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by Jayanudin Jayanudin

Submission date: 10-Mar-2023 11:31AM (UTC+0700)

Submission ID: 2033622070

File name: 2._BRAC_Jurnal_Internasional_bereputasi.pdf (243.49K)

Word count: 3929

Character count: 20018

Controlled Release Modeling of Urea from Chitosan Microspheres: Effect of Stirring Speed and Volume Ratio of Continuous to Dispersed Phase

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Received: 13.10.2021; Revised: 10.11.2021; Accepted: 14.11.2021; Published: 25.11.2021

Abstract: The purpose of this study was to determine the release kinetics and diffusion coefficient of chitosan microspheres containing urea based on changes in the stirring speed and the volume ratio of the continuous to dispersed phase (CP/DP). Chitosan microspheres filled with urea were prepared using the emulsion cross-linking method. The initial stage of this method has formed an emulsion then slowly dripped with glutaraldehyde saturated toluene as a crosslinker. Urea-loaded chitosan microspheres were washed and dried and then tested for release in an aqueous medium. The calculated cumulative release was used to determine the release kinetics and diffusion coefficient of chitosan microspheres. The appropriate release kinetics model was Simple Power Law with the Burst Effect because it produces an R^2 value of 0.99. The mechanism of urea release from chitosan microspheres is Case II the transport mechanism represents pure relaxation behavior. Determination of the diffusion coefficient values from $1,180 \times 10^{-14}$ up to $1,433 \times 10^{-14}$ cm^2/sec .

Keywords: release kinetics; urea; diffusion coefficient; emulsion cross-linking.

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1. Introduction

Urea fertilizer is one of the most widely used sources of nutrients for plant growth because of cheap. The nitrogen content of urea is the highest of all fertilizers, which is about 46% [1,2]. Conventional urea has the disadvantage that it is easily soluble in water even though the plant's absorption capacity for its nutritional needs is less than 35% [2,3]. Nitrogen that is not absorbed will be abundant in the environment and can cause nutrient imbalances in the soil and can cause the greenhouse effect [3,4].

Widely developed solutions are wrapping urea with a polymer/biopolymer to regulate the controlled release or mixing the urea with other materials like a composite for slow release. This form of fertilizer can increase the efficiency of nutrient absorption by plants. Methods for

the preparation of urea controlled release have been developed by many researchers. The emulsion cross-linking method for urea-loaded chitosan microspheres preparation was previously developed by Jayanudin *et al.* [5]. The release of urea from chitosan microspheres depends on the strength of the microsphere walls. The denser the walls of the microspheres, the less urea is released. The urea release behavior of chitosan microspheres was determined by the release kinetics to determine the achievement of the desired urea concentration. Analysis of the wall strength of chitosan microspheres determined by the diffusion coefficient. The release kinetics model and determining the diffusion coefficient refers to the research that has been reported by Malekjani [6]; Beig *et al.* [7,8]; Siepmann and Siepmann [9]. Cumulative release data of urea fertilizer from chitosan microspheres were taken, and research data was reported by Jayanudin *et al.* [5]. The purpose of this study was to determine the release kinetics and diffusion coefficient due to the influence of stirring speed and volume ratio of CP/DP.

2. Materials and Methods

2.1. Materials.

This research uses materials such as urea from PT. PUSRI, pro-analyst grade glutaraldehyde from Merck with a concentration of 25% (v/v), chitosan produced by PT. Biotech Surindo with DD = 87.2% and viscosity 37.10 cps, toluene, petroleum ether, and hexane are all technical grades obtained from CV. Tri Jaya Dinamika, vegetable oil produced by PT. Sarwana Nusantara, and glacial acetic acid from Merck.

2.2. Preparation of urea-loaded chitosan microspheres.

Preparation of urea-loaded chitosan microsphere refers to the study reported by Jayanudin *et al.* [5]. The first step was chitosan dissolved with 1% (v/v) glacial acetic acid to get a concentration of 4% (w/v) chitosan. Glutaraldehyde saturated toluene (GST) as a crosslinker was prepared using the same method from Jayanudin *et al.* [5]. Urea was dissolved in a chitosan solution (dispersed phase) and then added in vegetable oil (continuous phase) with a CP/DP ratio of 4:1, 6:1, and 8:1, then immediately stirred with a stirring speed of 10,000 rpm, 15,000 rpm, and 20,000 rpm to form an emulsion. GST was dropwise into the emulsion for the cross-linking process. The mixture was continuously stirred for the solidification process of chitosan microspheres. The last stage was chitosan microspheres filtered, washed, and dried. Urea release test from chitosan microspheres using water medium and analyzed using Nessel reagent to determine Nitrogen concentration.

2.3. Cumulative release analysis of urea from chitosan microspheres.

0.2 g of chitosan microspheres filled with urea were immersed in 50 mL of water for 1, 3, 7, 14, 21, and 30 days. The cumulative release analysis was carried out by determining the nitrogen content based on the immersion time using Nessler's reagent.

2.4. Release kinetics model.

The release kinetics model used in this study refers to the research reported by Malekjani and Jafari [6]; Beig *et al.* [7]; Beig *et al.* [8]. The release kinetics model was shown in equations 1-4.

Peppas-Sahlin model

$$\frac{M_t}{M_\infty} = k_1 t^m + k_2 t^{2m} \quad (1)$$

Sinclair and Peppas model

$$\frac{M_t}{M_\infty} = at^b \quad (2)$$

Modified hyperbola formula

$$\frac{M_t}{M_\infty} = \frac{at}{1+bt} \quad (3)$$

Modification of power law with burst effect

$$\frac{M_t}{M_\infty} = kt^n + b \quad (4)$$

where $\frac{M_t}{M_\infty}$ is cumulative release, k_1 , k_2 , a , and b are release kinetics constants, and t is release time.

2.4. Determination of diffusion coefficient.

The diffusion coefficient was determined using the equation formulated by Siepmann and Siepmann [9, 10] for reservoir systems with non-constant activity sources, as shown in equation 5.

$$\frac{M_t}{M_\infty} = 1 - \exp\left(-\frac{3R_0DKt}{R_i^2R_0 - R_i^3}\right) \quad (5)$$

where $\frac{M_t}{M_\infty}$ is cumulative release, R_0 is the outer radius, R_i is the inner radius, D is diffusion coefficient, K is constant, and t is release time. To determine using the equation $R_i = R_0 - \delta$, where δ is the wall thickness of chitosan microspheres is determined by the equation reported by Jayanudin *et al.* [11].

3. Results and Discussion

3.1. Release kinetics.

Cumulative release and diameter size data of chitosan microspheres taken from the study have been reported by Jayanudin *et al.* [5]. The release kinetics model used in this study was different from Jayanudin *et al.* [5], as shown in equations 1 – 4.

3.1.1. Determination of the release kinetics based on the change in stirring speed.

The kinetic model used in the study that has been reported by Jayanudin *et al.* [5] was the Higuchi and Korsmeyer-Peppas model, while this study used a different release kinetics model as shown in Equations 1 – 4. Figure 1 shows a comparison of cumulative release from experimental and calculation data using the kinetic release model.

The urea release kinetics model of chitosan microspheres was used to reveal the mechanism of urea release in the dissolution medium [12]. The mechanism of release of fertilizer from the carrier is the same as the release of drugs such as dissolution, erosion, diffusion, adsorption/desorption, and swelling [12,13]. The Sinclair and Peppas models reveal a diffusion mechanism of release through non-swelling devices (slabs, cylinders, and spheres). The modified hyperbola formula shows the release is first order at a low t value and decreases to zero-order when t increases [8]. The Peppas-Sahlin model explains two release mechanisms,

where the first term is the Fickian contribution and the second term is the case-II relaxation contribution. The coefficient m is the pure Fickian diffusion exponent for any set of geometric shapes that exhibits controlled release [6]. The modified Power-law model with burst effect shows a modification of Power-law or Korsmeyer-Peppas model by adding constant b , which indicates burst effect. Comparison of research data with calculation data using the release kinetics model (Equation 1-4) was shown in Figure 1.

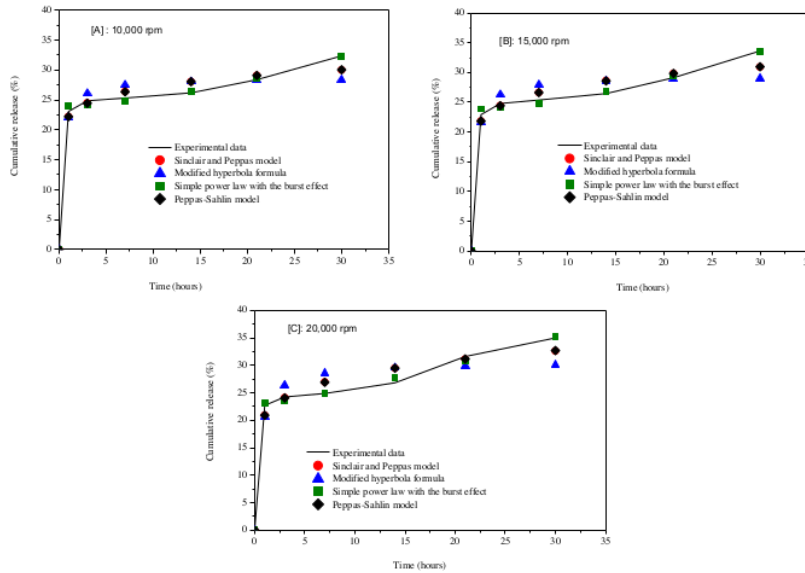


Figure 1. Comparison of experimental and calculated data using a release kinetics model based on changes in stirring speed [A]. 10,000 rpm, [B]. 15,000 rpm, and [C]. 20,000rpm

Figure 1 shows that the change in stirring speed affects the size of the chitosan microspheres and could directly affect the cumulative release of urea. This was because increasing the stirring speed decreases the diameter size of the chitosan microspheres. The smaller the size could increase the contact area between the chitosan microspheres and the release medium so that the cumulative release of urea from the chitosan microspheres increases [5].

The appropriate release kinetics model based on comparing the cumulative release of the experimental and calculations data using the release kinetics model was determined with the best fitting based on the R^2 value. Figure 1 shows the best fitting is a modified power-law model with a burst effect with an R^2 value for all variables (10,000 rpm, 15,000 rpm, and 20,000 rpm) of 0.99. Releases with burst effects were identical to purely diffusion-controlled kinetics. The value of n in this model indicates the release mechanism that occurs in the release of urea from chitosan microspheres. The resulting n values from this model were $n = 1.59$ for [A] 10,000 rpm, $n = 1.56$ for [B] 15,000 rpm, and $n = 1.25$ for [C] 20,000 rpm. The value of $n > 1$ indicates super case II transport [14].

3.1.2. Determination of the release kinetics based on the change in the volume ratio of the continuous to dispersed phase (CP/DP).

Changes in the volume ratio between CP/DP had an effect on the cumulative release of urea from chitosan microspheres. An increase in the volume ratio of CP/DP, decreases the

cumulative release of urea and vice versa. This was due to the chitosan microspheres produced using a large continuous phase volume resulting in harder microspheres due to a faster solidification process and reduced microsphere porosity [5]. Figure 2 shows a comparison between the cumulative release of the experimental and the calculation data results with the release kinetics model.

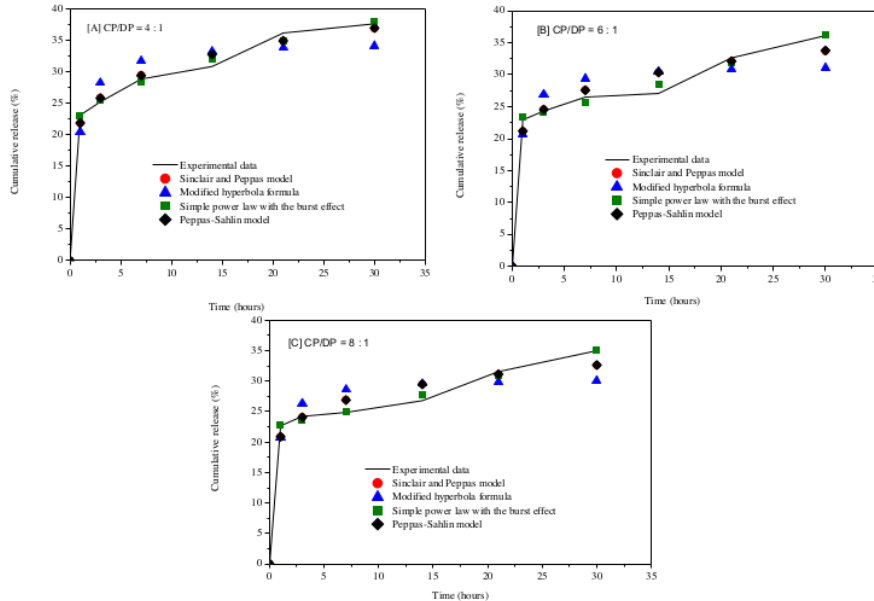


Figure 2. Comparison of experimental and calculated data using a release kinetics model based on changes in the volume ratio of CP/DP [A] 4 : 1, [B] 6 : 1, and [C] 8 : 1.

Table 1. The kinetic constant of urea release from chitosan microspheres

Variable	Peppas-Sahlin model				Sinclair and Peppas		
	m	k ₁	k ₂	R ²	a	b	R ²
Volume ratio between continuous phase and dispersed phase							
4 : 1	0.116	15.571	6.337	0.99	21.865	0.154	0.99
6 : 1	0.103	14.992	6.156	0.98	21.142	0.137	0.98
8 : 1	0.099	14.759	6.123	0.98	20.882	0.131	0.98
Stirring speed (rpm)							
10,000	0.067	15.460	6.765	0.99	22.225	0.088	0.99
15,000	0.077	15.275	6.551	0.98	21.825	0.103	0.98
20,000	0.099	14.762	6.120	0.98	20.882	0.131	0.98
Variable	Modified hyperbola formula			Simple Power Law with the Burst Effect			
	a	b	R ²	k	b	n	R ²
Volume ratio between continuous phase and dispersed phase							
4 : 1	49.189	1.405	0.97	2.861	20.273	0.538	0.99
6 : 1	59.953	1.897	0.96	0.253	23.132	1.161	0.99
8 : 1	63.795	2.088	0.96	0.247	22.617	1.151	0.99
Stirring speed (rpm)							
10,000	96.860	3.383	0.98	0.037	23.961	1.588	0.99
15,000	82.976	2.830	0.97	0.048	23.806	1.557	0.99
20,000	63.795	2.088	0.96	0.176	22.896	1.249	0.99

Comparison of experimental and calculation data as shown in Figure 1 produces the best fitting, namely the modified Power-law model with a burst effect. The highest R² value was owned by this model, with a value of 0.99. The mechanism of urea release from chitosan microspheres was determined by the value of n in this modified Power-law model. The value of n for CP/DP (4 : 1) was 0.54, CP/DP (6 : 1) was 1.16, and CP/DP (8 : 1) was 1.15. The value

of $n > 1$ indicates, according to Case II transport mechanism represents pure relaxation behavior [9]. Meanwhile, the value of n is $0.43 < n < 0.83$, including anomalous transport or non-Fickian transport, which was defined as having two mechanisms, namely diffusion and swelling (relaxation of polymer chains). The values of the release kinetics constants and R^2 for each variable of this study are shown in Table 1.

The release kinetic constants in Table 1 show that the appropriate release kinetics model was Simple Power Law with the Burst Effect because R^2 in all variables is 0.99. Figures 1 and 2 also show that the Simple Power Law with the Burst Effect model is good fitting.

3.2. Determination of the diffusion coefficient.

The mathematical model used to determine the diffusion coefficient was based on the equation compiled by Siepmann and Siepmann [9,10] for reservoir systems with non-constant activity sources. This mathematical model applies Fick's law of diffusion, where the nucleus exits the microsphere after the medium (water) penetrates the system, dissolving the microsphere nucleus, then the dissolved nucleus diffuses out of the system through the surrounding membrane. The surrounding bulk fluid provides perfect reservoir conditions. Furthermore, there was no excess of the active ingredient in the nucleus, so the released nuclear molecules were not replaced, and the concentration of the core material on the inner membrane surface decreased with time. This was called a "reservoir system with non-constant sources of activity" [6,9]. Determining the diffusion coefficient serves to determine the speed of the diffusion rate. Table 2 contains a collection of data on the diffusion coefficient resulting from calculations using equation 5.

Table 2. Diffusion coefficient of chitosan microspheres filled urea.

Variable	Diffusion coefficient (D) (cm ² /sec)
Volume ratio between the continuous phase and dispersed phase	
4 : 1	1.433 x 10 ⁻¹⁴
6 : 1	1.233 x 10 ⁻¹⁴
8 : 1	1.180 x 10 ⁻¹⁴
Stirring speed (rpm)	
10,000	1.308 x 10 ⁻¹⁴
15,000	1.270 x 10 ⁻¹⁴
20,000	1.197 x 10 ⁻¹⁴

Table 2 shows that increasing the stirring speed decreases the value of the diffusion coefficient, as well as the volume ratio of CP/DP where increasing the CP/DP volume ratio decreases the diffusion coefficient value. Besides being influenced by the concentration of the wall material because it was related to the density of the walls of the microspheres, the rate of diffusion was also influenced by the diffusion coefficient. Increasing the diffusion coefficient increased the rate of diffusion. The cumulative release of urea from chitosan microspheres reported by Jayaudin *et al.* [5] showed that the release time at 14, 21, and 30 days was higher than the stirring speed of 10,000 rpm and 15,000 rpm. The value of the diffusion coefficient of stirring at 20,000 rpm should also be greater than that of 10,000 rpm and 15,000 rpm.

This possibility occurs because the cumulative release value of the stirring speed of 20,000 rpm at 1, 3, and 7 days was greater than the speed of 10,000 rpm and 15,000 rpm. This was possible at 20,000 rpm having a smaller diffusion coefficient compared to 10,000 rpm and 15,000 rpm.

4. Conclusions

The urea release kinetics from chitosan microspheres was determined using the Peppas-Sahlin model, Sinclair and Peppas model, modified hyperbola formula, and modified power-law with burst effect. The model with a good fit is Simple Power Law with the burst effect with an R^2 value of 0.99 for all variables. The value obtained is $n > 1$, which indicates that the transport mechanism represents pure relaxation behavior according to Case II. The value of the diffusion coefficient is directly proportional to the rate of diffusion; the greater the diffusion coefficient, the rate of diffusion also increases. The value of the diffusion coefficient obtained starts from 1.180×10^{-14} to 1.433×10^{-14} cm^2/sec . The urea release mechanism from chitosan microspheres is a case II transport mechanism representing a pure relaxation behavior.

Funding

This research received no external funding.

Acknowledgments

Authors would like to say thank you to the *Lembaga Penelitian dan Pengabdian Kepada Masyarakat (LPPM)*-Universitas Sultan Ageng Tirtayasa for the opportunity to obtain an internal basic research grant in 2020. We also thank the Department of Chemical Engineering, Universitas Sultan Ageng Tirtayasa, for all the facilities provided so that this research has been a success.

Conflicts of Interest

The authors declare no conflict of interest.

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