

## The Effect of Cupric Ion on the Radiation Grafting of *N*-Vinyl-2-Pyrrolidone and other Hydrophilic Monomers onto Silicone Rubber

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### Synopsis

Radiation grafting systems containing cupric ion, *N*-vinyl-2-pyrrolidone (N-VP) and other hydrophilic monomers were studied. Such systems, in certain  $\text{Cu}^{++}$  ion concentration ranges were found capable of producing extremely high levels of graft on silicone rubber and other polymers. Gellation of the homopolymer surrounding the grafted film was inhibited by the presence of cupric salts. An increase in the graft water content and decrease in the wettability of the grafted film surface was noted as the  $\text{Cu}^{++}$  ion concentration in the grafting solution was increased. Based upon attenuated total reflectance infrared spectroscopic examination of the grafted materials, these effects could be explained by variations in the copolymer composition of the graft and increased penetration of the graft into the silicone rubber with increasing cupric ion concentration. The  $\text{Cu}^{++}$ /N-VP system allows many monomers which would ordinarily graft only with great difficulty to be readily grafted to polymeric surfaces. It also allows control over a number of graft parameters such as graft water content composition and penetration. Therefore, this system should be ideal for preparing a series of radiation grafted hydrogels to be used to evaluate important variables in the interactions of hydrophilic biomaterials and biological systems.

### INTRODUCTION

There is evidence to indicate that highly hydrated polymeric surfaces may be biocompatible and thromboresistant.<sup>1,2</sup> Hydrophilic polymers generally have low physical strength in aqueous environments, however, so that the production of useful, long-lived prosthetic devices is often not feasible. Techniques have been developed for radiation grafting monomers such as *N*-vinyl-2-pyrrolidone (N-VP) and 2-hydroxyethyl methacrylate (HEMA) onto silicone rubber and other polymeric supports.<sup>3-10</sup> This produces a composite material with a hydrophilic surface on a strong, stable backing.

The radiation graft is produced by the mutual irradiation technique. A polymeric substrate is fully immersed in a mixture of monomer and solvent and placed in a gamma radiation source. After irradiation for a specified period of time, the grafted polymer film is removed from the surrounding medium and cleaned. The surrounding medium, at this point, generally

consists of polymer, unreacted monomer, and solvent. Depending upon the precise conditions, it could be fully liquid, a tough, crosslinked gel, or some combination of liquid and gel. In this paper, the surrounding medium will be referred to as either the external polymer or the external solution.

A most desirable property for the grafting system is a nongelling (liquid) external polymer. Such a system allows the rapid, reproducible preparation of evenly grafted films. The extent of grafting should be such that the surface properties are due exclusively to the hydrophilic polymer. A high graft water content is also desirable since this may lead to increased biocompatibility.<sup>11</sup>

In an effort to prevent the gelling and/or precipitation of the external polymer,  $\text{Cu}^{++}$  and  $\text{Fe}^{+++}$  salts were added to the polymerization solvent.<sup>12-16</sup> Results obtained with the monomer-solvent combination N-VP/HEMA/ $\text{H}_2\text{O}$ / $\text{Cu}(\text{NO}_3)_2$  have been found to produce successful nongelling systems capable of exceptionally high graft levels. Many entirely unique effects have been noted in the behavior of this grafting system which are of particular interest from a theoretical as well as a practical standpoint. An initial report is presented here.

## EXPERIMENTAL

Dow-Corning nonreinforced Silastic films (and other polymeric materials for grafting) were washed for 5 min in 0.1% Ivory soap solution in an ultrasonic cleaner. They were subsequently given three 5-min rinses in freshly changed distilled water in the ultrasonic cleaner. The films were stored in a 52% R.H. chamber.

HEMA monomer was obtained from Hydron Laboratories, Inc., New Brunswick, N.J. The monomer obtained had a diester level of 0.02% and a methacrylic acid level of 0.02%. N-VP monomer (Monomer-Polymer Laboratories, Inc.) was purified by drying over Drierite and distilling at 42°C, 1 mm Hg. 2-Hydroxyethyl acrylate and propylene glycol monoacrylate (Monomer-Polymer Laboratories, Inc.) were purified by extracting three times with hexane to reduce dimethacrylate impurity levels. Acrylamide was purified by recrystallizing three times from chloroform (observed mp 84.2-84.7°C). Methacrylamide was recrystallized twice from benzene-ethanol (4:1) (mp 109.5-110.0°C). Methacrylic acid and ethylene glycol dimethacrylate (EGDMA) (Monomer-Polymer Laboratories, Inc.) were used as received. Cupric nitrate, cupric chloride, cupric sulfate, cupric acetate, and ferric nitrate were of reagent grade and used as received.

The cleaned films were suspended in monomer solutions (compositions expressed in volume per cent) without removal of air and irradiated at room temperature in a ca. 20,000 curie cobalt-60 source (courtesy of the College of Fisheries, University of Washington). The radiation dose used in all experiments was 0.25 Mrad.

After grafting, the films were removed from the bulk external polymer. Adhering bulk polymer (if any) was cleaned by vigorous rubbing with a sponge soaked in acetone-water (50:50 v/v). The films were then washed for 2 hr in two stirred acetone-water baths. Finally, the films were placed in a stirred distilled water bath for a minimum of 24 hr. The water in the bath was changed at least four times during this period. Films were always stored in distilled water.

Water contents of the grafted films were measured by blotting the films between two sheets of Whatman #1 filter paper for ten seconds using a 300-g weight to apply a uniformly distributed pressure and then weighing immediately. Per cent water in the graft was calculated using the relationship

$$\frac{W_w - W_d}{W_w - W_s} \times 100 = \% \text{ H}_2\text{O}$$

where  $W_w$  is the weight of the wet, grafted film;  $W_d$  is the weight of the grafted film dried in a desiccator over anhydrous at 1 mm Hg for 24 hr; and  $W_s$  is the weight of the untreated film. Reported water contents are the average of at least two determinations. Water content values were found not to have a coefficient of variation greater than 2.3% for films prepared with the same formulation on different days.

The amount of radiation graft formed on the substrate polymer has been expressed as the weight of graft per initial film area ( $W_g$ );  $W_g$  was calculated using the following relationship:

$$W_g = \frac{W_d - W_s}{\text{initial film area}}$$

It was determined in this work that in certain instances the radiation graft penetrates into the substrate polymer. Therefore, describing the degree of graft as graft/initial surface area is not in all cases a completely meaningful expression of the extent of grafting. The degree of graft has been expressed in other papers as the per cent of the graft in the final material. However, different Dow Corning Silastic rubber batches varied in thickness, and other polymeric substrates which were used in these experiments were not of uniform thickness. Therefore, for situations in which grafting occurred only on the surface, the degree of graft expressed as a per cent would appear to vary with the thickness of the substrate. As neither expression of the degree of graft is entirely satisfactory in all instances, the weight of graft/initial area was used arbitrarily in all situations.

For grafting experiments run on different days there was a coefficient of variation in the degree of grafting which, at times, amounted to as much as 8.7%. For a series of films prepared at the same time using Silastic sheeting from the same manufacturing lot, the shape of the various degree of graft curves was always reproduced. From day to day, however, the curves might appear shifted up or down with respect to the degree of graft axis. Therefore, the following protocols were adopted. For any continuous curve

presented in this paper, all experimental points were obtained from films grafted simultaneously. Where more than one curve is presented on a given plot, either all points on the plot were obtained at the same time, or an internally consistent experiment was run to determine the correct placement of the various curves with respect to the magnitude of the graft. Adherence to these protocols should ensure that all figures dealing with the degree of graft are both meaningful and comparable.

An attempt should be made to account for the large variation in the degree of graft for identical experiments repeated at different times. This variation was attributed to two factors. First, the monomer solutions were not deoxygenated. As there was no control on how much oxygen was dissolved in solution, the polymerization induction period, and therefore the final amount of graft, varied. Second, changes in the manufacturing procedure, and perhaps in the composition of the Silastic silicone rubber, were periodically made by Dow Corning Corporation. These changes were often quite obvious as the appearance of the material was clearly different from one batch to another. Direct comparisons showed that different rubber batches grafted different amounts of hydrogel under otherwise identical conditions.

Scanning electron micrographs were taken by the Materials Analysis Center, University of Washington, on a Cambridge Stereoscan instrument. Prior to examination, the grafted hydrogels were dried and coated with a vacuum-deposited layer of carbon and then gold and platinum.

ATR spectra were taken on a Beckman IR-4 spectrophotometer using an internal reflection angle of  $45^\circ$ . A polished KRS-5 crystal with both ends cut at  $45^\circ$  was used for all spectra. Grafted polymer films were pressed into intimate contact with both sides of the crystal in a solid sample holder sold by Beckman Instruments, Inc. The mirrors in the ATR unit were adjusted for maximum transmittance before each spectrum was run. An attenuator was used in the reference beam.

## RESULTS

The initial observations which prompted an in depth investigation of the radiation grafting systems described in the paper are shown graphically in Figure 1. Bars represent the average of at least two determinations. In systems containing HEMA as the only monomer, the addition of  $\text{Cu}(\text{NO}_3)_2$  to the solvent had little or no effect on the degree of grafting to the silicone rubber, the graft water content, or the appearance of the external polymer. For N-VP-water systems, there was a significant increase in graft water content upon the addition of cupric nitrate. The reduction in the viscosity of the external solution indicated that the salt probably inhibited polymerization in the external solution. The most striking effect was observed when both monomers were present. A graft level of approximately  $9.7 \text{ mg/cm}^2$  (approximately 36% graft for a 10-mil film) was produced when  $\text{Cu}(\text{NO}_3)_2$  was added to the solvent system. This is three times the graft for the same system using only water as a solvent. The graft level was

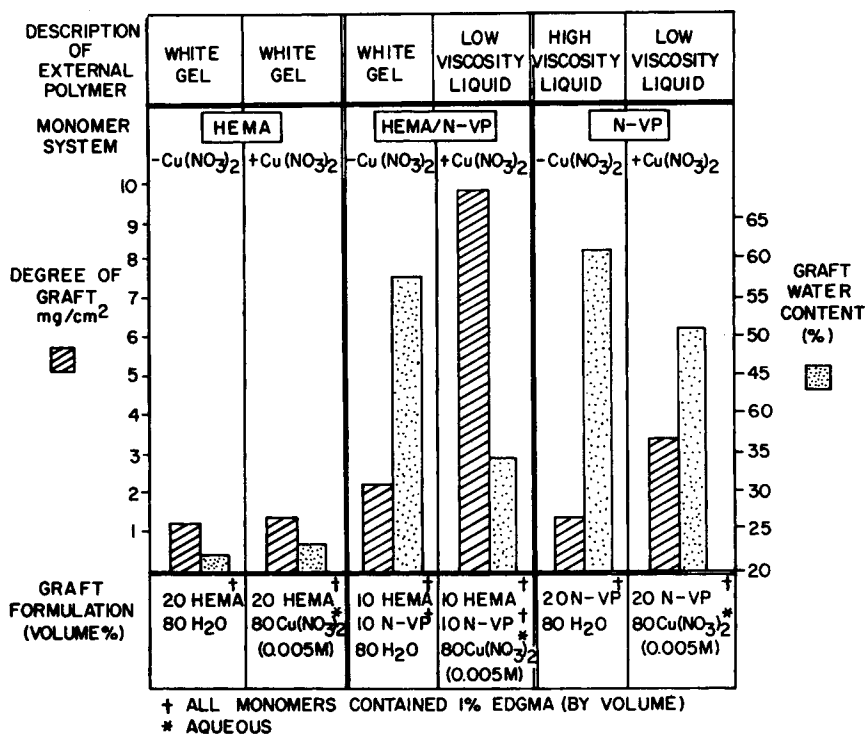


Fig. 1. Differences in grafting behavior of various monomer systems with and without  $\text{Cu}(\text{NO}_3)_2$  in the solvent.

higher than any which was observed in our previous hydrogel radiation grafting experiments.<sup>5</sup> Also, the graft water content was reduced almost in half when  $\text{Cu}(\text{NO}_3)_2$  was added to the system.

The graft increases seen in these systems in the presence of cupric nitrate might be interpreted as a simple effect due to decreased external polymer formation and thus higher monomer levels during the grafting process. However, the decreases in graft water content and the synergistic graft increase for the HEMA-N-VP system indicates a more complex process. Therefore, further experiments with this type of grafting system were performed.

Parts of the initial experiment were repeated comparing cupric chloride, cupric acetate, and cupric sulfate to cupric nitrate. Results with all cupric salts tested were basically similar and within the limits of experimental error (see Table I). It was therefore concluded that the observed effects were due to the cation rather than the anion.

Grafting experiments in the presence and absence of  $\text{Cu}(\text{NO}_3)_2$  were tried on various polymeric support materials (Table II). Silastic and Pellethane (a polyurethane-polyether copolymer) gave the expected results. For polyethylene, however, the degree of graft was highest in the absence of  $\text{Cu}(\text{NO}_3)_2$ . Thus, the support polymer may play some role in this process.

TABLE I  
Comparison of the Effects of Various  $\text{Cu}^{++}$  Salts on Radiation  
Grafting onto Silicone Rubber Using the Formulation  
10% HEMA, 10% N-VP, 80% Solvent (vol-%)<sup>a</sup>

Solvent	Graft, mg/cm <sup>2</sup>	H <sub>2</sub> O in graft, %	Description of external polymer
H <sub>2</sub> O	5.9	54.5	white viscous liquid + gel
$\text{Cu}(\text{NO}_3)_2$ (0.005 <i>M</i> )	8.8	41.2	clear liquid
$\text{CuCl}_2$ (0.005 <i>M</i> )	9.9	40.2	clear liquid
$\text{Cu}(\text{acetate})_2$ (0.005 <i>M</i> )	9.2	43.6	clear liquid
$\text{CuSO}_4$ (0.005 <i>M</i> )	9.4	40.4	clear liquid

<sup>a</sup> Radiation dose, 0.25 Mrad.

TABLE II  
Comparison of Substrate Polymer Effects on Radiation Grafting  
Using the Formulation 10% HEMA, 10% N-VP, 80% Solvent (vol-%)<sup>a</sup>

Substrate Polymer	Solvent	Graft, mg/cm <sup>2</sup>	H <sub>2</sub> O in graft, %	Description of external polymer
Silicone rubber	H <sub>2</sub> O	5.9	54.5	white viscous liquid + gel
Silicone rubber	$\text{Cu}(\text{NO}_3)_2$ (0.005 <i>M</i> )	8.8	41.2	clear liquid
Pellethane <sup>b</sup>	H <sub>2</sub> O	4.6	46.8	white viscous liquid + gel
Pellethane <sup>b</sup>	$\text{Cu}(\text{NO}_3)_2$ (0.005 <i>M</i> )	10.9	39.0	clear liquid
Polyethylene <sup>c</sup>	H <sub>2</sub> O	0.9	36.8	white viscous liquid + gel
Polyethylene <sup>c</sup>	$\text{Cu}(\text{NO}_3)_2$ (0.005 <i>M</i> )	0.8	20.3	clear liquid

<sup>a</sup> Radiation dose, 0.25 Mrad.

<sup>b</sup> Upjohn (2103-80A).

<sup>c</sup> Monsanto (A 2700-433).

The effect of  $\text{Cu}(\text{NO}_3)_2$  concentration on the degree of graft and graft water content for systems containing HEMA, N-VP, or various combinations of HEMA and N-VP is shown in Figures 2, 3, and 4. For systems containing both monomers, two peaks in the grafting curves were noted. Only one peak was evident where only one monomer was present. The peak for the formulations containing only HEMA monomer (Fig. 2, curve 5) occurred in a much higher range of  $\text{Cu}(\text{NO}_3)_2$  concentrations than the peak for the pure N-VP system (curve 1). As the HEMA concentration in the monomer mixtures was increased, the second, or high,  $\text{Cu}(\text{NO}_3)_2$  concentration peak seemed to increase in size and also shift to a higher  $\text{Cu}(\text{NO}_3)_2$  concentration range. To simplify discussion, this peak will be referred to as the "HEMA peak." The first peak always occurred in the rather narrow  $\text{Cu}(\text{NO}_3)_2$  concentration range of 0.001–0.005*M*, regardless of the system composition. This peak is shown in more detail in Figure 3. The data for this figure were gathered from an experiment done independently from that used to construct Figure 2. The three maxima each occur at slightly different copper nitrate concentrations. These variations in the location of the maxima do not correlate in any simple fashion with

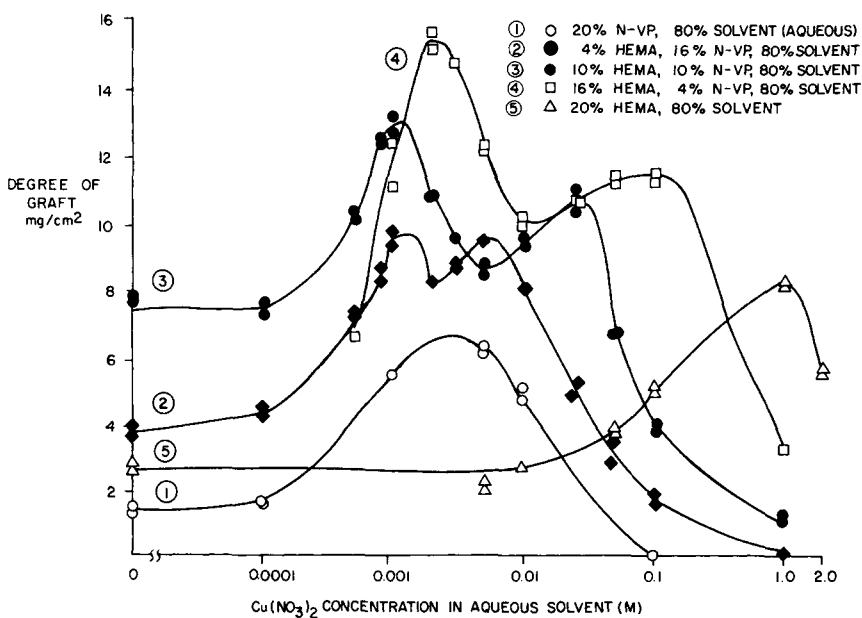


Fig. 2. Effect of  $\text{Cu}(\text{NO}_3)_2$  concentration in the solvent on the degree of graft for various monomer systems.

the composition of the monomer mixture. As the curve for the N-VP system shows a peak in this  $\text{Cu}^{++}$  concentration region and the HEMA system does not, this maximum will be referred to as the "N-VP peak." The "HEMA peak" and "N-VP peak" designations do not necessarily have significance with respect to the composition of the graft or the mechanism of the polymerization.

Certain correlations can immediately be made between various properties of these systems and the peaks seen in Figure 2. The water content of the graft drops or rises sharply in the same  $\text{Cu}(\text{NO}_3)_2$  concentration region in which the N-VP peak occurs (see Fig. 4). The surface properties of the grafted films undergo radical changes in the region of each of the peaks. In the low  $\text{Cu}(\text{NO}_3)_2$  concentration region of the plot below the N-VP peak, the grafted films were found to be relatively wettable in water. When lifted from a vessel of water, the water will flow over and evenly coat such films. In this respect, the low  $[\text{Cu}^{++}]$  films are indistinguishable from those formed with only water as the solvent. At a point in the  $\text{Cu}(\text{NO}_3)_2$  concentration region corresponding to the N-VP peak, the films made from N-VP containing systems suddenly become nonwetable. Water will bead up on the surface of these films. Another surface effect is seen to manifest itself in the HEMA peak region. The surface takes on a rough "orange peel" or reticulated texture. This texture is noted only in the portion of the HEMA peak where the graft level is very high. All other films along the curves in Figure 2 have smooth surfaces upon which no detail can be resolved even

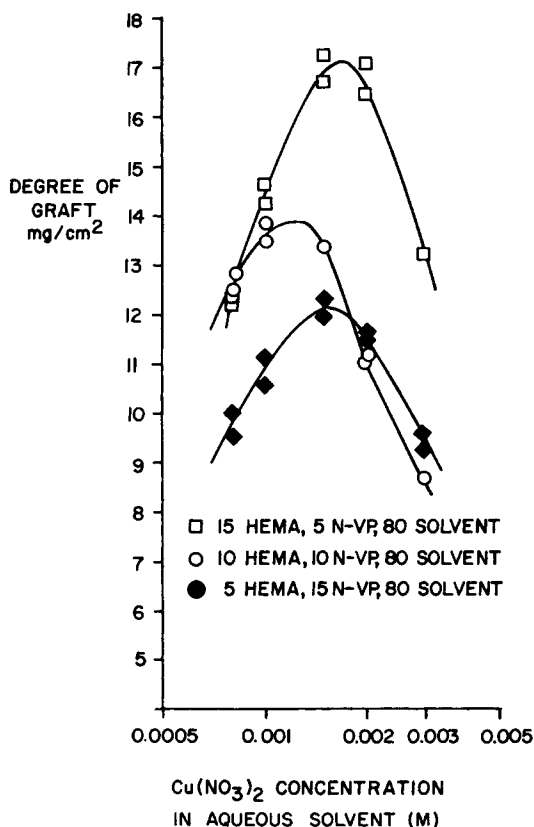


Fig. 3. Effect of  $\text{Cu}(\text{NO}_3)_2$  concentration in the solvent on the degree of graft for three copolymer systems in the concentration range  $0.0008M$ – $0.003M$ .

under scanning electron microscopic observation at  $2000\times$ . Examples of scanning electron micrographs of films in the region of the N-VP peak and the HEMA peak from curve 3 (Fig. 2) are shown in Figure 5. It should be mentioned that HEMA peak films could not be evaluated with respect to wettability by simple dipping tests due to the complicating effect of the rough surface texture.

The external polymer also underwent changes which could be correlated with the position of N-VP peak. For systems containing (by volume) 16% N-VP, 4% HEMA, and 80%  $\text{Cu}(\text{NO}_3)_2$  solution and 20% N-VP and 80%  $\text{Cu}(\text{NO}_3)_2$  solution (Fig. 2, curves 1 and 2), the external polymer was completely liquid after the 0.25-Mrad radiation dose at all  $\text{Cu}(\text{NO}_3)_2$  concentrations. However, at  $\text{Cu}(\text{NO}_3)_2$  concentrations of  $0.001M$  or lower, the solution had an extremely high viscosity while at concentrations above  $0.001M$  the viscosity was similar to that of the unirradiated grafting solution. For the systems shown in Figure 2, curves 3, 4, and 5, a white gelled



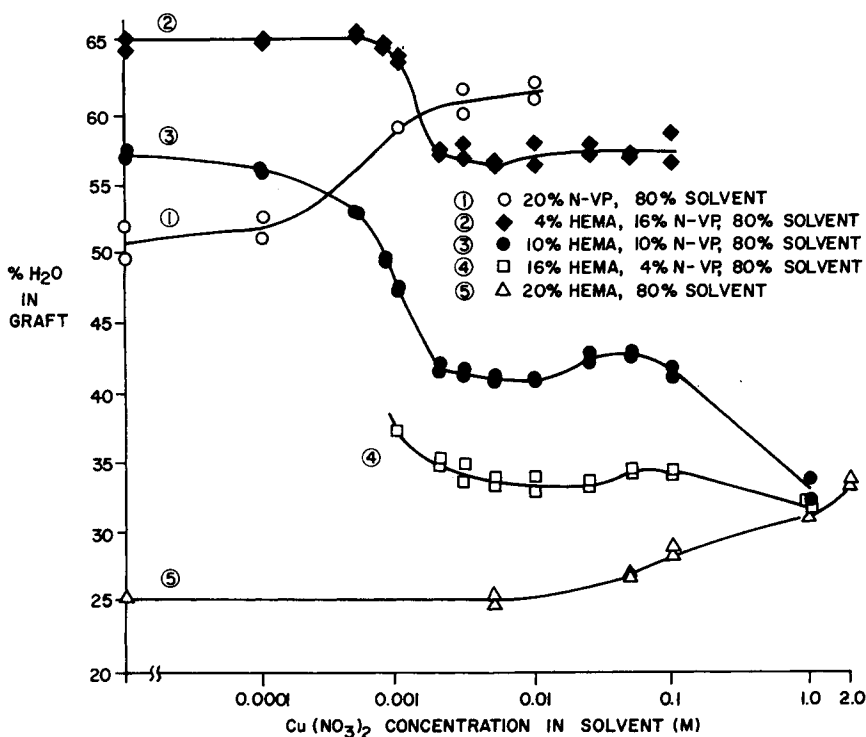
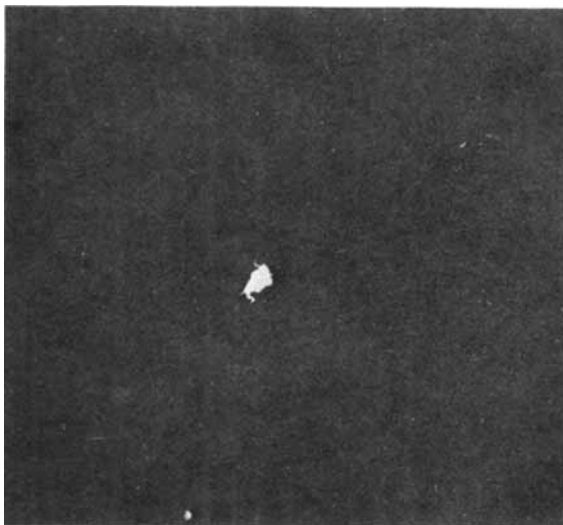


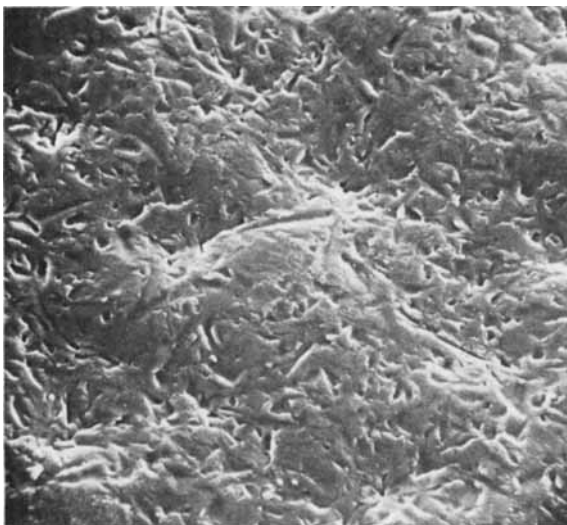
Fig. 4. Effect of  $\text{Cu}(\text{NO}_3)_2$  concentration in the solvent on the water content in the graft for various monomer systems.

external polymer formed at low  $\text{Cu}(\text{NO}_3)_2$  concentrations. For the system 16% HEMA, 4% N-VP, 80% solvent, the gel was so intractable that it could not be separated from the grafted film. In the region of the N-VP peak, this gel gradually became softer; and at a copper concentration of 0.002M, the external polymer was completely liquid. When both monomers were present in a 1:1 ratio (Fig. 2, curve 3), a soft, white gel which could be easily peeled from the grafted Silastic after irradiation was found only for cupric nitrate concentrations below 0.001M. Above 0.001M (the maxima of the N-VP peak), a low-viscosity liquid remained. For systems containing only HEMA monomer, a liquid external polymer was not observed until the  $\text{Cu}^{++}$  concentration was increased to 1.0M or above. In this case, the liquid-gel transition point occurred in the HEMA peak region.

It was noted that in the presence of two monomers the effects with respect to the amount of graft seemed most pronounced. Therefore, at a constant  $\text{Cu}^{++}$  concentration (0.005M), various ratios of HEMA and N-VP were radiation grafted to Silastic rubber. The results are shown in Figures 6 and 7. Again, 0.005M  $\text{Cu}(\text{NO}_3)_2$  was observed to have no effect on the



(a)



(b)

Fig. 5. Scanning electron micrographs at  $\sim 200\times$  of films prepared by radiation grafting Silastic in a solution consisting of 10% N-VP, 10% HEMA, and 80%  $\text{Cu}(\text{NO}_3)_2$  solution: (a)  $\text{Cu}(\text{NO}_3)_2$  concentration 0.002*M*; (b)  $\text{Cu}(\text{NO}_3)_2$  concentration 0.025*M*.

graft level in systems containing only HEMA monomer (Fig. 6). However, by adding only one part in twenty of N-VP to the monomer mixture, a massive increase in grafting is observed. The maximum effect is found at an 18:2 HEMA/N-VP ratio. With increasing N-VP in the mixture, a

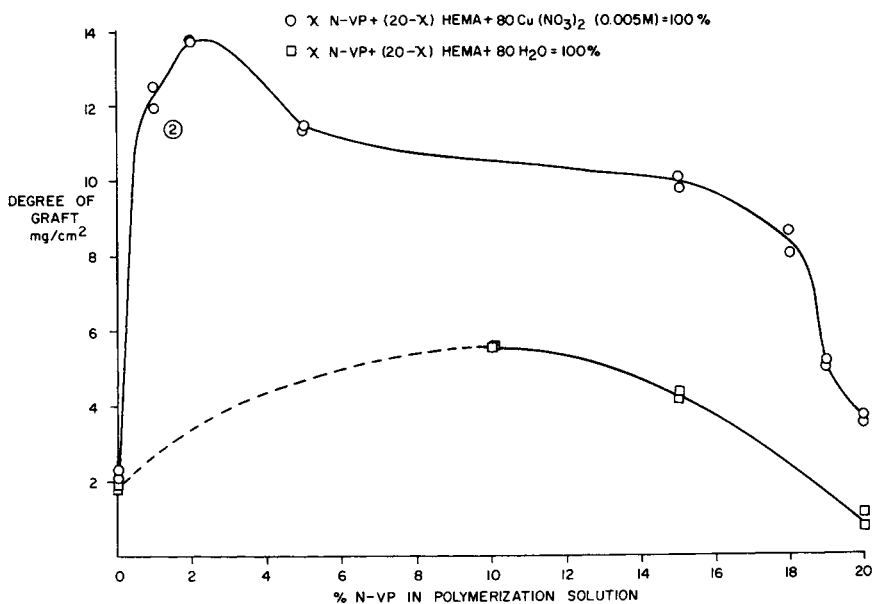


Fig. 6. Plot of the degree of graft as a function of the volume per cent N-VP in the monomer mixture for systems with and without  $\text{Cu}(\text{NO}_3)_2$  present.

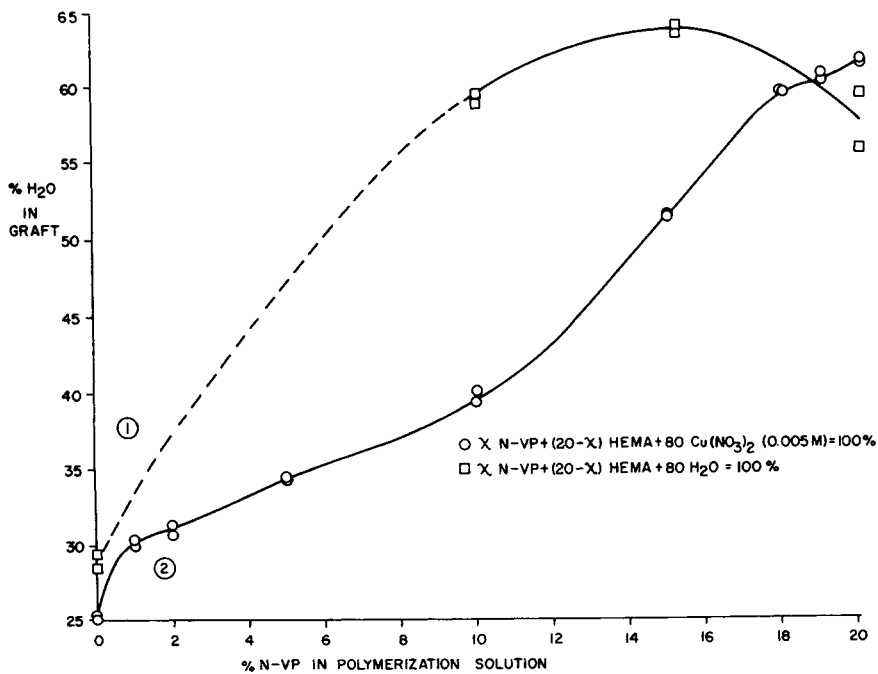


Fig. 7. Plot of the water content in the graft as a function of the volume per cent N-VP in the monomer mixture for systems with and without  $\text{Cu}(\text{NO}_3)_2$  present.

gradual fall-off in graft was produced. Still, for the system containing only N-VP monomer, there is a marked graft increase over the equivalent system without cupric ion present. The dashed sections in curve 1 in both Figures 6 and 7 represent formulations in which a gel external polymer is formed which cannot be cleaned from the surrounding film. Therefore, no reliable data could be taken in this region. The shape of curve 1 in Figure 6 in the "uncleanable" region would not be expected to match the shape of curve 2. The gels formed in this region are hard and crosslinked, and they would certainly hinder monomer diffusion to the film surface and also cause any monomer remaining after gelation to be used up at an accelerated rate in external polymer formation. The hardness and rapidity of formation of the gels increases with increasing HEMA in the monomer mixture. Therefore, it is unlikely that at the end of the curve representing high HEMA-N-VP ratios a sharp increase in film grafting would be noted as is seen in curve 2. Based upon these arguments, it is felt that the synergistic graft increase is due to the presence of  $\text{Cu}^{++}$  ion and not some particularly interaction between the two monomers.

The addition of small quantities of crosslinking agent (EGDMA) to the monomers was found to have interesting effects on graft and water content. These effects are shown in Figures 8 and 9.

Attenuated total reflectance (ATR) infrared spectrophotometry can be used to determine the ratio of HEMA units to N-VP units in the surface region of grafted films.<sup>5</sup> Such an analysis is made relatively simple due to the amide type carbonyl group on N-VP. Its infrared absorption will occur at a longer wavelength ( $\sim 6.0 \mu$ ) than that of the HEMA carbonyl ( $\sim 5.8 \mu$ ).<sup>17</sup> A typical ATR spectrum of a HEMA-N-VP radiation grafted hydrogel on Silastic rubber is shown in Figure 10 (Fig. 11 is the baseline spectrum for the ATR crystal used to obtain Fig. 10). The ratio of the HEMA carbonyl absorbance to the N-VP carbonyl absorbance is proportional to the fraction of each of the monomer units in the graft surface. In Figure 12, the ratio of the HEMA carbonyl peak to that of the N-VP carbonyl peak is plotted against the  $\text{Cu}^{++}$  concentration for systems containing a constant (1:1) initial monomer ratio.

In order to determine what structural features of the monomers might be involved in producing the sorts of effects observed for the HEMA-N-VP system in the presence of cupric ion, various other monomer systems were explored. Results are reported in Table III. In general, the most dramatic effects in terms of graft increases were found for systems which contained N-VP, another monomer and  $\text{Cu}^{++}$  ion. The HEMA/N-VP/ $\text{Cu}^{++}$  system, which was the only system explored in detail, falls into this category. The differences in grafting behavior between acrylamide and methacrylamide systems is worthy of note. Cupric ion increases graft in all cases when used in conjunction with acrylamide. For methacrylamide, the  $\text{Cu}(\text{NO}_3)_2$  is found to inhibit graft. It is assumed that the pendant methyl group on the backbone polymer chain is not the immediate cause of

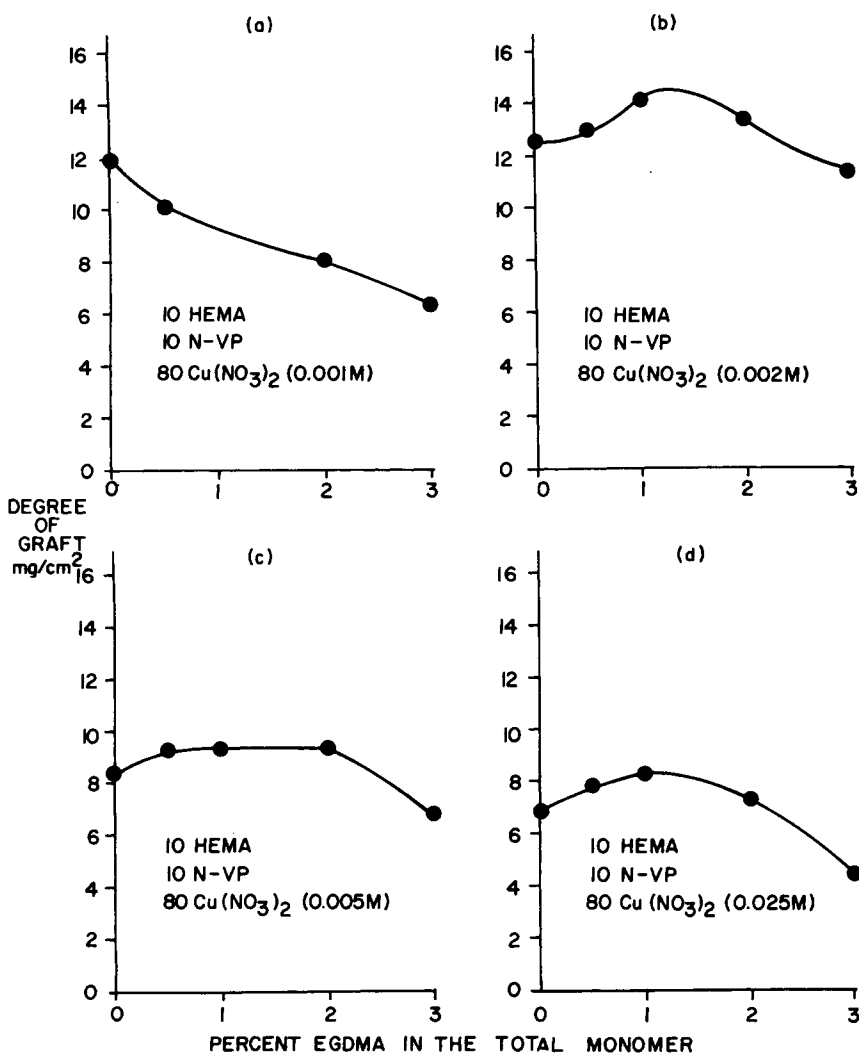


Fig. 8. Plot of the degree of graft vs. per cent EGDMA in the total monomer at four different  $\text{Cu}(\text{NO}_3)_2$  concentrations.

these graft decreases as 2-hydroxyethyl acrylate and 2-hydroxyethyl methacrylate both show the same sort of behavior (graft increases) in the presence of cupric ion and N-VP.

The effect of  $\text{Fe}^{+++}$  ion on grafting was tested by repeating the experiment described in Figure 1 using  $\text{Fe}(\text{NO}_3)_3$  instead of  $\text{Cu}(\text{NO}_3)_2$ . The results obtained were similar (see Table IV), except that the hydrogel graft appeared to be permanently stained yellow. This yellow staining has been previously reported.<sup>10</sup>

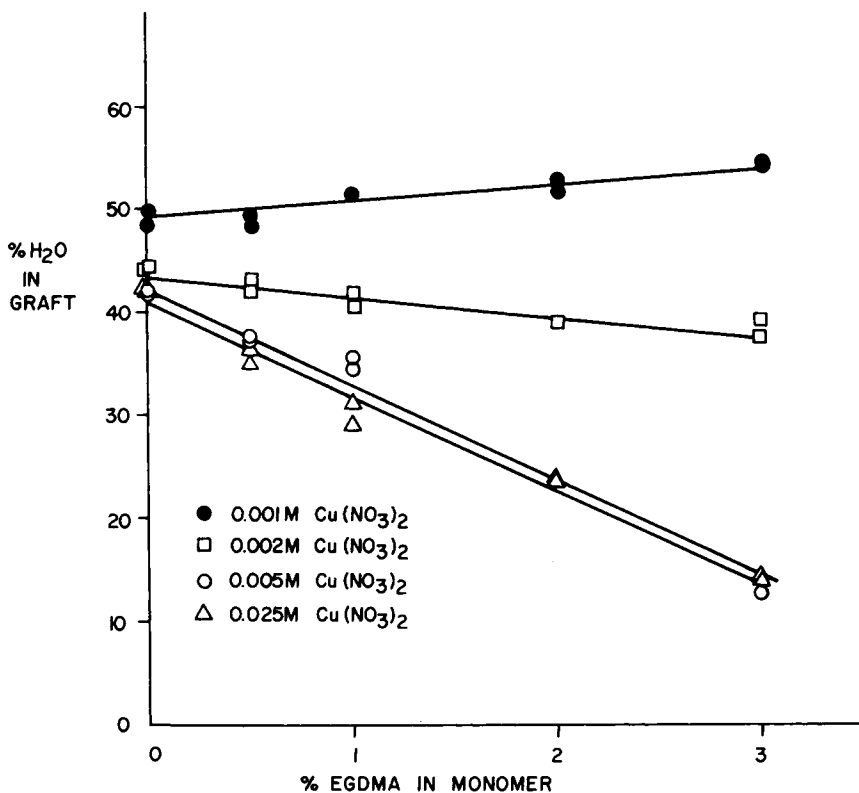


Fig. 9. Effect of increasing EGDMA in the monomer on the water content of the graft for the system 10% HEMA, 10% N-VP, 80% solvent (by volume) at four different  $\text{Cu}(\text{NO}_3)_2$  concentrations.

## DISCUSSION

It has been previously reported that  $\text{Cu}^{++}$  and  $\text{Fe}^{+++}$  ions are effective free-radical scavengers.<sup>12,13</sup> Metal ions have been used for many years in radiation grafting systems to inhibit external polymer formation.<sup>14,15,16</sup> Collinson et al. have proposed that a metal ion with an incomplete *d*-shell can transfer to itself an electron from the propagating radical polymer chain thus terminating the chain.<sup>18</sup> Consistent with such a model, Huglin and Johnson determined that, for the graft copolymerization of acrylic acid to nylon 6, as the concentration of  $\text{CuCl}_2$  in the bulk solution was increased, the rate of graft polymer formation and external polymer formation was decreased.<sup>19</sup> However, the inhibitory effect of the  $\text{Cu}^{++}$  was considerably higher in the bulk solution than in the graft.

The complicated effects noted for the radiation grafting behavior of the system HEMA/N-VP/ $\text{Cu}^{++}$  lead to the belief that something more than simple polymerization inhibition in the external solution is occurring. The

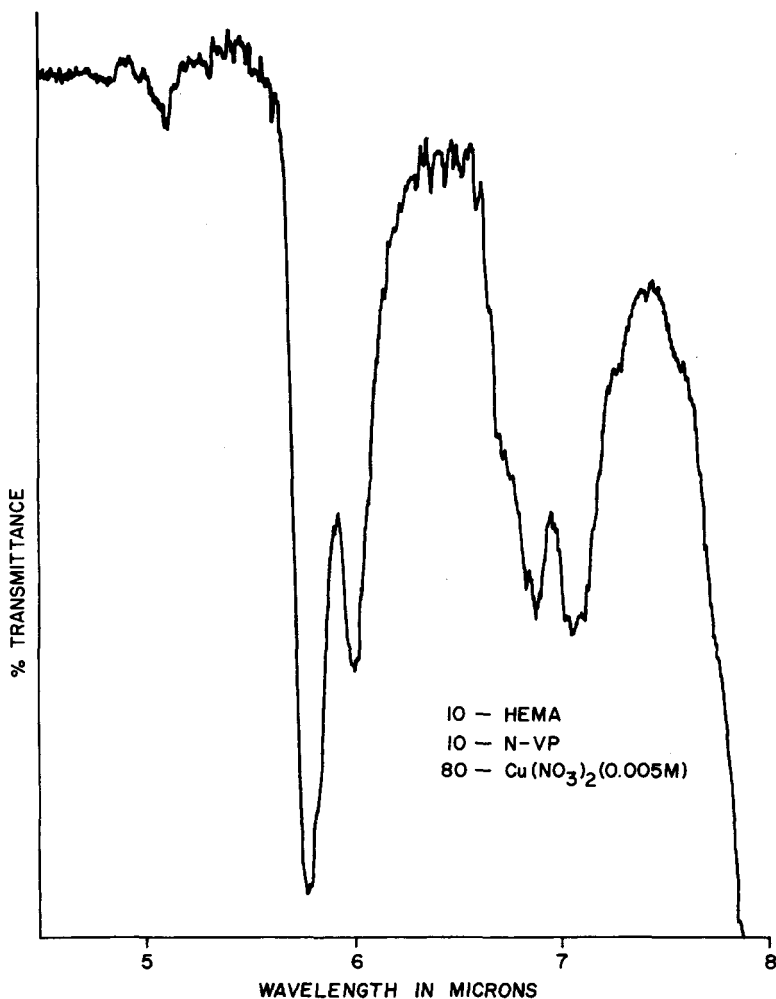


Fig. 10. ATR spectrum between 4.5 and 8  $\mu$  of a silicone rubber film radiation grafted with HEMA and N-VP.

experiments described were done in order to gain further insight into the mechanism of this process.

ATR spectra were taken of the grafted films so that a comparison could be made of the initial monomer ratio before irradiation with the ratio of HEMA to N-VP monomer units in the surface region of the graft. Based upon a comparison of the size of HEMA carbonyl IR peak to that of the N-VP (Fig. 12), it is apparent that for the 10 HEMA/10 N-VP system, the fraction of HEMA units in the graft is increasing with increasing copper concentration. It has been previously determined that pure N-VP grafted films have water contents of  $\sim 55$ – $65\%$ , while pure HEMA-grafted films

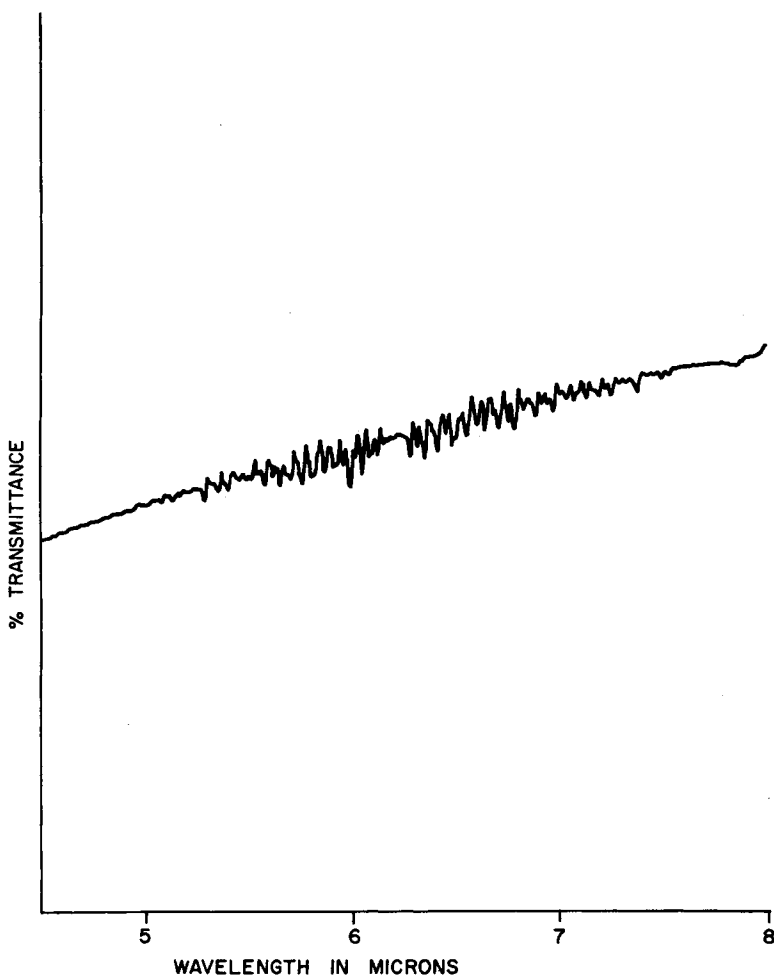


Fig. 11. Baseline spectrum of the KRS-5 crystal used to produce Fig. 10 between 4.5 and 8 $\mu$ .

contain  $\sim 25\text{--}30\%$  water in the graft.<sup>5</sup> The decrease in water contents for curves 2-4 in Figure 4 also suggests that the fraction of HEMA in these grafts is increasing with increasing  $\text{Cu}^{++}$  in the solvent. In Figure 2, the systems which are richer in N-VP monomer are seen to reach a zero graft level sooner as the  $\text{Cu}(\text{NO}_3)_2$  concentration is increased. The data all point to a mechanism in which the  $\text{Cu}^{++}$  ions are inhibiting the (graft) polymerization of N-VP to a greater extent than that of HEMA. This inhibition might occur through a reduction of  $\text{Cu}^{++}$  ion to  $\text{Cu}^+$ , as suggested by Collinson et al.<sup>18</sup>

It is also conceivable that the behavior of this system may be regulated by complex formation between the N-VP and the copper ion. *N*-Methyl-2-pyrrolidone complexes with a number of salts have been reported.<sup>20</sup> This behavior has been attributed to a strong affinity for cations by the negative



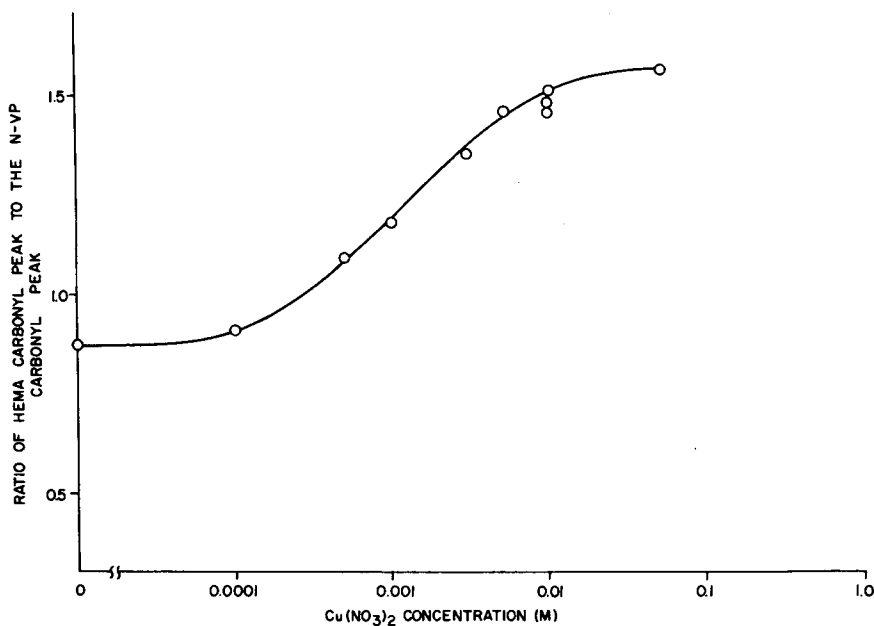


Fig. 12. Plot of the ratio of the HEMA carbonyl peak to the N-VP carbonyl peak as a function of  $\text{Cu}^{++}$  concentration in the solvent for the system 10% HEMA, 10% N-VP, 80% solvent (by volume).

TABLE III  
Effect of  $\text{Cu}(\text{NO}_3)_2$  on Radiation Grafting for Various Monomer Systems

Monomer 1 <sup>a</sup>	Monomer 2 <sup>a</sup>	Solvent (80%)	Extent of graft, mg/cm <sup>2</sup>	H <sub>2</sub> O in graft, %
2-Hydroxyethyl acrylate (10%)	N-VP (10%)	H <sub>2</sub> O <sup>b</sup>	0	—
2-Hydroxyethyl acrylate (10%)	N-VP (10%)	0.005M $\text{Cu}(\text{NO}_3)_2$	13.3	57.5
Acrylamide (10 g)	N-VP (10 g)	H <sub>2</sub> O <sup>b</sup>	0	—
Acrylamide (10 g)	N-VP (10 g)	0.005M $\text{Cu}(\text{NO}_3)_2$	2.5	60.2
Acrylamide (10 g)	HEMA (10 g)	H <sub>2</sub> O <sup>b</sup>	2.3	52.0
Acrylamide (10 g)	HEMA (10 g)	0.005M $\text{Cu}(\text{NO}_3)_2$	2.7	46.3
Acrylamide (20 g)	—	H <sub>2</sub> O <sup>b</sup>	0	—
Acrylamide (20 g)	—	0.005M $\text{Cu}(\text{NO}_3)_2$	1.3	68.0
Propylene glycol acrylate (10%)	N-VP (10%)	H <sub>2</sub> O <sup>b</sup>	0	—
Propylene glycol acrylate (10%)	N-VP (10%)	0.005M $\text{Cu}(\text{NO}_3)_2$	9.6	54.2
Methacrylamide (10 g)	N-VP (10 g)	H <sub>2</sub> O <sup>b</sup>	8.1	62.9
Methacrylamide (10 g)	N-VP (10 g)	0.005M $\text{Cu}(\text{NO}_3)_2$	4.2	60.5
Methacrylamide (5 g)	N-VP (15 g)	H <sub>2</sub> O <sup>b</sup>	6.8	66.2
Methacrylamide (5 g)	N-VP (15 g)	0.005M $\text{Cu}(\text{NO}_3)_2$	5.2	66.2

<sup>a</sup> Volume per cent or weight.

<sup>b</sup> External solution was found to be gelled after irradiation.

TABLE IV  
Effect of  $\text{Fe}(\text{NO}_3)_3$  on the Radiation Grafting of HEMA and N-VP  
onto Silicone Rubber

Monomer, vol-%	Solvent (80% by volume)	Graft, mg/cm <sup>2</sup>	H <sub>2</sub> O, %	Description of external polymer
20 HEMA	0.005M $\text{Fe}(\text{NO}_3)_3$	—	—	white gel <sup>a</sup>
10 HEMA-10 N-VP	H <sub>2</sub> O	6.73	57.8	white gel
10 HEMA-10 N-VP	0.005M $\text{Fe}(\text{NO}_3)_3$	13.76	41.2	low-viscosity liquid
20 N-VP	H <sub>2</sub> O	0.58	49.4	viscous liquid
20 N-VP	0.005M $\text{Fe}(\text{NO}_3)_3$	4.81	62.0	low-viscosity liquid

<sup>a</sup> Could not be completely cleaned from films.

oxygen atom. Complexes such as  $\text{Cu}(\text{ClO}_4)_2 \cdot 4\text{-}(N\text{-methyl-2-pyrrolidone})$  have been isolated and characterized.<sup>21</sup> Such complexes may also form with N-VP and influence the radiation grafting process in an as yet undetermined way.

In examining the ATR spectra for the set of films analyzed to produce Figure 12, it was noted that the size of the peaks due to the hydrogel decreased with increasing concentration of  $\text{Cu}(\text{NO}_3)_2$  in the solution used to prepare the films. Quantitative evaluation of ATR spectra based upon the intensity of single peaks is fraught with difficulties.<sup>22</sup> However, semi-quantitative judgments can often be made if care is taken to maintain some internal standard. As a rough standard in these experiments the intensity of an atmospheric absorption peak at  $\sim 6.5 \mu$  (see Fig. 10) was used. The "noise-like" peaks seen between  $5.3 \mu$  and  $7.9 \mu$  are caused by unequal path-lengths of atmospheric H<sub>2</sub>O in the sample and reference beams of the infrared spectrophotometer.<sup>23</sup> These absorptions are more clearly shown in the KRS-5 crystal baseline spectrum in Figure 11. It should be emphasized that these are true absorbance peaks and are completely reproducible with respect to shape and location as opposed to random noise.

In Figure 13, the ratio of the intensity of the peak at  $\sim 6.5 \mu$  to the arithmetic sum of the two carbonyl peaks (representing approximately the total absorption due to carbonyl type groups in the grafted hydrogel) is plotted against the  $\text{Cu}(\text{NO}_3)_2$  concentration in the aqueous solvent for the grafting solution 10% HEMA, 10% N-VP, 80% solvent. A clearly increasing trend with increasing  $\text{Cu}^{++}$  concentration is noted. Experiments were performed to be certain that this effect was not due to the gradual degeneration of the soft, easily deformable KRS-5 ATR crystal with repeated use. It was determined that no artifact of this sort was being observed. As the magnitude of the atmospheric absorption peaks should remain relatively constant, the intensity of the graft carbonyl peak must be decreasing.

The ATR technique examines the surface layer only of a material to a depth of perhaps a few microns. The above results imply that the con-

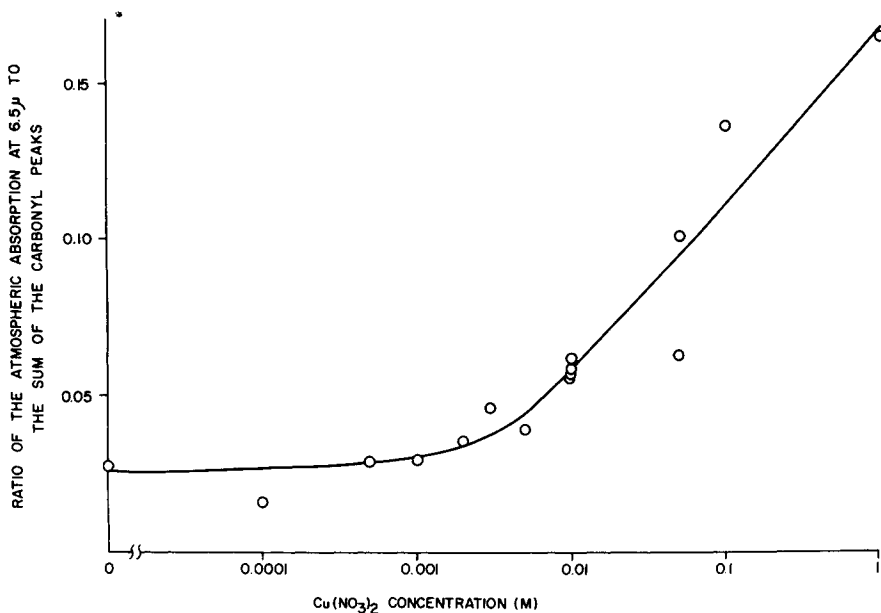


Fig. 13. Plot of the ratio of the atmospheric absorption at  $6.5 \mu$  to the sum of the carbonyl peaks as a function of  $\text{Cu}^{++}$  concentration in the solvent for the system 10% HEMA, 10% N-VP, 80% solvent (by volume).

centration of hydrogel graft at the surface changes as a function of the cupric ion concentration. At a cupric nitrate concentration of  $0.05M$ , high graft levels ( $\sim 6.7 \text{ mg/cm}^2$ ) are observed. Yet the peak intensity and therefore the surface concentration of graft is low. This implies the graft is internalized within the silicone rubber. For films prepared with  $0.1M$  and  $1.0M$   $\text{Cu}(\text{NO}_3)_2$ , the peak intensity was so low that the HEMA/N-VP ratio could not be obtained. The  $1.0M$  film had  $\sim 1 \text{ mg/cm}^2$  of graft. In other experiments using grafting systems without  $\text{Cu}^{++}$  ion, excellent spectra have been recorded from films with graft levels of this order of magnitude. The conclusion is that at higher  $\text{Cu}^{++}$  concentrations grafting occurs mainly within the Silastic matrix while at lower concentrations grafting takes place mainly on the surface.

The wettability of the films was found to decrease when prepared using copper concentrations of  $\sim 0.002M$  or above. If these high copper films were of a homogeneous nature with hydrophobic dimethylsiloxane chains and hydrophilic HEMA chains intermingled, one would expect a surface in which both structures were present. The wettability of the surface should be related to the fraction of hydrophilic groups in the surface. In the highest graft region of the HEMA peak, the hydrogel only accounts for  $\sim 37\%$  by weight of the total grafted material. Therefore, the surface might consist of as much as  $63\%$  hydrophobic regions. Such a surface could well demonstrate a nonwetable character. A surface coated with

hydrogel would not have visible hydrophobic sites and should appear wettable. These wettability observations are consistent with the graft penetration model formed on the basis of the ATR results.

The effect of  $\text{Cu}^{++}$  concentration on graft polymer penetration into the Silastic might be explained in the following way: It would be expected that the  $\text{Cu}^{++}$  concentration within the grafting substrate and in the graft itself should be considerably lower than that in the external solution. If there were a certain copper concentration at which grafting could no longer occur on the surface due to complete inhibition of polymerization, grafting might preferentially take place within the Silastic where the  $\text{Cu}^{++}$  concentration would be expected to be considerably lower. Based upon our own swelling measurements, it has been determined that HEMA monomer does not significantly penetrate the Silastic matrix. N-VP monomer, however, will swell Silastic to a small degree ( $\sim 3\%$ ). Therefore, in the presence of N-VP, the Silastic matrix is opened up somewhat to allow further monomer penetration and internal grafting. These swelling observations might help to explain how such small quantities of N-VP in the grafting system can cause huge increases in the degree of graft (Fig. 6).

Swelling observations may also help to explain why the expected effect of  $\text{Cu}^{++}$  ion on the graft polymerization is not seen with polyethylene (Table II). Neither HEMA nor N-VP can penetrate into the highly crystalline polyethylene matrix. Grafting can only occur at the surface where it is subject to inhibition by cupric ion. Therefore, in the presence of cupric ion the extent of grafting is even lower than without the salt present. Pellethane, on the other hand, is swollen by N-VP and the expected  $\text{Cu}^{++}$  effect is seen.

Based upon some of the data, it can be surmised that the presence of  $\text{Cu}^{++}$  ion in these grafting systems has a great influence upon the rates at which various monomers will graft to the support material. Curve 1 in Figure 7 describes the water content in the graft as a function of an increasing N-VP:HEMA ratio in the monomer solution for a system in which no  $\text{Cu}^{++}$  ion is present. From the previous discussion of the relationship between the graft water content and graft composition for the HEMA/N-VP system it is evident that by the time the monomer mixture contains equal quantities of both monomers (on a mole basis this occurs at approximately 10.8 vol-% N-VP) the graft is composed almost entirely of N-VP. When  $\text{Cu}^{++}$  ion is present, the fraction of N-VP in the graft increases much more gradually as the N-VP:HEMA ratio in the monomer solution is increased. This effect has already been attributed to the stronger inhibitory effect of  $\text{Cu}^{++}$  ion on the polymerization of N-VP than on that of HEMA.

$\text{Cu}^{++}$  ion may exert a significant effect upon the uptake of monomers into the graft when the divinyl crosslinking agent EGDMA is present. The effects of small quantities of this compound in the monomer mixture are of interest because it is a common HEMA impurity and because it is used in the preparation of crosslinked poly(HEMA) gels for biomedical applications.<sup>24</sup> Crosslinker concentration effects upon the degree of graft are

shown in Figure 8. The shape of the curve of degree graft versus cross-linking agent concentration apparently depends upon whether the solvent  $\text{Cu}^{++}$  concentration is in the range below the N-VP peak or above it. This concentration effect is again mirrored in Figure 9. At higher copper concentrations, the water content decreases with increased EGDMA. At  $0.001M$   $\text{Cu}(\text{NO}_3)_2$  (just below the region of the N-VP peak maxima), there is a slight increase in  $\text{H}_2\text{O}$  content with increasing EGDMA. The  $\text{Cu}^{++}$  concentration of  $0.002M$  perhaps represents an intermediate state. The decreasing water content trend can be explained by proposing that the hydrophobic EGDMA is being added to the graft. As the graft water content decrease is quite sharp at higher  $\text{Cu}^{++}$  concentrations, the possibility that the EDGMA is being added to the graft at a rate in excess of that expected based upon its low concentration must be considered. With grafting occurring within the Silastic at higher  $\text{Cu}^{++}$  concentrations, it is reasonable to speculate that the hydrophobic EGDMA may find internal hydrophobic Silastic sites preferable for attachment.

## CONCLUSIONS

Radiation grafting systems consisting of N-VP, another monomer, and cupric ion have been found to be unique, versatile, and potentially of great value, particularly for the preparation of new biomedical materials. The following interesting characteristics have been noted and explored for these cupric ion systems:

1. They can be used to produce levels of graft higher than are possible using other solvent systems on certain polymer supports.
2. They will prevent gellation of the external polymer.
3. The copolymer composition of the final film can be altered by varying the  $\text{Cu}^{++}$  concentration.
4. The surface texture of the final films can be modified by varying the  $\text{Cu}^{++}$  ion concentration.
5. Graft penetration into the substrate, and therefore the wettability of the films, is dependent upon the  $\text{Cu}^{++}$  ion concentration.
6. The  $\text{Cu}^{++}/\text{N-VP}$  system allows many monomers to be readily grafted which would graft not at all (or would graft only with great difficulty) in more conventional radiation grafting systems.

Certain aspects of the workings of these cupric ion grafting systems have been elucidated. In particular, the variations in the copolymer graft composition and graft penetration as a function of cupric ion concentration are now understood. However, the precise mechanisms which control this system are still unclear.

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