PREPARATION OF ALGINATE-CARBOXYMETHYL CELLULOSE HYDROGEL BEADS FOR CONTROLLED RELEASE OF COPPER OXYCHLORIDE*

Mya Theingi[1]

Abstract

In the present study, controlled release formulations have been developed by encapsulating the fungicide, copper oxychloride, for reducing the environmental impact of fungicides within the macromolecular network of alginate and carboxymethyl cellulose based microspheres. Alginate-carboxymethyl cellulose beads were prepared in three formulae with various concentrations of carboxymethyl cellulose (SACMC I for 0.25 %, SACMC II for 0.5 %, and SACMC III for 1 % w/v) as a copolymer of sodium alginate and calcium chloride as a cross- linker. The chemical structure, morphology, and thermal properties of the prepared hydrogel beads were characterized by Fourier Transform Infrared Spectroscopy (FT IR), Scanning Electron Microscope (SEM) and Simultaneous Thermogravimetric and Differential Thermal Analysis (TG-DTA), respectively. The swelling ratios of the prepared hydrogel beads were studied by the ASTM method, and the maximum swelling ratio of the SACMC I sample was found to be 80 %. In most of the formulations, the release efficiency of copper oxychloride from the SACMC II sample was 13 % within 7 days. The results were fitted with the Korsmeyer-Peppas kinetics model and the diffusion exponent ‘n’ for all samples were found to be less than 0.89, which shows that the release of fungicides from the samples was diffusion mechanism.

Keywords: Alginate-carboxymethyl cellulose beads, controlled release, fungicides, swelling ratio, diffusion exponent

Introduction

In the modern agricultural technology, agrochemicals (pesticides, herbicides, fungicides, etc.) have an important contribution and become essential for the crop protection and pest control. Their use to increase the agricultural production results in dispersal of these hazardous substances in soil, atmosphere and water through various natural processes. These chemicals are applied to the field in the form of different formulations viz. dusts, sprays, wettable powders, flowables, emulsifiable concentrates, etc. to make them safer, easier, more accurate handling and release. The effectiveness of the fungicides applied to the field depends mainly on its specific concentration maintained for a definite time. It is not possible for the above-mentioned formulations to maintain this concentration because of evaporation, leaching, degradation and volatilization of the active ingredient from these formulations. This will force to apply fungicides repeatedly, which creates environmental, ecological and economic problems along with the possible risks to human health. In addition to cause irreversible environmental damages, these exogenous chemicals also enter into food chains, which are of particular concern to human health (Feng *et al.*, 2019 and Roy *et al.*, 2019).

An ideal fungicides formulation would be one, which limits the amount available at any time to be adequate for crop protection from fungus diseases and leave minimum residues on crops and in environment. This can be achieved by encapsulating the chemicals in the polymeric matrix. The polymer-encapsulated formulations are superior to non-encapsulated commercial formulations in extending activity, reducing evaporative and degradation losses, reducing leaching and decreasing dermal toxicity. Different types of alginate-based controlled release formulations of fungicides for application in crop production developed. When release mechanisms and rates of fungicides from these formulations and conventional control have been compared, it has been observed that release from conventional formulations was completely

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[1] Department of Chemistry, Shwebo University

finished within 1 day, whereas release from calcium alginate formulations lasted up to 2 weeks. Alginates based gel formulation of fungicides retards rate of release of fungicides from the formulation. Carboxymethyl cellulose has been used to strengthen alginate stability because it has more stability, viscosity, binding ability, good water solubility and homogenous mixing with sodium alginate. The use of copolymer, carboxymethyl cellulose was used in alginate basic formulation have further reduced the release rate of the fungicides from the formulation which has retarded and reduced mobility of fungicides in the soil which have reduced the risks of groundwater pollution (Pepperman and Kuan, 1993 and Balgit *et al*., 2008).

Copper oxychloride ($Cu_2 (OH)_3Cl$) is one of the widely used fungicide in Myanmar that controls fungal and bacterial attack on plants and vegetables. It is greenish substance having molecular weight 213.56 g mol $^{-1}$($Cu_2(OH)_3Cl$). The fungicide is slightly soluble in water. Although copper is essential for metabolic processes in all organisms when in trace amounts, the use of copper-based fungicides has been ecologically harmful. Excess copper can produce reactive oxygen species (ROS) such as superoxide anion radical (O_2^-), hydroxyl radicals and hydrogen peroxide (H_2O_2) and can trigger an important reorganization of the root system architecture. In plants, ROS are highly reactive and toxic and cause damage to proteins, lipids, carbohydrates and DNA, which ultimately results in oxidative stress. Hence, a reduction or replacement of copper compounds in disease control is desirable (Ferreira *et al.*, 2014).

In view of the importance of copper oxychloride fungicide and its adverse effects on the environment and human health, controlled and sustained delivery devices are required for its release. The present study is an attempt to prepare calcium alginate-carboxymethyl cellulose composite beads as a controlled release delivery device for copper oxychloride fungicide. FT IR, SEM and TG-DTA techniques were used to characterize the prepared beads and swelling study was also carried out on the prepared beads. The beads of different composition have been prepared by varying the carboxymethyl cellulose (CMC) contents to study their effect on the release dynamics of the fungicide.

Materials and Methods

Materials

Sodium alginate (SA) and carboxymethyl cellulose (CMC) were obtained from Able chemical store Mandalay, Myanmar and used without pretreatment. Calcium chloride (dihydrate) (Able chemical store, Mandalay, Myanmar) was used as a crosslinker and Copper oxychloride was purchased from a local agrochemical supplier (Shwebo Twonship, Sagaing Region). All chemicals used in this study were of analytical quality, and distilled water was used throughout the experiments.

Preparation of Alginate-Carboxymethyl Cellulose Beads

Sodium alginate (SA) and carboxymethyl cellulose (CMC) in distilled water were prepared by weighting respective solids to give (7 % w/v) for SA and (0.25, 0.5 and 1.0 % w/v) for CMC and designated as SACMC I, SACMC II and SA CMC III. Three formulations of SACMC are shown in Table 1 and they were prepared by mixing the two polymers under continuous stirring until the solution become viscous and homogeneous. The formation of the hydrogel beads was based on the ionic gelation technique. Using a 3 mL syringe the viscous solution was transferred dropwise from a distance of 10 cm into 7 % w/v $CaCl_2.2H_2O$ solution, which was under magnetic stirring. Hydrogel beads were formed instantly and they were left in contact with the solution for 30 min. in order to complete the gelation. Finally, they were rinsed gently with distilled water and dried at 50 ºC (Sayeda *et al.*, 2013).

Loading of Copper Oxychloride

Beads containing copper oxychloride were prepared by dissolving 2 % (w/v) of copper oxychloride in an aqueous solution containing 7 % SA and (0.25, 0.5 and 1.0 % w/v) CMC solution. After mixing copper oxychloride with the polymeric solution, beads were fabricated as described above using 7 % $CaCl_2.2H_2O$ as a crosslinking agent. Three formulations of fungicide loaded aginate-carboxymethyl cellulose beads are shown in Table 1 and they are designated as SACMCCu I, SACMCCu II and SACMCCu III.

Table 1. Preparation of Copper Oxychloride Unloaded and Loaded Beads

Formulation	Sodium Alginate (%w/v)	CMC (%w/v)	$Cu_2(OH)_2Cl$ (%w/v)
SACMC I	7	0.25	0
SACMC II	7	0.5	0
SACMC III	7	1.0	0
SACMCCu I	7	0.25	0.2
SACMCCu II	7	0.5	0.2
SACMCCu III	7	1.0	0.2

Physical Properties of the SACMC Beads

The parameters such as diameter, porosity, yield percentage and swelling properties of the prepared fungicide unloaded and loaded beads were determined in order to understand the physical properties of the beads.

Diameter of beads.

About 20 beads were taken in random and its diameter was measured using a caliper. Diameter of the beads can also be measured from SEM images.

Porosity

The porosity of the SACMC beads without and with copper oxychloride were determined by volume/density method reported by Nnamonu *et al.*, 2012. A definite mass of beads were taken in a 10 mL measuring cylinder and tapped well. Total volume (V_t) and the volume occupied by the beads (V_b) were noted. The pore volume (V_p) was calculated using the following formula:

$$\text{Pore volume } (V_p) = \text{Total volume } (V_t) - \text{Volume of beads } (V_b)$$

$$\text{Percentage of porosity} = \frac{V_p \times 100}{V_t}.$$

Yield percentage

The yield percentage of beads was determined by the following formula:

$$\text{Yield of beads (\%)} = \frac{W_1 - W_2}{W_1} \times 100$$

where, W_1 is sum of the weight of fungicide, polymer and cross-linking agents and W_2 is weight of the beads generated.

Swelling properties

Conventional gravimetric procedure was adopted for monitoring the progress of water sorption process. In a typical experiment, known weigh of beads were taken and immersed in a definite volume of water at definite pH at room temperature for a period of 2 h. The swollen beads so taken out at a periodic time interval of 10 min and were gently pressed in between the two filter papers to remove excess water and finally weighed. The swelling (%) was calculated by the following equation (Lami *et al.*, 2012):

$$\text{Swelling Ratio (\%)} = (W_2 - W_1) / W_1 \times 100$$

where, W_1 and W_2 represents the weight of the dry and wet beads, respectively.

FT IR Spectroscopic Analysis

FT IR spectrophotometer model Shimadzu was used for FT IR measurements over the range 500-4000 cm^{-1}.

Scanning Eelectron Microscope (SEM)

The surface morphologies of unloaded and copper oxychloride loaded beads were performed by SEM. The micrographs were taken with a Qunata, SEM instrument manufactured by Thermo Fisher.

Thermogravimetric Analysis (TG-DTA)

TG-DTA studies were carried out using a DTG-60 apparatus (Shimadzu, Kyoto, Japan), at a heating rate of 20 ºC min^{-1} in special atmosphere gases, over a temperature range from room temperature to 600 ºC.

Release of Copper Oxychloride

The release of copper oxychloride, the loaded beads of known weights (0.1 g) were placed in a measured volume (100 mL) of distilled water (release medium) was studied under unstirred condition were studied. The released amount of copper oxychloride was determined at different time intervals (each 24 h within 7 days) by recording the absorbance of the release medium by UV-vis spectrophotometer (UH 5300, Hitachi, America) at maximum wavelength 292 nm. The recorded absorbance was then related to the amount of released copper oxychloride using a calibration plot. To understand the release process of copper oxychloride from the beads, mathematical modeling of the release was applied. The release kinetics were studied by Korsmeyer-Peppas kinetics model and it empirical formula is $M_t / M_\infty = k^n t$. Here, M_t / M_∞ is the partial release of the active ingredient at time t; 'k' is the constant characteristic of the fungicide loaded polymer system; and 'n' is the diffusion exponent of the release mechanism and Korsmeyer-Peppas Model Drug Release Mechanism for exponent n are shown in Table 2 (Ahmed, *et al.*, 2019 and Ritger and Pappas,1987)

Table 2. Korsmeyer-Peppas Model Drug Release Mechanism

Exponent (n)	Drug Release Mechanism
$n \leq 0.45$	Fickian diffusion (Case I diffusional)
$0.45 < n < 0.89$	Anomalous (non-Fickian) diffusion
$n = 0.89$	Zero order release (Case II transport)
$n > 0.89$	Super case II transport

Results and Discussion

Physical Characteristics of Bead

Some physical characteristic of fungicide unloaded and loaded alginate-CMC composite beads are shown in Table 3. The dry weight of beads increased with the increase of added CMC content. The diameters of the beads varied from 1.8 to 2.3 mm and the mean diameter of all bead are approximately 2 mm. It was shown that the size of the beads are not much change in the content of CMC.

Table 3. Some Physical Characteristics of the Fungicide Unloaded and Loaded Beads

Parameter	Fungicide Unloaded and Loaded Beads					
	SACMC I	SACMC II	SACMC III	SACMCCu I	SACMCCu II	SACMCCu III
Mean Diameter (mm)	0.2	0.2	0.2	0.2	0.2	0.2
Yield (%)	64	65	66	65	66	67
Porosity (%)	20	25	30	15	20	25

Swelling behaviour of the beads

Table 4. Swelling Ratio $Cu_2(OH)_3Cl$ Unloaded and Hydrogel Beads

Time (min)	Swelling Ratio (%)		
	SACMC I	SACMC II	SACMC III
10	25	20	15
20	25	30	15
30	30	35	20
40	30	40	30
50	40	40	30
60	45	50	35
70	50	50	40
80	55	55	45
90	60	60	45
100	70	60	50
110	80	65	55
120	80	65	60

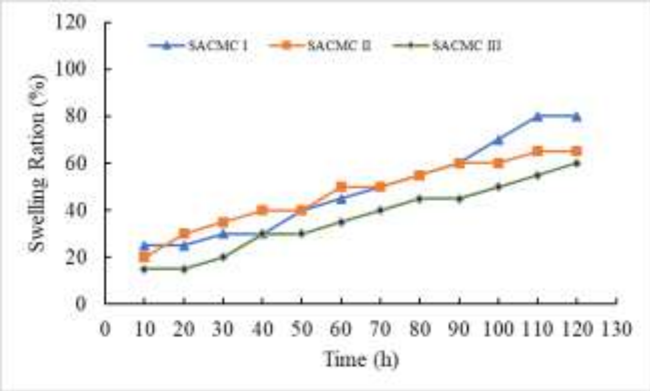
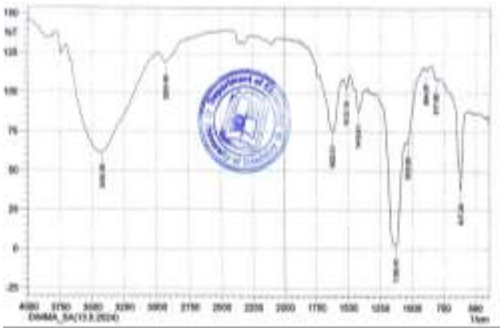


Figure 1. Swelling ratio fungicide $Cu_2(OH)_3Cl$ unloaded and loaded beads as a function of time

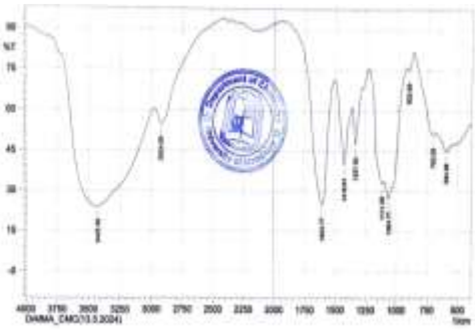
The swelling ratio of alginate-CMC beads after incubation in water for 2 h is presented in Table 4 and Figure 1. The swelling of prepared beads (SACMC I, SACMC II and SACMC III) can be explained that by filling the void regions of the polymer network and the center of the larger pores and macro pores after absorbing free water and binding water. It was found that the addition of CMC in alginate beads decreased the swelling ratio. The alginate-CMC beads showed a swelling ratio of 80, 65 and 60 %, which decreased with the increasing combination of CMC 0.25, 0.5 and 1.0 % in the formulation. The stronger the cross-linked hydrogels, the lower the swelling ratio. The reason for this may be that the amount of hydrophobic groups increased with the increasing amount of CMC, which reduced the water absorption capacity. So SACMC II sample was selected to analyze its functional group, surface morphology and thermal stability.

Characterization of Beads

FT IR spectroscopy analysis



(a)



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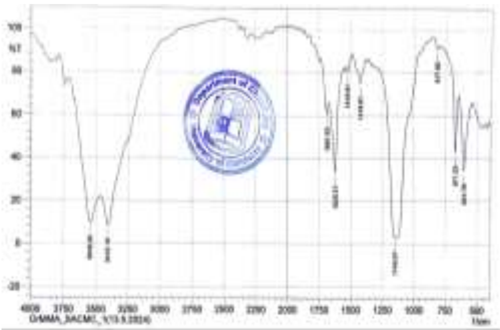

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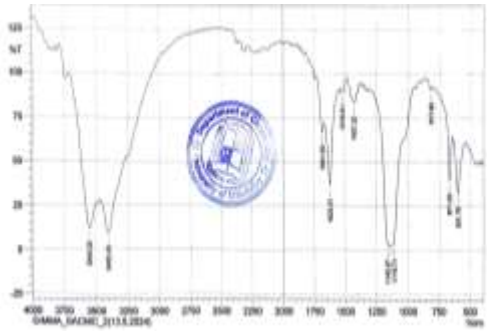

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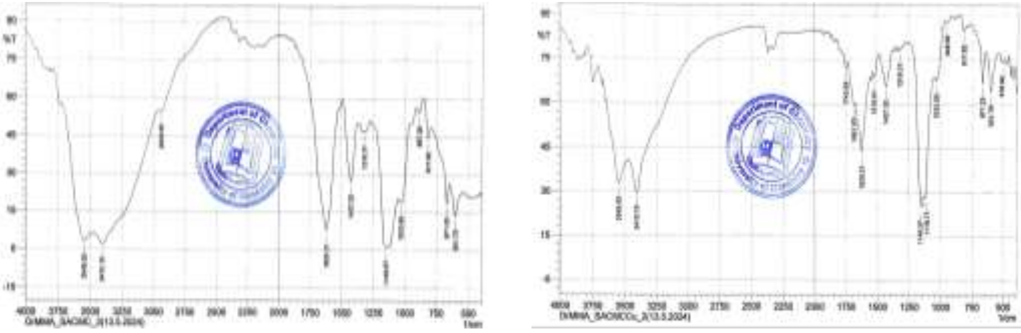


(e) (f)

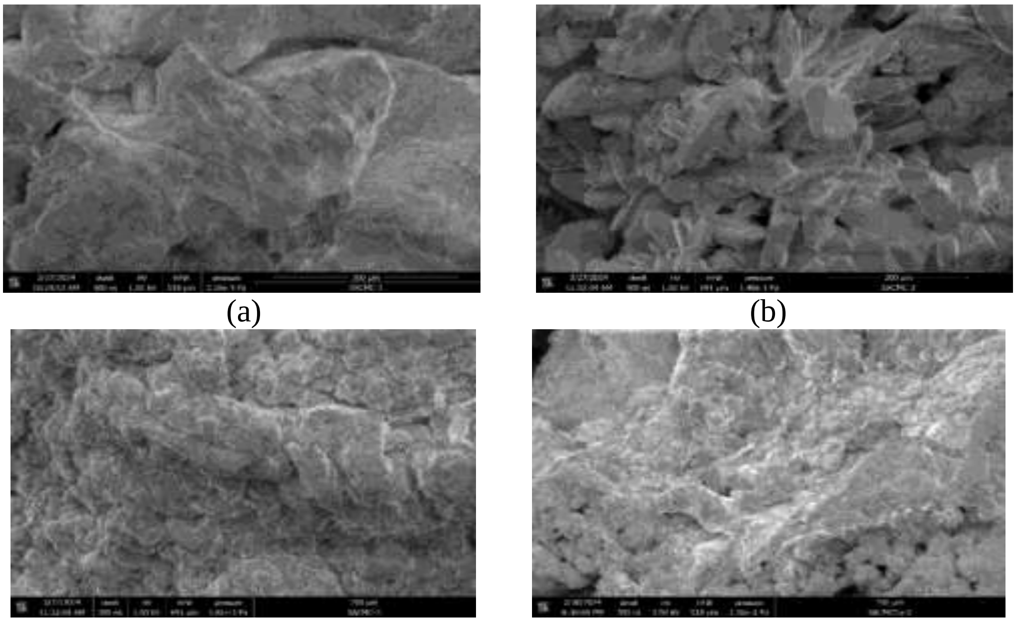
Figure 2. FT IR spectra of (a) SA, (b) CMC, (c-e) SACMC I, SACMC II, SACMC III and (f) SACMCCu II

Figure 2 (a)-(f) and Table 5 show the FT IR spectra and their assignment data of SA, CMC, SACMC I, SACMC II, SACMC III and SACMCCu II from 500 to 4000 cm^{-1}. The characteristic band at 3425 cm^{-1} shows the hydrogen bonding OH stretching region. The small hump at 2924 cm^{-1} shows the attributable to C-H stretching vibration. The sharp peak observed at 1604 cm^{-1} confirms the presence of COO^- is assigned to asymmetric stretching of the carboxyl group. The band around 1419 cm^{-1} is assigned to asymmetric stretching of the carboxyl group and 1327 cm^{-1} are assigned to OH stretching in-plane and C-H stretching in symmetric of CMC. The IR spectra of SA, CMC, unloaded and loaded composite beads showed the bands at 1149-1033 cm^{-1} were characteristic of the C-O stretching on polysaccharide skeleton. Unloaded and loaded composite beads showed the characteristic bands of metal oxygen stretching vibration at 671 and 601 cm^{-1}. Fungicide, copper oxychloride, loaded beads (SACMCCu II) showed Cu-O stretching vibration at 516 cm^{-1} (Daemi and M Barikani, 2012). FT IR revealed a reduction in intensity of the carboxylate peaks of alginate and CMC, present in the FT IR of the matrices signifying interactions between the formulation components that make good for slow release.

Table 5. FT IR Spectral Data of SA, CMC, Fungicide Unloaded and Loaded Beads

Observed Wavenumber (cm^{-1})						Band assignment
SA	CMC	SACMC I	SACMC II	SACMC III	SACMCCu II	
3425	3425	3549 3410	3549 3402	3549 3410	3549 3410	the hydrogen bonding & O-H stretching
2924	2924	-	-	2939	-	C-H stretching
1604	1620	1681 1620	1681 1620	1620	1681 1620	Asymmetric stretching of the carboxyl group (COO-)
1419	1419	1419	1427	1427	1427	Symmetric stretching of the carboxyl group (COO-)
1327	-	-	-	1319	1319	C-H stretching
1111 1064	1126 1033	1149 -	1149 -	1149 1033	1149 1033	C-O stretching
902 702	894 817	817	817	817	817	C-O-C ring vibration
-	-	671 601	671 601	671 601	671 601	Na-O stretching
-	-	-	-	-	516	Cu-O stretching

SEM Analysis



(a) (b) (c) (d)

Figure 3. SEM micrographs of (a) SACMC I (b) SACMC II, (c) SACMC III and (d) SACMCCu II

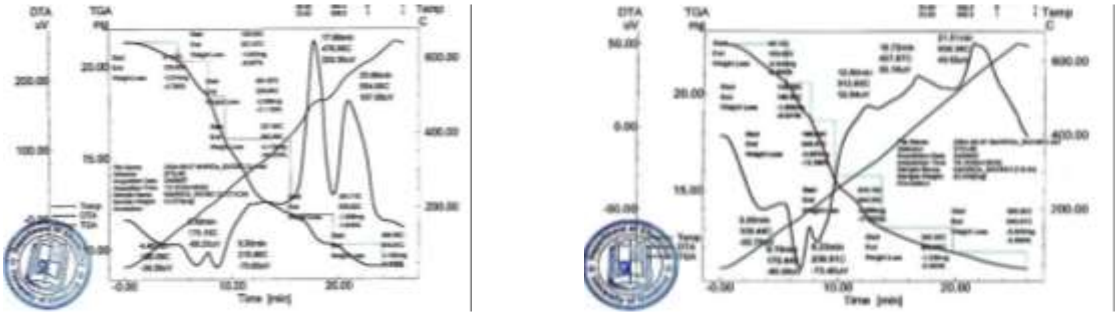
Figure 3 (a-d) present the SEM micrographs of SACMC I, SACMC II, SACMC III and SACMCCu II beads. It was found that the surface of unloaded beads is quite heterogeneous and possesses a rough and irregular morphology containing agglomerated cluster of alginate and CMC. On the other hand, a clear, compact, and metallic luster surface was observed for the copper oxychloride loaded beads. The addition of copper oxychloride within the polymer matrix had a significant impact on the morphology of alginate-CMC composite beads.

Thermogravimetric and Diffraction Thermal Analysis

Table 6. TG-DTA Interpretation Data of SACMC II and SACMCCu II

Temperature Range (°C)		Weight Loss (%)		Nature of peak	Remark
SACMC II	**SACMCCu II**	**SACMC II**	**SACMCCu II**		
40-150	41-139	8.904	4.700	endothermic	Removal of absorbed water
150-196	139-201	8.521	9.007	exothermic	Decomposition of the polymer
196-245	201-239	13.106	11.116	exothermic	Decomposition of the organic substance
245-340	239-393	11.622	19.079		
340-508	393-501	5.384	7.676	exothermic	Decomposition of carboxylic group
508-640	501-618	3.698	5.525		

TGA-DTA was employed to characterize the thermal stability of the unloaded and loaded beads. TGA-DTA curves of unloaded SACMC II, loaded beads SACMCCu II are shown in Figure 4, and their interpretation data are listed in Table 6. From the figures, it was found that the thermal stability is approximately the same for loaded and unloaded beads. As for example at ~ 500 ºC the weight loss is equal to 48 and 51 % for loaded and unloaded beads, respectively. Finally, these results show that the loaded or unloaded beads possess good thermal stability suitable for all the domain of practical application in which these beads are used.



(a) (b)

Figure 4. TG-DTA Thermograms of (a) SACMC II and (b) SACMCCu II beads

Copper Oxychloride Release Kinetics

The Fractional release of copper oxychloride from alginate-CMC based beads are shown in Table 7 and Figure 5 (a-c). As demonstrated for the release of copper oxychloride, the release rate of SACMCCu I was much slower than that of II and III. The amount of released copper oxychloride from SACMCCu I, II and III after 168 h was 10.25 %, 13.00 % and 11.44 %, respectively. The values of ‘n’ and ‘k’ were calculated by Korsmeyer-Peppa’s Model equation. The diffusion mechanism for the release dynamics of copper oxychloride were determined according to the exponential value of ‘n’ and are presented in Tables 8. In terms of copper oxychloride release, all values of ‘n’ were less than 0.89 %. The release mechanism of SACMCCu I and SACMCCu II show non-Fickian diffusion and SACMCCu III shows Fickian diffusion. The main difference between Fickian and non-Fickian diffusion is the presence or absence of boundaries; there are no boundaries in Fickian diffusion, whereas non-Fickian diffusion has a sharp boundary separating the highly swollen region from a dry, glassy region.

Table 7. Fractional Release (%) of $Cu_2(OH)_3Cl$ from SACMCCu I, II and III During 7 Days

Time (h)	Release (%)			Fitted Data by Korsmeyer-Peppa’s Model (%)		
	SACMCCu I	SACMCCu II	SACMCCu III	SACMCCu I	SACMCCu II	SACMCCu III
0	0	0	0	0	0	0
24	2.209	4.279	5.790	2.559	3.504	4.786
48	4.581	5.209	5.837	4.170	5.598	6.454
72	5.860	6.209	7.232	5.548	7.362	7.687
96	6.883	9.720	8.720	6.794	8.942	8.702
120	6.953	10.653	8.860	7.951	10.397	9.581
144	9.372	11.674	10.883	9.041	11.760	10.364
168	10.255	13.000	11.441	10.078	13.051	11.077

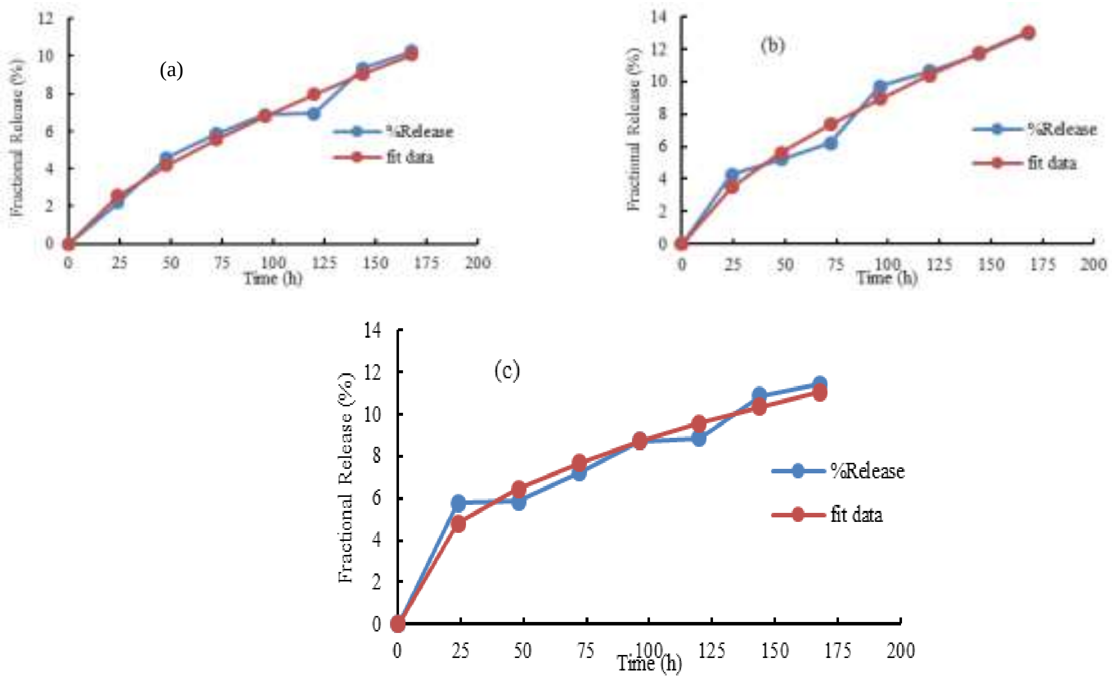


Figure 5. The fractional release of copper oxychloride from the (a) SACMCCu I, (b) SACMCCu II and (c) SACMCCu III beads

Table 8. Diffusion constants and mechanism involved in the release process of copper oxychloride from different formulations of beads

Formulation	n	K	R^2	Mechanism
SACMCCu I	0.704	0.273	0.991	Non-Fickian diffusion
SACMCCu II	0.675	0.409	0.990	Non-Fickian diffusion
SACMCCu III	0.431	1.215	0.986	Fickian diffusion

Conclusion

Alginate-CMC based beads were successfully developed by the ionic gelation method using calcium chloride as a crosslinking agent. Copper oxychloride was encapsulated in the beads confirmed by the measurement of FT IR, SEM and TG-DTA. It is concluded that the release of copper oxychloride from the beads was controllable and sustainable, which is important in the biocontrol of fungicides' harm to the environment and ecosystem. The increase in CMC contents in these constitutions decreased the release of fungicide. The fungicides' release kinetics Korsmeyer-Peppa's Model non-Fickian diffusion for SACMCCu I and SACMCCu II and Fickian diffusion for SACMCCu III. According to the release percent of the fungicide loaded samples, the samples can control fungicide for at least 2 months' duration time. The prepared hydrogel composite beads could be considered carriers of fungal biocontrol in the field of biological control and prevention, and have the effect of a slow release of fungicide.

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