Polymeric Sodium Alginate Interpenetrating Network Beads for the Controlled Release of Chlorpyrifos

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ABSTRACT: Novel polymeric sodium alginate (Na-Alg) interpenetrating network (IPN) beads have been prepared by crosslinking Na-Alg blend with gelatin (GE) or egg albumin (EA) using glutaraldehyde (GA) as the crosslinking agent. These beads were used for the controlled release of chlorpyrifos. The swelling experiments were performed in water at different temperatures, and these data were used to calculate the molecular mass (M_C) between crosslinks as well as diffusion coefficients. Diffusion coefficients calculated from desorption data were lower by about two orders of magnitude than those calculated from sorption results. Higher values of M_C were obtained for the gelatin-based IPNs than the neat Na-Alg and egg albumin-based matrices. Size of the beads did not vary significantly either by the network or by increasing the exposure time to the crosslinking agent. The scanning electron microscopy (SEM) was used to understand the surface characteristics of the beads. Differential scanning calorimetry (DSC) indicated a molecular level dispersion of chlorpyrifos in the polymer matrix. The percentage entrapment efficiency showed a dependence on the type of network polymer as well as time of exposure to the crosslinking agent. The encapsulation efficiency decreased with an increase in time of exposure to the crosslinking agent. *In vitro* release experiments have been performed to follow the release kinetics of chlorpyrifos from the matrices. © 2002 Wiley Periodicals, Inc. J Appl Polym Sci 85: 911–918, 2002

Key words: chlorpyrifos; sodium alginate; interpenetrating network; controlled release

INTRODUCTION

Chlorpyrifos, an organo-phosphorous insecticide (see Structure 1), has been used[1] to control Coleoptera, Diptera, Homoptera, and Lepidoptera in soil or on foliage of citrus, coffee, cotton, maize, and sugar beat. It is also used against household pests (Blattellidae, Muscidae, Isoptera), mosquitoes (larvae and adults), and controls ectoparasites on cattle and sheep. It has a solubility of 6.36 mg/L of water at 25°C.[2] Direct use of pesticides in the field pollute the surface/ground water, resulting in adverse effects on the biological systems. To minimize the toxicity of chlorpyrifos it is necessary to encapsulate it by a environmentally friendly polymer. Our earlier efforts addressed different types of hydrophilic polymers for the encapsulation of various pesticides.[3–8] The use of

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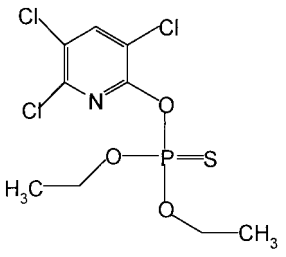

(O, O-Diethyl O- (3,5,6-trichloro-2-pyridinyl) phosphorothioate)

Structure 1 Chlorpyrifos.

interpenetrating polymer networks (IPNs) for the controlled release (CR) of agrochemicals was attempted.[9] The IPNs are more advantageous because they contain two polymers, each in a network form, which are crosslinked in the presence of each other to give a three-dimensional network structure giving the more free volume to facilitate encapsulation.

Chun et al.[10] have developed the blends of Na-Alg with deoxycholate, pluronic F68LF, dodecyltrimethyl ammonium bromide, poly(vinyl alcohol) and poly(ethyloxazoline), along with gelatin, polyallylamine, and chitosan as the coating materials to effectively control the release of bioactive molecules. The controlled release of interleukin-2 for tumor immunotherapy using alginate/chitosan porous microspheres has been reported by Liu et al.[11] The bioartificial pancreas, a medical device entrapping islets of Langerhans (islets) in various modifications of alginate-chitosan microcapsules have been attempted for the inclusion of polyethylene glycol (PEG) along with the crosslinkers such as carbodiimide (EDC) and glutaraldehyde (GA) in the core and onto the microcapsule membrane surface.[12] In our ongoing research, we found it to easy using a common crosslinking agent for both the polymers. This article reports our new experimental CR data of chlorpyrifos on three different formulations of Na-Alg beads: the neat Na-Alg, and the other two are IPNs, of which one is based on the gelatin matrix and the other is based on the egg albumin.

EXPERIMENTAL

Materials

Gift sample of chlorpyrifos, technical (85% pure) and AR grade (95% pure) samples were received from Rallis Research Center, Bangalore, India. Sodium alginate (approximate molecular mass 240,000), egg albumin (EA), gelatin (GE), glutaraldehyde (25% w/v) solution (GA), and AR grade methanol were all purchased from s.d. Fine Chemicals, Mumbai, India. Water used was double distilled and its purity was checked by measuring density and conductance at 25°C.

Preparation of Beads Containing Chlorpyrifos

The Na-Alg and its IPN polymeric beads were prepared by the procedures suggested earlier.[8] However, a small modification was adopted, i.e., a 4% of Na-Alg solution in distilled water or its blend with GE or EA (5 and 10% of dry mass of Na-Alg) were prepared by gentle heating. After a complete cooling of the polymer solution a weighed amount of chlorpyrifos (20% of dry mass of Na-Alg or its blend) was added and mixed homogenously using a magnetic stirrer. The polymer solution containing chlorpyrifos (10 mL) was then added drop-wise into gelation media of 100 mL of 30% ethanol in distilled water, 8% glutaraldehyde, and 1% of 1 N HCl using a 25-mL hypodermic syringe through a needle # 21 under constant stirring. Experimental conditions such as distance between syringe and gelation media, the number of drops of polymer solution into gelation media per minute, and the temperature were maintained uniform. Thus formed beads were removed from the gelation media at a selected time interval of 5 and 10 min. The beads were washed with water and then allowed to dry.

Drying of the Beads

The beads formed were allowed to dry in an oven (WTB Binder, Germany) maintained at 35°C (initial mass of the beads should be nearly equal). The masses of the beads were taken at definite intervals of time until a constant mass was achieved indicating complete equilibrium. All the mass measurements were done on a Mettler microbalance (Model AE 240, Switzerland) within an accuracy of ± 0.01 mg.

Bead Size Measurement

The particle size was measured by taking 5–10 particles on a glass slide under regular polarized light. The mean diameter was calculated by measuring the number of divisions of ocular micrometer covering the microspheres. The stage micro-

meter previously standardized the ocular micrometer.

Fourier Transform Infrared Spectra (FTIR)

All the FTIR measurements were taken on a Nicolet, Model Impact 410, USA. About 2 mg of the samples were ground with KBr and the pellets were made under a hydraulic pressure of 600 kg/cm^2.

Scanning Electron Microscopy (SEM)

The sample was deposited on brass holder and sputtered with gold. The SEM photographs were taken with JSM 6400 Scanning Microscope (Japan) at the required magnification in room temperature. A working distance of 39 mm was maintained and the acceleration voltage used was 20 kV, with the secondary electron image (SEI) as a detector. These experiments were performed at the RSIC in Indian Institute of Technology, Mumbai, India.

Differential Scanning Calorimetry (DSC)

Thermal analysis experiments on the polymer, pure chlorpyrifos and the polymers embedded with chlorpyrifos were performed using a DuPont-2000 microcalorimeter. The samples were heated at the rate of 5°C/min under a constant flow rate of nitrogen gas.

Swelling of the Beads

Swelling of the individual beads was studied by a measurement of the percentage uptake of water by the beads at a regular time intervals. Five different beads exposed to GA at different time intervals were selected and kept in distilled water on a watch glass in an incubator. Then the mass of five beads was taken at different intervals of time and the average value was calculated.

Content Uniformity

Beads were evaluated for chlorpyrifos content by incubating the known mass of the beads with 5 mL of water for complete swelling. The swollen beads were then crushed in an agate mortar with pestle and the solution thus formed was sonicated (Ikasonic U50, IKA Labortechnik, Germany) for 2 min using 60 MHz of frequency. Water was evaporated to form a thick paste to which about 10 mL of methanol was added to extract all the chlorpyrifos. The precipitated Na-Alg was removed from methanol by centrifugation (Remi R24, India) for about 5 min at 10,000 rpm speed. The absorbance of chlorpyrifos solution prepared in methanol was measured at the λ_{max} value of 230 nm using a UV spectrophotometer (Secomam, Anthellie, France) using pure methanol as a blank.

Dissolution Studies

The *in vitro* static dissolution experiments were performed in 250-mL conical flasks containing the dissolution media (30% methanol in distilled water) with the closer caps, which were kept in an incubator (WTB Binder, Germany) maintained at 35°C. Two to three beads weighing about 10 mg were taken in the dissolution media. At definite intervals of time, the conical flasks were shaken thoroughly and a 10-mL aliquot of this solution was used for the analysis of chlorpyrifos using UV spectrophotometer at a λ_{max} value of 230 nm. To minimize the error variations, experiments were performed in triplicate and the average values were used for data treatment and plotting.

RESULTS AND DISCUSSION

The aqueous solution of Na-Alg when dropped into a nonsolvent mixture viz., methanol/acetone will produce beads, which can be hardened by crosslinking with GA.[8] But, the encapsulation of chlorpyrifos, which is highly soluble in the external media containing methanol/acetone mixture by the above method, was not be suitable because of the possible low encapsulation efficiency of the final product. This prompted us to encapsulate the ethanol soluble chlorpyrifos successfully by adopting a modification in the earlier formulation procedure.[8] The Na-Alg beads were formulated in a 30% ethanol solution containing a higher concentration (8%) of the crosslinking agent.

The results of % encapsulation efficiency and size of the beads are presented in Table I. The beads are almost spherical in shape, with the particle sizes ranging between 890 and 910 μm. The SEM photographs as shown in Figure 1 indicate the smooth surfaces of the beads. Chlorpyrifos embedded into the polymeric beads did not show any interaction with either the polymer or the crosslinking agent during the formulation step as evidenced by FTIR spectra (see Fig. 2). The characteristic absorption peaks of chlorpyrifos (curve a) due to P=S has shown around 750–800 cm^{-1}, and the absorption band for the

Table I Results of % Entrapment Efficiency, Bead Size, Diffusion Coefficients, and Estimated Values of k and n from Eq. (2) for 20% Chlorpyrifos-Loaded Beads at 25°C

Polymer	Time of Exposure to GA (min)	Beads Size (μm)	% Encapsulation Efficiency	k (min^{-1})	n	$D_{sorption}$ $\times 10^6$ (cm^2/s)	$D_{desorption}$ $\times 10^8$ (cm^2/s)
Na-Alg	5	891 ± 55	77.11 ± 0.01	0.0071	0.63	8.42	2.97
	10	890 ± 48	75.50 ± 0.13	0.0076	0.62	7.23	1.2
Na-Alg + 5% gelatin	5	911 ± 94	78.17 ± 0.31	0.0052	0.58	4.77	3.31
Na-Alg + 10% gelatin	5	901 ± 62	78.91 ± 0.11	0.0051	0.51	4.35	4.12
Na-Alg + 5% egg albumin	5	908 ± 68	77.24 ± 0.04	0.0054	0.62	3.27	3.14
Na-Alg + 10% egg albumin	5	889 ± 50	78.03 ± 0.31	0.0062	0.61	2.35	3.26

P—O—C alkyl group appeared at 990 cm^{-1}. FTIR spectra of the encapsulated beads (curve b) also show peaks at 750–800 cm^{-1} and 990 cm^{-1} along with the crosslinked Na-Alg peaks. This clearly indicates that the chlorpyrifos did not produce any chemical interactions between the polymer or the crosslinking agent used. From the DSC scans (not shown in the figure), the endothermic peaks of chlorpyrifos observed at about 43°C does not appear in the DSC scan of chlorpyrifos-loaded crosslinked Na-Alg beads; therefore, a complete molecular dispersion of the chlorpyrifos has taken place. The particle sizes, which generally range between 889 and 908 μm did not vary significantly either by the network formation or by increasing the exposure time to the crosslinking agent. The % encapsulation efficiency varied from 75 to 79%, showing a dependence on the time of exposure to the crosslinking agent, i.e., extent of crosslinking of the matrix material used. Generally, % encapsulation efficiency decreased with an increase in the time of exposure to the crosslinking agent. This may be attributed to the release of chlorpyrifos to the external media after when it is exposed to a longer time.

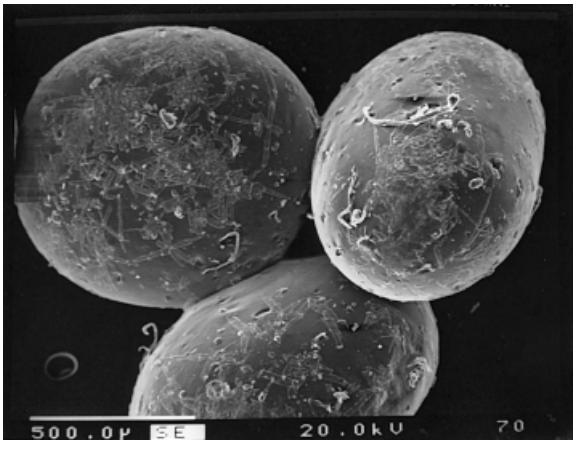

Figure 1 SEM photograph of Na-Alg beads.

Both sorption and desorption (drying rate) data have been used to calculate the diffusion coefficients, D for sorption and desorption of the liquid from the beads using the following equation:[13]

$$D = \left(\frac{r\theta}{6M_\infty}\right)^2 \pi \tag{1}$$

where θ is the slope of the linear portion of the plot of M_t/M_∞ vs. $t^{1/2}$, r is radius of the beads, and M_∞ is the maximum sorption value. To calculate D for liquid desorption from the beads during the drying process, we have calculated θ by plotting

$$\ln\left(1 - \frac{M_t}{M_\infty}\right)$$

results vs t. The calculated results of D for sorption and desorption experiments are also included in Table I. The diffusion coefficient for sorption experiments are higher by two orders of magnitude than those calculated from the desorption experiments. These data show a dependence on the nature of the bead polymer. For instance, with the Na-Alg beads, higher values of D are observed for sorption ranging between 8.42×10^{-6} cm^2/s for 5 min of exposure to GA and slightly lower values, i.e., 7.23×10^{-6} cm^2/s are observed for 10-min exposure to GA. The lower values of D ranging between 3.27×10^{-6} and 2.35×10^{-6} cm^2/s are observed for the egg albumin-based IPNs. The intermediate values ranging between 4.77×10^{-6} and 4.35×10^{-6} cm^2/s are observed for the gelatin-based IPNs. The D values for desorption range from 1.20 to 4.12×10^{-8} cm^2/s.

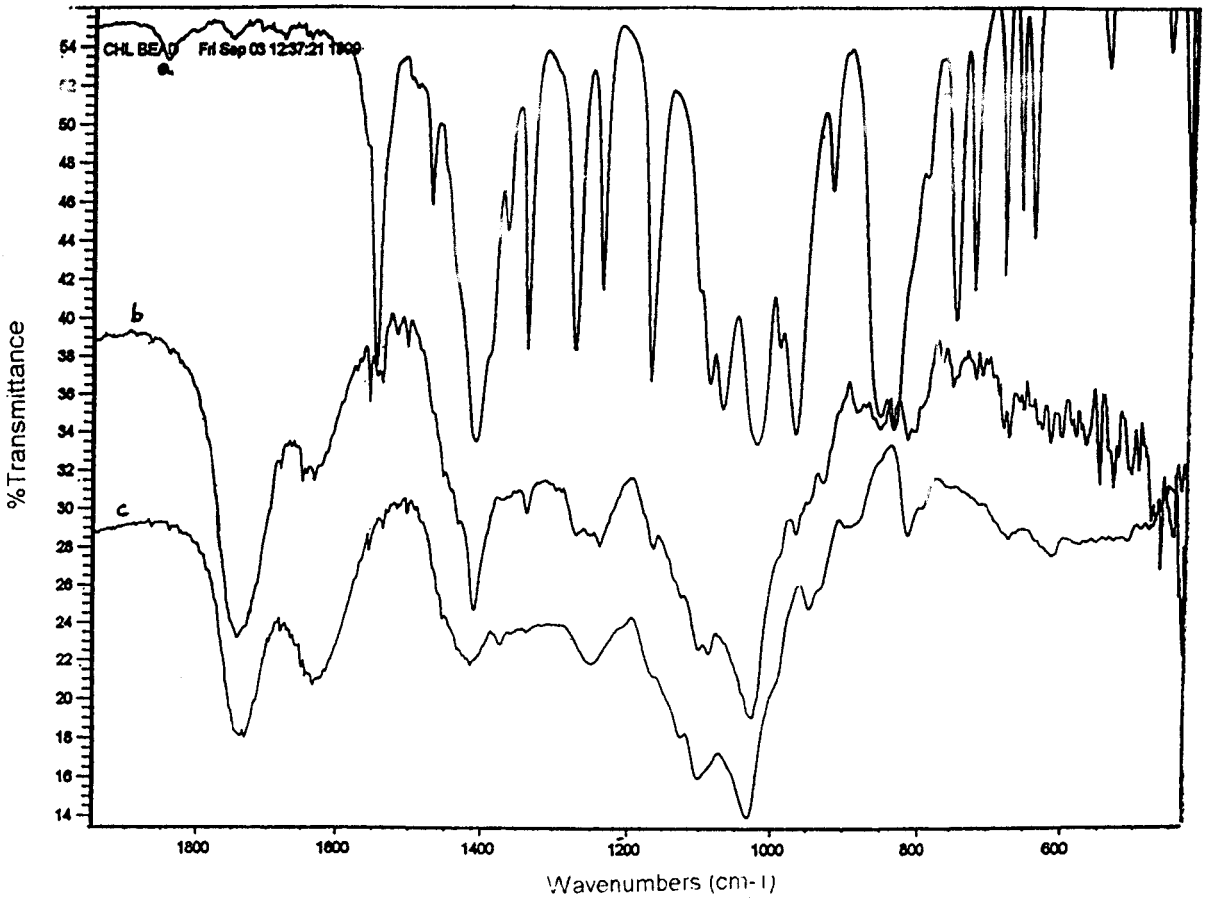

Figure 2 FTIR spectra of chlorpyrifos (curve a), beads containing chlorpyrifos (curve b), and empty Na-Alg beads (curve c).

Such a large difference in the values of D between sorption and desorption experiments is attributed to the slower rates of drying of the beads. These observations follow the same trends as published earlier on the drying rates of solvent from the elastomer membranes.[14] The D values for desorption are generally higher for the IPNs when compared to the neat Na-Alg beads.

The fraction release data, i.e., M_t/M_∞ of chlorpyrifos during the initial 60% release of chlorpyrifos have been fitted to the following equation:[15]

$$\left(\frac{M_t}{M_\infty}\right) = kt^n \tag{2}$$

to calculate the values of n and k by using the least-squares procedure. These data are also included in Table I. The n values calculated for all the systems vary between 0.51 and 0.63 with the correlation coefficients, r, at 95% confidence limit, indicating a slight variation from the Fickian transport.[16,17] Slightly lower values of n (0.51 to 0.58) are observed for the gelatin-based IPNs than the egg albumin-based IPNs, for which n varies between 0.61 and 0.62. Similarly, for the Na-Alg beads, n varies between 0.62 and 0.63. The lower k values for all the systems indicate a lesser interaction between the bead material and chlorpyrifos.

Swelling characteristics of the network polymer and the release of chlorpyrifos from the polymer matrix depends upon the extent of crosslinking. Therefore, it is possible to model the diffusion process and study parameters of interest like effect of amount of crosslinking and percentage loading of chlorpyrifos. The diffusion process involves immersing the beads into the medium of interest and provoking absorption of the liquid by the spherical polymer. To study this effect, swelling experiments were performed by monitoring the percentage uptake of water. From these data, the molecular mass (M_C) between crosslinks of

Table II Values of ϕ, χ, and M_C Calculated from Eqs. (3–5) for 20% Chlorpyrifos-Loaded Beads at Different Temperatures

Temperature (°C)	System	ϕ	χ	M_C
25	Na-Alg	0.544	0.559	195
30		0.538	0.563	207
35		0.528	0.563	224
25	Na-Alg +	0.662	0.887	465
30	5% gelatin	0.644	0.863	508
35		0.631	0.848	555
25	Na-Alg +	0.760	0.892	109
30	5% egg	0.755	0.895	116
35	albumin	0.742	0.874	124

the polymers was calculated using the Flory-Rehner equation[18] in the following simplified form:

$$M_C = - \rho_P V_S \phi^{1/3} [\ln(1 - \phi) + \phi + \chi \phi^2]^{-1} \quad (3)$$

The volume fraction, ϕ of the swollen polymer was calculated using:

$$\phi = \left[1 + \frac{\rho_P}{\rho_s} \left(\frac{M_a}{M_b} \right) - \frac{\rho_P}{\rho_s} \right]^{-1} \quad (4)$$

In the above equations ρ_P and ρ_S represent the densities of polymer and solvent, respectively; M_b and M_a are, respectively, the mass of the polymer before and after swelling; V_S is molar volume of the solvent used.

The interaction parameter, χ, was calculated as per the procedure published by Aithal et al.[16,17] using the following equation.

$$\chi = [\phi(1 - \phi)^{-1} + N \ln(1 - \phi) + N\phi] \times [2\phi - \phi^2 N - \phi^2 T^{-1} (d\phi/dT)^{-1}]^{-1} \quad (5)$$

where

$$N = \left(\frac{\phi^{2/3}}{3} - \frac{2}{3} \right) \left(\phi^{1/3} - \frac{2\phi}{3} \right)^{-1}$$

and $d\phi/dT$ is the slope obtained by plotting volume fraction vs. temperature in Kelvin. These data are presented in Table II. The Na-Alg and its IPNs are hydrophilic in nature and, hence, the transport of water through such polymers is dependent upon the rigidity of the polymer as well as the extent of crosslinking. The results of % uptake of water by the beads presented in Figure 3 indicate that all the Na-Alg beads show equilibrium water absorption up to 5 h, whereas the Na-Alg IPNs attain equilibrium at the end of 2 h. Thus, the IPN formation significantly reduces the swelling of Na-Alg beads. Further, the gelatin-based IPN beads are more rigid than the egg albumin containing beads, as evidenced by the higher values of M_C for the gelatin-based IPNs (for which M_C = 465–555) when compared to the egg albumin-based IPNs for which M_C varied from 109 to 124. The higher values of M_C are further supportive of the fact that the gelatin-based beads are more rigid structures than either the egg albumin-based beads or the neat Na-Alg beads. Increased rigidity of the gelatin-based matrix shows lower release rates probably due to a retarded leaching of chlorpyrifos to the external medium. The M_c values increase by increasing the temperature from 25 to 35°C, and this is probably due to an increase in the crosslinking at higher temperature. These results also support that the % increase in encapsulation efficiency for the gelatin- or the egg albumin-based IPNs is attributed to an increased rigidity of the matrix after the formation of IPNs, thereby retarding the leaching rate of chlorpyrifos to the external medium. The results of χ for the encapsulated Na-Alg matrices vary from 0.559 to 0.563, but for the IPN matrices of gelatin or egg albumin, these values are higher and range from 0.848 to 0.895, indicating the mild-type of interactions between the polymer and chlorpyrifos.

To calculate the drying rates, some samples of Na-Alg and their IPN beads were selected such that the initial mass should be nearly equal. Re-

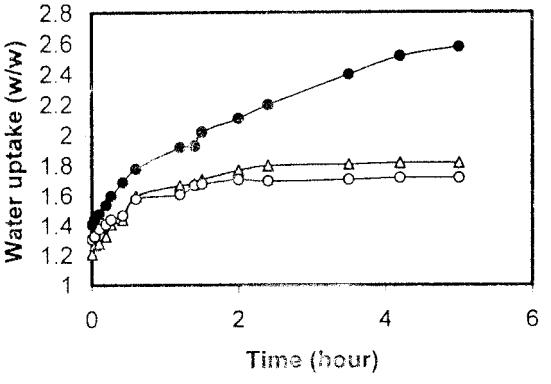

Figure 3 Effect of IPN formation on percentage uptake of water for (●) Na-Alg, (△) egg albumin IPNs, and (○) gelatin IPNs.

sults of drying rate presented in Figure 4 indicate that the IPN beads took longer drying time than the Na-Alg beads. The gelatin-based IPNs exposed for 5 min to the crosslinking agent dried quicker than the egg albumin-based IPNs. This is due to an increased rigidity of the wall polymer formed after the formation of IPN, thereby showing a decreased desorption rate of the liquid from the beads.

Because chlorpyrifos is sparingly soluble in water, and hence, for the *in vitro* dissolution study, we have used a 30% methanol solution as the dissolution media to maintain the sink conditions. The release of chlorpyrifos from the beads was subjected to a number of physical and chemical parameters including those related directly to the release medium (mass % of methanol in the dissolution), release conditions (temperature), and those resulting from a change in the characteristics of the CR device (beads). To study the effect of the nature of networking (i.e., IPNs) on the release kinetics, the beads containing 20% chlorpyrifos were selected. These results are depicted in Figure 5. The release rates of chlorpyrifos are much faster for the Na-Alg matrix than its IPNs of either gelatin or egg albumin, which is due to an increased rigidity of the IPNs. As suggested earlier by Murata et al.,[19] the Na-Alg matrix materials when treated with chitosan showed the decreased erosion rates. In a similar manner the presence of either gelatin or egg albumin has an effect in reducing the release rate of chlorpyrifos. Further, the release of chlorpyrifos from the gelatin-based IPNs and the egg albumin-based IPNs are quite similar. About, 70% of chlorpyrifos was released from the Na-Alg matrix on the sixth day (i.e., after 144 h) whereas, only about 58 and 60% release occurred for the gelatin and egg albumin containing IPNs, respectively. It is thus possible that the Na-Alg matrix beads might have become denser after when the IPNs are formed, thereby resulting in a decreased rate of diffusion of chlorpyrifos through the swollen beads.

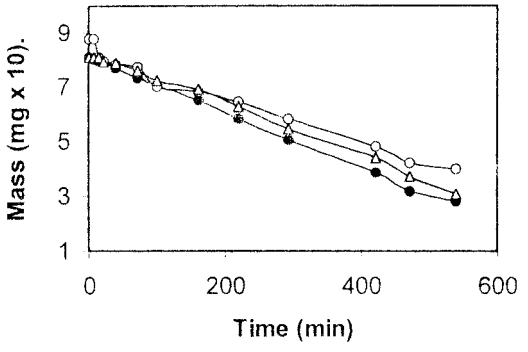

Figure 4 Effect of IPN formation on the drying rate of (●) Na-Alg, (△) egg albumin IPNs, and (○) gelatin IPNs.

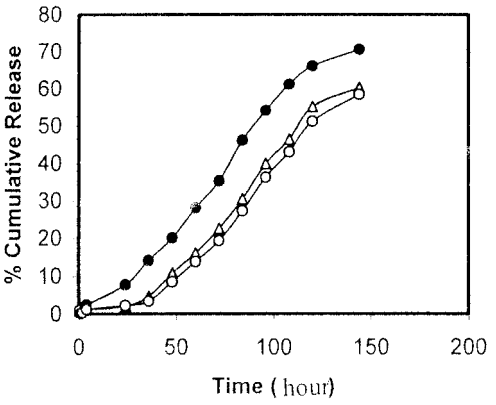

Figure 5 Effect of IPN formation on chlorpyrifos release from (●) Na-Alg, (△) egg albumin IPNs, and (○) gelatin IPNs.

CONCLUSIONS

In the present study, we have shown that chlorpyrifos can be successfully encapsulated using the crosslinked matrices of Na-Alg or its IPNs with either gelatin or egg albumin. The characterization of IPNs was done by measurement of swelling in water, which indicated that all the Na-Alg beads show a maximum amount of water absorption at about 5 h, but the Na-Alg IPN beads absorb water at 2 h. The molecular mass between crosslinks was calculated for all the IPNs, and these results are higher for the gelatin-based IPNs when compared to other matrices. However, the particle size did not vary significantly either by the network formation or by increasing the exposure time to the crosslinking agent. The *in vitro* static release data indicated that the release pattern deviates slightly from Fickian transport. It is demonstrated that the presence of either gelatin or egg albumin in Na- Alg delayed the release of chlorpyrifos.

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