Thermal Analysis of Controlled-Release Formulations Based on Entrapment of a Larvicide in Cross-Linked Carboxymethylcellulose*

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SYNOPSIS

Thermal analysis of controlled-release formulations of fenthion, prepared by its entrapment in cross-linked carboxymethylcellulose and carboxymethylcellulose–gelatin matrices was carried out by thermogravimetric analysis and under accelerated storage conditions. Thermograms of samples of sodium carboxymethylcellulose, cross-linked polymer samples, and the formulations were studied. The thermogravimetric analysis showed improved heat resistance and retention of fenthion or its decomposition products in the formulated samples. The decomposition maximum of technical-grade fenthion was 260°C and the corresponding weight loss was about 90%, whereas fenthion or its decomposition products appear to be retained up to temperatures ranging from 400 to 500°C in the formulations. The half-life of fenthion in the mechanical mixture with the carrier polymer was found to range from 19.92 to 29.98 days, whereas in the formulated samples, it was found to range between 41.54 and 113.35 days. © 1994 John Wiley & Sons, Inc.

INTRODUCTION

The controlled-release formulations of various larvicides were developed by the physical entrapment in polymer matrices of plastics and rubbers. Incorporation of insecticides in nonbiodegradable polymer matrices resulted in the residual loss of the larvicide and its biomagnification in the environment.[1-3] Fenthion (O,O-dimethyl-O-4-methylthio-m-tolyl-phosphorothioate) is widely used as a mosquito larvicide and its low persistence in the polluted aquatic habitats necessitates repeated application at short intervals.[4] Therefore, studies were undertaken in this laboratory to develop controlled-release formulations of larvicides using environmentally compatible polymers that undergo biodegradation following the device exhaustion.

Controlled-release monolithic formulations of fenthion were prepared using a chemically modified cellulose derivative, sodium carboxymethylcellulose

(NaCMC), as the entrapping matrix followed by ionotropic cross-linking with cupric or ferric ions under ambient conditions of temperature and pH.[5-7] Formulations were also prepared with an interactive polymer gelatin in combination with carboxymethylcellulose.[7,8] The controlled-release matrices thus obtained were found to release the larvicide for a prolonged duration following, more or less, a constant release rate.

Thermogravimetric analysis (TGA) is a useful technique to study the thermal resistance of the incorporated active agents in polymers[9] and the characterization of pesticide metal complexes.[10] The storage stability of pesticide formulations is an important parameter to assess their suitability for large-scale production and applications. It is influenced by both the inherent stability of the active agent and the formulation adjuvants.[11,12] The storage stability tests are generally performed under accelerated conditions of temperature.[9] The present study deals with the thermal analysis of controlled-release formulations of fenthion by thermogravimetric analysis and under accelerated storage conditions and the results are compared with the mechanical mixture of the carrier polymers and fenthion.

EXPERIMENTAL

Preparation of Controlled-release Formulations

Formulations were made by entrapping fenthion in NaCMC or NaCMC–gelatin (10 : 1) matrices by aqueous solution casting. The dried matrices containing fenthion thus obtained were further cross-linked with cupric or ferric ions to produce water-insoluble formulations.[5–8] Thus, formulations of fenthion at two different concentrations in the matrices of CuCMC, A1 (12.14%) and A2 (4.42%), were prepared. Similarly, formulations were also made that contained fenthion in the matrices of FeCMC, B1 (10.11%) and B2 (4.61%). Matrices of NaCMC–gelatin (10 : 1) containing fenthion were also prepared and insolubilized by the ionotropic cross-linking with the metal ions: cupric ion, A3 (3.17%), and ferric ion, B3 (3.61%).

Preparation of Cross-linked Polymer Samples and Mechanical Mixtures

The polymers, copper(II) carboxymethylcellulose (CuCMC) and ferric(III) carboxymethylcellulose (FeCMC), were prepared by the addition with continuous stirring of a 10% neutral aqueous slurry of NaCMC into a 1.0M solution of the respective gelling agents. The precipitate formed was filtered and dried in a hot-air oven at 50°C. The weighed quantities of the polymer and fenthion were ground to obtain the mechanical mixtures containing fenthion in CuCMC, A0 (6.15%), and FeCMC, B0 (8.38%).

Analysis of the Mechanical Mixtures and Formulations for Fenthion Content

The percentage of fenthion present in each formulated sample and mechanical mixture was estimated prior to storage stability tests. A weighed quantity (10 mg) of the formulation or the mechanical mixture was transferred into an agate mortar and triturated with 10 mL of spectroscopic grade n-hexane (E. Merck, Bombay). The contents were filtered and washed with n-hexane through a 0.5 μ PTFE filter and the filtrate and washings (2 × 5.0 mL) were collected and made up to 25 mL in a standard flask. One milliliter of this solution was diluted to 4.0 mL with n-hexane and UV absorbance was directly measured using a UV spectrophotometer (Spectronic-2000, Bausch & Lomb, U.S.A.) at 249 nm. The absorbance of the formulation blank, without

fenthion, was zero at 249 nm when n-hexane was used as the reference.

Five standard solutions of fenthion in n-hexane, viz., 1.0, 2.0, 3.0, 4.0, and 5.0 ppm, were used for standardization. The concentration of fenthion in the test solutions was calculated from the regression equation obtained by the linear regression of absorbance on concentration (R = 0.9930, SE = 0.2460, and P = 7.33 × 10^{-5}) and, hence, the percentage of fenthion in the formulations and the mechanical mixtures. The results were counterchecked by the HPLC analysis.[6] ANOVA (one-way analysis of variance)[13] was carried out using an IBM computer to compare data obtained by the spectroscopic and HPLC methods at a 5% critical difference. The variation in the values was not significant (P > .05).

Thermogravimetric Analysis (TGA)

The thermograms of the mechanical mixtures and the formulated samples, prepared for storage stability tests, were run at the heating rate of 20°C/min from 35 to 800°C using a DuPont 951 thermogravimetric analyzer and 990 thermal analyzer in a nitrogen atmosphere. Thermograms were also run with technical-grade fenthion of 94.5% purity (Bayer AG 5090, Leverkusen, Germany) and samples of NaCMC, CuCMC, and FeCMC. The thermograms were obtained as a plot of percentage weight loss against temperature and the derivative plot as the rate of change of weight loss with respect to temperature. All thermograms were run in duplicate.

Storage Stability Test

The storage stability test was performed as per the reported procedure.[9] A weighed quantity (10.0 mg) of the formulations and the mechanical mixtures was taken in 5 mL open glass vials and kept in an air oven at 60 ± 1°C for 2 weeks. After the storage period, the contents in the vials were cooled to room temperature and the percentage of fenthion present in the residue obtained was determined by the spectrophotometric analysis. Storage tests were conducted in triplicate.

The values of the rate constants (k) of the fenthion loss and the half-lives ($t_{1/2}$) of fenthion under the accelerated storage stability conditions were determined using first-order rate equations:

$$k = (2.303/t) \times \log(a/b) \tag{1}$$

and

$$t_{1/2} = 0.693/k \qquad (2)$$

where a and b are the concentrations of fenthion (%) present in the samples before and after the storage stability test, respectively.

RESULTS AND DISCUSSION

Thermogravimetric Analysis

The thermograms obtained with technical-grade fenthion and polymer samples of NaCMC, CuCMC, and FeCMC are presented in Figure 1(a)–(d), respectively. The results obtained from the thermo-
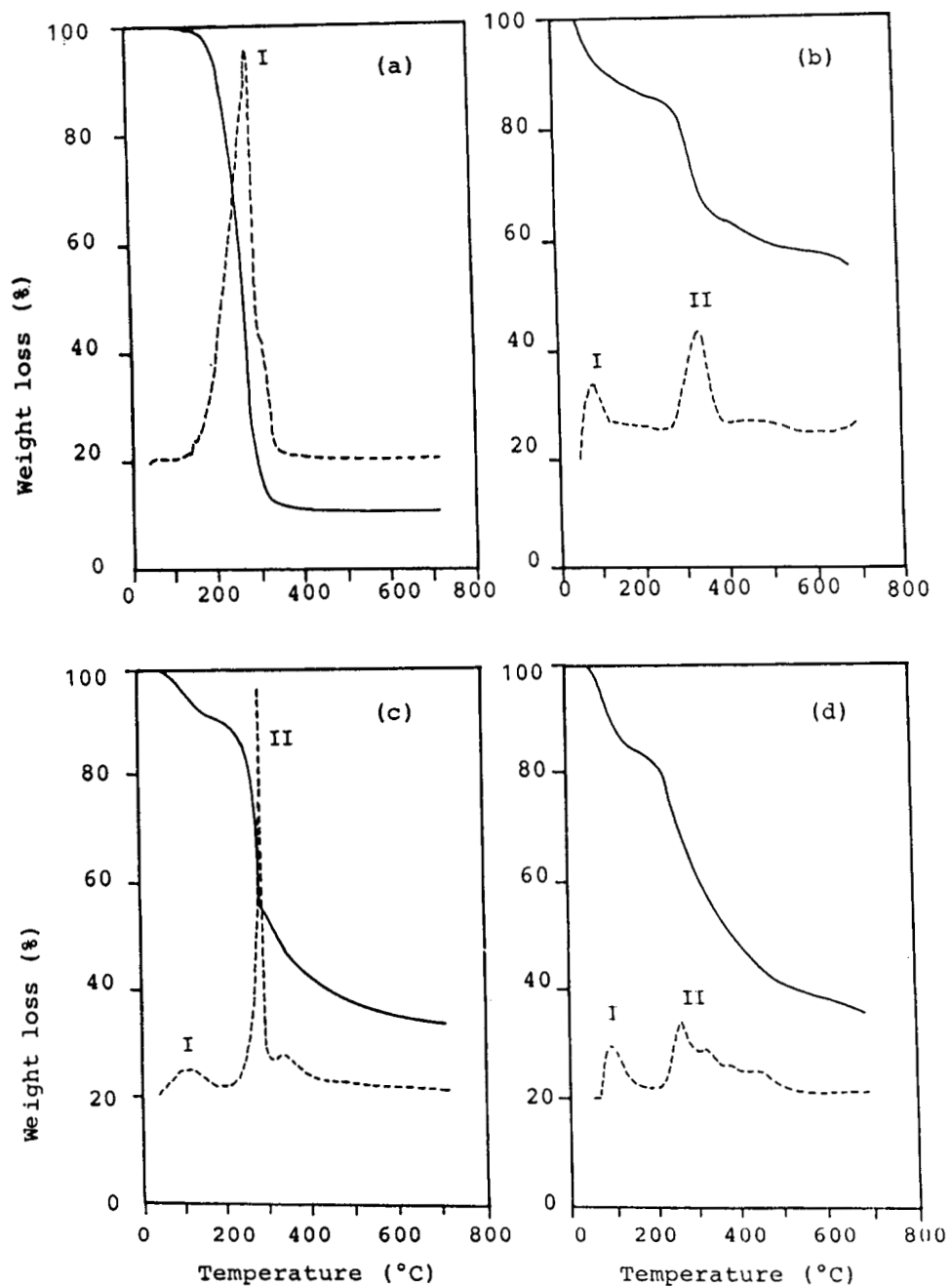

Figure 1 Thermograms of (a) fenthion, (b) NaCMC, (c) CuCMC, and (d) FeCMC.

Table I   Thermogravimetric Analysis Results of the Polymer Samples and the Samples Containing Fenthion

Sample	Fenthion Content (%)	Temperature Range (°C) and Weight Loss[a]		
		Peak I	Peak II	Peak III
Fenthion	94.5	130–320 (90.0)	—	—
NaCMC	0.0	35–105 (9.6)	230–380 (22.4)	—
CuCMC	0.0	35–180 (10.0)	200–430 (50.0)	—
FeCMC	0.0	35–155 (16.0)	180–530 (43.2)	—
A0	6.1475	35–130 (4.8)	230–380 (39.6)	470–570 (3.8)
A1	12.1375	35–130 (5.2)	145–400 (52.0)	400–500 (12.8)
A2	4.4163	80–155 (7.6)	155–440 (51.2)	440–500 (4.0)
A3	3.1698	35–155 (7.2)	155–480 (54.8)	—
B0	8.3750	35–150 (18.6)	150–480 (38.8)	—
B1	10.1063	35–175 (11.2)	175–380 (42.8)	380–480 (13.6)
B2	4.6125	35–155 (10.0)	180–405 (42.0)	405–480 (5.2)
B3	3.6084	35–155 (11.6)	155–410 (40.0)	410–480 (6.8)

[a] Percentage weight loss is given in parentheses.

grams are given in Table I. About 90% of fenthion was lost as a result of thermal decomposition and evaporation within the temperature range of 130–320°C when technical-grade fenthion was analyzed. The decomposition maximum (D_{max}) of fenthion, NaCMC, CuCMC, and FeCMC were 260, 315, 275, and 245°C. The weight loss noticed with the samples of polymers may be due to the thermal decomposition resulting in the evolution of CO_2, CO, and H_2O.[14,15]

Thermograms of the mechanical mixture, A0, and formulations A1, A2, and A3 containing fenthion in CuCMC matrices are presented in Figure 2(a)–(d), respectively. The thermogram of pure CuCMC [Fig. 1(c)] did not exhibit any appreciable weight loss above 400°C, as evident from the flat portion of the derivative plot. The mechanical mixture of CuCMC and fenthion (6.15%) also did not exhibit any sharp weight loss above 400°C, but about a 3.8% weight loss [peak II, Fig. 2(a)] was noticed within the range of 470–570°C, whereas the formulations of fenthion A1 (12.14%) and A2 (4.42%) exhibited sharp weight losses corresponding to 12.8% [peak III, Fig. 2(b)] and 4% [peak III, Fig. 2(c)], respectively, at temperatures above 400°C. Formulation A3 also exhibited a weight loss above 400°C and the weight loss could not be calculated due to the presence of a shoulder peak.

The analysis of the thermograms of pure FeCMC [Fig. 1(d)] and the mechanical mixture B0 (8.34%) [Fig. 3(a)] did not exhibit any sharp weight loss at temperatures above 400°C. The formulations based on the matrices of FeCMC, B1 (10.12%), B2 (4.61%), and B3 (3.61%) exhibited sharp weight losses of 13.6% (380–480°C), 5.2% (405–480°C), and 6.8% (410–480°C), respectively [peak III in Fig. 3(b)–(d)].

The above results indicate that the weight losses noticed in the thermograms of the formulated samples of fenthion may be due to the evolution of fenthion or its decomposition products. Therefore, fenthion or its decomposition products were retained in the formulations above 400°C compared to that of technical-grade fenthion (D_{max} = 260°C) or the mechanical mixtures.

Accelerated Storage Stability Test

The results of the accelerated storage stability tests conducted with the mechanical mixtures and the formulations are presented in Table II. The mechanical mixture of CuCMC–fenthion (A0) exhibited a percentage loss of 27.64 for fenthion after the storage period of 2 weeks at 60°C and the FeCMC–fenthion mixture (B0) showed a percentage loss of 38.54.

Among the formulations of fenthion in the cupric ion cross-linked matrices, a minimal loss of fenthion (8.20%) and maximum half-life (113 days) under accelerated storage conditions were observed when the formulation contained the interactive polymer, gelatin (A3). The maximum loss of fenthion (20.14%) and minimum half-life (43 days) under
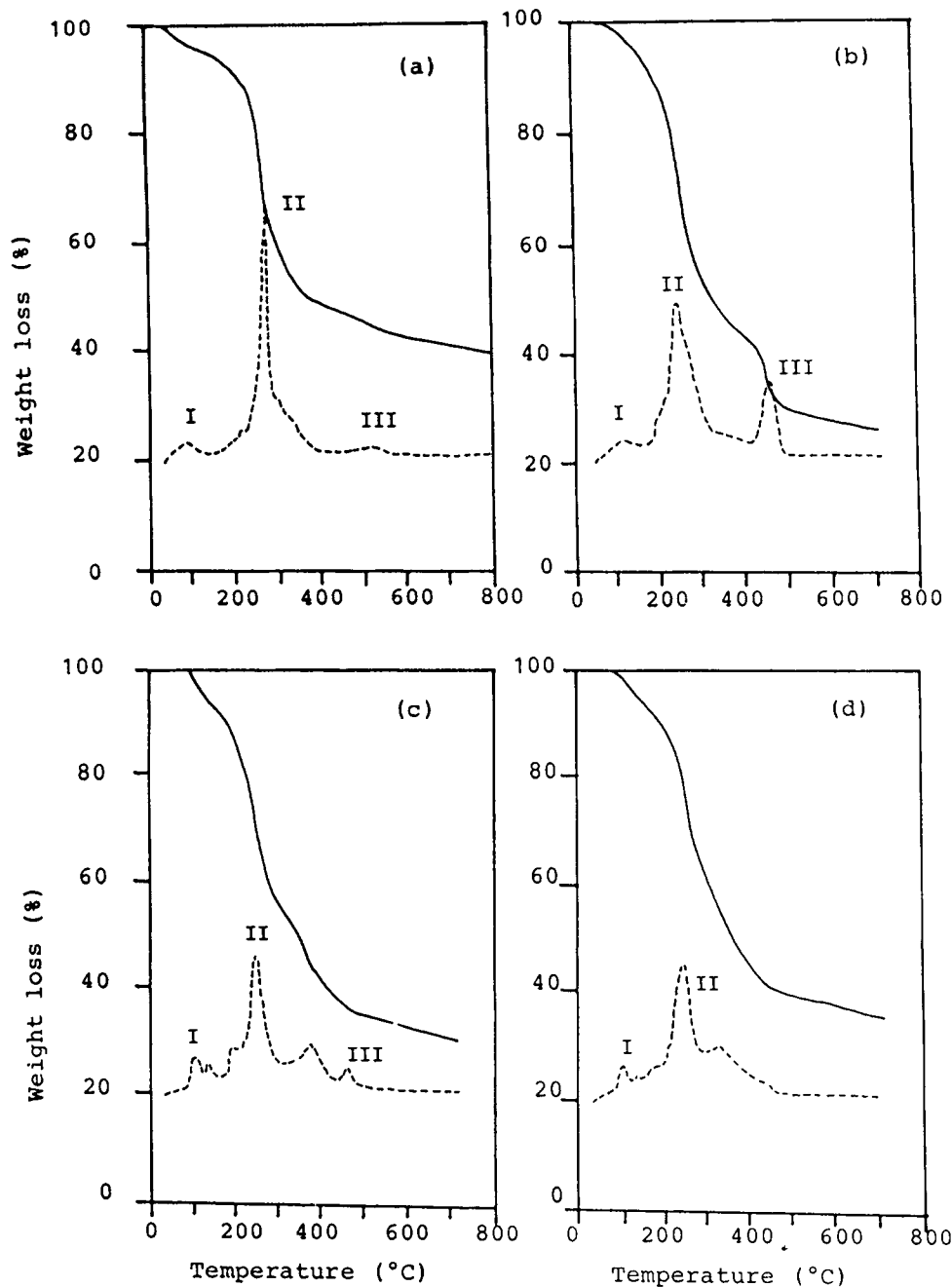
Figure 2   Thermograms of (a) A0, (b) A1, (c) A2, and (d) A3.

these conditions was noticed with A2 among the formulated samples of cupric ion as the cross-linking agent. When ferric ion cross-linked samples were analyzed, the matrices containing the gelatin (B3) exhibited a minimal loss of fenthion (9.42%) and a maximum half-life (98 days).

The values of the rate constants of the mechanical mixtures were higher than those of the formulations

and the values were very low when the matrices contained the interactive biopolymer gelatin. The loss of fenthion from the samples may be due to the evaporative loss as well as to the chemical degradation. These results of the stability tests under accelerated storage conditions revealed that fenthion in the formulated samples, B1 and B2, exhibited improved stability over that of the mechanical mix-
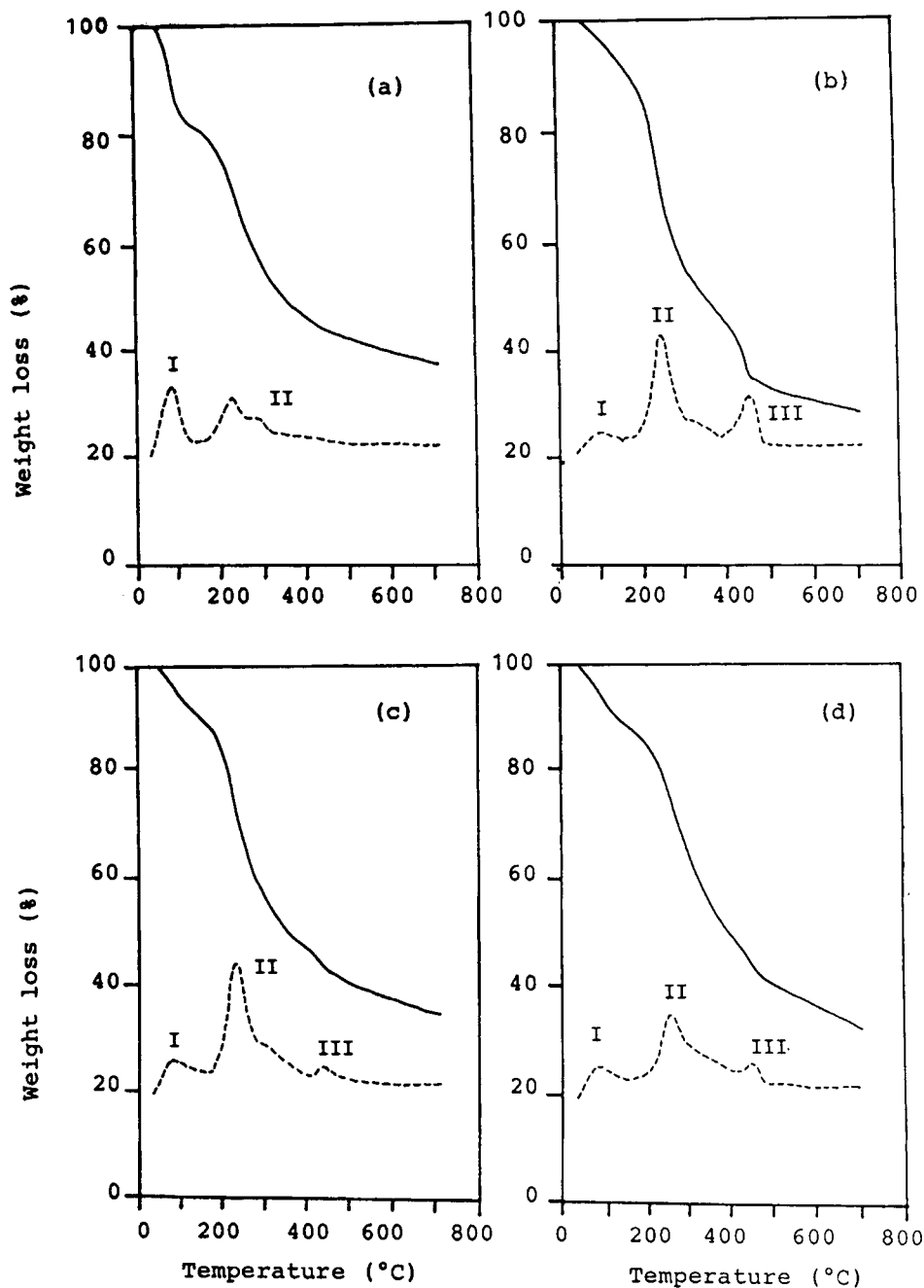
Figure 3   Thermograms of (a) B0, (b) B1, (c) B2, and (d) B3.

tures. A further improvement in storage stability was noticed when the interactive polymer gelatin was used in combination with carboxymethylcellulose (B3).

In conclusion, the results obtained with the storage stability tests under accelerated storage conditions and thermogravimetric analysis show improved thermal stability and retention of fenthion or its decomposition products in the formulated samples over those of the mechanical mixtures as a result of the physical entrapment of fenthion in these polymer matrices. Since the incorporation of fenthion into these polymer matrices improved the thermal stability as well as its controlled release for a prolonged duration,[7-9] these formulations may be useful in mosquito-control programs.

Table II Storage Stability of Fenthion in the Samples Under Accelerated Storage Conditions

| Sample | Fenthion Content (%) | | % Loss | Rate Constant (k) (per Day) | Half-life (Days) |
	Initial	Final			
A0	6.15	4.45	27.6423	0.02311	29.9809
A1	12.14 ± 0.16	10.52	13.3443	0.01023	67.7261
A2	4.42 ± 0.08	3.53	20.1357	0.01606	43.1426
A3	3.17 ± 0.11	2.91	8.2019	0.00611	113.3491
B0	8.38	5.15	38.5441	0.03478	19.9245
B1	10.11 ± 0.21	8.19	18.9911	0.01505	46.0576
B2	4.61 ± 0.18	3.65	20.8243	0.01668	41.5427
B3	3.61 ± 0.09	3.27	9.4183	0.00707	98.0638

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