Controlled Release Formulations of Carbaryl Based on Copper Alginate, Barium Alginate, and Alginic Acid Beads

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ABSTRACT: A controlled release system for reducing environmental impact was produced by encapsulating the pesticide carbaryl (Carb) in the alginate beads. The various bead formulations were prepared by using sodium alginate (NaAlg) as a polymer, $CuCl_2$, $BaCl_2$ as a crosslinking agent, and HCl as a linking agent. The surface morphology of prepared beads was characterized with scanning electron microscopy (SEM). SEM confirmed the spherical nature and surface morphology of the particles. Bead characteristics, such as Carb entrapment efficiency, particle size, swelling degree, and Carb release kinetics, were determined. The effects of crosslinker or linker concentration, type, and carbaryl/sodium alginate (Carb/NaAlg) ratio on Carb release from the beads were investigated for 20 days at 25°C. It was observed that Carb release from the beads increased with the increase of Carb/NaAlg ratio whereas decreased with the increase of crosslinker concentration. At the end of 20 days, the Carb release from alginic acid beads was found to be higher than that of copper alginate (Cu-Alg) and barium alginate (Ba-Alg) beads. The swelling measurements of the beads supported the release results. Release kinetics were described by Fickian and non-Fickian approaches. © 2006 Wiley Periodicals, Inc. J Appl Polym Sci 102: 4245–4253, 2006

Key words: water soluble polymers; controlled release; carbaryl; insecticide; beads

INTRODUCTION

Agriculture represents one of the most important areas of international needs to health, nutrition, and economic developments. The rapidly growing demand for food is the main impetus behind the need for more efficient operation in both agriculture and industrial protection that afford higher yields and better quality.

Agrochemicals are concerned with the utilization of chemicals to control plant or animal life and to improve production of crops both in quality and quantity. However, the potential hazards of the conventional agrochemicals to public health and wildlife result in greatly increasing stringent limitations on their use.[1]

In the past few years, the problem of the environmental fate of pesticides had caused great concern.[2] The major inconvenience of their use is both the high (and possible toxic) doses initially applied, and the need for repeated applications to achieve the required efficiency. In fact, pesticides accumulate in soil, air, and water exerting toxic effects on animals and plants. Moreover, when a crop protection chemical is applied, its performance, safety to applicators, and the environment in conventional use are affected by the way the product is formulated. Recently, controlled release technology emerged as an alternative approach, which promises to solve problems accompanying the use of some agrochemicals while avoiding the possible side effects.

The production of pesticides in controlled release formulations could offer several advantages. First, the possibility of protecting pesticides from environmental degradation processes would decrease the effective dose needed over a given period. Second, the continuous release of the pesticide from an adequate formulation would maintain a minimum effective level and achieve an optimal performance.[2] If a pesticide is chemically combined or dissolved or encapsulated in a polymeric material, its application to soil or any other medium would result in release of the active agent by hydrolysis or diffusion at a controlled rate. Therefore, the loss of the active agent by degradation, evaporation, or leaching would be minimized. Application of such combinations would therefore result in a much more efficient use of the active agent per unit weight as well as a much longer period of protection for the same amount than application of conventional methods. Several research works have contributed to the development of formulations for the controlled release of chemicals in agriculture.[3–9]

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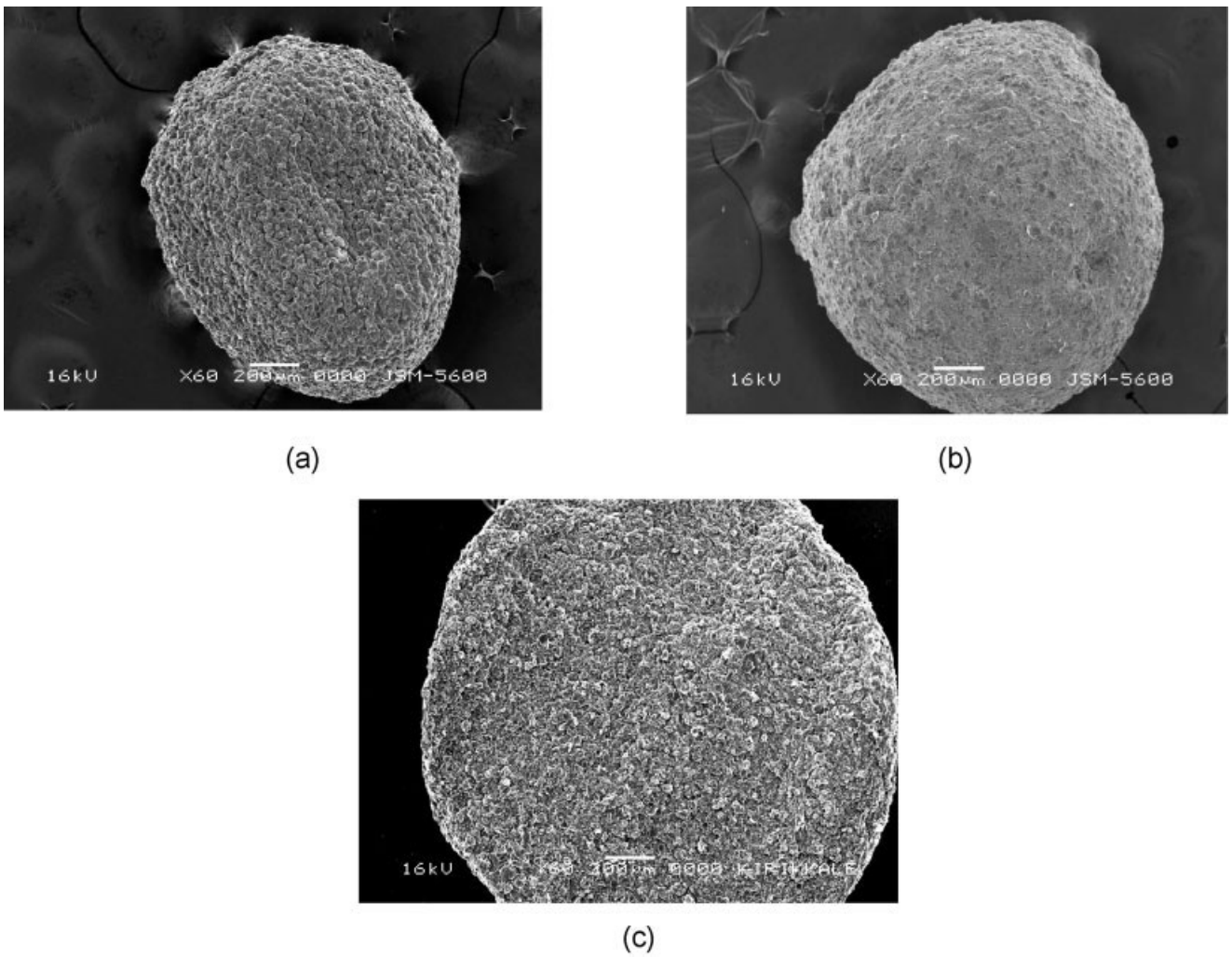

Figure 1 Scanning electron microscopic photographs of Cu-Alg (a), Ba-Alg (b), and AA (c) beads (magnification, ×60).

Alginic acid (AA) is a polysaccharide composed of β-D-mannuronic acid (M) and α-L-guluronic acid (G).[10] It is found in brown seaweeds and is commercially available as sodium salt. Being biodegradable and biocompatible, it is an attractive polymer for the development of drug carriers and controlled release delivery systems.[11–15]

Connick et al.[3] have described a series of alginate-kaolin based 2,6-dichlorobenzonitrile controlled release formulations. In an aquatic release experiment, the authors reported that the release of active ingredient becomes longer as kaoline concentration is increased.

Pepperman and Kuan[16] investigated the controlled release of alachor release from calcium alginate microspheres. In a water release study, significant control of alachor release rates was obtained with the addition of linseed oil.

Fernandez-Perez et al.[17] studied the mobility of isoproturan from an alginate-bentonite controlled release formulation in layered soil. They observed that the use of the alginate-bentonite controlled release formulation produced less vertical mobility of active ingredient when compared with the technical product.

Carbaryl (Carb) (chemical name: α-napthyl-*n*-methyl carbamate) is a wide spectrum insecticide used for 100 species of insects on citrus, fruit, cotton, forests, lawns, nuts, ornamentals, shade trees, and other crops as on poultry, livestock, and pets.[18] It is formulated as wettable powder, which makes its handling very difficult, mainly because of the fast absorption by nasal, oral, and transdermal routes. It has also low chemical stability that is due to the rapid hydrolyzes to 1-naphthol in alkaline medium.[2]

One way to overcome these disadvantages of Carb is to achieve controlled release formulations of it. In this article, we have carried out optimization studies for the release of Carb choosing sodium alginate as main support material, which is a cheap polymer with no toxic residue. The effects of various processing parameters such as the type of crosslinking or linking agent, concentration and carbaryl/sodium alginate ratio were

TABLE I
Particle Size and Percentage Entrapment Efficiency of the Beads Prepared by Using Different Crosslinking or Linking Agents

Cation	Carbaryl/ sodium alginate (w/w)	Crosslinker or linker concentration (*M*)	Bead diameter (mm)	Entrapment efficiency (%)
Cu^{2+}	1 : 1.5	0.025	1.31 ± 0.06	97.9
Cu^{2+}	1 : 1.5	0.05	1.23 ± 0.10	98.1
Cu^{2+}	1 : 1	0.1	1.28 ± 0.06	97.3
Cu^{2+}	1 : 1.5	0.1	1.19 ± 0.13	99.2
Cu^{2+}	1 : 2	0.1	1.73 ± 0.06	99.4
Cu^{2+}	1 : 1.5	0.2	1.14 ± 0.07	99.5
Ba^{2+}	1 : 1.5	0.025	1.26 ± 0.03	98.1
Ba^{2+}	1 : 1.5	0.05	1.48 ± 0.07	98.4
Ba^{2+}	1 : 1	0.1	1.06 ± 0.05	97.4
Ba^{2+}	1 : 1.5	0.1	1.53 ± 0.04	98.9
Ba^{2+}	1 : 2	0.1	1.15 ± 0.04	99.5
Ba^{2+}	1 : 1.5	0.2	1.28 ± 0.04	98.9
H^+	1 : 1.5	0.05	2.27 ± 0.23	94.2
H^+	1 : 1	0.1	2.12 ± 0.04	96.2
H^+	1 : 1.5	0.1	2.20 ± 0.15	97.2
H^+	1 : 2	0.1	2.63 ± 0.08	99.0
H^+	1 : 1.5	0.2	2.07 ± 0.06	96.0

studied. Release properties were also supported by swelling measurements.

EXPERIMENTAL

Materials

Hektavin 85 (85% (w/w) in carbaryl) was supplied from Hektaş T.A.Ş. in Turkey. Sodium alginate, medium viscosity (viscosity of 2% solution at 25°C is approximately 3500 cps), was obtained from Sigma Chemical Company (Louis, USA). $CuCl_2{\cdot}2H_2O$ and $BaCl_2{\cdot}2H_2O$ were obtained from Merck (Darmstadt, Germany). All the other solvents and chemicals were of analytical grade and were used without further purification.

Preparation of carbaryl loaded beads

The beads were prepared from homogenous solution of sodium alginate in water (1–2% w/v) and 0.2 g of carbaryl (Carb) was added and mixed for 30 min. About 100 mL of crosslinking or linking solution of $CuCl_2$ or $BaCl_2$ and HCl of known molarity (0.025–0.2*M*) was taken in a beaker and stirred magnetically. Twenty milliliters of polymer solution containing Carb was pumped through nozzle (needle of 1 mm internal diameter) at a flow rate of 80 mL/h, using a peristaltic pump (Unitest, Turkey) at a temperature of 25°C, and the size of the droplets was controlled by applying a coaxial airstream. The beads formed were stirred for 30 min more for hardening then filtered, washed with distilled water, and allowed to dry at room temperature until constant weight was attained. The hardening and the washing solutions were tested for the evaluation of Carb content spectrophotometrically (Unicam UV2-100, UK) at 280 nm to calculate the actual amount of the Carb in the beads (for entrapment efficiency). Concentration of Carb was determined from a calibration curve prepared as concentration vs. absorbance. The percentage of entrapment efficiency was then calculated as:

$$\text{Entrapment Efficiency (\%)} = \frac{\text{Practical carbaryl loading}}{\text{Theoretical carbaryl loading}} \times 100 \quad (1)$$

Swelling experiments

Beads (50 mg) of constant mass were added to 100 mL distilled water and allowed to swell for 48 h at 25°C. The excess surface-adhered liquid drops were removed by blotting, and the swollen beads were weighed using electronic balance (Shimadzu AEG-120). The beads were then dried in an oven (Nuve FN 120, Turkey) at 40°C till to constant weight. The swelling degrees were calculated from the mass increase as follows:

$$\text{Swelling Degree (\%)} = \frac{(M_s - M_d)}{M_d} \times 100 \quad (2)$$

where M_s and M_d are mass of swollen beads and mass of dry beads, respectively.

Beads size measurements

Ten samples of completely dried beads from different formulations were selected and their sizes were

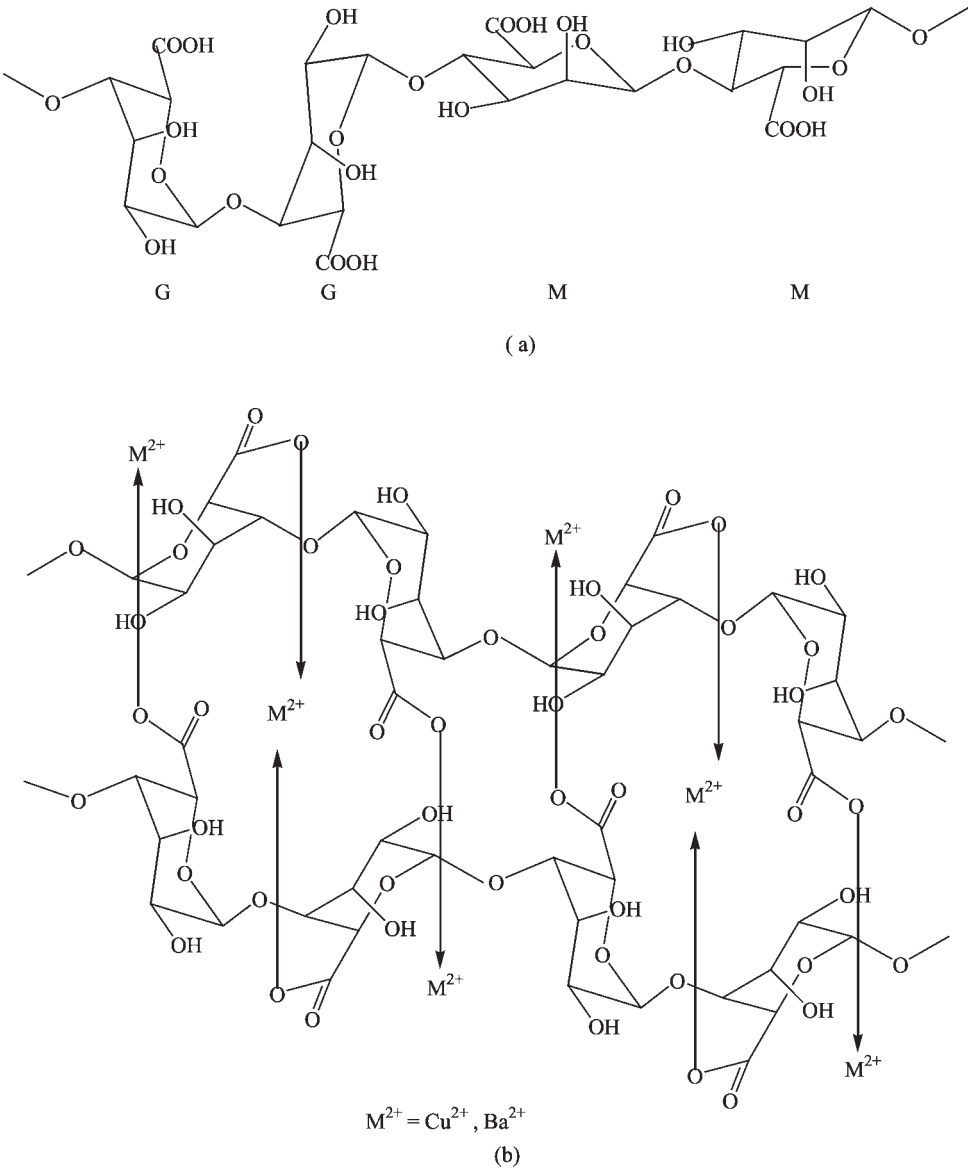

Figure 2 Expected structure between sodium alginate matrix and hydrogen cations (a), and copper or barium cations (b).

measured by using binocular microscope (Prior, England) with an accuracy of ±0.2 mm.

Scanning electron microscopy

The bead structure and surface morphology of the samples were studied using JSM 5600 model scanning electron microscope (Japan) after coating with gold under vacuum.

Insecticide release studies

The release behavior of Carb loaded beads were studied placing the loaded beads (50 mg) into a conical flask with 500 mL distilled water at 25°C. Flask was stirred with magnetic stirrer and 3 mL of sample was taken at specified time intervals for the analysis of Carb content, using distilled water as a blank in UV spectrophotometer at 280 nm.

RESULTS AND DISCUSSION

Bead formation and crosslinking

Bead formation was achieved using sodium alginate. Cu-Alg, Ba-Alg, and AA beads formed have almost spherical shape as revealed by the SEM photographs shown in Figure 1(a–c). As it is seen from the figure, Cu-Alg and AA beads had rough surface structure whereas Ba-Alg beads had a smooth surface structure. The results of percentage entrapment efficiency and particle sizes are presented in Table I. The beads formed have particle sizes ranging from 1.06 ± 0.05 to 2.63 ± 0.08 mm in diameter. The particle size of beads was

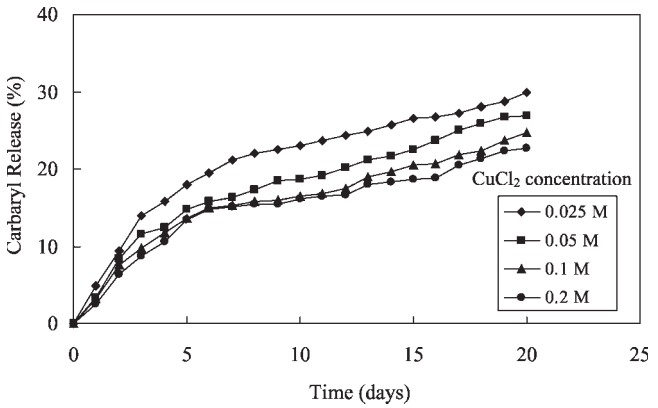

Figure 3 Effect of $CuCl_2$ concentration on the carbaryl release from Cu-Alg beads. Carb/NaAlg ratio: 1 : 1.5.

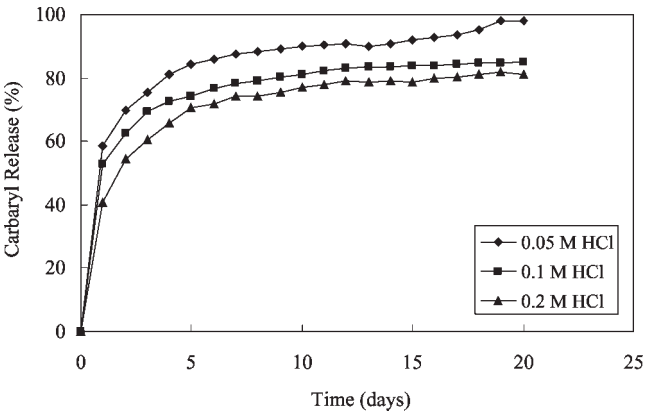

Figure 5 Effect HCl concentration on the carbaryl release from AA beads. Carb/NaAlg ratio: 1 : 1.5.

prepared using $CuCl_2$ approximately the same as that of those prepared with $BaCl_2$. However, diameters of the beads prepared with HCl are much larger than the other beads. The particle size did not vary significantly either with increasing crosslinker concentration or with changing Carb/NaAlg ratio. The explanation of these results could be related to the mechanism of the bonding of copper, barium, and hydrogen cations to alginate anions. Since copper and barium cations are divalent, and its bonding to alginate is expected to occur in a planer two-dimensional as illustrated in Figure 2. Two-dimensional bonding causes the crosslinking through the beads. Thus, a more compact structure and smaller size for Cu-Alg and Ba-Alg beads occurs than that of AA beads. However, the percentage entrapment efficiency increased slightly with the decrease in Carb/NaAlg ratio. With the decrease in Carb/NaAlg ratio, polymer concentration increases. The increase in polymer concentration increases the polymer viscosity, hence trap more Carb molecules thus entrapment efficiency increases. Similar results were found in literature.[19–21] Arıca et al.[19] investigated *in vitro* studies of enteric coated diclofenac sodium carboxymethylcellulose (CMC) microspheres. They observed that increased CMC concentration resulted in an increase encapsulation efficiency and % yield value.

Effect of crosslinker or linker concentration on Carb release

The release of Carb from the Cu-Alg, Ba-Alg, and AA beads were carried out at 25°C in distilled water, and the amount of insecticide release within a given time was evaluated by UV spectroscopy. Effect of $CuCl_2$, $BaCl_2$, and HCl concentration on the cumulative Carb release profile of beads was shown in Figures 3–5, respectively. Generally, it was found that as the concentration of $CuCl_2$, $BaCl_2$, and HCl increases from 0.025 to 0.2*M*, release of Carb decreases. At the end of the 20 days, maximum amount of Carb released from Cu-Alg, Ba-Alg, and AA beads prepared with 0.025*M* $CuCl_2$, 0.025*M* $BaCl_2$, and 0.05*M* HCl were found to be 32, 9, and 96%, respectively. Effect of crosslinking agent concentration on the cumulative release of Carb from beads was also supported by swelling measurements, which were presented in Figure 6. As can be seen from the

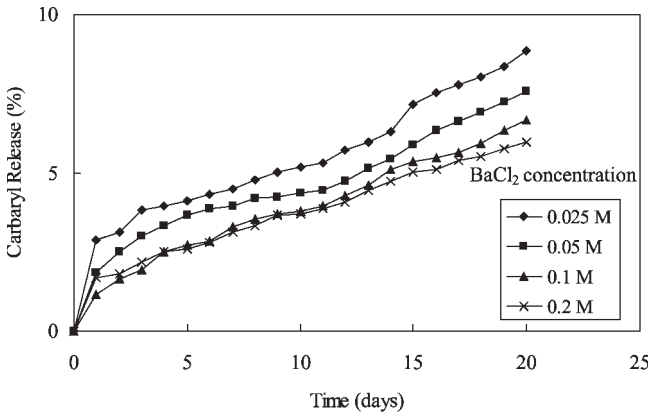

Figure 4 Effect of $BaCl_2$ concentration on the carbaryl release from Ba-Alg beads. Carb/NaAlg ratio: 1 : 1.5.

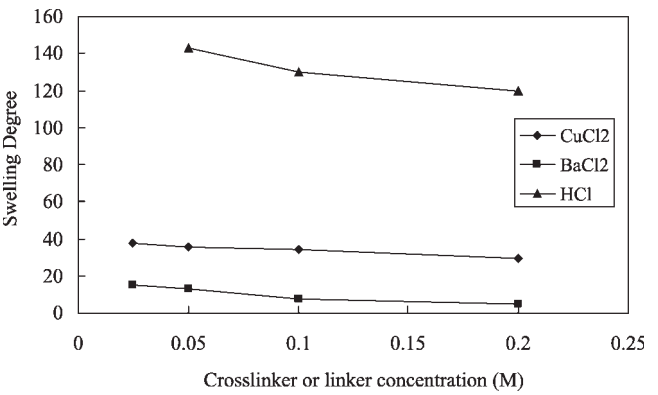

Figure 6 Effect of crosslinking or linking concentration on swelling degree of the beads.

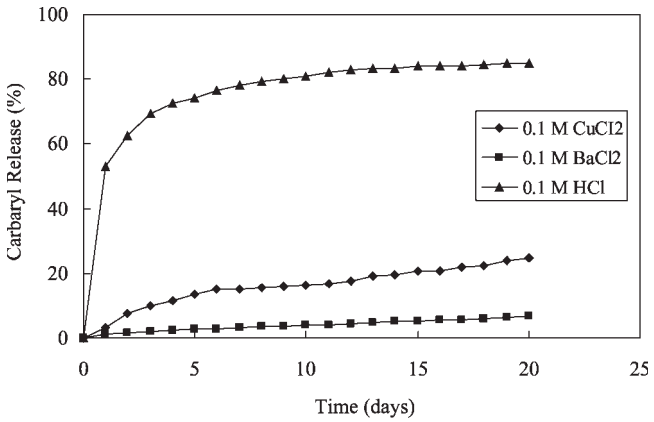

Figure 7 Effect of cation type on release of carbaryl. Carb/NaAlg ratio: 1 : 1.5.

figure, swelling degree of beads decreases with the increase in crosslinker or linker concentration. When the crosslinking agent concentration increases number of bounded carboxyl groups, hence degree of crosslinking, rigidity of the polymer increases, consequently, Carb release from the beads decreases. Similar results were reported by other workers.[22–25]

Darvari et al.[22] investigated pesticide aldicarb for the release from carboxymethyl cellulose microspheres. They observed that increase in $AlCl_3$ concentration reduced release of aldicarb from microspheres.

Thimma et al.[23] crosslinked carboxymethyl guar gum with barium chloride. They have compared swelling degree of barium chloride crosslinked carboxymethyl guar gum with that of crosslinked calcium chloride. They have reported similar results.

The effect of type and valency of the ions in the crosslinking agents on the cumulative release of Carb and swelling degree were shown in Figures 6 and 7. It is reflected from the figures that cumulative Carb release from beads follow the order of AA>Cu-Alg>Ba-Alg.

The explanation of this observation could be related to mechanism of the bonding of hydrogen, copper, and barium cations to alginate anions. Since copper and barium cations are divalent, their bonding to alginate is expected to occur in a planar two-dimensional manner as represented in the egg-box model illustrated in Figure 8.[26] The gelation and crosslinking of the polymers are mainly achieved by the exchange of sodium ions from the guluronic acid with the divalent cations and the stacking of these guluronic groups to form the egg-box structure. In contrast, univalent hydrogen cation is expected to form a one dimensional univalent bonding structure with the alginate. Two-dimensional bonding model is expected to be the reason for the extended crosslinking through the whole body of the matrix. Therefore, swelling of these beads is smaller than that of AA beads (Fig. 6), which leads to lower release of carbaryl.

On the other hand, Carb release of the beads crosslinked with $BaCl_2$ solution is lower than that of crosslinked with $CuCl_2$ solution. It is expected that divalent salts $CuCl_2$ and $BaCl_2$ crosslink the alginate in a similar mechanism. The difference could be explained by noting that the degree of crosslinking depends on the ability of crosslinker ions to diffuse through the matrix. This diffusion ability is a function of the ionic size.[27] Since barium ion has a radius of 1.35 Å compared with 0.73 Å for copper ion, barium ions are expected to fill larger space between the alginate chains producing a tight arrangement, leading to low release. Similar observation was found in the literature. Al-Musa et al.[28] studied evaluation of parameters involved in preparation and release of drug loaded in crosslinked matrices of alginate. They have investigated that effect of Al^{3+}, Ca^{2+}, and Ba^{2+} ions on the drug release.

The micrographs of Cu-Alg, Ba-Alg, and AA beads are shown in Figure 9(a)–9(c). The micrographs show that the surface textures of all the beads are amorphous. The AA and Cu-Al matrix was more porous, and Ba-Alg matrix was much tight than the others, supporting the release studies.

Effect of carbaryl/sodium alginate ratio on the Carb release

The effect of Carb/NaAlg ratio on the Carb release of Cu-Alg, Ba-Alg, and AA beads were shown in Figures 10–12, respectively. The figures show that when the Carb/NaAlg ratio decreased, Carb release from beads decreased. The maximum Carb release from Cu-Alg, Ba-Alg, and AA beads prepared with 0.1*M* crosslinking or linking concentration were found to be 28, 11, and 93%, respectively. This result can be explained as follows: decrease in Carb/NaAlg ratio causes an increase in polymer concentration. Consequently, crosslinking degree of beads increased with decrease in Carb/NaAlg

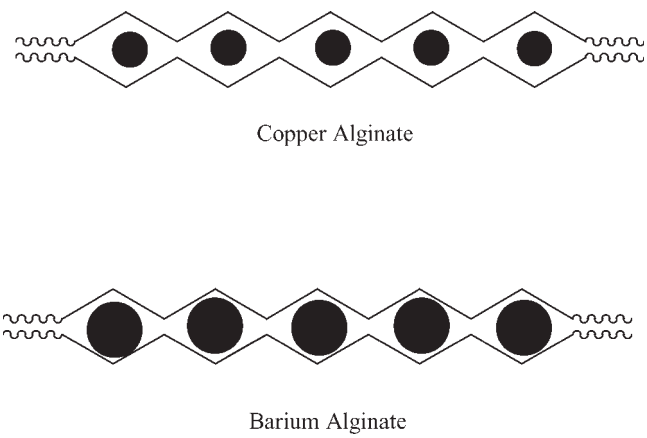

Figure 8 Egg-box model representing copper and barium cations reacting with alginates.

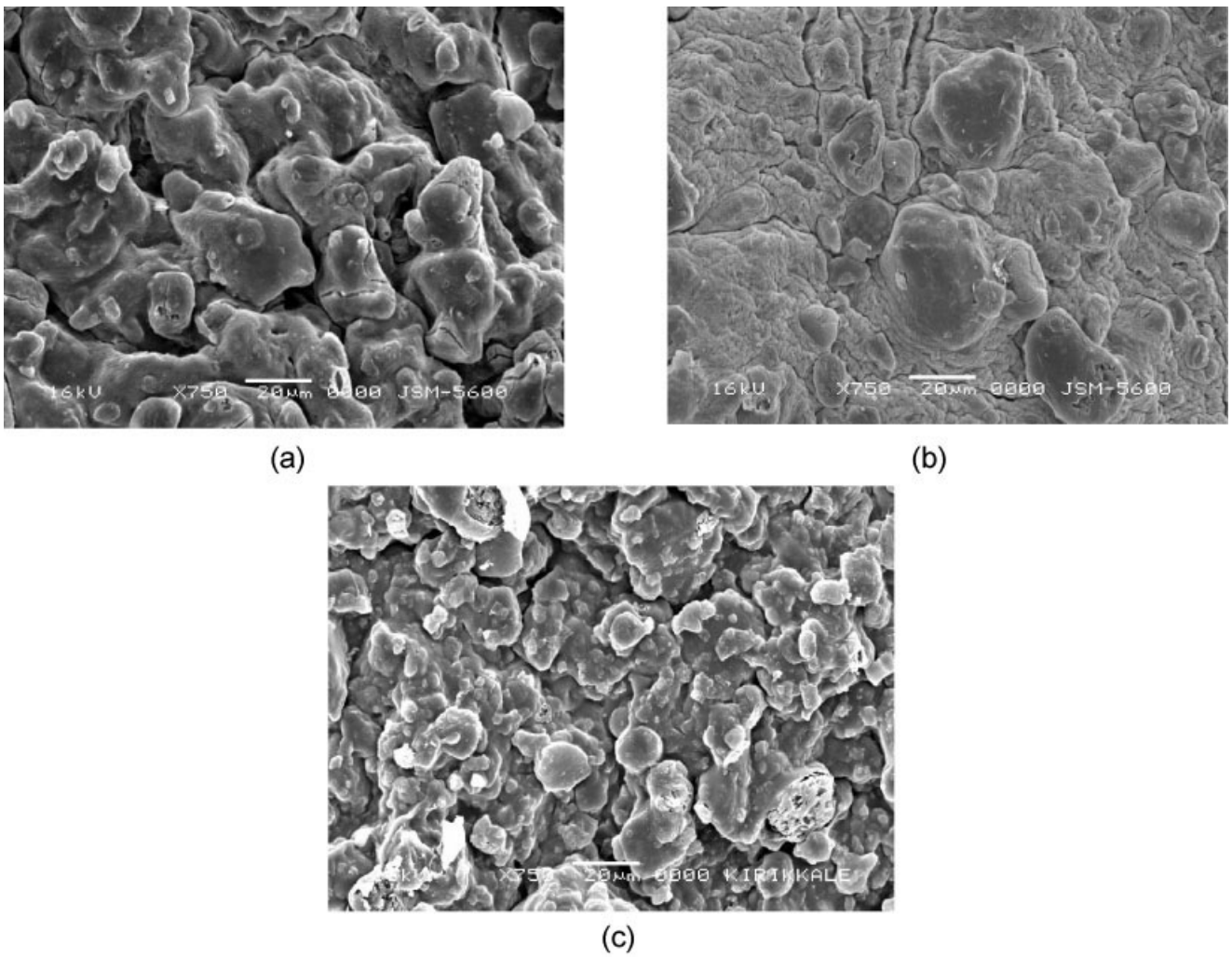

Figure 9 Surface morphology of Cu-Alg (a), Ba-Alg (b), and AA (c) beads (magnification, ×750) by scanning electron microscope.

ratio. Hence Carb release decreases with decreasing Carb/NaAlg ratio. This result was also attributed to the decreasing driving force for Carb diffusion with decreasing Carb content.

Swelling measurements also supported these results. Figure 13 shows the change of the swelling degree with Carb/NaAlg ratio. As can be seen AA beads have higher swelling degree for all of the Carb/NaAlg ratios. Generally, swelling degree of the beads decreased with the decrease in Carb/NaAlg ratio because of the increase in crosslinking density. Diffusion of water molecules through high crosslinked beads will be difficult. Similar findings were reported for liquid pesticide neem seed oil loaded formulations by Kulkarni et al.[11]

Bajpai and Giri[29] studied swelling dynamics of macromolecular hydrophilic network and evaluation of its potential for controlled release of KNO_3 as a model agrochemical. They have observed that the amount of released KNO_3 increased with increasing percent loading of hydrogel.

In previous study of Işıklan,[30] Carb release was studied from the NaAlg beads crosslinked with glutaraldehyde. In a study, it was observed that cumulative

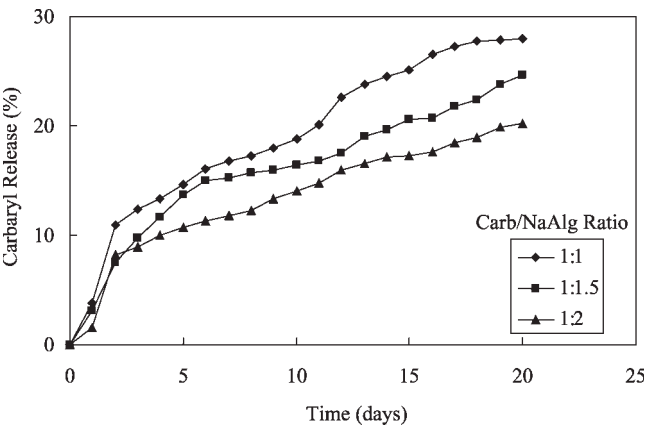

Figure 10 Effect of Carb/NaAlg ratio on the carbaryl release from Cu-Alg beads. $CuCl_2$ concentration: 0.1*M*.

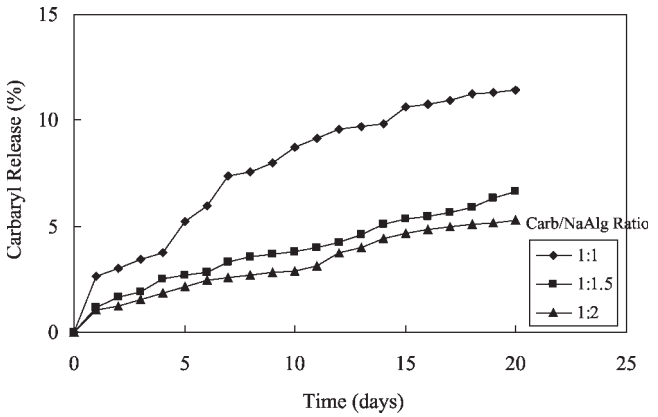

Figure 11 Effect of Carb/NaAlg ratio on the carbaryl release from Ba-Alg beads. $BaCl_2$ concentration: 0.1*M*.

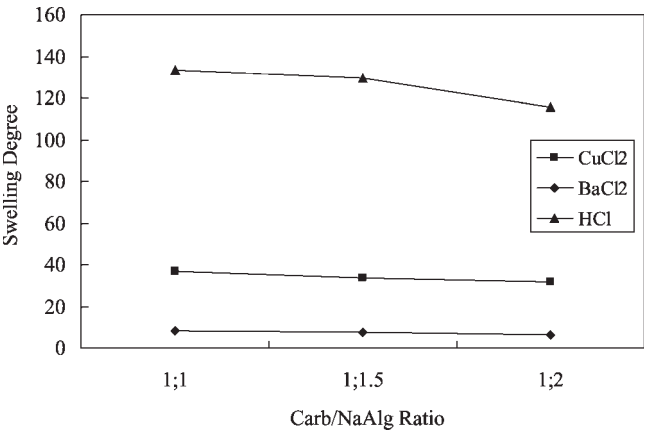

Figure 13 Effect of Carb/NaAlg ratio on swelling degree of beads.

release of 1 : 1 Carb/NaAlg ratio beads have shown 67% release whereas that of 1 : 8 Carb/NaAlg ratio beads have shown 35% at 25 days.

Empirical correlations of the release data

The release data of all the systems have been further substantiated by fitting the fraction release data M_t/M_∞ to an empirical equation proposed by Peppas.[31]

$$(M_t/M_\infty) = kt^n \tag{3}$$

where M_t is the amount of Carb at time t and M_∞ is the Carb released at equilibrium time; k, a constant characteristic of the pesticide–polymer system; and n is the diffusional exponent, which suggests the nature of the release mechanism. A value of $n = 0.5$ indicates Fickian transport, while $n = 1$ is of Case II transport. The intermediary values ranging between 0.5 and 1.0 are indicative of the anomalous transport.[30,31] The least-squares estimations of the fractional release data along with the estimated correlation coefficient values, r with 95% confidence limit are presented in Table II. Generally, the k values decrease with the increase in crosslinker and linker concentration and decrease in Carb/NaAlg ratio. However, the n values increase, with the increase in crosslinker or linker concentration and with the decrease Carb/NaAlg ratio. The values of n for the release of Carb from the Cu-Alg and Ba-Alg beads range between 0.38 and 0.71 indicating that the release in these systems deviates slightly from Fickian transport to non-Fickian transport whereas for AA beads range between 0.14 and 0.27 indicating Fickian transport.

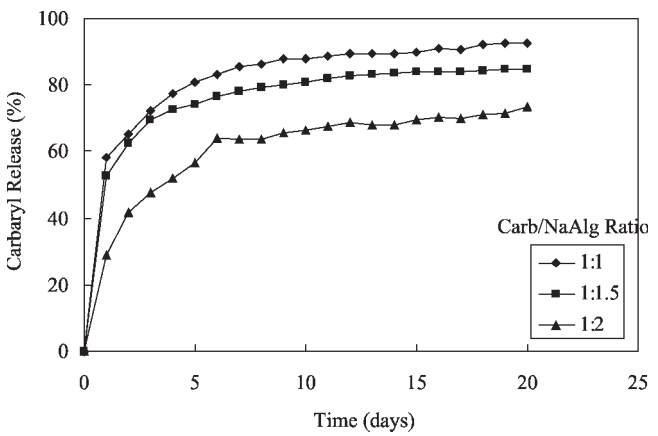

Figure 12 Effect of Carb/NaAlg ratio on the carbaryl release from AA beads. HCl concentration: 0.1*M*.

CONCLUSIONS

In this study, Carb was successfully encapsulated in Alginate polymer. The particle size did not vary much neither by increasing crosslinker or linker concentration, nor by increasing carbaryl/sodium alginate ratio. But the diameter of AA beads was found to be larger than that of other beads. In contrast, increase in percentage entrapment efficiency was observed by decreasing carbaryl/sodium alginate ratio. The crosslinker type is shown to have a prominent influence on the drug release. For the beads prepared with high concentration of crosslinker or linker agent, cumulative Carb release was found to be slower than the other beads. Carb release from the AA beads was observed much higher than Cu-Alg and Ba-Alg beads. Swelling measurements also supported the release studies. The n values calculated for the release of Carb from AA beads indicate that Carb release has Fickian transport whereas release from Cu-alginate and Ba-alginate beads deviates from Fickian transport. From these results, alginate beads appear to be interesting as a controlled released system for agrochemical applications to improve pesticide sta-

TABLE II
The Results of *k*, *n* and *r* Calculated from eq. (3)

Cation	Carbaryl/ sodium alginate (w/w)	Crosslinker or linker concentration (*M*)	*k*	*n*	*r*
Cu^{2+}	1 : 1.5	0.025	6.76	0.52	0.966
Cu^{2+}	1 : 1.5	0.05	5.02	0.58	0.969
Cu^{2+}	1 : 1	0.1	5.75	0.55	0.956
Cu^{2+}	1 : 1.5	0.1	4.60	0.57	0.965
Cu^{2+}	1 : 2	0.1	2.69	0.71	0.954
Cu^{2+}	1 : 1.5	0.2	3.95	0.61	0.954
Ba^{2+}	1 : 1.5	0.025	2.39	0.38	0.950
Ba^{2+}	1 : 1.5	0.05	1.76	0.44	0.977
Ba^{2+}	1 : 1	0.1	2.15	0.58	0.981
Ba^{2+}	1 : 1.5	0.1	1.08	0.58	0.994
Ba^{2+}	1 : 2	0.1	0.85	0.60	0.986
Ba^{2+}	1 : 1.5	0.2	1.36	0.46	0.978
H^{+}	1 : 1.5	0.05	63.38	0.15	0.967
H^{+}	1 : 1	0.1	61.25	0.14	0.971
H^{+}	1 : 1.5	0.1	57.42	0.14	0.967
H^{+}	1 : 2	0.1	34.61	0.27	0.957
H^{+}	1 : 1.5	0.2	47.29	0.20	0.951

bility, and to reduce the risks both to people who handle the product and to groundwater.

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