CHAPTER VII

SYNTHESIS AND CHARACTERIZATION OF SODIUM ALGINATE INTERPENETRATING NETWORK SYSTEMS FOR CONTROLLED RELEASE OF CHLORPYRIFOS

VII.1. Abstract

In this chapter, the Na-Alg IPN beads have been prepared by crosslinking the Na-Alg blend with gelatin and egg albumin using GA as the crosslinking agent. The characterization of IPN was done by measuring its swelling in water. From the swelling data, molecular mass between crosslinks, $M_C$ was calculated for all the IPNs and these results indicated that $M_C$ increases for only gelatin IPN. However, the particle size did not vary significantly either by the network formation or by increasing the exposure time to the crosslinking agent. Percentage entrapment efficiency varied considerably with the type of network and the time of exposure to crosslinking agent. The percentage entrapment efficiency decreased with an increase in the time of exposure to the crosslinking agent. The in-vitro static dissolution experiments have been performed and efforts have been made to study the release kinetics of chlorpyrifos from the matrices using the empirical equation.

Part of the work described in this chapter has been submitted to 27th International Symposium on Controlled Release of Bioactive Materials", to be held in Paris, France, July 7-13, 2000. Also, the entire work is submitted to Journal of Controlled Release, (2000).
VII. 2. Introduction

Over the past few decades, many hydrophilic polymers have been used as the effective controlled delivery systems for the release of bioactive molecules [1-3]. The parameters which affect the properties of the controlled release (CR) formulations are dependent upon the nature and type of the polymer used to develop such systems. Investigations are in active progress to use the appropriate polymers to achieve an effective delivery system. In this direction, the use of interpenetrating polymer networks (IPNs) as the coating materials [4] for the agrochemicals constitutes an interesting class of encapsulated products. The release mechanisms of such products can be evaluated precisely. In these applications, the major task of polymer chemists is to design and evaluate a suitable wall material. However, the real commercial acceptance of such products will necessitate a cost benefit of the product and hence, it is helpful to find the alternative and cheaper materials to encapsulate agrochemicals for the CR application. Some of the natural products or by-products from many chemical process industries fulfills these requirements [5].

It has been shown earlier [6] that one of the easiest ways to control the release of drug through the polymeric matrices is to blend with the low molecular mass additives or coating with another polymer. The crosslinked sodium alginate (Na-Alg) has been used as a CR matrix material in medicine [7] and in agriculture [8]. Alginates (polysaccharides) are generally known to be haemocompatible that do not accumulate in any organs of the human body. Recently, the blends of sodium alginate with deoxycholate, pluronic F68LF, dodecyltrimethyl ammonium bromide, polyvinyl alcohol and poly ethyloxazoline have been used along with gelatin, polyallylamine and chitosan as the coating materials [6] to effectively control the release of bioactive molecules. An easy method to produce IPNs is to crosslink the polymer blend with a common crosslinking agent for both the
polymers as otherwise, if one of the polymers is crosslinked, then it will be a semi-IPN.

In this chapter, the preparation of Na-Alg IPN beads by crosslinking Na-Alg blend with gelatin and egg albumin using GA as the crosslinking agent is reported. The characterization of IPN was done by measuring its swelling capacity in water. From these data, the molecular mass between crosslinks, $M_C$ has been calculated so as to understand the extent of networking in the IPN matrices.

Release of the active agent from the polymer matrix depends upon the extent of crosslinking. In order to understand the crosslinking of polymer network, it is important to know the $M_C$ values between crosslinks of the network polymer. The network structure in crosslinked polymers has been studied by a number of techniques [9], but the most popular technique is from a study of swelling of the polymer in the presence of a solvent. Whenever a polymer is placed in a solvent, it swells until the osmotic retractive forces are balanced by the elastic forces due to stretched segments of the polymer chains. These elastic retractive forces are inversely proportional to the $M_C$ of the polymer. When $M_C$ is large, then the polymer network is more elastic and swells rapidly especially in the presence of a compatible solvent. The $M_C$ values were calculated using Flory-Rehner equation [7-12] as per the procedures outlined in Chapter V.

From the sorption and desorption experiments of the IPN polymer, the concentration-dependent diffusion coefficient, $D$ for water absorptions as well as desorption by the beads were calculated [7,8] using Eq. (V.9). The values of $D$ for desorption from the beads during the drying process were calculated as explained before in Chapter V, under section V.4.D. Chlorpyrifos is a well known commercial pesticide, which finds widespread applications as a liquid formulation

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in controlling the pests like white grub and holotrichi consanguine blanch, which mainly affect the groundnut crop. It is an organo-phosphorous compound, which was encapsulated by the newly synthesized Na-Alg IPN polymer to produce the CR product for soil application.

VII.3. Experimental

The materials used along with the detailed experimental procedures have already been given in Chapter II under section II.8.

VII. 4. Results and Discussion

The aqueous solution of Na-Alg when dropped into an anti-solvent such as methanol/acetone mixture will produce beads, which can be hardened by crosslinking with GA [7,8]. But, the encapsulation of an active agent, which is highly soluble in external media containing methanol/acetone mixture by the above method, may not be suitable because of the possible low encapsulation efficiency of the final product. In this research, the ethanol-soluble chlorpyrifos was successfully encapsulated by adopting some modifications in the formulation procedure [8]. The formation of Na-Alg beads was carried out in 30 % ethanol solution containing higher concentration (8 %) of the crosslinking agent.

The results of % entrapment efficiency and size of the beads are presented in Table VII.1. The beads formed are almost spherical in shape with the particle sizes ranging between 890 and 910 μm. The particle size did not vary significantly either by the network formation or by increasing exposure time to the crosslinking agent. But, the % entrapment efficiency varied considerably with the type of network and the time of exposure to the crosslinking agent. The % entrapment 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 long-term exposure. On the other hand, the % entrapment efficiency increased with the formation of IPN of gelatin and egg albumin. Increased rigidity of the matrix after IPN formation might have retarded leaching of the chlorpyrifos to the external medium.

Table VII.1. Results of % Entrapment Efficiency, Estimated Values of k, n and r for Various Systems from Eq. (IV.1) for 20 % Chlorpyrifos-Loaded Beads Formed at 298.15 K

<table>
<thead>
<tr>
<th>Polymer</th>
<th>Time of exposure to GA (min)</th>
<th>% Entrapment efficiency</th>
<th>k (10⁻²) (min⁻¹)</th>
<th>n</th>
<th>D_{desorption} x 10⁶ (cm²/s)</th>
<th>D_{desorption} x 10⁸ (cm²/s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Na-Alg</td>
<td>5</td>
<td>77.11 ± 0.01</td>
<td>0.0071</td>
<td>0.63</td>
<td>8.42</td>
<td>2.97</td>
</tr>
<tr>
<td></td>
<td>10</td>
<td>75.50 ± 0.13</td>
<td>0.0076</td>
<td>0.62</td>
<td>7.23</td>
<td>1.2</td>
</tr>
<tr>
<td>Na-Alg + 5 % gelatin</td>
<td>5</td>
<td>78.17 ± 0.31</td>
<td>0.0052</td>
<td>0.58</td>
<td>4.77</td>
<td>3.31</td>
</tr>
<tr>
<td>Na-Alg + 10 % gelatin</td>
<td>5</td>
<td>78.91 ± 0.11</td>
<td>0.0051</td>
<td>0.51</td>
<td>4.35</td>
<td>4.12</td>
</tr>
<tr>
<td>Na-Alg + 5 % egg albumin</td>
<td>5</td>
<td>77.24 ± 0.04</td>
<td>0.0054</td>
<td>0.62</td>
<td>3.27</td>
<td>3.14</td>
</tr>
<tr>
<td>Na-Alg + 10 % egg albumin</td>
<td>5</td>
<td>78.03 ± 0.31</td>
<td>0.0062</td>
<td>0.61</td>
<td>2.35</td>
<td>3.26</td>
</tr>
</tbody>
</table>

Swelling of the polymer matrix and release of the active agents from the swollen matrix depend upon the rigidity of the network polymer. In order to understand this, the M_C values between crosslinks of the polymer were calculated per the procedures suggested in Chapter V. These data are presented in Table VII.2. It is observed that the χ values for the encapsulated Na-Alg matrices are in the range of 0.559-0.563, but with the IPN matrices, these values show an increase.
and vary from 0.848 to 0.895 (see Table VII.2). On other hand, the $M_C$ values for the Na-Alg matrices vary in the range from 195 to 224, but for the gelatin and egg albumin IPN matrices, the $M_C$ values range between 465-555 and 109-124, respectively indicating that after the formation of gelatin IPN, the $M_C$ values increased.

### Table VII.2. Values of $N$, $\phi$, $\chi$ and $M_C$ for the 20 % Chlorpyrifos-Loaded Beads at Different Temperatures.

<table>
<thead>
<tr>
<th>Swelling of beads at K</th>
<th>System</th>
<th>$N$</th>
<th>$\phi$</th>
<th>$\chi$</th>
<th>$M_C$</th>
</tr>
</thead>
<tbody>
<tr>
<td>298.15</td>
<td>Na-Alg</td>
<td>-1.234</td>
<td>0.544</td>
<td>0.559</td>
<td>195</td>
</tr>
<tr>
<td>303.15</td>
<td>Na-Alg+ 5% gelatin</td>
<td>-1.266</td>
<td>0.662</td>
<td>0.887</td>
<td>465</td>
</tr>
<tr>
<td>308.15</td>
<td>Na-Alg+ 5% egg</td>
<td>-1.313</td>
<td>0.760</td>
<td>0.892</td>
<td>109</td>
</tr>
<tr>
<td>298.15</td>
<td>Na-Alg+ albumin</td>
<td>-1.303</td>
<td>0.742</td>
<td>0.874</td>
<td>124</td>
</tr>
<tr>
<td>303.15</td>
<td>Na-Alg+ albumin</td>
<td>-1.310</td>
<td>0.755</td>
<td>0.895</td>
<td>116</td>
</tr>
<tr>
<td>304.15</td>
<td>Na-Alg+ albumin</td>
<td>-1.303</td>
<td>0.742</td>
<td>0.874</td>
<td>124</td>
</tr>
</tbody>
</table>

### VII. 4. A. Drying Rate of the Beads

In order to optimize the drying conditions, some samples of Na-Alg and its IPN beads were selected such that the initial mass should be nearly equal. Results of drying presented in Fig.VII.1 indicate that the IPN beads take longer drying time than the Na-Alg beads. The gelatin IPN beads exposed for 5 min to crosslinking agent dried quickly when compared to the egg albumin IPN beads. This may be due to the increased rigidity of the wall polymer formed after IPN, thereby showing the decreased desorption rate of the liquid from the beads. The drying data were further analyzed to calculate the diffusion coefficients, $D$ for the desorption of liquid from the beads using Eq. (V.9), and these results are presented in Table VII.1. It is observed that the $D$ values for desorption are small i.e., these
Fig. VII.1. Effect of IPN formation on drying rate of (●) Na-Alg, (Δ) egg albumin IPNs and (O) gelatin IPN beads.

Fig. VII.2. Effect of IPN formation on percentage uptake of water for (●) Na-Alg, (Δ) egg albumin IPNs and (O) gelatin IPN beads.
values range from $1.15$ to $4.12 \times 10^{-8}$ cm$^2$/s and this may be attributed to the slow drying of the beads. However, the D values for desorption did not show any systematic dependence on the type of IPN system chosen. In the majority of cases, lower D values are observed for the IPNs when compared to the Na-Alg beads.

VII.4.B. Swelling of the Individual Beads

In order to find the effect of formation of various IPNs and to study the extent of crosslinking on the release rates of chlorpyrifos from the polymeric matrices, the swelling experiments were performed by monitoring the percentage uptake of water by the beads. Na-Alg and its IPNs are the hydrophilic polymers and hence, transport of water through such polymers is dependent upon the rigidity of the polymer as well as the extent of crosslinking. In the present research, swelling of the beads was measured as the % uptake of water by the beads at a particular time interval. The results of % uptake of water by the beads are presented in Fig.VII.2. These data indicate that all the Na-Alg beads show a maximum amount of water absorption at about 5 h, but the Na-Alg IPN beads tend to absorb water during the second hour. It may be noted that the IPN formation significantly reduces swelling of the Na-Alg beads. Further, the gelatin-based IPN beads are more rigid than the egg albumin beads as evidenced by the smaller extent of swelling of the gelatin IPN when compared to egg albumin IPN. These results also confirm the % entrapment efficiency results i.e., entrapment efficiency increased with the formation of IPNs of gelatin and egg albumin, which may due to an increased rigidity of the matrix after the formation of IPN, might have retarded the leaching out of the chlorpyrifos to external medium.

The values of diffusion coefficients calculated from Eq. (V.9.) for the three types of beads are also included in Table VII.1. The values of D for sorption are
higher than those observed for desorption experiments. These data also show a dependence on the IPN formation. The higher values of D for sorption ranging between $8.42 \times 10^{-6}$ and $7.23 \times 10^{-6}$ cm$^2$/s for the Na-Alg beads and the lower values ranging between $3.27 \times 10^{-6}$ and $2.35 \times 10^{-6}$ cm$^2$/s are observed for the gelatin IPN. However, the intermediate values ranging between $4.77 \times 10^{-6}$ and $4.35 \times 10^{-6}$ cm$^2$/s are observed for the egg albumin IPNs.

VII. 4. C. Static Dissolution Study

Since chlorpyrifos is less soluble in water and hence, for the in-vitro dissolution study, we have used 30% methanol solution as the dissolution media in order to maintain the sink conditions. Chlorpyrifos release from the beads were 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). In order to observe the effect of the nature of networking (i.e., IPNs) on the release kinetics, the beads containing 20% of chlorpyrifos loading were selected and these results are depicted in Fig. VII.3.

The release rates of chlorpyrifos are much faster for the Na-Alg matrix than its IPNs with either gelatin or egg albumin because the formation of IPNs might have increased the rigidity of the polymer. Further, the release of pesticide from the gelatin IPNs is slower than the egg albumin IPNs. 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 to be noted that the Na-Alg matrix beads might have become more denser after the formation IPNs, thereby resulting in the decrease of rate of diffusion of chlorpyrifos through the swollen beads.
Fig. VII.3. Effect of IPN formation on the release of (●) Na-Alg, (Δ) egg albumin IPN and (O) gelatin IPN beads.
VII.4.D. Empirical Correlations

The fraction release data i.e., \( \frac{M_t}{M_{\infty}} \) of chlorpyrifos during the initial 60% release of the pesticide were fitted to Eq. (IV.1) proposed by Ritger Peppas [13]. The values of \( n \), the diffusional exponent and \( k \), have been estimated by the least-squares procedure. These results along with the correlation coefficients, \( r \), at 95% confidence limit are also included in Table VII.1. The \( n \) values calculated for all the systems vary between 0.51 and 0.63 indicating the release in these systems to be slightly deviating from the regular Fickian transport [14-16]. However, lower values of \( n \) are observed for the gelatin IPN than the egg albumin IPN. The lower \( k \) values for all the systems indicate a lesser interaction between the matrix material and the active agent.

VII.5. Conclusions

Chlorpyrifos can be successfully encapsulated in Na-Alg and its IPN with gelatin and egg albumin beads. The characterization of IPN was done by measuring its swelling capacity in water 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 during the second hour. The molecular mass between crosslinks, \( M_c \) was calculated for all the IPNs and these results indicated that \( M_c \) increases for only gelatin IPN. However, the particle size did not vary significantly either by the network formation or by increasing the exposure time to crosslinking agent. The % entrapment efficiency decreased with an increase in the time of exposure to crosslinking agent. The in-vitro static dissolution experiments have been performed to study the release kinetics of chlorpyrifos and these data indicated that the release pattern deviates slightly from the regular Fickian transport.
VII.6. References