Controlled Release and Absorption of Cetylpyridinium Chloride Using Polymer Hydrogels

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ABSTRACT: Interest in the biocide cetylpyridinium chloride (CPC) has resurged based on new studies showing its effectiveness against a wide variety of pathogens. Hydroxyethyl methacrylate (HEMA)-based hydrogels have been developed for the controlled release of CPC. Initial burst release of the biocide can be controlled and sustained release can be achieved for more than two weeks. The burst and sustained release can be adjusted by varying the amount of anionic monomer (AMPSA), crosslink content (DEGDMA), release media, hydrogel surface area, and CPC loading. After removing the CPC-loaded hydrogel from solution and drying, the release of CPC can also be reactivated. Very interesting swelling behavior was observed for CPC-loaded hydrogels due to the electrostatic and hydrophobic interactions between the polymer hydrogel and CPC. In addition, HEMA-based hydrogels can be used to recover or absorb CPC from aqueous solutions. By increasing the amount of AMPSA in the HEMA-based hydrogel, more CPC can be absorbed from solution. The absorption is also enhanced by agitating the solution. © 2005 Wiley Periodicals, Inc. J Appl Polym Sci 99: 3153–3162, 2006

Key words: hydrogels; biocompatibility; photopolymerization; cetylpyridinium chloride; controlled release; biocide; hydroxyethyl methacrylate

INTRODUCTION

The surfactant cetylpyridinium chloride has been used for over 40 years as an antiseptic agent for oral care. This quaternary ammonium compound exhibits antimicrobial activity against Gram-positive and, at higher concentrations, Gram-negative microorganisms.[1] Interest in CPC has resurged with recent reports of its effectiveness as a biocide against a wide variety of pathogens often found contaminating meat and produce. These pathogens include *Escherichia coli* O157 : H7, *Listeria monocytogenes,* and *Staphylococcus aureus* on beef,[2–4] as well as *Campylobacter* and *Salmonella typhimurium* on poultry.[5–7] Pathogen growth is also inhibited on fresh produce by rinsing with dilute CPC solutions.[8–11] The U.S. Food and Drug Administration recently approved the use of CPC in antibacterial sprays for use on raw poultry.[12] Potential homeland defense applications also exist for CPC-containing materials. The National Research Council has identified the need for biocidal materials and surfaces to meet homeland defense challenges for the chemical sciences in the 21st century.[13]

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To date, studies involving the controlled release of CPC have focused largely on dental applications in which low levels (less than 10 mg) of CPC were loaded within a polymer matrix. Erodible adhesive patches, resins and varnishes containing CPC have been prepared for the treatment of plaque and gingivitis.[1,14–16] Nafee et al. prepared adhesive patches from polyvinylalcohol (PVA), hydroxyethylcellulose (HEC), and chitosan.[1] Over 95% of CPC was released from PVA-based patches after 7 h, whereas only 50% of CPC was released from HEC-based patches. Compared to the PVA- and HEC-based patches, a considerable drop in CPC release was observed from chitosan-based patches containing polyvinyl pyrrolidone and gelatin additives.[1] Ali et al. found that almost 95% of CPC was released from modified cellulose disks after 6 h. The disks showed growth inhibition of common microorganisms found in oral infections.[14] Ehara et al. observed that methacrylic acid-based dental resins released CPC only at pH $\leq$ 6. Once CPC was fully desorbed from the resin, the resin could readsorb some of the CPC when immersed in an aqueous solution.[15] Compared to the polymer matrices described above, higher levels of CPC loading were achieved using albumin microspheres: 10–25 mg in 100 mg of albumin microspheres.[17]

Polymer hydrogels have become a popular vehicle for the controlled release of a variety of materials. Hydrogels based on 2-hydroxyethyl methacrylate

(HEMA) are attractive for a variety of applications due to their high water content, nontoxicity, and biocompatibility. By employing photopolymerization techniques, hydrogel disks or coatings can be produced conveniently and rapidly. Polymer properties can be adjusted for slow release by varying the polymer formulation.

In this work, the release of cetylpyridium chloride (CPC) from HEMA-based polymer hydrogels was explored and controlled by varying the anionic monomer content, crosslinker content, release media, and hydrogel surface area. High levels of CPC loading (up to 35 wt %) were achieved while maintaining the polymer's physical integrity. The initial burst release of the biocide was controlled and sustained release was achieved for more than two weeks. Release of CPC was reactivated after drying the polymer hydrogels. HEMA-based hydrogels were also prepared without CPC loading. These "blank" hydrogels were used to study the absorption of CPC from aqueous solutions. The absorption of CPC was adjusted by increasing the amount of AMPSA (2-acrylamido-2-methyl-1-propanesulfonic acid) in "blank" HEMA-based hydrogels. The absorption is also enhanced by agitating the solution.

EXPERIMENTAL

Materials

HEMA, AMPSA, diethyleneglycol dimethyacrylate (DEGDMA), cetylpyridinium chloride monohydrate (CPC), and the photoinitiator, 2,2-dimethoxy-2-phenylacetophenone (DMPA) were purchased from Aldrich (Milwaukee, WI) and used as received. Gram-Pac phosphate buffer, pH 7.41, was purchased from Fisher Scientific (Pittsburgh, PA). Teflon sheets were purchased from Plastic Supply, Inc. (Albuquerque, NM) and circular photopolymerization molds were machined with a 0.050 in. (1.27 mm) depth and varying diameters.

Photopolymerization

HEMA-based hydrogels containing AMPSA were prepared with 0.3 mol % DMPA, 2 or 4 mol % DEGDMA, and 0, 2.5, 5, or 10 mol % AMPSA (15 mmol total monomer, crosslinker and initiator content). To fully dissolve the anionic monomer, 0.2 g of deionized water was added to the formulation. Based on the total mass of the monomer, crosslinker and initiator, ~11.5 wt % CPC was added.

HEMA-based hydrogels without the anionic monomer, AMPSA, were also prepared with 0.3 mol % DMPA and 2, 4, or 6 mol % DEGDMA. CPC loading levels ranged from 11.5–35 wt %. Sample labels for the hydrogels represent the sample as DEGDMA (mol %):AMPSA (mol %):CPC (wt %) (Table I).

TABLE I
HEMA-Based Hydrogel Disks Prepared to Study the Controlled Release and Absorption of CPC in Aqueous Solutions

Sample	DEGDMA (mol %)	AMPSA (mol %)	CPC (wt %)	AMPSA : CPC
2 : 0 : 11.5	2	—	11.5	—
2 : 2.5 : 11.5	2	2.5	11.5	1 : 2.2
2 : 5 : 11.5	2	5	11.5	1 : 1
2 : 10 : 11.5	2	10	11.5	1 : 0.5
2 : 0 : 0	2	—	—	—
2 : 2.5 : 0	2	2.5	—	—
2 : 5 : 0	2	5	—	—
2 : 10 : 0	2	10	11.5	—
4 : 0 : 11.5	4	—	11.5	1 : 22
4 : 2.5 : 11.5	4	2.5	11.5	1 : 1
4 : 5 : 11.5	4	5	11.5	1 : 0.5
4 : 10 : 11.5	4	10	21.5	—
2 : 0 : 21.5	2	—	25	—
2 : 0 : 25	2	—	30	—
2 : 0 : 30	2	—	35	—
2 : 0 : 35	2	—	21.5	—
4 : 0 : 21.5	4	—	25	—
4 : 0 : 25	4	—	30	—
4 : 0 : 30	4	—	35	—
4 : 0 : 35	4	—	11.5	—
6 : 0 : 11.5	6	—	21.5	—
6 : 0 : 21.5	6	—	25	—
6 : 0 : 25	6	—	30	—
6 : 0 : 30	6	—	35	—
6 : 0 : 35	6	—	11.5	—

Sample label represents DEGDMA (mol %): AMPSA (mol %): CPC (wt %).

In all cases, the polymer formulation was stirred or ultrasonically irradiated to dissolve all materials. The solution was pipetted into a circular Teflon mold with a 0.050 in. (1.27 mm) depth and 0.500 in. (12.70 mm) diameter. Polymerization was initiated by irradiation for 5 min with a 4500 $\mu W/cm^2$ UV source (UVP B-100A flood lamp) in a black exposure box (UVP #76–00-55–01). The lamp intensity was monitored daily with a Spectroline DRC-100X digital radiometer and DIX-365A sensor. The lamp was allowed to warm up for 1 h before use. The temperature within the exposure box was 40–45°C.

Two additional Teflon molds with a 0.050 in. (1.27 mm) depth were used to produce polymers with larger surface area. One mold had a diameter of 0.7500 in. (19.05 mm) and the other had a diameter of 1.0000 in. (25.40 mm).

CPC release measurement

The CPC-loaded hydrogel disk was immersed in 25 mL deionized water or pH 7.41 phosphate buffer and agitated on a Labquake shaker with rocking action. To monitor the release, 250 μL samples were removed at regular time intervals. Hydrogels with 25 wt % CPC or

more were immersed in 40 mL of deionized water or phosphate buffer and similarly agitated. To monitor the release, 100 μL samples were removed and diluted with 150 μL deionized water at regular time intervals. The release of CPC was measured with liquid chromatography coupled with mass spectroscopy (Waters Integrity LC/MS with Symmetry C8 columns). The flow rate was 0.4 mL/min with an injection volume of 50 μL and UV detection at 260 nm.

Reactivation release measurement

During the first cycle, the CPC-loaded hydrogel was monitored for 24 h in the manner described in the aforementioned section (cycle 1). The hydrogel was then removed from solution and dried at room temperature under reduced pressure for 24 h. This release-drying process was repeated twice on the same sample (cycles 2 and 3).

Swelling

The percent swelling was calculated for hydrogels containing 2 mol % DEGDMA, varying amounts of AMPSA, and an initial CPC content of 11.5 wt %. The swollen weight of each sample was measured after being immersed in deionized water for 24 h. The percent swelling was calculated as follows.

$$\%\text{Swelling} = \left[\frac{W_s - W_d}{W_d}\right] 100$$

where W_s is the weight of the swollen hydrogel and W_d the weight of the dry hydrogel.

CPC absorption

HEMA-based hydrogels were prepared without CPC loading. These "blank" hydrogels were used to study the absorption of CPC from aqueous solutions. Hydrogels with 2 mol % DEGDMA and varying degrees of AMPSA were prepared (samples 2 : 0 : 0, 2 : 2.5 : 0, 2 : 5 : 0, and 2 : 10 : 0). The hydrogels were immersed in deionized water for three weeks and allowed to swell to equilibrium. The water was replaced daily to remove residual amounts of unreacted monomer and initiator and to bring the hydrogels to their fully swelled volume. The hydrogels were removed from deionized water and the surface water was removed with a Kim Wipe. The hydrogels were then immersed in 20 mL of 75 ppm CPC solution in deionized water or in 20 mL of 75 ppm CPC solution in pH 7.41 buffer. The solutions were allowed to stand (static conditions) or were agitated on a Labquake reciprocal shaker (dynamic conditions). To monitor CPC absorption, the CPC reservoir concentration was monitored at 260 nm using an HP 8452A UV–Vis at regular time intervals.

RESULTS AND DISCUSSION

Polymer properties

Photopolymerization of the HEMA-based formulations was achieved in 5 min with a 4500 μW/cm^2 UV source. The hydrogel disks were hard and transparent. The thickness of the disks was maintained at 0.050 in. (1.27 mm) to ensure uniform photopolymerization across the thickness of the disk. The photopolymerization of acrylate monomers with comparable UV intensity has been extensively studied.[18–23] In addition, the hydrogels swelled uniformly in aqueous solutions and maintained their physical integrity even with high levels of CPC loading.

Variation of anionic monomer, release media, and crosslinker content

Release studies indicate that there are several factors that influence the release of CPC into solution. The first factor is the amount of anionic monomer incorporated into the polymer hydrogel. Figure 1 compares the release of CPC into deionized water for polymer hydrogels with varying degrees of anionic monomer, AMPSA (0, 2.5, 5, and 10 mol %). A burst release of CPC is observed in the first 24 h, with the exception of the hydrogel containing 10 mol % AMPSA (2 : 10 : 11.5). This initial burst is thought to arise from the release of CPC from the surface of the hydrogel. The CPC release is greatest for the polymer hydrogel containing no AMPSA. As the AMPSA concentration increases, the CPC release decreases. The suppressed release of CPC is largely due to the stoichiometry between the polyanion and the CPC cation. The molar ratio of AMPSA to CPC is 1 to 2.2 for the sample containing 2.5 mol % AMPSA and 11.5 wt % CPC. Increasing the AMPSA content to 5.0 mol % yields a 1 : 1 ratio between AMPSA and CPC. At 10 mol % AMPSA, the molar ratio between AMPSA and CPC is 1 : 0.5 and almost no CPC is released from the polymer matrix.

The second factor that influences the release of CPC is the release media. Figure 1 shows the release of CPC in deionized water and Figure 2 shows the release in pH 7.41 phosphate buffer. The same polymer formulations were used for both studies. The same release trends are observed in both studies: increasing the AMPSA concentration decreases the CPC release. However, the overall release of CPC is considerably suppressed in the phosphate buffer. After 5 days, the total release of CPC in phosphate buffer is only one-quarter of the total amount released in deionized water from the same polymer. Lee and Lin found that release of the cationic dye, crystal violet, was sup-

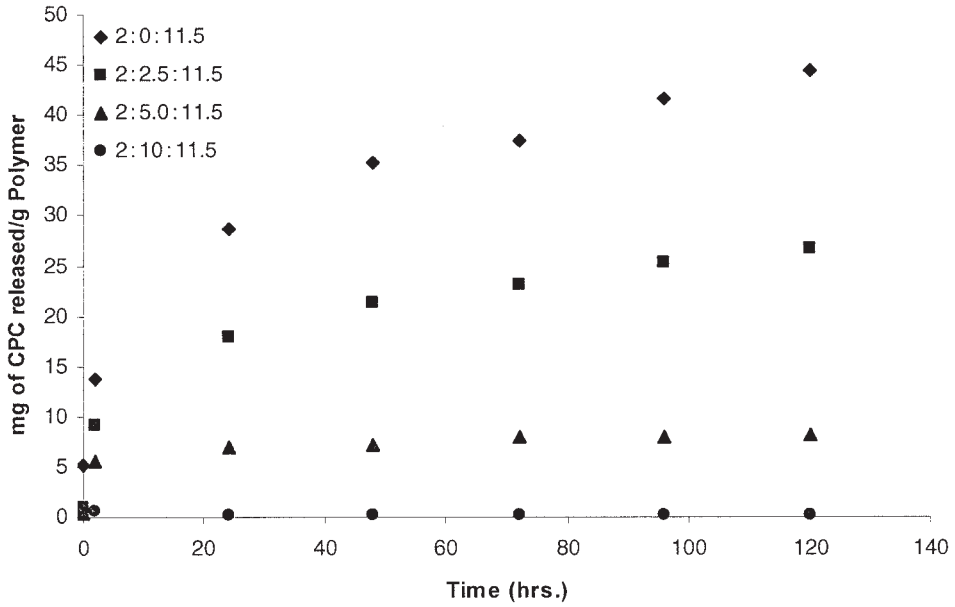

Figure 1 Comparison of CPC release in deionized water with varying degrees of anionic monomer (AMPSA) in polymer hydrogel. ◆ = 2 : 0 : 11.5, ■ = 2 : 2.5 : 11.5, ▲ = 2 : 5.0 : 11.5, ● = 2 : 10 : 11.5, where sample label represents DEGDMA (mol %) : AMPSA (mol %) : CPC (wt %).

pressed in saline solutions.[24] Exchange between ions in solution and the polymeric complex (cationic CPC/polyanion) is established. This ion-exchange effect may suppress the release of the cationic material CPC in ionic solutions.

The third factor that influences the release of CPC is the amount of crosslinking. A series of HEMA-based hydrogels were prepared with varying amounts of crosslinker, (2, 4, or 6 mol % DEGDMA). The CPC loading level was 11.5 wt %. The release results are shown in Figure 3. Increasing the degree of crosslinking suppresses the release of CPC as has been observed for other polymers.[17] Altering the degree of crosslinking is commonly used to control the release of various materials from polymer hydrogels. Compared to varying the anionic monomer content, vary-

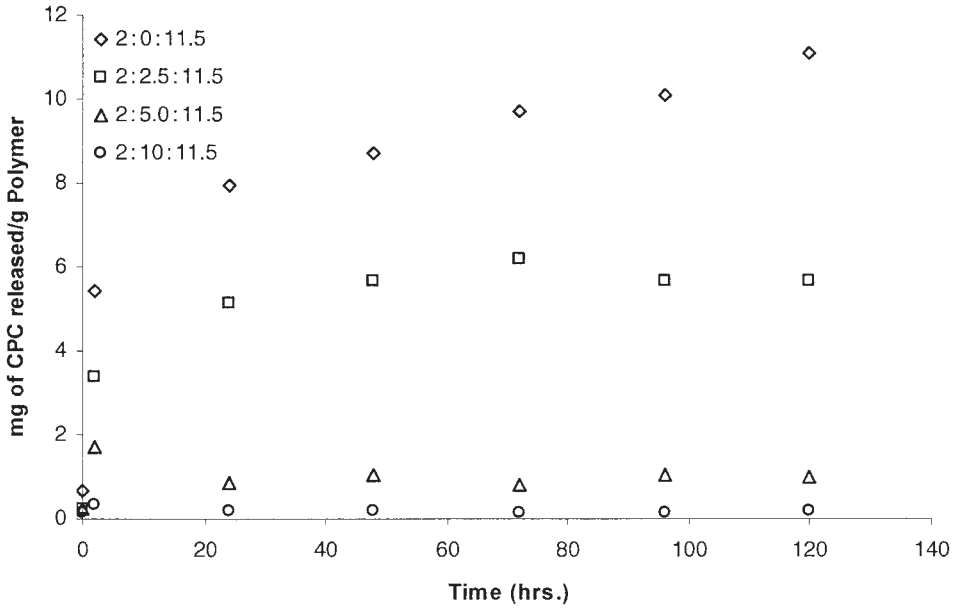

Figure 2 Comparison of CPC release in pH 7.41 phosphate buffer with varying degrees of anionic monomer (AMPSA) in polymer hydrogel. ◇ = 2 : 0 : 11.5, □ = 2 : 2.5 : 11.5, △ = 2 : 5.0 : 11.5, ○ = 2 : 10 : 11.5, where sample label represents DEGDMA (mol %) : AMPSA (mol %) : CPC (wt %).

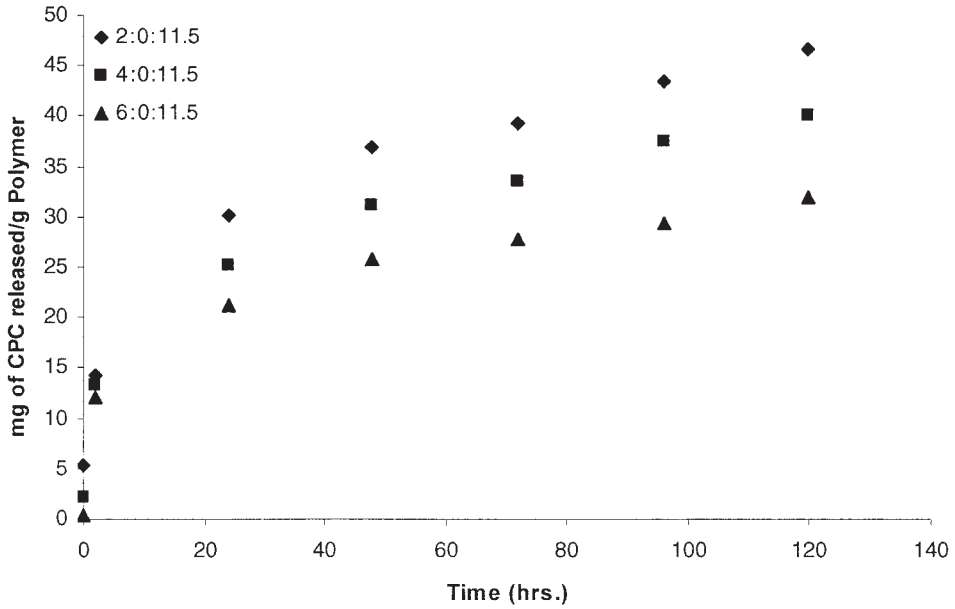

Figure 3 Comparison of CPC release in deionized water with varying degrees of crosslinker (DEGDMA) in polymer hydrogel. Hydrogel does not contain AMPSA. ◆ = 2 : 0 : 11.5, ■ = 4 : 0 : 11.5, ▲ = 6 : 0 : 11.5, where sample label represents DEGDMA (mol %) : AMPSA (mol %) : CPC (wt %).

ing the degree of crosslinking has a less dramatic effect on the release of CPC and can be used to fine-tune the release from HEMA-based hydrogels. Increasing the amount of DEGDMA crosslinker did not impact the CPC loading ability of these materials.

Variation of CPC loading

Most studies involving the controlled release of CPC have used low levels (less than 10 mg) of CPC loaded within the polymer matrix.[1,14–16] In this work, the amount of CPC loaded in the polymer hydrogel was studied. Hydrogels containing 11.5, 21.5, 25, 30, and 35 wt % CPC were prepared. High levels of loading could be achieved without compromising the physical integrity of the hydrogel disk. The upper limit of CPC loading was restricted by the CPC solubility in the HEMA-based polymer formulation. Beyond 35 wt %, CPC was not completely soluble. The release data of CPC from hydrogels with various loading levels are shown in Figure 4. High levels of CPC can be delivered rather quickly (24 h or less) or delivery can be sustained over several days.

Variation of hydrogel surface area

By employing photopolymerization techniques, hydrogel disks with different surface areas were produced conveniently and rapidly, further illustrating the applicability of this system. The release of CPC was monitored for hydrogels with different surface areas. The disks had identical compositions and surface areas of 3.12, 6.56, and 11.34 cm^2. The disk thickness for all samples was 0.050 in. (1.27 mm). Figure 5 shows that the release rate is proportional to the surface area exposed to solution. Larger exposed surface area results in greater CPC release. The dependence on exposed surface area is confirmed by the fact that the amount of CPC released per square centimeter is uniform for all three samples.

Extended release of CPC

The extended release of CPC was also explored. The long-term release of CPC from a HEMA-based hydrogel with 2 mol % DEGDMA and 11.5 wt % CPC was studied. Analysis of the solution after 15 days indicated a CPC concentration of 950 ppm. This concentration corresponds to the theoretical concentration if all CPC incorporated into the hydrogel was released. The long-term release of CPC from a HEMA-based hydrogel with 4 mol % DEGDMA and 11.5 wt % CPC was also studied. After 11 days, 43% of CPC was released. It was estimated that full release would be achieved after 35 days. Once again, the controlled and sustained release of CPC is clearly illustrated. Simply by increasing the amount of crosslinker DEGDMA, the extended release is more than doubled. Controlled biocide delivery can be achieved for one week, two weeks, or even a month (Fig. 6).

Burst release and polymer–CPC interactions

Burst release is typically defined by an initial large release of material from a controlled release matrix

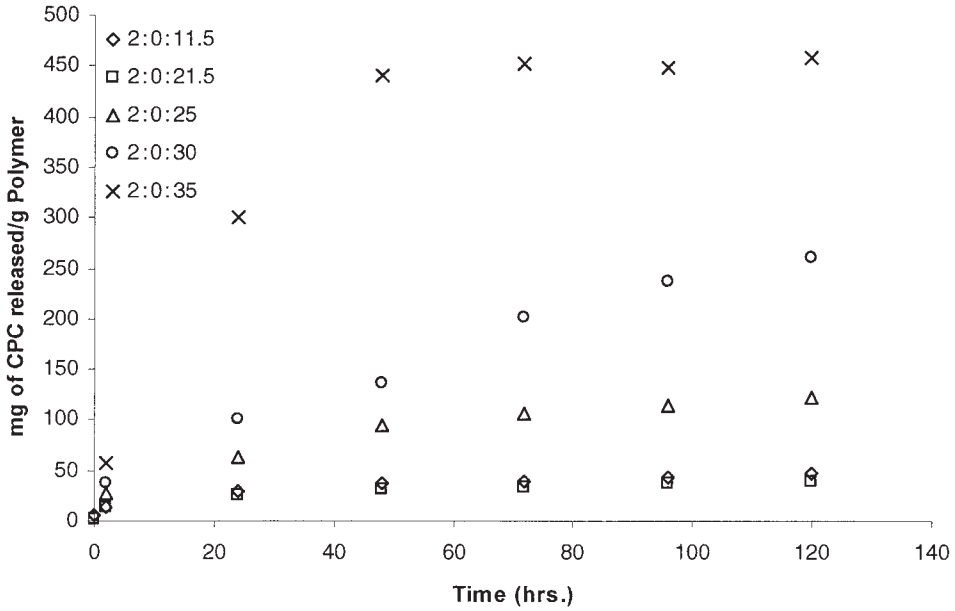

Figure 4 Comparison of CPC release in deionized water with varying degrees of CPC loading. Hydrogel does not contain AMPSA. ◇ = 2 : 0 : 11.5, □ = 2 : 0 : 21.5, △ = 2 : 0 : 25. ○ = 2 : 0 : 30, × = 2 : 0 : 35, where sample label represents DEGDMA (mol %) : AMPSA (mol %) : CPC (wt %)

before the release rate stabilizes.[25] Burst release is commonly observed in controlled delivery systems but the phenomenon is not completely understood. The mechanism of burst release may not be universal and may largely depend on the specific release material and matrix interactions.[25] Burst release of CPC was observed in this work and was generally complete in 24 h or less before a stable, linear release rate was achieved. The amount of CPC released during the 24 h burst release period is shown in Table II for several different hydrogels. The amount of CPC released during the burst release period decreases with an increase in the anionic monomer, AMPSA. The CPC burst release also decreases with an increase in

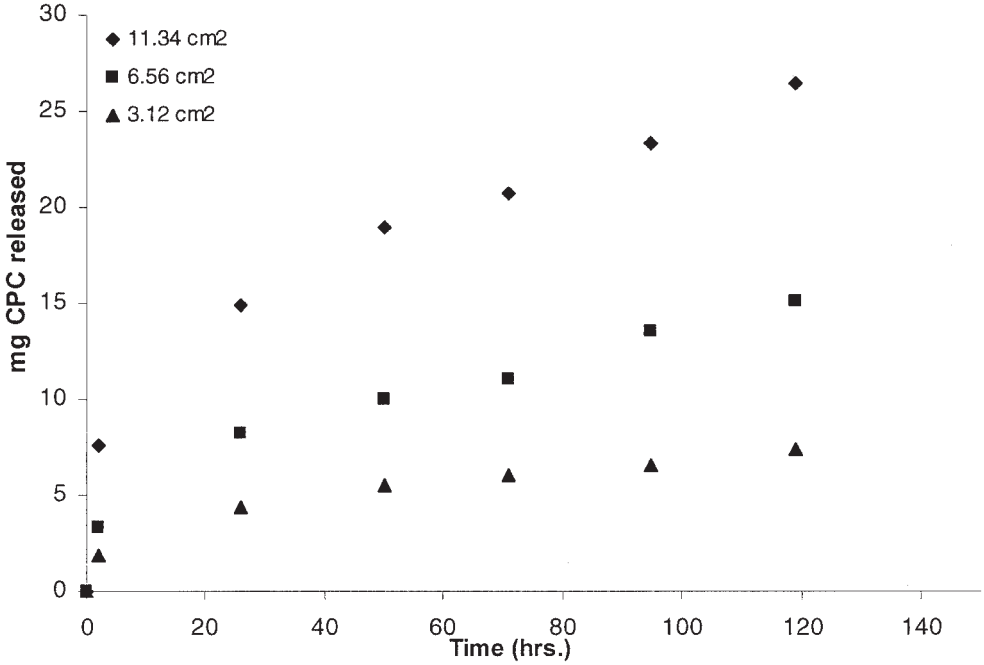

Figure 5 Comparison of CPC relcase in deionized water with varying hydrogel surface areas. Hydrogel does not contain AMPSA and is based on 4 mol % DEGDMA and 11.5 wt % CPC. ♦ = 11.34 cm^2, ■ = 6.56 cm^2, ▲ = 3.12 cm2.

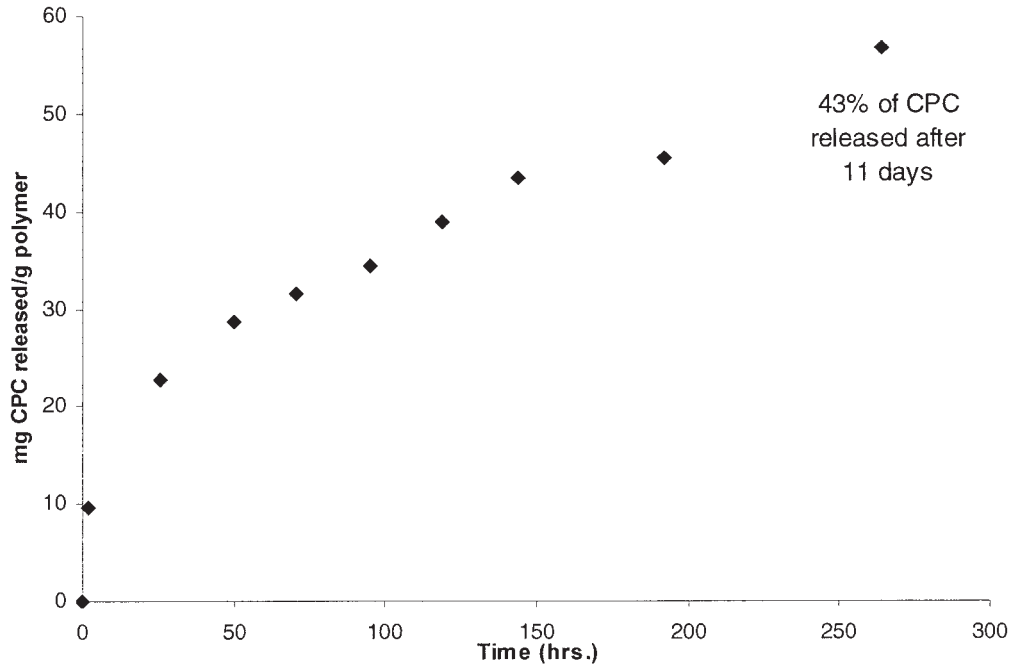

Figure 6 Extended release of CPC in deionized water. Hydrogel does not contain AMPSA and is based on 4 mol % DEGDMA and 11.5 wt % CPC.

crosslinker, DEGDMA. The amount of CPC released during the burst period dramatically increases when the CPC loading is increased and when the CPC is loaded within an uncharged HEMA-based hydrogel.

There are several potential reasons for burst release from a controlled release matrix. One possible reason for burst release is dissolution of unbound material present on the surface of the matrix or hydrogel.[25] In this case, a fairly simple method for reducing the burst release is by surface extraction of the drug or material. Lee showed that surface extraction or pretreatment is an effective method for reducing the burst release of oxprenolol HCl from HEMA-based hydrogels.[24] In this work, the repeat release of CPC was measured to probe the burst release profile from an uncharged hydrogel and to determine if release could be reactivated from hydrogels after they are removed from solution and dried. We found that the burst release of CPC from an uncharged HEMA-based hydrogel is largely attributed to CPC present on the surface of the hydrogel (Fig. 7). HEMA-based hydrogels with 4 mol % DEGDMA and 11.5 wt % CPC were prepared. An initial burst release was observed for the first release cycle and may be attributed to CPC released from the surface of the hydrogel. After the first release cycle, the hydrogel was removed from solution and dried. The CPC release was reactivated in cycles 2 and 3 and followed a more stable, linear release profile. After the first cycle, ~22% of the total amount of CPC had been released. After the second cycle and third cycle, ~28 and 34% of the total amount of CPC had been released, respectively. After multiple release-drying cycles, the physical integrity of the hydrogel remained intact. Not only have we probed the burst release of these materials, we have also shown that the release can be reactivated from these materials after removing from solution and drying.

TABLE II
Milligrams CPC Released Per Gram Polymer After 24 h in Deionized Water

Sample	CPC (mg)
2 : 0 : 11.5	28.7
2 : 2.5 : 11.5	17.9
2 : 5 : 11.5	6.98
2 : 10 : 11.5	0.13
4 : 0 : 11.5	25.2
6 : 0 : 11.5	21.2
2 : 0 : 21.5	45.13
2 : 0 : 25	63.94
2 : 0 : 30	100.76
2 : 0 : 35	300.29

Sample label represents DEGDMA (mol %): AMPSA (mol %): CPC (wt %).

Another potential reason for burst release may be the degree of swelling of the matrix or hydrogel.[25] Brazel and Peppas observed burst release for the drug theophylline in hydrogels with a large degree of swelling and thus larger pore volume for diffusion of the drug upon swelling.[26] In this work, the degree of swelling does not correlate with the amount of CPC released from the hydrogel–CPC matrix during the

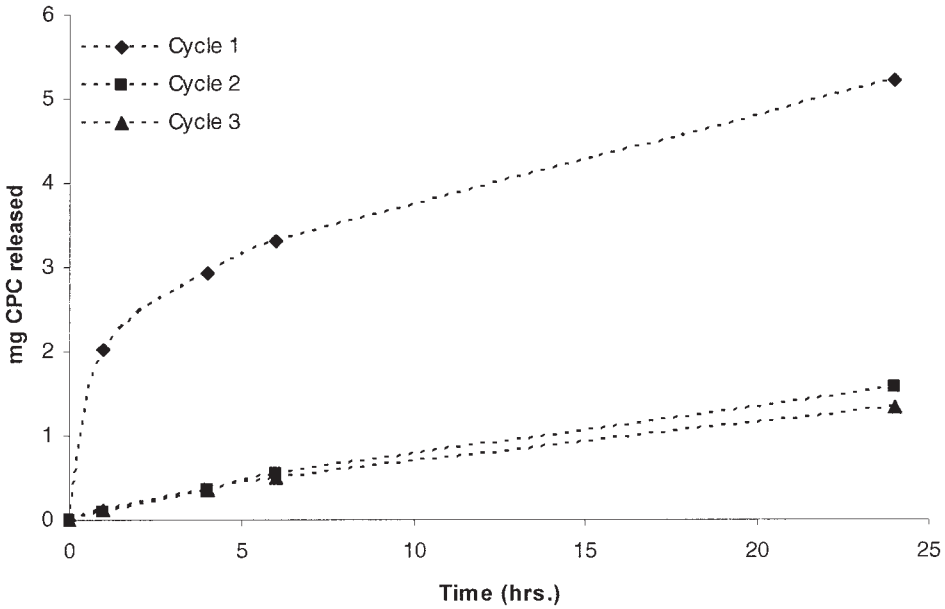

Figure 7 Reactiviation of CPC release in deionized water. Hydrogel does not contain AMPSA and is based on 4 mol % DEGDMA and 11.5 wt % CPC.

burst period. In fact, there is a very dramatic difference in swelling between hydrogels prepared with and without CPC loading. The percent swelling is shown in Table III for HEMA hydrogels based on 2 mol % DEGDMA, 0–10 mol % AMPSA, and with and without 11.5 wt % CPC (Fig. 8). Without CPC in the hydrogel matrix, the percent swelling increases linearly as the amount of anionic, hydrophilic AMPSA increases. The same samples prepared with 11.5 wt % CPC loading have a very different swelling profile that points to distinct polymer–CPC interactions.

There has been a large interest in polymer–surfactant interactions in recent years.[27–33] The focus has been on the interaction of swollen hydrogels or polymer solutions with surfactant solutions, including CPC. The swollen charged hydrogels typically collapse when exposed to oppositely charged surfactant solutions. The minimum collapsed volume is often observed when charge neutralization occurs between the charged hydrogel and the oppositely charged surfactant.[27,30,33,34] There appears to be little information on the swelling behavior of hydrogels prepared with surfactant encapsulated in the matrix during polymerization. Table III shows that the smallest degree of swelling was observed for sample 2 : 5 : 11.5 in which the molar ratio between the anionic monomer AMPSA and cationic CPC is approximately 1 : 1, i.e., the hydrogel is neutral. The percent swelling more than doubles for sample 2 : 10 : 11.5 where the molar ratio between AMPSA and CPC is 1 : 0.5. The hydrogel is charged and the hydrophilic nature of AMPSA dramatically enhances swelling. The percent swelling in-

TABLE III
Percent Swelling of Hydrogels After 24 h in Deonized Water

Sample	% Swelling	AMPSA : CPC	Overall charge of the polymer–CPC hydrogel	mg CPC released/g polymer
With CPC loading				
2 : 0 : 11.5	59.2 ± 4.9	—	+	28.7
2 : 2.5 : 11.5	50.2 ± 2.9	1 : 2.2	+	17.9
2 : 5 : 11.5	40.4 ± 3.0	1 : 1	Neutral	6.98
2 : 10 : 11.5	102.5 ± 2.5	1 : 0.5	−	0.13
Without CPC loading				
2 : 0 : 0	42.0 ± 1.4			
2 : 2.5 : 0	71.1 ± 1.3			
2 : 5 : 0	130.0 ± 2.4			
2 : 10 : 0	250.6 ± 2.9			

Hydrogels are based on 2 mol % DEGDMA, 0–10 mol % AMPSA, and 11.5 wt % CPC. Average and standard deviation are obtained from four samples.

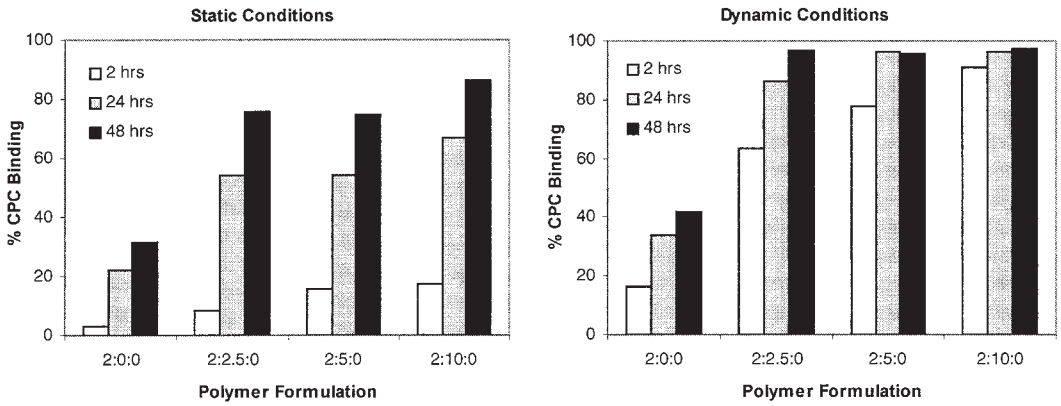

Figure 8 CPC absorption in deionized water under static and dynamic conditions. Hydrogels contain 2 mol % DEGDMA and varying amounts (0, 2.5, 5, or 10 mol %) ofAMPSA. Sample label represents DEGDMA (mol %) : AMPSA (mol %) : CPC (wt %).

creases slightly for samples 2 : 0 : 11.5 and 2 : 2.5 : 11.5 due to the overall positive charge of the hydrogel compared to the neutral polymer matrix 2 : 5 : 11.5. The hydrophobic nature of CPC dominates, preventing a large increase in swelling.

Not only have we probed the burst release profile of CPC from HEMA-based hydrogels, we have also observed interesting swelling behavior due to both electrostatic and hydrophobic interactions within the CPC-loaded hydrogel. We have found that the stoichiometry between the anionic monomer AMPSA and cationic CPC largely determines the swelling behavior of the hydrogel material. The hydrophobic nature of CPC has a less dramatic impact on swelling. We have also found that CPC burst release is largely attributed to dissolution of unbound CPC from the surface of the hydrogel and not the swelling of the hydrogel–CPC matrix.

CPC absorption under static and dynamic conditions

Ehara et al. found that CPC could be absorbed from aqueous solutions with polymer resins based on methacrylic acid.[15] In this work, we wanted to determine if HEMA-based hydrogels could not only be used for the controlled release but also for the controlled absorption of CPC. "Blank" hydrogels with 2 mol % DEGDMA and varying degrees of AMPSA were prepared. The hydrogels were immersed in CPC solutions (in deionized water or pH 7.41 buffer) with an initial concentration of 75 ppm CPC. CPC binding was measured over 48 h under both static and dynamic (with agitation) conditions. In this work, very little change in swelling was observed for the hydrogels because the CPC concentration was lower than that usually required for collapse in similar hydrogels.[34] The most rapid absorption (t = 2 h) of CPC was observed under dynamic conditions for hydrogels containing AMPSA. After 2 h, more than 60% of CPC was absorbed from water or buffer. Because of ionic interactions, CPC absorption increased as the amount of anionic monomer, AMPSA, increased in the hydrogel. The absorption results agree with our release data where we found that the stoichiometry between the polyanion and CPC cation largely controls release (Fig. 9). In addition, CPC binding increased under dynamic conditions due to increased exposure of the hydrogel to the CPC solution. Absorption is also possible without the addition of AMPSA. This may be due to the hydrophobic nature of the CPC molecule and its affinity for the nonionic hydrogel. Thus, HEMA-based hydrogels containing DEGDMA and AMPSA can not only be used for the controlled release but also for the absorption of CPC from solution.

CONCLUSIONS

With the increased interest in the biocidal surfactant CPC, more effective controlled release methods are needed. HEMA-based hydrogels with good physical integrity can be prepared quickly and conveniently with photopolymerization. High levels of CPC can be loaded in the polymer hydrogel. Release can be controlled by varying the amount of anionic monomer (AMPSA), crosslinker (DEGDMA), release media, exposed surface area, and CPC loading. The burst release of CPC is largely due to material on the surface of the hydrogel and not the degree of swelling. After the hydrogel is removed from solution and dried, linear release of CPC is observed from the same hydrogel. We have also observed interesting swelling behavior due to both electrostatic and hydrophobic interactions within the CPC-loaded hydrogel. In addition, the polymer formulation can not only be used for the controlled release of CPC but also for the controlled absorption of CPC from solution. For both the

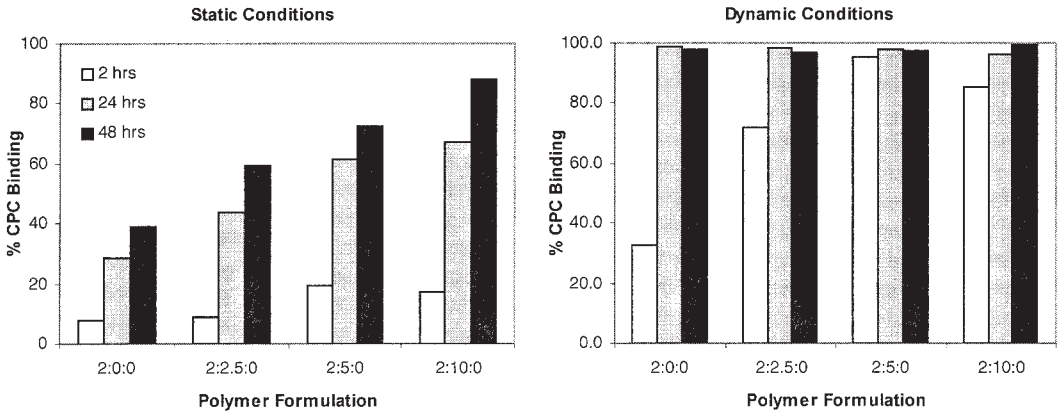

Figure 9 CPC absorption in pH 7.41 phosphate buffer under static and dynamic conditions. Hydrogels contain 2 mol % DEGDMA and varying amounts (0, 2.5, 5, or 10 mol %) of AMPSA. Sample label represents DEGDMA (mol %) : AMPSA (mol %) : CPC (wt %).

release and absorption of CPC, ionic interactions between AMPSA and CPC dominate. We have found that the anionic/cationic stoichiometry of the material dictates release, absorption, and also swelling. Because of the ease of preparation, effectiveness of the biocide CPC, and biocompatibility of the HEMA monomer, this controlled-release system could be used in variety of materials or coatings exposed to pathogens.

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