A Method for Determining the Optimum Peroxide-to-Amine Ratio for Self-Curing Resins

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Synopsis

The rate of polymerization of a methacrylate monomer was influenced by the molar ratio of benzoyl peroxide to an aromatic tertiary amine accelerator when the product of the concentrations of these was kept constant. The maximum rate, measured as the minimum gel time, occurred in monomer solutions containing about 1.5 moles of peroxide per mole of amine.
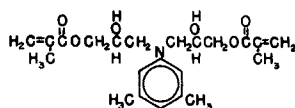
INTRODUCTION

Most dental composites, some direct filling resins, and some pit and fissure sealants for caries prevention are formulated as two or more components that are mixed together just prior to use. In a number of these products, the hardening reaction involves a peroxide, usually benzoyl peroxide in one component, and a tertiary aromatic amine such as N,N-dimethyl-p-toluidine,[1] N,N-dimethyl-3,5-xylidine,[2] or p-tolyldiethanolamine[3] in the other component.

A number of other amine accelerators have been reported[4–6] that may be useful in dental or other biological applications. One of these amines[5] (Fig. 1) was used in the present study.

The primary purpose of this work was to find a method to determine the optimum molecular ratio of benzoyl peroxide to the amine accelerator to bring about the most efficient polymerization of a two-component methacrylate resin formulation. The present report describes the use of the method with only one formulation, but it is expected that it will prove more generally useful, including other methods or criteria of determining "overall" polymerization.

At the time of formulation, it is important to know the appropriate concentration of peroxide for one portion and of amine for the other portion, so that when the components are mixed together in specified amounts, the peroxide and amine will have the proper stoichiometry. The amine and peroxide molecules interact[7] to produce free radicals that react with the methacrylate groups, bringing about polymerization. It is undesirable to have an excess of amine or peroxide remaining in the polymer because of possible adverse effects on such properties as color stability and biocompatibility.

$$H_2C=\overset{O}{\underset{H_3C}{C}}OCH_2\overset{H}{\underset{H}{C}}CH_2\underset{N}{\underset{\underset{CH_3}{\underset{H_3C}{\bigcirc}}}{}}CH_2\overset{H}{\underset{H}{C}}CH_2O\overset{O}{C}=CH_2\overset{}{\underset{CH_3}{}}$$

BMX

Fig. 1. Structural formula of the amine accelerator BMX [N,N-bis(2-hydroxy-3-methacryloxypropyl)-3,5-xylidine][5] used in this study.

Not much has been found in the literature to indicate the molar proportions of peroxide to amine that should be used to polymerize methacrylate monomers such as those used in dentistry. One relationship repeatedly cited[7−9] is that the initial rate of polymerization, R_0, is equal to an empirical constant k times the molar concentrations (moles solute per liter of solution) of the peroxide, [BP], and amine, [A], each to some exponential power, for example:

$$R_0 = k[\text{BP}]^{1/2}[\text{A}]^{1/2} \qquad (1)$$

This equation implies that the initial rate of polymerization depends only upon the product [BP][A] and not on the individual concentrations [BP] and [A] or their ratio.[9] At the time when the components are first mixed together, the initial reaction is considered to be a bimolecular reaction between peroxide and amine.[7−9] This calls for a 1:1 molar relationship for greatest efficiency at the beginning of the reaction.

However, as polymerization proceeds, there is reason to believe that some of the benzoyl peroxide is wasted by a form of radical-induced decomposition that does not produce additional free radicals.[7,10] Furthermore, the fate or subsequent reactions of an amine molecule, after it has reacted once with a peroxide molecule, is not known. According to some of the conceivable (although not established) sequential reactions, certain derivatives of the amine formed after the original reaction might be capable of decomposing one or more additional benzoyl peroxide molecules.[10,11]

Some tertiary aromatic amines have an inhibiting effect on polymerization, perhaps because of chain transfer reactions.[12,13] Thus, there are a number of factors that might influence the optimum peroxide to amine ratio during the course of polymerization.

Consequently, the present experiments were designed to measure the overall rates of polymerization of a methacrylate type monomer wherein the product [BP][A] was held constant and the ratio of [BP] to [A] was the independent variable.

EXPERIMENTAL

Materials and Methods

First Experiment. The monomer used was 1,1,1-trimethylolpropane trimethacrylate (Monomer X-980, Rohm & Haas, Philadelphia, Pennsylvania), as supplied with 220 ppm of the monomethyl ether of hydro-

TABLE I
Molal Concentrations of Amine, Peroxide, Ratios of These, and Average Gel Times
of Their Mixtures

Peroxide molality[a]	Amine molality	$\dfrac{[\text{Peroxide}]}{[\text{Amine}]}$	Gel times, min	
			First experiment	Second experiment
0.005	0.2	0.025	>90	—
0.01	0.1	0.1	>90	—
0.0125	0.08	0.15625	42.8	—
0.02	0.05	0.4	43.7	53.8
0.025	0.04	0.625	34.2	38.0
0.031623	0.031623	1.0	37.4	37.8
0.04	0.025	1.6	32.2	32.7
0.05	0.02	2.5	35.0	36.4
0.08	0.0125	6.4	38.0	—
·0.1	0.01	10.0	43.6	—
0.2	0.005	40.0	>90	—

[a] Moles per kilogram of inhibited monomer; these are the nominal values and do not represent the precision of measurement. Based on the estimated errors of measurement, the coefficient of variation of the ratio of peroxide to amine is about 2%.

quinone. Eleven pairs of solutions were prepared with this monomer, one of each pair containing benzoyl peroxide (Lucidol-98, Pennwalt Corp., Buffalo, New York) in solution, and the other, the amine accelerator shown in Figure 1. The individual solutions were prepared from the two most concentrated solutions that were each 0.2 molal (moles of solute per kilogram of inhibited monomer) with respect to either peroxide or amine, by volumetric dilution with monomer. As given in Table I, the concentrations in each pair of the solutions were such that when equal volumes were mixed together, the product of the molal concentrations, [BP][A], was 0.001, with the ratio [BP]:[A] in the eleven pairs varying between 1:40 and 40:1.

The time required for polymerization of the mixture from each pair was measured with an automatic gel timer [Tecan, Techne (Cambridge) Ltd., Duxford, England]. One cc of one of the liquids was measured accurately using a syringe (B-D Yale 1 cc Tuberculin, Becton, Dickinson & Co.) with 0.001-cc calibrations having an 18-gauge needle with a blunted end. The liquid was injected into a 10×75 mm Pyrex test tube mounted under the gel timer. With a similar syringe, the other liquid of the pair was added to the test tube, so as to make a total of 2.00 cc of mixture. When the second solution was added, a stop watch was started. At 0.1 min, a disposable wooden cylindrical probe (2.2 to 2.3 mm in diameter) was used to stir the solutions manually for 0.3 min, at which time the same probe was attached to the gel timer. At 0.5 min, the gel timer was started; it automatically raised and lowered the probe in the liquid mixture, further stirring the combined solutions. The probe had been adjusted to approach to within 2 to 3 mm of the bottom of the test tube. When the monomers gelled or solidi-
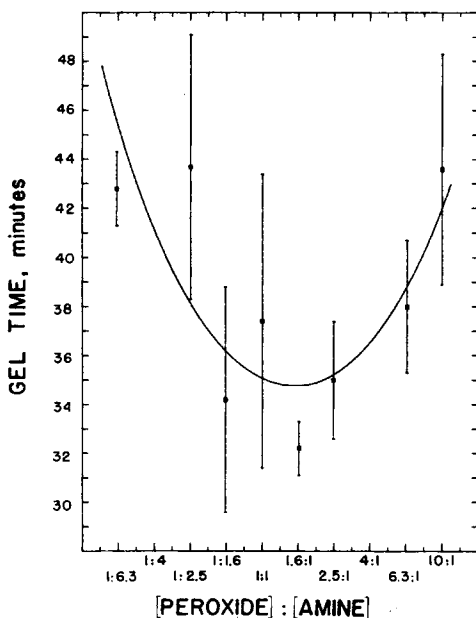
Fig. 2. Gel time as a function of the ratio of the molal concentration of benzoyl peroxide to that of aromatic amine accelerator. The gel times are indicated as the mean ± one standard deviation. The scale for the ratios is logarithmic, in which each large calibration mark represents a ratio of 1.585 times the preceeding one in going from left to right. The measured ratio indicated approximately above the mark designated 6.3:1 is, more precisely, 6.4:1; and, similarly, at the mark 1:6.3, it is 1:6.4. In the cases of the ratios 1:40, 1:10, and 40:1, the monomer formulations had not gelled by 90 min.

fied, the probe became immobilized, automatically stopping the timer. The original 0.5 min was added to the digital read-out of the timer, given in 0.1-min intervals. Five such measurements were made with each pair of solutions, and the averages and standard deviations of the gel times for each pair were plotted against the peroxide to amine ratios, as shown in Figure 2. Figure 2 was drawn with an X-Y plotter (Hewlett-Packard 9125A plotter and 9100B calculator) controlled by a programmed calculator.

Second Experiment. In an attempt to reduce the experimental error of the gel (hardening) time determinations, replicate measurements were made (with the five "central" pairs of solutions) under slightly different conditions. In these, the method was the same except that: to conserve the remaining material, 0.5 cc of each liquid was used, making 1.00 cc of mixture; the tests were done in a different laboratory in which the temperature was more closely controlled (and recorded as varying between 22.8° and 23.4°C, and 44% and 52% relative humidity), and the bottom of the probe was enlarged by screwing onto it a nut (2-56) brass hexagonal, 0.187 in., or 4.76 mm, across the outside flat surface). This latter change

presumably gave better mixing and broader "sampling" of the mixture as it gelled.

RESULTS

The hardening (gel) time values were fitted using the method of least squares[14] to the equation[15−17]

$$\log T = a + b(\log r) + c(\log r)^2 \tag{2}$$

where T is the gel time (in minutes) and r is the ratio of the initial molal concentration of benzoyl peroxide to that of aromatic amine accelerator.

First Experiment. The least-squares estimates of the coefficients, their standard errors, and covariances, indicated as $\hat{\imath}$, $s_{\hat{\imath}}$, $s_{\hat{\imath}\hat{\jmath}}$, are: a, 1.545, $s_{\hat{a}}$, 0.012; $\hat{b}$, −0.043, $s_{\hat{b}}$, 0.017; $\hat{c}$, 0.121, $s_{\hat{c}}$, 0.027; $s_{\hat{a}\hat{b}}$, 3.2×10^{-5}; $s_{\hat{a}\hat{c}}$, −2.1×10^{-4}; $s_{\hat{b}\hat{c}}$, − 2.2×10^{-4}. The standard error of regression is 0.051. This fitted curve of the hardening time as a function of the ratios of the molal concentrations of benzoyl peroxide to amine is shown in Figure 2.

The value of r (moles of peroxide per mole of amine) which minimizes the hardening time is calculated to be 1.51, with a 95% confidence interval of 1.13 to 2.01.

Second Experiment. The least-squares estimates of the coefficients, their standard errors, and covariances are: $\hat{a}$, 1.542, $s_{\hat{a}}$, 0.018; $\hat{b}$, −0.200,
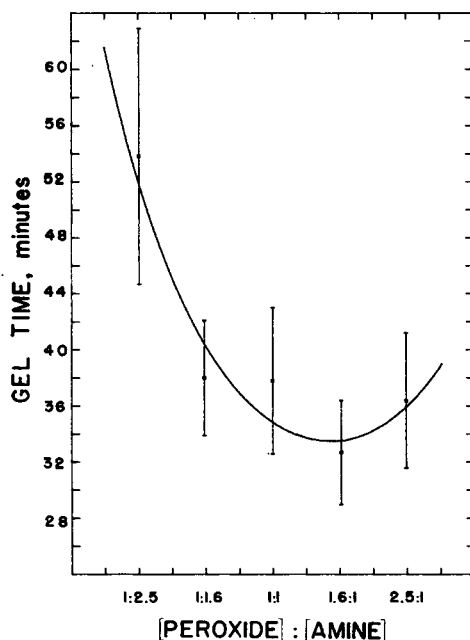

Fig. 3. Data from the second experiment, plotted in same manner as in Fig. 2 (first experiment). In both cases, the minimum gel times, as indicated by the least-squares fitted curves, occur when the molar ratio of benzoyl peroxide to amine (BMX) is about 1.5.

$s_{\hat{b}}$, 0.043; $\hat{c}$, 0.59, $s_{\hat{c}}$, 0.18; $s_{\hat{a}\hat{b}}$, 1.5×10^{-5}; $s_{\hat{a}\hat{c}}$, -2.5×10^{-3}; $s_{\hat{b}\hat{c}}$, -5.9×10^{-4}. The standard error of regression is 0.058. The fitted curve of the hardening time as a function of the benzoyl peroxide-amine ratio is shown in Figure 3.

The value of r which minimizes the hardening time is calculated to be 1.48, with a 95% confidence interval of 1.09 to 2.01.

DISCUSSION

Previous investigations[7,8,18] have shown that a relationship between the initial rate of polymerization of vinyl monomers and the initial concentrations of tertiary aromatic amine and benzoyl peroxide is given by

$$R_0 = k[A]^m[BP]^m \tag{3}$$

where R_0 is the initial rate of polymerization, k is an empirical constant, and [A] and [BP] are the initial concentrations (in moles/l.) of amine and benzoyl peroxide in the monomer, and the exponent m may depend on the conditions of the experiment.[8,9] To our knowledge, no study has been made on the overall polymerization rate of methacrylate monomers, especially those capable of crosslinking, as a function of amine and benzoyl peroxide concentrations.

If we were to assume that the initial rate determines the overall rate, than

$$R = k'[A]^{m'}[BP]^{m'} \tag{4}$$

where R is the overall rate of polymerization (the reciprocal of the time required to gel as measured experimentally). Since the coefficients are the same,

$$R = k'([A][BP])^{m'}. \tag{5}$$

In other words, the rate should be determined solely by the product of the concentrations of amine and benzoyl peroxide. However, in this investigation with the product of the concentrations held constant, the rate of polymerization was not constant as the ratio of amine and peroxide was varied from 1:40 to 40:1.

Since the purpose of this investigation is the determination of the optimum ratio of peroxide to amine with respect to hardening time, eq. (2) was used.

STATISTICAL TREATMENT OF THE DATA

In fitting eq. (2) by least squares, an implicit assumption is made that all the experimental errors are in the hardening time determination while none exist in the values of the ratio r. This assumption is not completely valid when the experimental conditions are considered, because, in reality, the error in the hardening time is due to two sources: (1) error in measurement of the hardening time and (2) error in measuring volumes of the

formulations, which, in turn, influences the observed value of the hardening time. Although statistical treatment of similar data, where error in the independent variable causes error in the dependent variable, has been worked out (where the relationship between the variables is linear[19] or a polynomial of low degree[20]), a general treatment for the curvilinear case in which exact tests of significance for the parameters are developed apparently has not yet been done.[21] Therefore, the assumption is now made explicit that no error exists in the values of the ratio of the concentration of benzoyl peroxide to that of amine, allowing for the usual treatment by least squares.

Since the standard deviation for each group of hardening time determinations made at each ratio was approximately proportional to the mean of each group in each experiment, the logarithms of the measurements would be expected to be normally distributed.[22] After the hardening time data were converted to their logarithms, a test for outliers[23] showed the presence of an outlier at the 95% confidence level in each of several groups in the two experiments.

After omitting the outliers from the calculations, the groups were tested for constancy of variance.[24] At the 95% confidence level, the groups in each experiment had the same variance. With inclusion of outliers, constancy of variance could not be assumed.

After fitting eq. (2) to the data, a statistical test was performed to determine if the error from regression was consistant with the within group error. In the first experiment, at the 95% confidence level, the error for regression was greater than the within group error; but at the 99% confidence level, the two measures of experimental error were consistant with each other. Thus, the data of the first experiment are correlated with moderate success by eq. (2). In the second experiment, the error for regression was consistant with the within group error at the 95% confidence level.

A "Student's" t-test of significance (see Appendix) was used to compare the eq. (2) values of the coefficients from the data of the first with those of the second experiment. At the 95% confidence level, the constant term in the one case was insignificantly different from that in the other. On the other hand, the other coefficients from the second experiment were significantly larger than the corresponding ones in the first.

Equation (2) may be used to calculate the value of r giving the minimum value of the hardening time. According to differential calculus,[25] a relative minimum or maximum is present in a curve where the first derivative of the equation of the curve is zero and the value of the second derivative is not zero. An examination of the data shows that a minimum is present.

Differentiating eq. (2) with respect to log r and setting the result equal to zero[25] gives

$$\frac{d \log T}{d \log r} = b + 2c(\log r') = 0 \tag{6}$$

where r' is the value of the ratio which causes log T to be a minimum. After substituting the least-squares estimates of the parameters of the first experiment, log r' is calculated to be 0.179 and r' is 1.51. From the propagation of error formula,[26] the standard error of log r' is 0.061. From these results, the 95% confidence interval for r' is 1.13 to 2.01. From the results of the second experiment, log r' is 0.170 and r' is 1.48. The standard error of log r' is 0.064. From these results, the 95% confidence interval for r' is 1.09 to 2.01. The best estimate of r' on combining the data of the two experiments is 1.49 with a 95% confidence interval of 1.22 to 1.83 and a 99% confidence interval of 1.14 to 1.95.

CONCLUSIONS

A comparison of the results of the first experiment with those of the second shows that the standard errors are approximately equal; the fit of eq. (2) is decidedly better using the data of the second experiment; the value of a in eq. (2) is essentially equal in both cases; the values of b and c are significantly larger in the second experiment, and the optimum ratio of the molar concentrations of peroxide to amine in both cases is approximately 1.5:1. This experimentally determined ratio is significantly greater than 1:1 for the overall polymerization rate.

Although the present experimental results lead to the conclusion that approximately 1.5 moles of benzoyl peroxide may be optimal for use with each mole of the amine accelerator BMX (Fig. 1), it does not necessarily follow that other amines, peroxides, or monomers would require the same ratio.

Nonetheless, the experimental method should be applicable to the evaluation of the optimal ratios of diverse peroxides and amine accelerators.

Appendix

The significance test for comparing corresponding coefficients of two regression equations when the standard errors for the two equations are assumed equal is the following:[27]

$$t = \frac{\theta_1 - \theta_2}{s_p \sqrt{\left(\frac{s_{\theta_1}}{s_1}\right)^2 + \left(\frac{s_{\theta_2}}{s_2}\right)^2}}$$

where θ_1 and θ_2 are the corresponding coefficients from experiments 1 and 2; s_{θ_1} and s_{θ_2} are the corresponding standard errors of the coefficients; s_1 and s_2 are the standard errors of regression, and s_p is the pooled standard error, calculated as

$$s_p = \sqrt{\frac{(n_1 - P)s_1^2 + (n_2 - P)s_2^2}{n_1 + n_2 - 2P}}$$

where n_1 and n_2 are the number of experimental points in experiments 1 and 2, respectively, and P is the number of coefficients in each regression equation.

The value of t is distributed as "Student's t" with $(n_1 + n_2 - 2P)$ degrees of freedom if the two coefficients estimated by θ_1 and θ_2 are equal.

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