RESULTS & DISCUSSION
IV. RESULTS AND DISCUSSION

Mosquitoes are the most important single group of insects in terms of public health significance. Choice of control measures against mosquitoes must be based on a fundamental understanding of the ecology, bionomics and behaviour of the target species and its relation to its host and environment. The larval control measures are generally preferred as preventive measures in areas which are prone to frequent outbreaks of mosquito borne diseases and in situations, where, for technical or operational reasons, adult control alone or combined with drug administration fails to interrupt disease transmission. Mosquito larval control programmes are hampered mostly due to the enormous number of breeding places which need treatment generally at either weekly or fortnightly intervals.

During the last few decades, controlled release technology has received increasing attention in the face of a growing awareness that substances ranging from drugs to insecticidal chemicals are frequently toxic and sometimes ineffective when administered or applied by conventional means. Controlled release pesticide technology holds great promise for improving the efficacy of some of the existing pesticides and reducing the environmental problems associated with their application. Optimum design or selection of polymers for controlled release system requires the understanding of factors related to the structure and morphology of the polymer and properties related to the diffusion process. From a material point of
view, optimum release conditions can be achieved by controlling the crystalline phase, porous structure, degree of swelling, mesh size of the crosslinked macromolecular chain, thermodynamic transitions related to the macromolecular relaxations and chemical erosion of the polymer (Yasuda et al., 1969; Yasuda and Lamaze, 1971; Langer and Peppas, 1981; Korsmeyer and Peppas, 1981; Andreopoulos, 1987).

Among the natural polymer derivatives, chemically modified products of starch, cellulose and cyclodextrins find wide application in controlled release formulations of pesticides. They can be processed to various controlled release products having desired characteristics by altering the processing parameters and since they are biodegradable, the environmental impact due to their application is minimal.

Cellulose, a polymer of β-D-glucopyranose units linked 1-4, is the principal polysaccharide in plant cell walls. Synthetic cellulose modifications belonging to the general category of ethers, comprise alkyl and hydroxyalkyl celluloses. In addition to these nonionic derivatives, sodium carboxymethylcellulose (NaCMC) is an anionic polyelectrolyte prepared by the reaction of sodium chloroacetate and alkali cellulose and used in industrial applications where thickening, suspending, stabilizing and film forming properties are important. Monovalent cations form soluble salts with NaCMC; divalent ions are borderline and trivalent cations form insoluble salts causing gelling. The effect, however, varies with salt type, pH and
degree of substitution (Norbert and Leon, 1971; Mark et al., 1987; Allen and Bevington, 1989).

4.1. Identification of Suitable Crosslinking Agents and Standardisation of Procedure for Insolubilisation:

NaCMC is highly soluble in water and this semisynthetic cellulose derivative requires further modification to be useful as a controlled release matrix for mosquito larvicides. Different chemical crosslinking procedures have been reported to prepare water insoluble derivatives of NaCMC.

Yureva (1973) studied the insolubilisation of NaCMC using formaldehyde, dimethylol urea at room temperature resulting in reduction of water solubility. But the insolubilised matrix underwent hydrolysis when placed in water for few days. When crosslinking was carried out at 150°C and in presence of either 5% acetic acid, 2.5% sulphuric acid or 8% sodium hydroxide, water insoluble films were obtained which lost 21.8% weight when kept in water for 22 days. Crosslinking of NaCMC using epichlorohydrin and sodium hydroxide was also reported at a temperature of 50°C for 12 hours (Satake, 1974). Crosslinked cellulose derivatives were prepared by a dry ball milling procedure using copper carbonate and sodium hexametaphosphate at 130°C for 2 hours (Fukunuga, 1976).
Ionotropic network formation with chemical reaction or ion-exchange due to ionic crosslinking of polyionic chains with multivalent counter ions is an important technique for the development of erodible controlled release systems resulting in porous and water swellable matrices (Salif et al., 1976; Lee et al., 1991). After considering the factors involved in the insolubilisation procedures for NaCMC at ambient conditions of temperature and pH, the inorganic salts of aluminium, barium, magnesium, copper, zinc and ferric ions were screened.

Addition of an aqueous solution (1.0 M) of the salts into a stirred aqueous slurry of NaCMC, which was found necessary to impart appreciable matrix stability to the slabs, resulted in gelling followed by localized precipitation at higher levels of gellant concentration. In an alternative procedure to insolubilise NaCMC, dried sheet was made from a neutral aqueous slurry of NaCMC by solution casting. Insolubilisation of the dried sheets was carried out by immersing the sheets in 1.0 M aqueous solution of aluminium sulphate, magnesium sulphate, copper sulphate, barium chloride, zinc sulphate and ferric chloride for 24 hours.

4.1.1. Physical integrity of insolubilised matrices:

The samples obtained with different crosslinking agents were dried at room temperature and introduced in water to monitor their physical stability. The samples obtained by gelling in aluminium,
magnesium, barium and zinc salt solutions were found to disintegrate within a week. Whereas the sheets obtained by crosslinking with copper and ferric salts were quite stable for more than 20 weeks with the respective weight losses of 15.68 and 19.44% after three months. Thus, the two metal ion salts, viz., copper sulphate and ferric chloride were selected for the insolubilisation of NaCMC to prepare controlled release matrices of mosquito larvicides.

4.1.2. Matrices of NaCMC containing an interactive polymer, gelatin:

NaCMC is compatible with certain water soluble nonionic polymers like methylcellulose, hydroxyethylcellulose and hydroxypropylcellulose (Mark et al., 1987; Rao et al., 1988; Rao et al., 1989). It is also compatible with positively charged polymer, gelatin below its isoelectric point to form interactive polymer network (Peppas, 1987b). Therefore polymer blends of NaCMC and gelatin were made to study the influence of gelatin on matrix stability and release behaviour of active agent in such matrices.

Dried matrix of NaCMC containing gelatin in the proportion of 4:1 was made by blending an aqueous slurry of gelatin to that of NaCMC. It was found to swell enormously and disintegrate within 24 hours in water. The stability of this matrix in water was not sufficient enough to be used as controlled delivery system of larvicides. Further crosslinking of this matrix with the gelling agents resulted in matrices with higher stability.
When this matrix was crosslinked with 1.0 M solution of copper sulphate for 24 hours, the weight loss of matrix was 33.55% and that of the matrix crosslinked with ferric chloride under the same conditions was 50.05% after introducing the matrices in water for three months.

4.2. Studies on Crosslink Density:

The insolubilisation reaction of NaCMC matrices with multivalent ions involves the ion exchange process. In general the ion exchange properties vary with salt type and its concentration, pH, degree of substitution of NaCMC and the manner in which NaCMC and the salts are contacted (Bikales and Segal, 1971; Mark et al., 1987).

The results from the studies on the resistance of the insolubilised polymer samples to undergo hydrolysis indicated that the samples obtained with copper sulphate and ferric chloride as gelling agent were found to have the required matrix integrity in water to be useful as controlled release matrices for mosquito larvicides.

4.2.1. Influence of crosslinking parameters:

Since higher temperatures and extreme pH conditions would adversely affect the stability of the insecticides, crosslinking was carried out at 30±1°C and neutral pH. Studies on crosslink density
of NaCMC samples were made with respect to (i) two gelling agents, copper sulphate and ferric chloride, (ii) two concentrations of the gelling agent, 0.5 and 1.0 M aqueous solutions, (iii) different extents of crosslinking periods, 3, 6, 12, 24 and 48 hours in the respective gelling mediums and (iv) incorporation of an interactive polymer, gelatin in the ratios of 10:1 and 4:1 (10 and 25%) with respect to NaCMC. The estimation of the percentage of metal ion present in each crosslinked sample was carried out and the results are expressed as the percentage of metal ion present in each sample.

4.2.1.1. Crosslinking with 1.0 M copper sulphate:

The crosslink density was found to increase rapidly during the initial periods of crosslinking up to 12 hours and slowly afterwards when the crosslinking reaction was carried out at 1.0 M solution (Fig. 1). Pure NaCMC exhibited a crosslink density of 5.41% at 3 hours and increased to 10.13% within 48 hours. When the NaCMC matrix containing 10% gelatin was crosslinked, the crosslink density was 4.92% at 3 hours and increased to 9.63% at 48 hours. The polymer sample containing 25% gelatin had a crosslink density of 4.36% at 3 hours and increased to 9.27% by 48 hours.

4.2.1.2. Crosslinking with 0.5 M copper sulphate:

Polymer samples crosslinked in 0.5 M solution showed relatively low crosslink densities (Fig. 1). The crosslink densities of NaCMC
matrices were 4.62% and 8.44% at the respective periods of 3 and 48 hours. The crosslink densities of the matrices containing 10 and 25% of gelatin were also low with the respective values of 7.79% and 7.35% at 48 hours of crosslinking.

4.2.1.3. Crosslinking with 1.0 M ferric chloride:

The crosslink density was found to increase less rapidly during the crosslinking period of 48 hours as shown in Fig. 2. Pure NaCMC exhibited a crosslink density of 2.72% at 3 hours and increased to 11.24% within 48 hours. When the NaCMC matrix containing 10% gelatin was crosslinked, the crosslink density was 2.12% at 3 hours and increased to 7.02% at 48 hours. The polymer sample containing 25% gelatin had a crosslink density of 1.66% at 3 hours and increased to 6.41% by 48 hours.

4.2.1.4. Crosslinking with 0.5 M ferric chloride:

Polymer samples crosslinked in 0.5 M solutions showed relatively higher crosslink densities (Fig. 2). The crosslink densities of NaCMC matrices were 3.78% and 10.96% at the respective periods of 3 and 48 hours. The crosslink densities of the matrices containing 10 and 25% of gelatin were 8.31% and 6.22% at 48 hours of crosslinking.

The crosslinking reaction was less rapid in the case of ferric chloride than copper sulphate during the initial periods of
Fig. 1. Crosslink densities of the polymer samples insolubilised with copper sulphate as the gelling agent.

Fig. 2. Crosslink density of the polymer samples insolubilised with ferric chloride as the gelling agent.

NaCMC in 1.0 M (□) and 0.5 M (○) gellant,
NaCMC-gelatin (10:1) in 1.0 M (○) and 0.5 M (*) gellant and
NaCMC-gelatin (4:1) in 1.0 M (▽) and 0.5 M (◇) gellant.
crosslinking. The crosslink density was almost same during the initial periods of crosslinking in 0.5 and 1.0 M solutions of copper sulphate. The increase in the crosslink density in 0.5 M solution compared to 1.0 M solution observed in the case of ferric ion may be due to the fact that the trivalent ferric ion forms more networks than the divalent copper ion and the crosslinked network formed on the surface of the polymer sample would have prevented further permeation of ferric ions into the inner portions of the matrix.

4.3. **Standardisation of Fenthion, Temephos and Diflubenzuron**

by using UV-Spectrophotometer and HPLC:

The absorption maxima of the technical grade insecticides were measured using a UV-Spectrophotometer and found to be 249, 252 and 262 nm respectively for fenthion, temephos and diflubenzuron. A linear regression equation was obtained with concentration on optical density using standard solutions of the insecticides. The amount of active agent present in unknown samples was estimated using the regression equation.

HPLC procedures were standardised to analyse the concentration of the insecticides viz., fenthion, temephos and diflubenzuron present in the water samples. The retention times were found to be 3.11, 3.18 and 2.96 minutes respectively for fenthion, temephos and diflubenzuron and chromatograms of the three insecticides are
Fig. 3. Chromatograms (HPLC) of fenthion (A), temephos (B) and diflubenzuron (C) using acetonitrile-water (7:1) mobile phase, 2 ml/min flow rate, Zorbax-C8 column (4.6 mm i.d x 25 cm) at 60°C, and UV-detector at 249, 252 and 262 nm for the respective insecticides.
presented in Fig. 3. A two point calibration method was used for determining the quantity of the agents present in unknown samples.

4.4. Geometry of the Matrices:

Monolithic erodible systems, possessing either a slab or disc geometry release the active agent at a constant rate if erosion takes place only on the surface of the device (heterogeneous erosion) and the total surface area does not change with time by neglecting the edge effects (Brooke and Washkuhen, 1977; Langer and Peppas, 1980; Rhine et al., 1980a and 1980b; Langer and Peppas, 1981; Langer and Peppas, 1983; Carstensen, 1987). Therefore for the present investigation, a slab geometry has been selected since the insolubilised CMC matrices eroded when released in water.

The advantages of using floating type devices of mosquito larval control agents are well known (Das et al., 1983). Insolubilised NaCMC matrices have been found to sink in water. In order to make the device suspend on water surface, two low density materials, cork powder and expanded polystyrene beads are incorporated into the matrices at the stage of initial NaCMC matrix preparation. The incorporation of 5% expanded polystyrene with respect to NaCMC has been found to give appropriate suspending characteristics without affecting matrix intactness.
4.5. Stability of Matrices in Relation to Concentrations of Fenthion:

Formulation was made which contained 30% of the larvicide, fenthion, using an 82.5% Emulsifiable Concentrate (EC) in NaCMC and crosslinked for 48 hours in 1.0 M copper sulphate. This matrix exhibited physical integrity only for a period of 14 weeks. When the insecticide load was reduced to 20%, the matrix obtained showed intactness up to 36 weeks for the same crosslinking period. Thus the maximum load of the larvicide studied was 20% in the matrix and the study was extended to 10% also at different crosslinking conditions.

4.6. Formulations of fenthion:

The following formulations of fenthion were prepared and the release profiles of the larvicide were studied in the laboratory to optimise the formulation conditions for developing matrices with desired characteristics. Thus formulations were made with two concentrations of fenthion in NaCMC followed by crosslinking with the two gelling agents and at three different periods of crosslinking. Twelve formulations of fenthion thus prepared were evaluated under laboratory conditions.

4.6.1. Formulations of fenthion (20%) in NaCMC:

The NaCMC slabs incorporated with 20% fenthion with respect to
the weight of NaCMC were crosslinked for the duration of 12, 24 and 48 hours in 1.0 M solutions of the gelling medium. The slabs thus obtained were coded as CuF1, CuF2 and CuF3 with copper sulphate and FeF1, FeF2 and FeF3 with ferric chloride in the increasing order of crosslinking periods (Recipe-1).

4.6.1.1. Formulations based on the matrices of CuCMC:

Release studies: The three matrices, CuF1, CuF2 and CuF3 were introduced in measured volume of water in glass troughs under static condition at 30±1 C. The quantity of the active agent released from each matrix was monitored at daily intervals by the standardised HPLC and spectrophotometric techniques. Laboratory evaluation of these slabs was continued till the matrices lost their physical integrity. The three matrices, CuF1, CuF2 and CuF3 were evaluated in the laboratory for 31, 34 and 36 weeks respectively (Table 2).

Release profile analysis: The release profiles showing the quantity of fenthion released in mg/week are presented in Figs. 4a, 5a & 6a respectively for the matrices CuF1, CuF2 and CuF3. Release profiles indicated that the formulations exhibited an initial high release of 95.83, 82.81 and 74.79 mg respectively from CuF1, CuF2 and CuF3 during the first week of study and stabilised thereafter during the entire period of evaluation. These initial higher values may be due to the release of fenthion on the surface of the device and the
Fig. 4. Release profile of fenthion from CuF1.

Fig. 5. Release profile of fenthion from CuF2.
Fig. 6. Release profile of fenthion from CuF3.

Fig. 7. Release profile of fenthion from FeF1.
initial influx of water into the matrices followed by the counter-current diffusion of fenthion from the matrix into water.

The cumulative release profiles of the formulations are presented in Figs. 4b, 5b & 6b for CuF1, CuF2 and CuF3 respectively. The average release rate was obtained from the linear regression of the cumulative quantity of fenthion released on time. The values of the average release rates, given by X-coefficient of the regression equations, were 11.91, 9.28 and 8.47 mg/week respectively for CuF1, CuF2 and CuF3 and the respective values of the linear regression coefficients (R1) are 0.9803, 0.9830 and 0.9811 (Table 2).

The Figs. 4c, 5c & 6c represent the plot of cumulative amount of fenthion released against square-root of time and the values of the regression coefficients (R2) were 0.9787, 0.9898 and 0.9942 respectively for formulations CuF1, CuF2 and CuF3 (Table 2).

The values of the regression coefficients, R1 and R2, obtained by the regression of cumulative amount released on time and square-root of time showed a more or less square-root time release profile of fenthion from these three matrices. The maximum square-root time release behaviour was observed with the formulation CuF3.

Values of the release exponent, n and the kinetic constant, k in the equation (11),
Table-2: Duration of evaluation, average release rate and coefficients of linear regressions of cumulative release on time (R1) and cumulative release on square-root of time (R2) of formulations of fenthion (20%) with CuCMC and FeCMC matrices.

<table>
<thead>
<tr>
<th>Code</th>
<th>Duration of evaluation(wk)</th>
<th>Release rate (mg/wk)</th>
<th>Coeft. of linear regression R1</th>
<th>Coeft. of linear regression R2</th>
</tr>
</thead>
<tbody>
<tr>
<td>CuF1</td>
<td>31</td>
<td>11.9109</td>
<td>0.9803</td>
<td>0.9787</td>
</tr>
<tr>
<td>CuF2</td>
<td>34</td>
<td>9.2788</td>
<td>0.9830</td>
<td>0.9898</td>
</tr>
<tr>
<td>CuF3</td>
<td>36</td>
<td>8.4717</td>
<td>0.9811</td>
<td>0.9942</td>
</tr>
<tr>
<td>FeF1</td>
<td>16</td>
<td>26.7995</td>
<td>0.9623</td>
<td>0.9973</td>
</tr>
<tr>
<td>FeF2</td>
<td>19</td>
<td>22.3380</td>
<td>0.9854</td>
<td>0.9914</td>
</tr>
<tr>
<td>FeF3</td>
<td>21</td>
<td>18.8020</td>
<td>0.9732</td>
<td>0.9948</td>
</tr>
</tbody>
</table>

Table-3: Values of release exponent (n), kinetic constant (k), regression coefficient of the log of fraction of fenthion released on log of time (R3) and the apparent diffusion coefficient (D) of fenthion (20%) from CuCMC and FeCMC matrices.

<table>
<thead>
<tr>
<th>Code</th>
<th>Release exponent, n</th>
<th>Constant, k</th>
<th>Coeft. of regression, R3</th>
<th>Dx10^{-9} (cm^2/sec)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CuF1</td>
<td>0.5171</td>
<td>0.1483</td>
<td>0.9755</td>
<td>8.8785</td>
</tr>
<tr>
<td>CuF2</td>
<td>0.4976</td>
<td>0.1542</td>
<td>0.9836</td>
<td>7.4667</td>
</tr>
<tr>
<td>CuF3</td>
<td>0.5001</td>
<td>0.1489</td>
<td>0.9906</td>
<td>7.2111</td>
</tr>
<tr>
<td>FeF1</td>
<td>0.5827</td>
<td>0.2096</td>
<td>0.9955</td>
<td>32.9242</td>
</tr>
<tr>
<td>FeF2</td>
<td>0.6817</td>
<td>0.1363</td>
<td>0.9944</td>
<td>36.5228</td>
</tr>
<tr>
<td>FeF3</td>
<td>0.5999</td>
<td>0.1676</td>
<td>0.9928</td>
<td>26.2222</td>
</tr>
</tbody>
</table>
were obtained from the linear regression of log of the fraction released (log MT/Mz) on log of time (log t). The constant of the regression equation was taken as log k and the x-coefficient was taken as the release exponent, n. The values of n and k were 0.5171 and 0.1483 for the matrix CuF1, 0.4975 and 0.1542 for the matrix CuF2 and 0.5001 and 0.1489 for CuF3, respectively (Table 3).

The apparent diffusion coefficient, D of fenthion from these slabs was obtained by substituting the values of n, k and the thickness of the slab, l in cm in the equation (12)

\[ k = 4(D/\pi l)^{2n} \]  \hspace{1cm} (12)

and the diffusion coefficients were \(8.88 \times 10^{-9}\), \(7.47 \times 10^{-9}\) and \(7.21 \times 10^{-9}\) cm/sec respectively for matrices CuF1, CuF2 and CuF3. (Table 3).

Among these three formulations of 20% fenthion in copper carboxymethylcellulose (CuCMC) matrices, CuF1 exhibited a higher release rate and values of diffusion coefficient. The value of n was higher in the case of formulation CuF1 compared to the rest two. The values of the release exponent n (> 0.45) indicated that all the three matrices exhibited a non-Fickian release pattern.
4.6.1.2. **Formulations based on the matrices of FeCMC:**

Release studies conducted with the matrices containing 20% fenthion, insolubilised by crosslinking in 1.0 M solution of ferric chloride exhibited physical integrity of 16, 19 and 21 weeks (Table 2) for the formulations, FeF1, FeF2 and FeF3 with the respective crosslinking periods of 12, 24 and 48 hours (Recipe-1).

The weekly release profiles of FeF1, FeF2 and FeF3 are presented in Figs. 7a, 8a and 9a respectively. The quantities of fenthion released in the first week were 95.3917, 69.7828 and 37.4972 mg respectively for the matrices FeF1, FeF2 and FeF3. The release rate decreased slowly thereafter and the average release rates were 26.80, 22.34 and 18.80 mg/week (Table 2) for the three formulations in the increasing order of crosslinking duration.

The cumulative release profiles against time and square-root of time are presented in Figs. 7b & 7c for the matrix FeF1, Figs. 8b & 8c for FeF2 and Figs. 9b & 9c for the formulation FeF3 respectively. The values of linear regression coefficients of the cumulative release profiles on time (R1) and square-root of time (R2) were 0.9623 and 0.9973 for FeF1, 0.9854 and 0.9914 for FeF2 and 0.9732 and 0.9948 for formulation FeF3 respectively (Table 2). The values of the regression coefficients indicate that the matrix FeF2 exhibited maximum linear release behaviour compared to the other two matrices.
Fig. 8. Release profile of fenthion from FeF2.

Fig. 9. Release profile of fenthion from FeF3.
and FeF1 exhibited maximum tendency towards square-root time release pattern.

The values of the release exponent, n were 0.5826, 0.6817 and 0.5999 and the kinetic constant, k were 0.2096, 0.1363 and 0.1676 respectively for matrices FeF1, FeF2 and FeF3 (Table 3). The values of n indicate that these three formulations exhibited non-Fickian release characteristics. FeF2 (n=0.6817) showed maximum value of n followed by FeF3 and FeF1.

The values of the apparent diffusion coefficient, D of fenthion from these formulations FeF1, FeF2 and FeF3 were 32.92x10^-9, 36.52x10^-9 and 26.22x10^-9 cm/sec respectively (Table 3).

The laboratory analysis of these formulations showed that these formulations underwent faster erosion than the matrices obtained by crosslinking with cupric ion. But there was an appreciable shift of release behaviour from square-root time profile towards non-Fickian one and the values of average release rate and the apparent diffusion coefficient revealed that these matrices exhibited higher values compared to CuCMC matrices.

4.6.2. Formulations of 10% fenthion in NaCMC:

4.6.2.1. Formulations based on CuCMC:

Fenthion formulations which contained 10% of active agent in
NaCMC and crosslinked with 1.0 M cupric ion, CuF4, CuF5 and CuF6 for the respective crosslinking duration of 12, 24 and 48 hours were evaluated for 39 weeks (Table 4) in the laboratory (Recipe-2).

The respective average release rates of fenthion from CuF4, CuF5 and CuF6 matrices were 6.51, 5.15 and 5.90 mg/week (Table 4). The weekly release profiles of these three matrices are presented in Figs. 10a, 11a & 12a and the quantities of the fenthion released during the first week were 67.67, 44.91 and 47.18 mg respectively from CuF4, CuF5 and CuF6.

The cumulative amount of fenthion released against time and square-root of time are presented respectively in Figs. 10b & 10c for CuF4, Figs. 11b & 11c for CuF5 and Figs. 12b & 12c for the matrix CuF6. The respective values of linear regression coefficients, R1 and R2 were 0.9797 and 0.9916 for CuF4, 0.9774 and 0.9912 for CuF5 and 0.9860 and 0.9911 for CuF6 (Table 4).

The values of release exponent, n were 0.4267, 0.4470 and 0.4830 and the kinetic constant, k were 0.1877, 0.1786 and 0.1562 respectively for matrices CuF4, CuF5 and CuF6 (Table 5). The apparent diffusion coefficients of fenthion from these matrices were $4.00 \times 10^{-9}$, $4.95 \times 10^{-9}$ and $6.31 \times 10^{-9}$ cm$^2$/sec respectively for CuF4, CuF5 and CuF6 (Table 5).
Table-4: Duration of evaluation, average release rate and coefficients of linear regressions, R1 and R2 of formulations of fenthion (10%) from CuCMC and FeCMC matrices.

<table>
<thead>
<tr>
<th>Code</th>
<th>Duration of evaluation (wk)</th>
<th>Release rate (mg/wk)</th>
<th>Coefs. of linear regression</th>
</tr>
</thead>
<tbody>
<tr>
<td>CuF4</td>
<td>39</td>
<td>6.5108</td>
<td>0.9797 0.9916</td>
</tr>
<tr>
<td>CuF5</td>
<td>39</td>
<td>5.1474</td>
<td>0.9774 0.9912</td>
</tr>
<tr>
<td>CuF6</td>
<td>39</td>
<td>5.8968</td>
<td>0.9860 0.9911</td>
</tr>
<tr>
<td>FeF4</td>
<td>26</td>
<td>9.9616</td>
<td>0.9740 0.9968</td>
</tr>
<tr>
<td>FeF5</td>
<td>27</td>
<td>7.6944</td>
<td>0.9446 0.9946</td>
</tr>
<tr>
<td>FeF6</td>
<td>27</td>
<td>7.2852</td>
<td>0.9271 0.9889</td>
</tr>
</tbody>
</table>

Table-5: Values of release exponent (n), kinetic constant (k), regression coefficient (R3) and the apparent diffusion coefficient (D) of formulations of fenthion (10%) from CuCMC and FeCMC matrices.

<table>
<thead>
<tr>
<th>Code</th>
<th>Release exponent, n</th>
<th>Constant, k</th>
<th>Coef. of regression, R3</th>
<th>Dxx10^-9 (cm^2/sec)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CuF4</td>
<td>0.4268</td>
<td>0.1877</td>
<td>0.9896</td>
<td>4.0025</td>
</tr>
<tr>
<td>CuF5</td>
<td>0.4470</td>
<td>0.1786</td>
<td>0.9911</td>
<td>4.9518</td>
</tr>
<tr>
<td>CuF6</td>
<td>0.4830</td>
<td>0.1562</td>
<td>0.9906</td>
<td>6.3083</td>
</tr>
<tr>
<td>FeF4</td>
<td>0.5846</td>
<td>0.1471</td>
<td>0.9945</td>
<td>18.2549</td>
</tr>
<tr>
<td>FeF5</td>
<td>0.5083</td>
<td>0.1941</td>
<td>0.9911</td>
<td>13.4945</td>
</tr>
<tr>
<td>FeF6</td>
<td>0.4529</td>
<td>0.2310</td>
<td>0.9862</td>
<td>9.5718</td>
</tr>
</tbody>
</table>
Fig. 10. Release profile of fenthion from CuF4.

Fig. 11. Release profile of fenthion from CuF5.
Fig. 12. Release profile of fenthion from CuF6.

Fig. 13. Release profile of fenthion from FeF4.
It has been observed that there was a decrease in release rate and the values of diffusion coefficient as the concentration of fenthion was halved. The formulations CuF4 and CuF5 exhibited square-root time release profile whereas CuF6 followed a non-Fickian release as seen from the values of n and the regression coefficients.

4.6.2.2. Formulations based on the matrices of FeCMC:

Formulations containing 10% fenthion in FeCMC matrices with the crosslinking periods of 12, 24 and 48 hours (FeF4, FeF5 and FeF6 respectively) displayed matrix stability for 26, 27 and 27 weeks (Table 4) during the laboratory evaluation (Recipe-2).

The release profiles of the three matrices, FeF4, FeF5 and FeF6 are presented in Figs. 13, 14 & 15 respectively. The values of X-coefficient of the linear regression of the cumulative release (Mt) on time were 9.96, 7.69 and 7.29 respectively for formulations FeF4, FeF5 and FeF6 and corresponding values of D were $18.25 \times 10^{-9}$, $13.49 \times 10^{-9}$ and $9.57 \times 10^{-9}$ cm/sec (Tables 4 & 5).

Values of regression coefficients, release exponent and kinetic constant are given in Tables 4 & 5. Comparison of the diffusion coefficient and release rate between formulations with cupric and ferric ions, FeCMC matrices exhibited higher values. The values of n, R1 and R2 showed that these matrices exhibited a non-Fickian release behaviour.
Fig. 14. Release profile of fenthion from FeF5.

Fig. 15. Release profile of fenthion from FeF6.
Among the twelve formulations based on CuCMC and FeCMC matrices studied in the laboratory for matrix stability and release characteristics, formulations prepared by crosslinking with copper ion were found to have more physical integrity in water for 39 weeks compared to 27 weeks observed with FeCMC matrices. The formulations based on CuCMC matrices exhibited either square-root time or non-Fickian release profile whereas formulations based on FeCMC matrices followed non-Fickian mode of release. All these formulations were suspending in water during the entire evaluation period in the laboratory.

4.6.3. Formulations of 20% fenthion in NaCMC-gelatin (4:1):

4.6.3.1. Formulations based on CuCMC-gelatin:

Matrices containing 20% fenthion with respect to NaCMC in NaCMC-gelatin (4:1) matrices were further crosslinked with 1.0 M cupric ion to get CugelF1, CugelF2 and CugelF3 respectively when the crosslinking durations were 12, 24 and 48 hours (Recipe-3). These three matrices were evaluated for 48, 55 and 54 weeks (Table 6) respectively in the increasing order of crosslinking duration.

The release profiles of fenthion are given in Figs. 16, 17 & 18 respectively for CugelF1, CugelF2 and CugelF3 and the quantities of fenthion released from these matrices during the first week of release were 28.31, 33.70 and 39.19 mg. The average release rates,
Table 6: Duration of evaluation, average release rate and coefficients of linear regressions, R1 and R2 of formulations of fenthion (20%) from CuCMC-gelatin (4:1) and FeCMC-gelatin (4:1) matrices.

<table>
<thead>
<tr>
<th>Code</th>
<th>Duration of evaluation (wk)</th>
<th>Release rate (mg/wk)</th>
<th>Coefts. of linear regression</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>R1</td>
</tr>
<tr>
<td>CugelF1</td>
<td>48</td>
<td>8.4980</td>
<td>0.9879</td>
</tr>
<tr>
<td>CugelF2</td>
<td>55</td>
<td>7.7916</td>
<td>0.9869</td>
</tr>
<tr>
<td>CugelF3</td>
<td>54</td>
<td>7.7117</td>
<td>0.9898</td>
</tr>
<tr>
<td>FegelF1</td>
<td>7</td>
<td>21.7607</td>
<td>0.9907</td>
</tr>
<tr>
<td>FegelF2</td>
<td>7</td>
<td>21.3884</td>
<td>0.9978</td>
</tr>
<tr>
<td>FegelF3</td>
<td>11</td>
<td>16.4258</td>
<td>0.9961</td>
</tr>
</tbody>
</table>

Table 7: Values of release exponent (n), kinetic constant (k), regression coefficient (R3) and apparent diffusion coefficient (D) of formulations of fenthion (20%) from CuCMC-gelatin (4:1) and FeCMC-gelatin (4:1) matrices.

<table>
<thead>
<tr>
<th>Code</th>
<th>Release exponent, n</th>
<th>Constant, k</th>
<th>Coef. of regression, R3</th>
<th>Dx10^-9 (cm²/sec)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CugelF1</td>
<td>0.7280</td>
<td>0.0607</td>
<td>0.9950</td>
<td>16.4840</td>
</tr>
<tr>
<td>CugelF2</td>
<td>0.6809</td>
<td>0.0664</td>
<td>0.9967</td>
<td>12.6435</td>
</tr>
<tr>
<td>CugelF3</td>
<td>0.6693</td>
<td>0.0682</td>
<td>0.9976</td>
<td>11.8328</td>
</tr>
<tr>
<td>FegelF1</td>
<td>1.3752</td>
<td>0.0849</td>
<td>0.9942</td>
<td>175.6399</td>
</tr>
<tr>
<td>FegelF2</td>
<td>1.0320</td>
<td>0.0929</td>
<td>0.9960</td>
<td>135.4922</td>
</tr>
<tr>
<td>FegelF3</td>
<td>0.9765</td>
<td>0.0690</td>
<td>0.9926</td>
<td>81.2213</td>
</tr>
</tbody>
</table>
Fig. 16. Release profile of fenthion from Cugel Fl.

Fig. 17. Release profile of fenthion from Cugel F2.
Fig. 18. Release profile of fenthion from Cugel F3

Fig. 19. Release profile of fenthion from Fegel F1 (□), Fegel F2 (○) and Fegel F3 (△).
the values of the release exponent, kinetic constant, apparent diffusion coefficients and the values of linear regression coefficients are presented in Tables 6 & 7.

The value of the release exponent, n was found to be higher than that of the matrices of CuCMC containing 20% fenthion. A maximum value of 0.7280 was obtained with formulation CugelF1, followed by 0.6809 for CugelF2 and 0.6693 for CugelF3. All these three formulations thus exhibited a non-Fickian release pattern with a proximity towards zero-order kinetics.

The initial burst effect observed with CuCMC formulations was considerably reduced when the matrices contained the interactive polymer, gelatin. The matrices containing 25% of gelatin in NaCMC were found to have improved physical integrity and the average release rate was found to be slightly less than that of the respective formulations based on CuCMC matrices.

4.6.3.2. **Formulations based on FeCMC-gelatin:**

Formulations of fenthion (20%) in FeCMC-gelatin (4:1) matrices (Recipe-3) with the crosslinking durations of 12, 24 and 48 hours in 1.0 M ferric ion, FegelF1, FegelF2 and FegelF3 were intact for 7, 7 and 11 weeks (Table 6) respectively during the release profile studies conducted in the laboratory.
The weekly release profiles of fenthion are given in Fig. 19. The average release rates, values of \( n \), \( k \), \( D \) and regression coefficients are presented in Tables 6 & 7. The formulations of fenthion based on FeCMC-gelatin were found to have reduced physical integrity compared to those without gelatin. This may be due to the lower crosslink densities and excessive swelling of the matrices followed by hydrolysis of the crosslinks.

4.6.4. Formulations of 10% fenthion in NaCMC-gelatin (4:1):

4.6.4.1. Formulations based on CuCMC-gelatin:

Formulations, CugelF4, CugelF5 and CugelF6, containing 10% fenthion in CuCMC-gelatin (4:1) matrices with the respective crosslinking durations of 12, 24 and 48 hours, were prepared (Recipe-4) and evaluated for 54 weeks (Table 8). The release profiles are presented in Figs. 20, 21 & 22. The quantities of fenthion released during the first week from these formulations were 13.77, 14.55 and 16.02 mg respectively in the order of increasing crosslinking period. The average release rate, values of the release exponent, kinetic constant, diffusion coefficient and the regression coefficients are presented in Tables 8 & 9. CugelF4 exhibited a higher value of the release exponent, 0.7934 followed by 0.7346 for CugelF5 and 0.7243 for CugelF6.

Among the formulations obtained by crosslinking with cupric ion,
Square-root of time (weeks)

Fig. 20. Release profile of fenthion from Cugel F4.

Fig. 21. Release profile of fenthion from Cugel F5.
Fig. 22. Release profile of fenthion from Cugel F6.

Fig. 23. Release profile of fenthion from Fegel F4 (□), Fegel F5 (○) and Fegel F6 (△).
Table-8: Duration of evaluation, average release rate and coefficients of linear regressions, R1 and R2 of formulations of fenthion (10%) from CuCMC-gelatin (4:1) and FeCMC-gelatin (4:1) matrices.

<table>
<thead>
<tr>
<th>Code</th>
<th>Duration of evaluation (wk)</th>
<th>Release rate (mg/wk)</th>
<th>Coefts. of linear regression</th>
</tr>
</thead>
<tbody>
<tr>
<td>CugelF4</td>
<td>54</td>
<td>7.1796</td>
<td>0.9742</td>
</tr>
<tr>
<td>CugelF5</td>
<td>54</td>
<td>6.0032</td>
<td>0.9690</td>
</tr>
<tr>
<td>CugelF6</td>
<td>54</td>
<td>5.8669</td>
<td>0.9738</td>
</tr>
<tr>
<td>FegelF4</td>
<td>8</td>
<td>19.7393</td>
<td>0.9894</td>
</tr>
<tr>
<td>FegelF5</td>
<td>14</td>
<td>14.1972</td>
<td>0.9832</td>
</tr>
<tr>
<td>FegelF6</td>
<td>15</td>
<td>12.9923</td>
<td>0.9962</td>
</tr>
</tbody>
</table>

Table-9: Values of release exponent (n), kinetic constant (k), regression coefficient (R3) and the apparent diffusion coefficient (D) of formulations of fenthion (10%) from CuCMC-gelatin (4:1) and FeCMC-gelatin (4:1) matrices.

<table>
<thead>
<tr>
<th>Code</th>
<th>Release exponent, n</th>
<th>Constant, k</th>
<th>Coeft. of regression, R3</th>
<th>D x 10^{-9} (cm^2/sec)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CugelF4</td>
<td>0.7934</td>
<td>0.0487</td>
<td>0.9807</td>
<td>20.0581</td>
</tr>
<tr>
<td>CugelF5</td>
<td>0.7346</td>
<td>0.0606</td>
<td>0.9778</td>
<td>17.3043</td>
</tr>
<tr>
<td>CugelF6</td>
<td>0.7243</td>
<td>0.0628</td>
<td>0.9872</td>
<td>16.7817</td>
</tr>
<tr>
<td>FegelF4</td>
<td>1.2234</td>
<td>0.0858</td>
<td>0.9832</td>
<td>224.5526</td>
</tr>
<tr>
<td>FegelF5</td>
<td>1.2540</td>
<td>0.0778</td>
<td>0.9848</td>
<td>224.3034</td>
</tr>
<tr>
<td>FegelF6</td>
<td>1.1839</td>
<td>0.0609</td>
<td>0.9889</td>
<td>151.3685</td>
</tr>
</tbody>
</table>
matrices which contained gelatin (25%) showed better physical integrity and constant release behaviour of fenthion during the laboratory evaluation. Also, the maximum value of the release exponent observed with CuCMC matrices was 0.5171 (CuF1) whereas matrices which contained gelatin exhibited a higher value for the release exponent, 0.7934 (CugelF4).

4.6.4.2. Formulations based on FeCMC-gelatin:

Laboratory evaluation of the formulations, FegelF4, FegelF5 and FegelF6, with the respective crosslinking duration of 12, 24 and 48 hours in 1.0 M ferric ion (Recipe-4) was conducted for 8, 14 and 15 weeks respectively till the matrices started extensive erosion. Weekly release profiles of the three formulations are presented in Fig. 23. The values of average release rate, n, k, D, R1, R2 and R3 are presented in Tables 8 & 9.

The values of the release exponent were relatively higher when the NaCMC-gelatin (4:1) matrix was crosslinked with ferric ion compared to the rest of the formulations of fenthion studied. But these matrices were found to have limited physical stability in water (7 to 15 weeks). The observed higher value of n was mainly due to the faster erosion of the matrices which resulted in higher release rate.
4.6.5. **Formulations insolubilised in 0.5 M gelling agents:**

The influence of the concentration of the gelling agent on the matrix stability and the release pattern of fenthion was also studied with matrices containing 10% of fenthion in NaCMC (Recipe-2) and NaCMC-gelatin (4:1) (Recipe-4) crosslinked with 0.5 M solution of both the gelling agents. Thus four matrices were obtained, CuF7 and CugelF7, crosslinked in 0.5 M solution of cupric ion and FeF7 and FegelF7, crosslinked in ferric chloride solution for 24 hours.

CuF7 and FeF7 were evaluated for 34 and 33 weeks respectively and the release profiles are presented in Figs. 24 & 25. The average release rate of fenthion from these matrices were 4.61 and 9.28 mg/week and the values of the release exponent were 0.4033 and 0.5725 for CuF7 and FeF7 respectively (Tables 10 & 11). Matrix CugelF7 was evaluated for 33 weeks and the average release rate was 5.32 mg/week. The release profile is presented in Fig. 26. FegelF7, obtained by crosslinking under the similar conditions with ferric ion was intact for only 8 weeks (Table 10) and the release profile is represented in Fig. 27a.

In the case of CuCMC matrices, when the crosslinking was carried out with 0.5 M solution of the gelling agent, the physical integrity as well as the value of the release exponent have been lowered as seen in CuF7 (34 weeks, 0.4033) compared to CuF5 (39 weeks, 0.4470) obtained with 1.0 M solution. But in FeCMC matrices, crosslinking in
Fig. 24. Release profile of fenthion from CuF7.

Fig. 25. Release profile of fenthion from FeF7.
Fig. 26. Release profile of fenthion from Egel F7.

Fig. 27. Release profile of fenthion from Fegel F7 (○), and Fegel F8 (●).
0.5 M solution has increased both these parameters as seen in FeF7 (33 weeks, 0.5725) compared to FeF5 (27 weeks, 0.5083) obtained with 1.0 M solution of the gelling agent. The observed variation in physical integrity may be due to the difference in the initial crosslink densities of the respective matrices (Figs. 1 & 2).

4.6.6. Formulations of 10% fenthion in crosslinked matrices of NaCMC-gelatin (10:1): 

Incorporation of 25% gelatin in NaCMC matrices and further crosslinking with cupric ion resulted in matrices with increased matrix stability and improved release characteristics of fenthion. When the gelling agent was ferric ion, the matrix integrity was found to be less than that of the respective matrices without the interactive biopolymer gelatin insolubilised under identical conditions. Matrices were made which contain 10% gelatin and 10% fenthion in NaCMC matrices and crosslinked with the two gelling agents.

4.6.6.1 Matrices crosslinked in 1.0 M gelling agent: 

Matrices obtained by crosslinking in 1.0 M solution of each cupric and ferric ion for 24 hours (Recipe-5), CugelF8 and FegelF8 exhibited physical integrity for 22 and 11 weeks and the release profiles are presented in Figs. 28 & 27b respectively. The values of n, k, D and the coefficients of the linear regression are presented
Fig. 28. Release profile of fenthion from Cugel F8.

Fig. 29. Release profile of fenthion from Cugel F9.
in Tables 10 & 11. The values of $n$ were 0.6457 and 1.0302 respectively for the matrices CugelF8 and FegelF8.

4.6.6.2. Matrices crosslinked in 0.5 M gelling agent:

Two formulations, which contained 10% fenthion and 10% gelatin (Recipe-5) crosslinked in 0.5 M solution of the crosslinking agents, copper sulphate and ferric chloride for 24 hours, CugelF9 and FegelF9 were found to have physical integrity for a period of 21 weeks. The matrix stability of the formulation CugelF9 was found almost equal to that crosslinked in 1.0 M solution of cupric ion (CugelF8, 22 weeks). But the stability of FegelF9 was considerably increased from 11 weeks to 21 weeks compared to FegelF8.

The release profiles of fenthion from CugelF9 and FegelF9 are presented in the respective Figs. 29 & 30. Values of $n$, $k$, $D$ and regression coefficients are presented in Tables 10 & 11.

Among the formulations of fenthion, the matrices crosslinked with cupric ion were found to have matrix integrity for 39 weeks during the laboratory evaluation with an average release rate of 5.15 to 11.91 mg/week. The formulations obtained with ferric chloride as the crosslinking agent were evaluated for 16 to 27 weeks with an average release rate ranging from 7.29 to 26.80 mg/week.
### Table-10: Duration of evaluation, average release rate and coefficients of linear regression, R1 and R2 of formulations of fenthion (10%) from crosslinked NaCMC and NaCMC-gelatin matrices.

<table>
<thead>
<tr>
<th>Code</th>
<th>Duration of evaluation (wk)</th>
<th>Release rate (mg/wk)</th>
<th>Coefts. of linear regression R1</th>
<th>R2</th>
</tr>
</thead>
<tbody>
<tr>
<td>CuF7</td>
<td>34</td>
<td>4.6142</td>
<td>0.9671</td>
<td>0.9954</td>
</tr>
<tr>
<td>CuF7L</td>
<td>34</td>
<td>5.3162</td>
<td>0.8523</td>
<td>0.9485</td>
</tr>
<tr>
<td>CuF8L</td>
<td>22</td>
<td>6.6727</td>
<td>0.9837</td>
<td>0.9954</td>
</tr>
<tr>
<td>CuF9L</td>
<td>21</td>
<td>4.9869</td>
<td>0.9825</td>
<td>0.9934</td>
</tr>
<tr>
<td>FeF7</td>
<td>33</td>
<td>9.2783</td>
<td>0.9558</td>
<td>0.9950</td>
</tr>
<tr>
<td>FeF7L</td>
<td>8</td>
<td>38.5638</td>
<td>0.9864</td>
<td>0.9533</td>
</tr>
<tr>
<td>FeF8L</td>
<td>11</td>
<td>16.0425</td>
<td>0.9961</td>
<td>0.9697</td>
</tr>
<tr>
<td>FeF9L</td>
<td>21</td>
<td>10.9530</td>
<td>0.9809</td>
<td>0.9742</td>
</tr>
</tbody>
</table>

### Table-11: Values of release exponent (n), kinetic constant (k), regression coefficient (R3) and the apparent diffusion coefficient (D) of fenthion (10%) from crosslinked matrices of NaCMC and NaCMC-gelatin.

<table>
<thead>
<tr>
<th>Code</th>
<th>Release exponent, n</th>
<th>Constant, k</th>
<th>Coef. of regression, R3</th>
<th>Dx10⁻⁹ (cm²/sec)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CuF7</td>
<td>0.4033</td>
<td>0.2271</td>
<td>0.9945</td>
<td>4.2286</td>
</tr>
<tr>
<td>CuF7L</td>
<td>0.3605</td>
<td>0.3034</td>
<td>0.9554</td>
<td>4.0588</td>
</tr>
<tr>
<td>CuF8L</td>
<td>0.6457</td>
<td>0.1344</td>
<td>0.9986</td>
<td>27.1184</td>
</tr>
<tr>
<td>CuF9L</td>
<td>0.7004</td>
<td>0.1172</td>
<td>0.9915</td>
<td>33.6233</td>
</tr>
<tr>
<td>FeF7</td>
<td>0.5725</td>
<td>0.1405</td>
<td>0.9899</td>
<td>14.9592</td>
</tr>
<tr>
<td>FeF7L</td>
<td>1.0309</td>
<td>0.1321</td>
<td>0.9900</td>
<td>189.9138</td>
</tr>
<tr>
<td>FeF8L</td>
<td>1.0302</td>
<td>0.0900</td>
<td>0.9948</td>
<td>130.4921</td>
</tr>
<tr>
<td>FeF9L</td>
<td>1.0495</td>
<td>0.0176</td>
<td>0.9917</td>
<td>76.1061</td>
</tr>
</tbody>
</table>
Fig. 30. Release profile of fenthion from Pegel F9.
The release profile analysis of these formulations showed that the values of the release exponent were relatively higher with the formulations crosslinked with ferric chloride than with copper sulphate. The maximum value of the release exponent observed with the matrices with cupric ion was 0.5171 (CuF1) whereas with the ferric ion crosslinked matrices, the maximum value of the release exponent was 0.6817 (FeF2). The release of fenthion from these formulations has been found to follow a non-Fickian release pattern.

When an interactive polymer gelatin was used in combination with NaCMC followed by crosslinking with the two metal ions, the matrices crosslinked with cupric ion showed improved matrix stability than those with ferric ion. The former matrices were evaluated for 54 weeks whereas the matrices with ferric ion disintegrated within 11 weeks. The average release rate of fenthion from matrices crosslinked with cupric ion was found to range from 5.87 to 8.50 mg/week and the highest value of 0.7934 (CugelF4) for the release exponent was observed.

4.7. Formulations of Diflubenzuron:

The results on the release behaviour of fenthion from the matrices of crosslinked NaCMC and NaCMC in combination with the interactive polymer, gelatin, prompted us to develop formulations with diflubenzuron, an insect growth regulator known as a chitin synthesis inhibitor. The proportion of gelatin used in these
formulations was only 10% with respect to NaCMC as the matrix which contained 25% of gelatin was not able to keep its suspending nature when introduced in water.

4.7.1. **Formulations based on CuCMC and FeGMC matrices:**

Two formulations, CuDl and FeDl obtained, when NaCMC matrix containing 10% diflubenzuron (Recipe-6) was crosslinked in 1.0 M solution of copper sulphate and ferric chloride for 24 hours, were intact for a period of 33 weeks with the average release rate of 4.90 $\times 10^{-9}$ and 3.45 mg/week and apparent diffusion coefficient of 5.60$\times 10^{-9}$ and 3.02$\times 10^{-9}$ cm$^2$/sec respectively (Tables 12 & 13).

The release profiles of diflubenzuron from CuDl and FeDl are presented in Figs. 31 & 32 respectively. The values of n indicated that CuDl has only an approaching square root time release profile whereas FeDl deviated away from square root time release profile (Tables 12 & 13).

4.7.2. **Formulations based on crosslinked NaCMC-gelatin (10:1):**

Formulations, CugelDl and FegelDl were obtained when NaCMC-gelatin in the ratio of 10:1, containing 10% diflubenzuron (Recipe-7) was crosslinked in 1.0 M solution and CugelD2 and FegelD2 were obtained in 0.5 M solution of the insolubilising agents, copper sulphate and ferric chloride respectively for 24 hours.
### Table-12: Duration of evaluation, average release rate and coefficients of linear regressions, R1 and R2 of formulations of diflubenzuron.

<table>
<thead>
<tr>
<th>Code</th>
<th>Duration of evaluation (wk)</th>
<th>Release rate (mq/wk)</th>
<th>Coeffs. of linear regression R1</th>
<th>R2</th>
</tr>
</thead>
<tbody>
<tr>
<td>CuD1</td>
<td>33</td>
<td>4.8985</td>
<td>0.9486</td>
<td>0.9879</td>
</tr>
<tr>
<td>FeD1</td>
<td>33</td>
<td>3.4462</td>
<td>0.9194</td>
<td>0.9730</td>
</tr>
<tr>
<td>CugelD1</td>
<td>34</td>
<td>2.8289</td>
<td>0.9793</td>
<td>0.9868</td>
</tr>
<tr>
<td>FegelD1</td>
<td>16</td>
<td>4.5939</td>
<td>0.9576</td>
<td>0.9933</td>
</tr>
<tr>
<td>CugelD2</td>
<td>31</td>
<td>3.1059</td>
<td>0.9948</td>
<td>0.9841</td>
</tr>
<tr>
<td>FegelD2</td>
<td>20</td>
<td>3.6960</td>
<td>0.9893</td>
<td>0.9600</td>
</tr>
</tbody>
</table>

### Table-13: Values of release exponent (n), kinetic constant (k), regression coefficient, R3 and the apparent diffusion coefficient (D) of formulations of diflubenzuron.

<table>
<thead>
<tr>
<th>Code</th>
<th>Release exponent, n</th>
<th>Constant, k</th>
<th>Coeff. of regression, R3</th>
<th>Dx×10^{-9} (cm²/sec)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CuD1</td>
<td>0.4304</td>
<td>0.2113</td>
<td>0.9734</td>
<td>5.5963</td>
</tr>
<tr>
<td>FeD1</td>
<td>0.3640</td>
<td>0.2656</td>
<td>0.9625</td>
<td>3.0153</td>
</tr>
<tr>
<td>CugelD1</td>
<td>0.4960</td>
<td>0.1542</td>
<td>0.9924</td>
<td>7.3233</td>
</tr>
<tr>
<td>FegelD1</td>
<td>0.5414</td>
<td>0.2187</td>
<td>0.9787</td>
<td>24.2056</td>
</tr>
<tr>
<td>CugelD2</td>
<td>0.6269</td>
<td>0.1089</td>
<td>0.9862</td>
<td>16.5558</td>
</tr>
<tr>
<td>FegelD2</td>
<td>0.6337</td>
<td>0.1208</td>
<td>0.9830</td>
<td>20.7379</td>
</tr>
</tbody>
</table>
Fig. 31. Release profile of diflubenzuron from CuDL.

Fig. 32. Release profile of diflubenzuron from FeDL.
CuD1 and FeD1 maintained physical stability for 34 and 16 weeks respectively and the profiles are presented in Figs. 33 & 34. The values of n were 0.4960 and 0.5414 respectively for CuD1 and FeD1, showing that the addition of gelatin improved the release characteristics of the formulations to follow a non-Fickian mode of release (Tables 12 & 13).

CuD2 and FeD2 showed matrix stability for 31 and 20 weeks respectively (Figs. 35 & 36). The average release rates were 3.11 and 3.70 mg/week and the values of n were 0.6269 and 0.6337 respectively for the formulations CuD2 and FeD2. The values of D and the coefficients of linear regression are presented in Tables 12 & 13.

Among the six formulations of diflubenzuron studied, maximum matrix stability was observed with CuD1 and FeD1. But the release rate of diflubenzuron from these matrices was not constant. Addition of gelatin into these matrices resulted in improvement of release characteristics as seen in the formulation FeD2 eventhough the matrix was not relatively stable (20 weeks). Whereas CuD2 with appreciable matrix stability (31 weeks) and the value of n (0.6269) had desired characteristics.

4.8. Formulations of Temephos:

Four formulations of temephos were made containing 10% of temephos with respect to NaCMC in NaCMC-gelatin (10:1) (Recipe-8).
Fig. 33. Release profile of diflubenzuron from CugelD1.

Fig. 34. Release profile of diflubenzuron of FegelD1.
Fig. 35. Release profile of diflubenzuron from CugelD2.

Fig. 36. Release profile of diflubenzuron from PegelD2.
The formulations, CugelT1 and FegelT1 in 1.0 M solution and CugelT2 and FegelT2 with 0.5 M solution of the respective crosslinking agents, copper sulphate and ferric chloride for 24 hours.

The laboratory evaluation of CugelT1 and FegelT1 indicated that the matrices obtained by crosslinking in 1.0 M solution were intact for 34 and 11 weeks as shown in the respective Figs. 37 & 38. Whereas CugelT2 and FegelT2 were intact for 31 and 21 weeks (Figs. 39 & 40).

The values of n were 0.6001, 0.9774, 0.6614 and 0.9575 respectively for the matrices CugelT1, FegelT1, CugelT2 and FegelT2. The values of D and coefficients of linear regressions are presented in Tables 14 & 15. Among the four formulations of temephos, CugelT2 was found to have maximum physical integrity and desired release characteristics.

4.9. Dynamic and Equilibrium Swelling Properties of the Crosslinked Polymers:

Crosslinked polymeric materials can swell to a considerable degree with many organic solvents as well as with water. The degree of swelling is reduced by increasing crosslinking density. The solute diffusion coefficient also increases with increasing swelling and this can be used as a means of controlling the rate of release of incorporated solutes. The ability of a polymer to swell with a solvent is dependent on the free energy of mixing of the solvent with
Fig. 37. Release profile of temephos from CugelT1.

Fig. 38. Release profile of temephos from FegelT1.
Fig. 39. Release profile of temephos from CugelT2.

Fig. 40. Release profile of temephos from PegelT2.
Table-14: Duration of evaluation, average release rate and coefficients of linear regressions, R1 and R2 of formulations of temephos.

<table>
<thead>
<tr>
<th>Code</th>
<th>Duration of evaluation (wk)</th>
<th>Release rate (mg/wk)</th>
<th>Coefts. of linear regression</th>
</tr>
</thead>
<tbody>
<tr>
<td>CugelT1</td>
<td>34</td>
<td>7.3260</td>
<td>0.9878</td>
</tr>
<tr>
<td>FegelT1</td>
<td>11</td>
<td>14.5030</td>
<td>0.9946</td>
</tr>
<tr>
<td>CugelT2</td>
<td>31</td>
<td>5.9915</td>
<td>0.9714</td>
</tr>
<tr>
<td>FegelT2</td>
<td>21</td>
<td>13.4459</td>
<td>0.9949</td>
</tr>
</tbody>
</table>

Table-15: Values of release exponent (n), kinetic constant (k), regression coefficient (R3) and the apparent diffusion coefficient (D) of formulations of temephos.

<table>
<thead>
<tr>
<th>Code</th>
<th>Release exponent, n</th>
<th>Constant, k</th>
<th>Coeфт. of regression, R3</th>
<th>D x 10^{-9} (cm²/sec)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CugelT1</td>
<td>0.6001</td>
<td>0.1162</td>
<td>0.9986</td>
<td>14.2601</td>
</tr>
<tr>
<td>FegelT1</td>
<td>0.9774</td>
<td>0.0884</td>
<td>0.9925</td>
<td>105.0578</td>
</tr>
<tr>
<td>CugelT2</td>
<td>0.6614</td>
<td>0.1109</td>
<td>0.9926</td>
<td>22.9549</td>
</tr>
<tr>
<td>FegelT2</td>
<td>0.9575</td>
<td>0.0555</td>
<td>0.9953</td>
<td>59.6463</td>
</tr>
</tbody>
</table>
the polymer and inversely related to the crosslink density within the polymer (Yasuda et al., 1968; Yasuda et al., 1969; Yasuda and Lamaze, 1971; Hopfenberg and Hsu, 1978; Korsmeyer et al., 1986a and 1986b; Peppas and Lustig, 1986; Peppas et al., 1986; Lee and Peppas, 1987; Peppas, 1987b; Kost and Langer, 1987; Peppas and Korsmeyer, 1987; Lustig and Peppas, 1988; Harland et al., 1988; Harland and Peppas, 1989).

The insolubilised NaCMC samples were found to swell in water and therefore the studies on the dynamic and equilibrium swelling properties of the different insolubilised polymer samples were carried out. Polymer samples for the swelling studies were prepared by crosslinking the matrices of NaCMC, NaCMC-gelatin (10:1) and NaCMC-gelatin (4:1). The crosslinking was carried out in 1.0 M solution of copper sulphate and ferric chloride for 12, 24 and 48 hours.

4.9.1. Dynamic swelling of samples crosslinked with cupric ion:

The initial weight and volume of polymer samples dried to constant weight were determined. Volume of the each sample was measured by volume balance method (Brannon-Peppas and Peppas, 1990; Walker and Peppas, 1990; Thanoo and Jayakrishnan, 1990).

The dynamic swelling behaviour of different insolubilised samples as a plot of swelling ratio against time is presented in Fig. 41 for
CuCMC samples, Fig. 42 for CuCMC-gelatin (10:1) samples and Fig. 43 for CuCMC-gelatin (4:1) samples crosslinked for 12, 24 and 48 hours respectively in 1.0 M copper sulphate.

The swelling ratios of the samples increased rapidly during initial 24 hours and the increase was relatively slow thereafter till the equilibrium swelling ratio was reached.

4.9.2. Dynamic swelling of samples crosslinked with ferric ion:

Figs. 44, 45 & 46 show the dynamic swelling behaviour of the respective insolubilised FeCMC, FeCMC-gelatin (10:1) and FeCMC-gelatin (4:1) samples crosslinked for 12, 24 and 48 hours in 1.0 M ferric chloride. There was a marked difference in the dynamic swelling pattern of the polymer samples based on their extents of crosslinking.

4.9.3. Equilibrium swelling ratios of the polymer samples insolubilised with cupric ion:

The equilibrium swelling ratios of the insolubilised samples at different extents of crosslinking are presented in the Fig. 47. Samples with 12 hours of crosslinking exhibited maximum value for the equilibrium swelling ratio and the values were 2.06, 2.53 and 2.76 respectively for samples CuCMC, CuCMC-gelatin (10:1) and CuCMC-gelatin (4:1). The swelling ratios of the respective samples
Fig. 41. Dynamic swelling behaviour of NaCMC samples cross linked in 1.0 M copper sulphate for 12 (□), 24 (○) and 48 (△) hours.

Fig. 42. Dynamic swelling behaviour of NaCMC-gelatin (10:1) samples crosslinked in 1.0 M copper sulphate for 12 (□), 24 (○) and 48 (△) hours.
Fig. 43. Dynamic swelling behaviour of NaCMC-gelatin (4:1) crosslinked in 1.0 M copper sulphate for 12 (□), 24 (○), and 48 (△) hours.

Fig. 44. Dynamic swelling behaviour of NaCMC samples crosslinked in 1.0 M ferric chloride for 12 (□), 24 (○) and 48 (△) hours.
Fig. 45. Dynamic swelling behaviour of NaCMC-gelatin (10:1) samples crosslinked in 1.0 M ferric chloride for 12 (□), 24 (○) and 48 (△) hours.

Fig. 46. Dynamic swelling behaviour of NaCMC-gelatin (4:1) samples crosslinked in 1.0 M ferric chloride for 12 (□), 24 (○) and 48 (△) hours.
crosslinked for 24 hours were 2.02, 2.20 and 2.64. At 48 hours of crosslinking, the values of equilibrium swelling ratios were 1.85, 1.98 and 2.45 respectively for the above three samples. A minimum value of the equilibrium swelling ratio was observed with the CuCMC matrix crosslinked for 48 hours.

4.9.4. Equilibrium swelling ratios of the polymer samples

insolubilised with ferric ion:

The equilibrium swelling ratios of the samples crosslinked with ferric chloride for 12 hours were 2.50, 3.99 and 4.23 respectively for FeCMC, FeCMC-gelatin (10:1) and FeCMC-gelatin (4:1). At 24 hours of crosslinking, the swelling ratios were 1.34, 2.57 and 3.12 and the samples obtained after 48 hours of crosslinking duration exhibited the values of 1.18, 1.93 and 2.78 respectively for FeCMC, FeCMC-gelatin (10:1) and FeCMC-gelatin (4:1) (Fig. 47).

Among the polymer samples crosslinked with cupric and ferric ions at three different extents of crosslinking, FeCMC matrix crosslinked for 48 hours showed minimum value of equilibrium swelling ratio and FeCMC-gelatin (4:1) crosslinked for 12 hours exhibited the maximum value for swelling ratio.

The equilibrium swelling ratios of samples containing gelatin were higher than the crosslinked CMC samples at the respective extents of crosslinking with both the gelling agents. The equilibrium
Fig. 47. Equilibrium swelling ratios of the crosslinked polymer samples.

Fig. 48. Equilibrium water uptake per gm of the crosslinked polymer samples.

a) CuCMC; b) CuCMC-gelatin (10:1); c) CuCMC-gelatin (4:1)
d) FeCMC e) FeCMC-gelatin (10:1); f) FeCMC-gelatin (4:1).
swelling ratios were found to increase further when the gelatin content in the samples was increased from 10:1 to 4:1, NaCMC to gelatin. In all polymer samples the swelling ratios were found to decrease with increase in the crosslinking periods.

4.9.5. Equilibrium water content in the swollen samples:

The equilibrium water uptake per gm dry polymer weight of the samples at the equilibrium swelling is presented in Fig. 48. The values were 0.86, 0.75 and 0.74 respectively for CuCMC samples with the respective crosslinking extents of 12, 24 and 48 hours in 1.0 M cupric ion. The quantity of water absorbed was found to increase with the increase in gelatin content. A maximum quantity of water absorbed, 3.19 was found in the case of sample crosslinked for 12 hours which contained 4:1 NaCMC to gelatin, and the quantity of water absorbed was 2.8331 when the crosslinking period was 48 hours.

With ferric ion insolubilised matrices, the values of the quantity of the water absorbed per gm dry polymer weight of the samples were 1.39, 0.42 and 0.29 for FeCMC samples with the respective crosslinking periods of 12, 24 and 48 hours in 1.0 M ferric chloride. The quantity of water absorbed was found to increase with the increase in the gelatin content and the values were 2.70, 2.21 and 1.35 when the polymer samples contained NaCMC to gelatin in 10:1 proportion and at the ratio of 4:1, the quantities of water
absorbed per gm dry weight of samples were 4.71, 2.51 and 1.94 respectively for the crosslinking extents of 12, 24 and 48 hours.

Dehydrated hydrogels placed in water will swell to some equilibrium value. The driving force for water to enter the polymer is osmotic pressure. Strong interactions like hydrogen bonding between chemical structures of the polymer and water will further increase the driving force for swelling. The equilibrium swelling of a hydrogel is determined by the hydrophilicity, nature and extent of the crosslinking agent. Crosslink density of the hydrogels will cause lower degree of equilibrium swelling and result in decreased water content. The diffusion coefficient of the solute also decreases with increase in crosslinking density (Graham, 1986).

4.10. Studies on the Erosion of the Insolubilised Samples:

Matrices obtained by hydrophobic crosslinking of water soluble polymers when placed in water undergo erosion at the crosslinks as well as degradation of the backbone of the polymers. This may control the physical stability and the release rate of the incorporated active agent (Heller, 1980; Langer and Peppas, 1983). The insolubilised matrices obtained from NaCMC were found to undergo matrix erosion when placed in water. Therefore percentage of matrix erosion and erosion of the crosslinks were monitored after a period of three months in water.
4.10.1. Erosion of the crosslinks:

4.10.1.1. **Samples crosslinked with copper sulphate:**

The results of the percentage erosion of crosslinks after introducing in water for three months are presented in Fig. 49. The crosslink density of NaCMC sample when crosslinked with 1.0 M solution of the copper sulphate for 12 hours was found to decrease from 9.01% to 7.43% when released in water for three months with a percentage reduction in crosslink density of 17.55. The corresponding values of the percentage reduction in crosslink densities of the samples crosslinked for 24 and 48 hours were 21.50 and 25.23 with the respective initial crosslink densities of 9.62% and 10.13%.

When the insolubilised matrices containing 10% gelatin with respect to NaCMC with the initial crosslink densities of 8.12%, 8.91% and 9.63% for the respective crosslinked periods of 12, 24 and 48 hours in 1.0 M solution were subjected to erosion studies in water for three months, the values of the percentage reduction in copper ion were 19.73, 23.75 and 30.44 respectively.

The values of percentage loss in cupric ion were 25.47, 28.28 and 26.77 when the insolubilised samples of NaCMC-gelatin (4:1) with the crosslink densities of 7.83%, 8.26% and 8.44% for the respective crosslink periods of 12, 24 and 48 hours were studied for erosion in water for three months.
Fig. 49. Percentage erosion of the crosslinking agents after releasing in water for three months.

Fig. 50. Percentage erosion of the matrices after releasing in water for three months.

(a) CuCNC, (b) CuCNC-gelatin (10:1), (c) CuCNC-gelatin (4:1),
(d) FeCNC, (e) FeCNC-gelatin (10:1) and (f) FeCNC-gelatin (4:1)
4.10.1.2. **Samples crosslinked with ferric chloride:**

When NaCMC samples crosslinked in 1.0 M solution of ferric chloride for 12, 24 and 48 hours with the respective crosslink densities of 5.72%, 7.82% and 11.24% were released in water for a period of three months and studied for erosion, the values of percentage loss of ferric ion were 11.29, 14.25 and 12.32 respectively (Fig. 49).

When the insolubilised samples of NaCMC-gelatin (10:1) with initial crosslink densities of 5.42%, 5.99% and 7.11% were released in water for three months for monitoring erosion, the values of percentage loss of the ferric ion were 16.16, 17.95 and 25.80 respectively for the three crosslinking periods in the increasing order. Whereas with the samples containing 25% gelatin, the values for the percentage loss of ferric ion were 15.95, 23.50 and 38.51 respectively when the initial crosslinking densities were 3.46%, 4.48% and 6.41%.

The studies on the erosion of the crosslinking agent showed that the percentage loss of both copper and ferric ions from the matrices was proportional to the initial crosslink density. The percentage of metal ion erosion was found to increase with increase in gelatin content in the insolubilised matrices which may be due to the increased hydrophilicity facilitating the hydrolysis of the crosslinks.
4.10.2. Matrix erosion:

The results of the percentage erosion of the matrices during three months duration in water are presented in the Fig. 50. CuCMC matrices showed lower values of percentage matrix erosion than the matrices of CuCMC containing gelatin. The values were 15.69, 34.41 and 33.08% respectively when the samples of NaCMC, NaCMC-gelatin (10:1) and NaCMC-gelatin (4:1) were crosslinked for 48 hours in 1.0 M copper sulphate. The percentage of matrix erosion was found relatively higher when matrices containing 25% gelatin in the crosslinked matrices of FeCMC and the values were 65.61, 50.05 and 44.95% corresponding to the crosslinking duration of 12, 24 and 48 hours respectively. Out of the 18 samples studied for matrix erosion, the minimum value of the percentage matrix erosion was observed with CuCMC matrix obtained by crosslinking for 48 hours and the erosion was maximum in the case of sample of NaCMC-gelatin (4:1) obtained by crosslinking for 12 hours in 1.0 M ferric chloride. The erosion of the matrices was found to decrease with increase in the crosslinking duration and was directly proportional to the gelatin content in the matrices.

4.11. Scanning electron microscopic (SEM) studies:

The rate of release of active agent from polymer substrates is influenced by the texture of the controlled release product (Shasha et al., 1976; Korsmeyer and Peppas, 1981; Jeyanthi and Rao, 1990).
The surface texture of the products is reported to have more importance on the release profile than their internal structures (Schreiber and White, 1980). Therefore scanning electron micrographs of the surface of samples, NaCMC, NaCMC-gelatin (4:1), crosslinked polymer and formulated samples containing fenthion were studied at 300x magnification.

4.11.1. Micrographs of NaCMC and NaCMC-gelatin (4:1):

The scanning electron micrographs of NaCMC and NaCMC-gelatin (4:1) are presented in Plate 1. The micrographs show that by the addition of the interactive polymer gelatin, the crystalline surface texture of NaCMC is lost as a result of the strong electrostatic interaction between the macromolecular chains of NaCMC and gelatin, leading to agglomeration.

4.11.2. Micrographs of crosslinked polymers and formulations:

The micrographs of NaCMC sample crosslinked with cupric ion and CuCMC containing 20% fenthion are presented in Plate 2. The surface texture of the crosslinked samples show that CuCMC is amorphous and porous. The micrograph of CuCMC containing 20% fenthion shows that fenthion is uniformly dispersed in the crosslinked polymer as it interacts with the polymer structure.

The scanning electron micrographs of the samples obtained by
Scanning electron micrograph of the surface of NaCMC.

Scanning electron micrograph of the surface of NaCMC-gelatin (4:1).
Scanning electron micrograph of the surface of NaCMC crosslinked with cupric ion.

Scanning electron micrograph of the surface of the formulation of fenthion based on CuCMC matrix.
crosslinking NaCMC with ferric ion and FeCMC containing 20% fenthion are presented in Plate 3. The texture of pure FeCMC sample was found to be amorphous and porous but less porous than that obtained by crosslinking with cupric ion. In FeCMC sample containing 20% fenthion, the texture of the crosslinked matrix has been altered indicating that fenthion interacts with the crosslinked structure.

The micrographs obtained with the samples of crosslinked NaCMC-gelatin (4:1) matrices containing 20% fenthion with two crosslinking agents are shown in Plate 4.

The analysis of micrographs shows that the surface texture of NaCMC sample has been changed by the incorporation of the interactive polymer gelatin. The ionotropic crosslinking used for insolubilising NaCMC has also resulted in textural changes of the surface. The micrographs obtained with the crosslinked matrices containing fenthion show that fenthion may act as a plasticizer thereby reducing macromolecular interactions. The relatively high porous nature coupled with initial influx of water of CuCMC matrices compared to CuCMC-gelatin and FeCMC matrices may be responsible for the burst effect (high initial release rate) observed during the laboratory evaluation of the formulations with fenthion.

4.12. Mechanism of the Insecticide Release:

The release mechanism of an incorporated active agent from a
Scanning electron micrograph of the surface of NaCMC crosslinked with ferric ion.

Scanning electron micrograph of the surface of the formulation of fenthion based on FeCMC matrix.
Scanning electron micrograph of the surface of formulation of fenthion based on the matrix of NaCMC-gelatin (4:1) crosslinked with ferric ion.
polymeric monolithic device is determined by the rate limiting step of the release process (Langer and Peppas, 1980; Langer and Peppas, 1981). The release may be due to the pure active agent diffusion according to Fick's law (Crank, 1975), chemical reaction between the polymer and the dissolution medium (Heller, 1980 and 1984; Heller and Baker, 1980), or countercurrent diffusion of dissolution medium at a constant penetration velocity in the polymer (Hopfenberg and Hsu, 1978; Peppas, 1985; Korsmeyer et al., 1986; Rao and Padmalatha Devi, 1988; Vyavahare et al., 1990).

The scanning electron microscopic analysis of the crosslinked polymer samples and the samples containing fenthion showed that the crosslinked structure is highly amorphous and porous. Studies conducted on the dynamic and equilibrium swelling behaviour of the crosslinked polymers revealed that the water intake and swelling were very rapid in the initial hours (Figs. 41 to 46). The increase in the swelling ratios was not appreciable after a week period and therefore the advancement of the swelling interface at constant velocity was not observed. The studies conducted on the erosion of the crosslinks and the matrices showed that the ionotropic crosslinking was reversible when contacted with water resulting in the hydrolysis of the crosslinks. The matrix erosion is noticed when a critical number of crosslinks are hydrolysed.

The weekly release profile analysis of the formulations shows a high release rate of the active agent at the initial periods of the
release study. This burst effect may be due to the fact that the free insecticide on the surface is released into the medium as soon as the device is introduced in water. Besides, the initial rate of swelling followed by the penetration of swelling interface into the matrix is high and large amount of insecticide is released. The dynamic swelling ratios of FeCMC samples were relatively lower than those of CuCMC at the respective periods of swelling and the formulations based on the matrices of FeCMC (FeEl-FeF6) showed lower initial release rates compared to matrices of CuCMC (CuF1-CuF6). The formulations which contained the interactive polymer gelatin showed comparatively lower burst effect. This may be due to the less porous nature of the matrices resulting in the reduction of the interconnecting channels which assist the countercurrent diffusion of the insecticide during the initial ingression of water into the matrix. Such high initial rate of release from hydrophilic polymers has been noticed by many authors (Hopfenberg, 1976; Pramanick and Ray, 1990).

The values of the release exponent, determined for the entire period of the release study, showed that most of the formulations follow a non-Fickian or a profile which approaches zero-order kinetics. Therefore the release of fenthion may not be due to pure diffusion which generally follows Fickian release pattern. A swelling controlled release mechanism would not be possible as the continuous ingression of water followed by the movement of the swelling interface into the polymer matrix at constant velocity had not been
observed (Hopfenberg and Hsu, 1978; Thomas and Windle, 1982; Korsmeyer and Peppas, 1983).

The insolubilised matrices of NaCMC were found to erode in water. The hydrolytic crosslink cleavage of the matrices may occur on the surface as well as in the bulk. But the physical integrity of the matrices in water indicates that the crosslink cleavage takes place mainly on the surface than the bulk. Since the surface erosion generally takes place at a constant rate, the active agent release follows either non-Fickian or zero-order profile.

Eventhough the matrices of CuCMC underwent slower surface erosion than FeCMC and the crosslinked matrices of NaCMC-gelatin, the bulk erosion of CuCMC matrices was observed at an early period than in the case of CuCMC-gelatin. The physical integrity of FeCMC and CuCMC-gelatin was retained even after an appreciable reduction in their size.

The solute release from erodible matrices can be effected through diffusive mechanisms, by the erosion of the matrices or by the combination of diffusion and erosion (Heller, 1984). Matrices of CuCMC were found to erode slowly than FeCMC and crosslinked matrices of NaCMC-gelatin (Fig. 50). Eventhough CuCMC-gelatin matrices eroded faster than CuCMC matrices, the release rate of fenthion was higher in the latter matrices (Tables 2, 3, 4 and 5). This is due to the fact that the release of fenthion from CuCMC matrices is influenced
by both erosion of the matrices as well as the diffusion of the active agent. Whereas by incorporating the interactive polymer gelatin, the interconnecting channels of the water filled pores are reduced and the release of the active agent is mainly due to the erosion of the polymer. FeCMC matrices are also porous and undergo erosion and the release of the active agent from these matrices was faster than other matrices.

4.13. Thermal Analysis of the Formulations:

The storage life of pesticide formulations is influenced by both inherent stability of the active agent and the formulation adjuvants. The storage stability tests are generally performed under accelerated conditions of temperature.

4.13.1. Storage stability under accelerated temperature conditions:

Thermal stability tests of the formulations of fenthion under accelerated temperature condition, in open vials at 60 °C for two weeks were conducted as reported by Szente et al., 1990. The insolubilised NaCMC and NaCMC containing gelatin (10:1) samples with the two crosslinking agents in 1.0 M solution crosslinked for 24 hours were used for these tests. The loss of the insecticide observed during the testing procedure may be due to evaporation as well as the thermal degradation of fenthion which was determined by HPLC. Results
were compared with that of mechanical mixtures of the insecticide and the respective carrier polymers.

4.13.1.1. Mechanical mixtures of the polymer and fenthion:

Mechanical mixture of CuCMC containing 6.15% fenthion when subjected to the stability test, was found to contain 4.45% of fenthion and the corresponding percentage loss in active agent was 27.55. In the case of the mechanical mixture of FeCMC and fenthion, the active agent was reduced from the initial content of 8.38% to 5.15% after the stability test period and the percentage loss of fenthion was 38.52.

4.13.1.2. Formulations of fenthion:

When the formulated sample containing 12.14% of fenthion in CuCMC matrix was subjected to the thermal stability test, the content of fenthion was decreased to 10.52% and the corresponding percentage loss was 13.30. With the formulation of FeCMC, fenthion content was reduced to 8.19% from the initial concentration of 10.11% and the percentage loss of fenthion was 18.97.

Stability tests were also carried out with CuCMC and FeCMC samples containing fenthion at lower concentrations. In the samples which contained 4.42% and 4.61% of fenthion crosslinked with cupric and ferric ions respectively, fenthion content was reduced to 3.52%
and 3.64% with the corresponding values of percentage loss of active agent being 20.18 and 20.98.

When the formulated CuCMC sample containing 10% gelatin was studied, the percentage of fenthion was reduced to 2.91 from the initial content of 3.17 and the corresponding loss of fenthion was 8.08%. The similar formulation of FeCMC containing 10% gelatin showed a percentage loss of 9.43 with reduction in fenthion content from 3.61% to 3.27%.

The results of storage stability tests discussed above indicate that the thermal stability of fenthion was increased in the insolubilised NaCMC samples compared to the mechanical mixtures. The insolubilised matrices containing gelatin have been found to further improve the thermal stability of fenthion compared to CuCMC and FeCMC matrices.

4.13.2. Thermogravimetric analysis:

Thermogravimetric analysis (TGA) is a useful technique for the thermal characterisation of organic polymers (Anderson, 1966; Reich and Levi, 1967; Trask-Morrel and Andrews, 1991) and is also useful to study the thermal resistance of the incorporated active agents in controlled release pesticide formulations (Szente et al., 1990; Prasad et al., 1990). Thermograms of pure fenthion, NaCMC, CuCMC, FeCMC and the formulated samples were run from room temperature to
800°C. The heat resistance of fenithion in formulated samples was compared with pure fenithion and that in the mechanical mixture of fenithion and the carrier polymers.

4.13.2.1. Thermograms of pure fenithion and polymers:

The thermogram obtained with technical grade fenithion (Fig. 51) showed a weight loss which started at 130°C and attained a constant weight at 320°C, the total weight loss being 90%. Fig. 52 represents the thermogram obtained with NaCMC. The thermogram displayed a weight loss of 9.6% in the temperature range of 35 to 105°C corresponding to the moisture present in the sample and the major weight loss was between 230 and 380°C, accounting for 22.4%. This may be due to the decomposition of the carboxylate group with the evolution of CO and CO₂ (Bajaj et al., 1986). Pure CuCMC sample exhibited an initial weight loss of about 10% due to the absorbed moisture and the major weight loss was between 200 and 430°C and the total weight loss up to 600°C was around 50% (Fig. 53). The thermogram of FeCMC (Fig. 54) showed a weight loss of 43.2% in the temperature range of 180 to 530°C corresponding to the major peak in the derivative plot.

4.13.2.2. Thermograms of mechanical mixtures and formulations of fenithion crosslinked with cupric ion:

The mechanical mixture of CuCMC and fenithion containing 6.15%
Fig. 53. Thermogram of CuXC

Fig. 54. Thermogram of PoCMC.
fenthion, presented in Fig. 55 exhibited an initial loss of about 5% and the major weight loss of around 40% between 230 and 380°C. The weight loss was not appreciable afterwards as seen from the derivative plot.

The formulated sample containing 12.14% of fenthion in CuCMC matrix showed a weight loss of 5.2% (30 to 130°C) followed by a loss of around 52% between 145 and 400°C. A weight loss of about 13% was noticed from 400 to 500°C (Fig. 56). When the sample contained 4.42% of fenthion in CuCMC matrix, the thermogram (Fig. 57) exhibited a weight loss of 51% between 150 and 440°C and the weight loss afterwards up to 500°C was approximately 4%. The formulation which contained 10% gelatin and 2.91% fenthion when analysed by TGA (Fig. 58), an initial weight loss of 7.2% from 30 to 155°C and the weight loss of about 55% up to 480°C was observed.

4.13.2.3. Thermograms of mechanical mixtures and formulations of fenthion crosslinked with ferric ion:

The thermogram of mechanical mixture of FeCMC and fenthion presented in Fig. 59 showed around 45% weight loss corresponding to the major peak on the derivative plot. When the formulated sample containing 10.11% of fenthion in FeCMC matrix was subjected to thermogravimetric analysis, there was a weight loss of about 43% from 175 to 380°C corresponding to a major peak on the derivative curve.
Fig. 55. Thermogram of the mechanical mixtures of CuCMC and fenthion (6.15\%).

Fig. 56. Thermogram of the formulation of fenthion (12.14\%) in CuCMC.
Fig. 57. Thermogram of the formulation of fenthion (4.42%) in CuCMC.

Fig. 58. Thermogram of the formulation of fenthion (3.17%) in CuCMC-gelatin (10:1).
Fig. 59. Thermogram of the mechanical mixture of PEO and fentition (8.37%).

Fig. 60. Thermogram of formulation of fentition (10.11%) in PEOC.
and a minor peak between 380 and 480 °C which accounted for about 13% (Fig. 60).

When the formulated sample containing 4.61% fenthion in FeCMC matrix was analysed, the thermogram (Fig. 61) exhibited a weight loss of 42% in the temperature ranging from 180 to 405 °C and about 5% between 405 and 480 °C corresponding to a peak in the derivative plot. The thermogram of the formulation containing 3.61% of fenthion in the ferric ion crosslinked matrix of NaCMC-gelatin (10:1) showed a major peak in the derivative plot accounting for a weight loss of 40% in the temperature range of 155 to 410 °C and a minor one of 6.8% between 410 and 480 °C (Fig. 62).

4.14 Field Evaluation:

The field trial was carried out with one of the formulations of fenthion, CuF3, which contained 20% fenthion with respect to NaCMC and crosslinked with 1.0 M solution of copper sulphate for 48 hours. This formulation exhibited matrix stability for 39 weeks and was suspending on water surface during the entire laboratory evaluation. CuF3 formulation was prepared in large quantities for the field trial.

The trial was conducted in one of the villages in Shertallai taluk, Kerala, which is highly endemic for Malayan filariasis transmitted by *Mansonioides* mosquitoes. The evaluation was carried
Fig. 61. Thermogram of formulation of fenthion (4.61%) in FeOx-C.

Fig. 62. Thermogram of the formulation of fenthion in FeOx-gelatin (10:1).
out in husk retting ponds of surface area of 50-100 m² with depth 3-4 m.

The average breeding densities in the control and treated ponds were 813 and 703 larvae/dip respectively during the pretreatment period (Fig. 63). The breeding density in the treated ponds was decreased to 20 larvae/dip after 24 hours of application with the percentage reduction of 97.15 and the breeding density was zero for 25 weeks. From 26th week onwards, the treated ponds were found to be positive for breeding with the breeding density fluctuating between 5.5 and 177 larvae/dip upto 31st week. The breeding density in the control ponds was found to fluctuate between 109 and 752 larvae/dip during the evaluation period of 31 weeks. The results are comparable to those obtained with the PVC formulation of fenthion which showed effectiveness for 20 weeks at the same concentration (Wilkinson et al., 1971).

The bioassay conducted with the water samples from treated ponds against the fourth instar larvae of the field collected Mansonia annulifera showed more than 95% mortality for 14 weeks and the mortality fluctuated between 80 and 95% from 14 to 25 weeks. Concentration of fenthion analysed in the water samples from treated ponds was found to fluctuate between 0.006 and 0.095 ppm.
Fig. 63. Breeding densities of the Mansonoides larvae in the control (○) and the formulation treated (●) ponds.
Thus the fenthion formulation CuF3 has been found to be effective for 25 weeks at the application concentration of 2.5 ppm with the concentration of fenthion released below 0.1 ppm. Since the frequency of application can be restricted to twice in a year, cost of the control operation can be reduced by minimizing the quantity of insecticide and man-power requirement and avoiding the use of spray-equipments. Moreover, since the polymer used for entrapping the larvicide is biodegradable, the environmental impact due to the application of the formulation could be minimal.