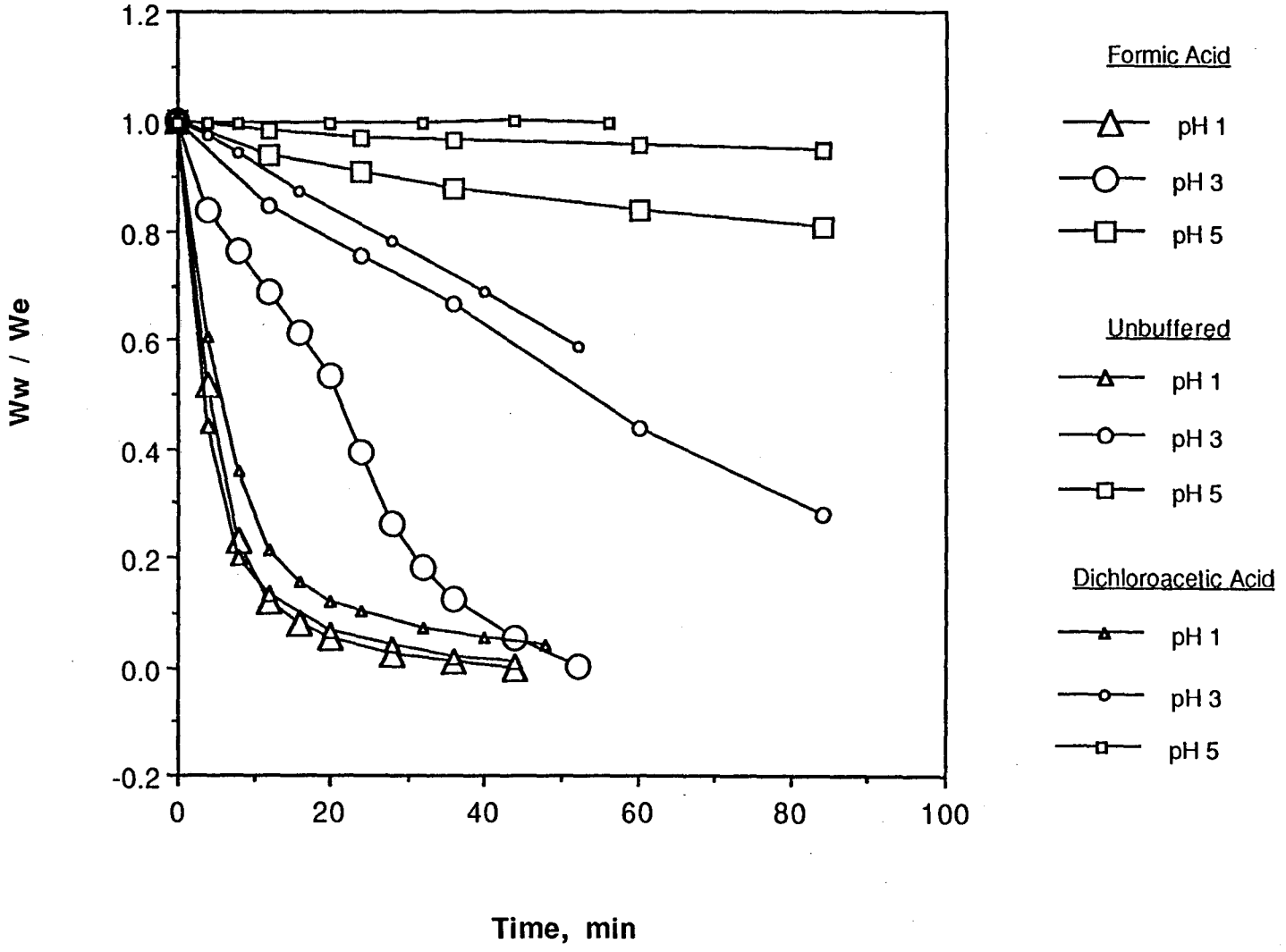

Figure 10: 78/22 mol % HEMA/MAA gel

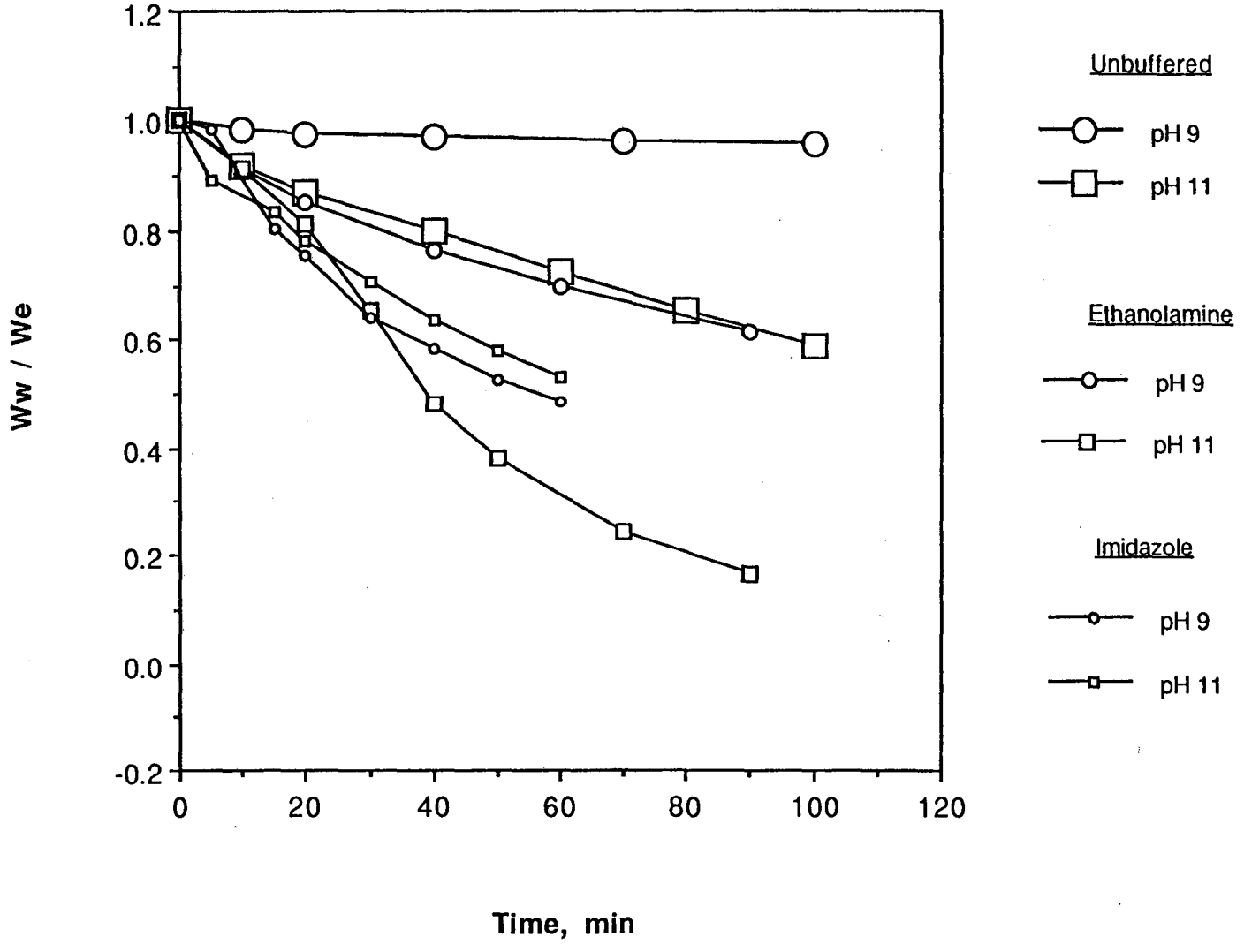

Figure 11: 78/22 mol % HEMA/DMA gel

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