Pharmaciana
Vol.14, No.3, Nov 2024, Page. 396-407
ISSN: 2088 4559; e-ISSN: 2477 0256
DOI: 10.12928/pharmaciana.v14i3.28104

The effect of HPMC-K15M and guar gum as polymer-coated for sustained-released tablet: disintegration and release kinetics

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Submitted: 29-12-2023 ***Reviewed: 31-03-2024*** ***Accepted: 06-11-2024***

ABSTRACT

Polymeric coating films are able to control tablet drug release rate depending on polymer physicochemical properties. Guar gum and HPMC-K15M (GG/HPMC-K15M) can be a coating polymer in sustained-release tablets. This study aims to characterize the disintegration and drug release kinetics on theophylline sustained-release tablets coated with GG/HPMC-K15M. The film coating was made with variations of the GG/HPMC-K15M ratio of 1:3 (F1), 1:4 (F2), and 1:5 (F3). Granules were preformulated regarding LOD, granule size distribution, packing, and flow properties. Film coating was carried out using a liquid spraying method. Coated tablets were tested for quality examination, and the drug release kinetics model was determined based on in-vitro dissolution. Granule pre-formulation result shows that the granules have excellent packing and flow properties with an LOD of 4.59–5.33% and a size of 553.28–627.28 πm. Tablets provided uniform size characteristics with a weight variation of 333.38–339.56 mg (CV 1.32–3.43% and acceptance value 6.53–13.58), hardness of 11.61–18.86 kgf, friability of 0.103–0.186%, disintegration time of 20.69–27.36 min, and drug content of 98.51–98.55%. The theophylline was dissolved by 95.24% (6h in FI), 97.04% (7h in F2), and 99.79% (8h in F3); all formulas followed zero-order kinetic ($r^2 \sim 1$). Suitable quality theophylline tablets GG/HPMC-K15M coating have been successfully produced. Increasing the concentration ratio of HPMC-K15M in the coating solution resulted in a significant increase in disintegration time and a slowing of the drug release rate. The drug release kinetics of all formulations followed the zero-order kinetic model.

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Keywords: dissolution, drug release kinetics, film coating, liquid spray, polymeric coating

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INTRODUCTION

Tablets provide many advantages, such as ease of administration, high patient compliance, and cost-effectiveness, making them one of the most preferred dosage forms. Coating is an essential step in the tablet manufacturing process regarding aesthetic and functional considerations (Seo et al., 2020). Film coating is the most widely used to solve various obstacles during drug production, distribution, storage, and clinical use compared to other types, such as sugar and press coating (Zaid, 2020). For example, film coating can regulate drug release from the dosage form in terms of time, speed, and location (Lee et al., 2020). It aims to facilitate the delivery of acid-sensitive drugs to the colon while minimizing adverse effects on the gastrointestinal system. Sustained-release tablets with film coating are commonly used to regulate the rate at which drugs dissolve in the gastrointestinal tract (Kapoor et al., 2019). Its tablet is designed to rapidly achieve therapeutic blood levels and sustain them within the therapeutic range through controlled release (Agustin & Ratih, 2015). Controlling the drug release rate is influenced by the physicochemical properties and the quantity of polymer utilized for surface coating (Seo et al., 2020; Shukla et al., 2019). Guar gum and hydroxypropyl methylcellulose (HPMC) are suitable polymers for this coating film.

Guar gum (GG) is obtained from *Cyamopsis tetragonoloba* (Leguminosae family) seeds, a water-soluble and non-ionic natural polysaccharide gum. Chemically, it consists of a linear polymer chain of (1 → 4)-ß-Ɗ-mannopyranosyl units, which have α-Ɗ-galactopyranosyl units linked by (1 → 6) bonds (George et al., 2018). Its use has been widely developed in various hydrophilic matrices as carriers to effectively control drug release by forming gels. GG expands in cold water and produces a colloidal dispersion so that its gel-forming network inhibits drug release from the preparation (Jana et al., 2019). HPMC, another polymer, has hydrophilic properties and is widely applied in modified-release tablet formulations. Its addition to the coating component can improve the mechanical properties of the tablet (Prusty & Patra, 2022). This polymer is commercially available in several grades depending on the viscosity and amount of substituents (Hirun, 2022). HPMC-K15M can control drug release for 24 hours in tablet matrix formulations with drug release mechanisms in the form of drug dissolution inside the hydrogel, drug diffusion across the hydrogel, and gel erosion (Yi et al., 2019).

Theophylline is a bronchodilator for treating asthma and stable chronic obstructive pulmonary disease (COPD) (Rahmawati et al., 2018). Sustained release preparations have become essential to dynamic changes in COPD pharmacotherapy over the last few years (Sharma & Kansal, 2023). After oral administration, theophylline changes rapidly and is completely retained in the digestive tract. The serum half-life of theophylline varies from 3 to 13, with an average range of 7-9 hours, and is toxic at doses of 7.5 mg/kg or higher (Palai et al., 2023).

Based on the explanation above, studying the disintegration characterization and drug release kinetics of sustained-release tablets coated with guar gum and HPMC-K15M is necessary. Guar gum, a natural gum, is favored over similar synthetic polymers because of its easy availability, lower toxicity, and cost-effectiveness (George et al., 2018). The incorporation of HPMC will enhance the limited properties of guar gum. Theophylline core tablets were produced using the wet granulation process, and the coating was applied using coating solutions comprising various ratios of guar gum and HPMC-K15M. The primary measurement to assess the coating performance of the two polymers is the disintegration and in-vitro dissolution.

MATERIALS AND METHOD

Materials

Materials consist of theophylline BPFI (BPOM, Indonesia), theophylline (Jilin Shulan Synthetic Pharm., China), HPMC K15M (Shanghai Honest Chem. China), explotab (Gujarat Overseas INC., India), lactose (DFE pharma, Germany), talc (Haicheng Xinda Mining, China), guar gum (Shreeji Agro, India), Mg stearate (Faci Asia Pacific, Singapore), povidone K30 (JH Nanhang LC., China), PEG 400 (PT. Purnomo Putra Kimia, Indonesia), ethanol and aquadest (Harum Kimia, Indonesia).

Methods

Theophylline Granules Preparation

Granules (300 mg in capsule) consist of 25% theophylline (75 mg, active ingredient), 5% PVP (15 mg, binder), 4% Explotab (12 mg, disintegrant), and 62% lactose (186 mg, filler). Theophylline and Explotab were mixed with a V-mixer (Tamaru) at 90 rpm for 10 min. Then, dissolved in 74 mL of distilled water, PVP was added slowly until a banana-breaking mixture was formed. The mixture was sieved with a #12 mesh sieve and dried at 60°C in the oven for 2 hours. The dry granules were sieved again with a #18 mesh sieve and mixed with 2% Mg stearate and 2% talc for evaluation.

Theophylline Granules Evaluation

Densities, Carr Index, and Hausner Ratio

Granules ± 50 g (w) were weighed and put into a 100 mL measuring cup installed on a tapped density tester (Tamaru). The initial volume (v_1) before tapping and the final volume (v_2) after tapping 500 times were recorded (Nining et al., 2020). Then, the bulk density, tapped density, Carr index, and Hausner ratio are calculated using equations (1), (2), (3), and (4).

$$\text{Bulk density (g/mL)} = \frac{W}{v_1} \quad \text{.....(1)}$$

$$\text{Tapped density (g/mL)} = \frac{W}{v_2} \quad \text{.....(2)}$$

$$\text{Carr index (\%)} = \frac{tapped\ density - bulk\ density}{tapped\ density} \text{ x } 100 \quad \text{.....(3)}$$

$$\text{Hausner ratio} = \frac{tapped\ density}{bulk\ density} \quad \text{.....(4)}$$

Flow rate and angle of repose

Granules ±100 g (w) were weighed and put into a funnel with the hole closed on the granule flow tester. Then, the funnel lid was opened, and the granules' flow time (t), the pile's diameter (d), and height (h) were recorded. The t data was used to calculate the flow rate, while the d and h data were used to calculate the angle of repose (Nining et al., 2020). Both are calculated using equations (5) and (6).

$$\text{Flow rate (g/s)} = \frac{w}{t} \quad \text{.....(5)}$$

$$\text{Angle of repose (°)} = tan^{-1}\frac{h}{r} \quad \text{.....(6)}$$

Loss on Drying (LOD)

Granules ± 1g (w_1) were weighed and placed in a weighing bottle that has been heated and weighed. The weighing bottle containing the sample with the lid open was heated at 105°C in the oven (Memmert) for 30 min. Then, the bottle was cooled in a desiccator with the lid closed and weighed. Its

procedure was repeated until a constant weight (w_2) was obtained, indicated by a weighing difference of no more than 0.50 g (Depkes RI, 2020). LOD was calculated using equation (7).

$$\text{LOD (\%)} = \frac{w_1 - w_2}{w_1} x\ 100 \quad \text{.....(7)}$$

Granule size distribution

Granule grouping was determined using the sieving method (Depkes RI, 2020). Mesh analytical sieves #12, #18, #20, #30, #40, and pans were weighed (w_1) and arranged vertically downwards from small to large numbers. Granules ±100.0 g were weighed and put into the top sieve, and the tool was run at 30 Hz for 25 minutes. Once completed, each sieve was weighed again (w_2), and the average granule size was calculated.

Theophylline tablet core compressing and coating process

The granules that have been evaluated were then put into the hopper of the tablet compressing machine (Rimek). The tablet weight and hardness were regulated using the upper and lower punch of the machine. If both were matched, the machine was run until the granules were finished. A 100 mL coating solution was prepared with the composition listed in Table 1. Both polymers were weighed and put into a glass beaker. Coating tablets was done by spraying the coating solution over the tablet's surface gradually and uniformly with a revolving coating pan (CP-2L). Afterwards, the tablets were rotated in the pan until they reached room temperature. The film-coated pills were weighed and kept in a clean, then dried container (Iswandana et al., 2018).

Table 1. Composition of theophylline tablet coating solution

Materials	Function	Coating component (%)		
		F1	F2	F3
Guar gum	Polymer	1	1	1
HPMC K15M	Polymer	3	4	5
PEG 400	Plasticizer	1	1	1
Ethanol 80% ad	Solvent	100	100	100

Theophylline coating tablets evaluation

Physical examination and size uniformity

Physical examination was done by observing the tablet's shape, colour, and size (Nining et al., 2020). The diameter and thickness of the tablet were measured with a calliper and recorded in mm.

Weights variation

Ten tablets as samples were prepared. Each tablet was weighed, and the estimated amount of drug in each tablet was calculated in percentage of the amount stated on the label. The acceptance value determines whether the preparation is the same (Depkes RI, 2020). Correlation coefficients can also be calculated with weighted data.

Hardness and friability

Hardness was measured using a hardness tester (YD-3) by applying pressure to the tablet until it was crushed. The test was carried out on ten tablets. Friability was measured using a friability tester (TFT 2D/C5.2). A total of 20 tablets were cleaned, weighed (W_1), and put into the tool. Then, the tool was run at 25 rpm for 4 min. The tablet was cleaned and weighed again (W_2). Friability was determined by calculating the weight loss percentage to the initial weight (Nining et al., 2020).

Disintegration time

A total of 6 tablets were placed into the disintegration tester basket (BJ-2), and a weighted disc was placed in each hole. The tool was run with water at 37° ± 2° as the medium. The basket was removed at the end of the time limit, and the tablets were observed (all tablets must be crushed entirely). If one or two tablets did not entirely disintegrate, repeat the test with an additional 12 tablets: At least 16 of the 18 tablets tested must fully disintegrate (Depkes RI, 2020).

Drug content

Drug content was determined spectrophotometrically (Agilent Cary 60) with phosphate buffer saline (PBS) pH 7.2. First, the standard solution variations were made with theophylline BPFI to determine λmax (270,0 nm) and the standard curve. Sample preparation for compressed theophylline tablets was done by grinding 20 until they became powder. A certain amount of powder (~10 mg theophylline) was weighed, dissolved in PBS pH 7.2 in a 100 mL volumetric flask, diluted, and measured for absorbance at the λmax obtained previously.

Dissolution

The test procedure utilized a dissolution tester (Hanson Research SR 8 plus) with a paddle stirrer type. PBS pH 7.2 was used as a dissolution medium with an agitation speed of 100 rpm and a temperature of 37 ± 0.5°C. The pH of PBS is adjusted to 7.2 in order to simulate the pH conditions in the proximal ileum during the fasting state (Hamed et al., 2016). The sampling process was conducted at 15, 30, 45, 60, 90, 120, 240, 300, 360, 420, and 480 min. The sample is replaced with a new dissolution medium of equal volume to maintain a constant medium volume. The sample absorbance was measured, and the dissolved drug content was determined using λmax and a standard curve previously determined (Ainurofiq et al., 2014).

Release kinetics modeling

The in-vitro studies results were entered into several kinetic model equations (8)-(11), such as zero-order, first-order, Higuchi, and Korsmayer-Peppas, to characterize kinetic release studies and determine the drug release mechanism (Kamboj et al., 2014). Each kinetic model's linear regression line equation was created using its principles.

(a) Zero-order kinetics: $Q_t = Q_0 + K_0 t$ ……(8)

where Q_t is the amount of drug dissolved at time t, Q_0 is the initial amount of drug in solution, and K_0 is the zero-order release constant. A linear graph shows the cumulative amount of drug the system releases (Q_t) and time (t).

(b) First-order kinetics: $\ln Q_t = \ln Q_0 - K$ …… (9)

where K is the first-order release constant. A linear graph shows the logarithm of the drug cumulative amount (In Q_t) and time (t).

(c) Higuchi model kinetics: $Q_t = K_H t^{½}$ …… (10)

where K_H is the Higuchi dissolution constant. A linear graph shows the drug cumulative amount (Q_t) and the root of time (t ½).

(d) Kinetics of the Korsmayer-peppas model: $M_t/M_\infty = Kt^n$ ……(11)

where M_t/M_∞ is the fraction of drug released over time t, and n is the release exponent. The exponent value (n) indicates the drug release mechanism.

A linear graph is shown between the logarithm of the drug released cumulative amount < 60% and the logarithm of time as indicated by a correlation coefficient value close to one (r^2 > 0,98). Determination of the kinetic model for drug release from tablets was determined from the r^2 value in the linear regression equation obtained by each formulation. If r^2 approaches one, the kinetics follows the release of the regression equation from that kinetic model (Nining et al., 2021).

Data Analysis

A theoretical approach was carried out on some evaluation data by comparing it with the requirements contained in compendial and other standard books. Statistical analysis was carried out on tablet evaluation data with one-way ANOVA (α=0.005), and then, the Tukey HSD test was continued to determine the significance of the differences between formulas.

RESULT AND DISCUSSION

Packing and flow properties

Granules were made using the wet granulation method. The packing and flow properties, such as bulk and tapped density, Hausner ratio, Carr index, flow rate, and angle of repose, are shown in Table 2. Some fundamental parameters that govern the efficiency of many processes include solid particle packing, density, and void proportion. Porosity is connected to the inner structure of the particle (affecting particle density), whereas vacancy is related to the gaps between the particles (affecting bulk density) (Kalman & Portnikov, 2020). The bulk and tapped density for all granules ranged from 0.51 g/mL to 0.54 g/mL, with drying losses ranging from 4.59% to 5.33%. The granules' moisture accumulates on the surface and creates water-bridging forces that reduce the bulk density. Bulk and tapped density estimate powder volume at a particular production scale. The test is one of the most straightforward approaches for determining "flowability" with the Carr index and Hausner ratio classification. These two indices represent powder packing behaviour with and without tapping (Akseli et al., 2019). The difference in bulk and tapped density values is between 0.2 and 0.3, which indicates that the volume has mostly stayed the same even though 500 tappings have been carried out. That confirms that the granule size is the same and reproducible (Singh et al., 2021). Carr index and Hausner ratio showed low values, < 10% and < 1.11, respectively, which predicted acceptable flow. Both were used to estimate powder flow since they are related to powder density and internal friction. In particular, both describe inertial forces generated by tapping (for tapped density) and interparticle friction relative to gravitational forces (for bulk density). Powders that exhibit low internal friction relative to their weight cannot withstand the force of their gravity and, therefore, will compact based on density measurements. Further rearrangement stimulated by tapping did not cause a significant reduction in volume, and the powder was characterized by a low Carr index and Hausner ratio (Akseli et al., 2019).

Table 2. Evaluation data of F1-F3 batches teophylline granule core

Parameter	F1	F2	F3
Bulk density (g/mL)	0.51 ± 0.00	0.51 ± 0.01	0.51 ± 0.00
Tapped density (g/mL)	0.54 ± 0.01	0.53 ± 0.01	0.54 ± 0.00
Carr index (%)	5.42 ± 1.16	3.75 ± 0.62	4.79 ± 0.58
Hausner ratio	1.06 ± 0.01	1.04 ± 0.01	1.05 ± 0.01
Flow rate (g/s)	13.77 ± 0.20	16.23 ± 0.22	16.44 ± 0.18
Angle of repose (°)	28.44 ± 1.63	27.44 ± 0.41	29.23 ± 1.38
Loss on drying (%)	5.33 ± 0.41	4.59 ± 0.01	4.69 ± 0.11
Granule size (πm)	553.28 ± 7.70	569.04 ± 11.04	627.28 ± 10.67

Solid particle flow is the movement of particles relative to neighbouring particles to create a sliding surface. At the same time, the angle of repose is defined as the angle of inclination of the free surface to the horizontal of the bulk solid pile. It is a criterion for the ability to flow solid particles and a fundamental parameter in bulk material storage (Kalman, 2021). The angle of repose obtained ranges from 27.44° to 29.23° with a granule size ranging from 553.28 πm to 627.28 πm, which means it is excellent to flow. Particles larger than 250 πm usually flow relatively freely in contrast to particles under 100 πm in size, which tend to become cohesive and have problems with the flow (Avbunudiogba et al., 2020).

Physicochemical properties of coating tablets

Various physicochemical properties of coating tablets, such as diameter and thickness, weight variations, hardness, friability, and tablet disintegration time, are presented in Table 3.

Table 3. Evaluation data of theophylline tablet

Parameter	F1 (1:3)	F2 (1:4)	F3 (1:5)
Size variation			
Diameter (mm)	9.24 ± 0.06	9.26 ± 0.05	9.24 ± 0.07
Thickness (mm)	5.15 ± 0.07	5.07 ± 0.07	5.07 ± 0.12
Weight variation (mg)	333.38 ± 4.40	334.99 ± 7.29	339.56 ± 11.65
Coefficient of variation (CV, %)	1.32	2.18	3.43
Acceptability value	6.53	7.70	13.58
Hardness (kgf)	11.61 ± 1.17	13.69 ± 0.01	18.86 ± 2.45
Friability (%)	0.186 ± 0.003	0.155 ± 0.003	0.103 ± 0.001
Disintegration time (min)	20.69 ± 0.38	24.25 ± 0.75	27.36 ± 1.09
Drug content (%)	98.51 ± 0.93	98.51 ± 0.08	98.55 ± 0.10

Tablets must have good dosage uniformity. Tablets with a drug content of ≥ 25 mg with an active substance ratio of ≥ 25% were tested for preparation uniformity using the weight variation method (Depkes RI, 2020). All formulas' variation coefficients are below 5%, and the acceptance value is below 15.0. Both prove that tablets have a similar amount of active substance in the dosage unit. The acceptability value was calculated by estimating the drug content in each tablet against the drug content of each dosage formula. The drug content obtained ranged from 98.51% to 98.55%. The granules' flow properties greatly influence the moulded mass's weight or dosage uniformity, including their porosity (Iswandana et al., 2018; Syukri, 2018).

Tablet hardness is a parameter of a tablet's resistance to mechanical stress, such as shock and tablet cracking during packaging, transportation, and usage (Syukri, 2018). Tablet hardness in all batches ranged from 11.61 kgf to 18.86 kgf. Increasing the coating concentration increases the tablet's hardness. This observation may be caused due to the stronger bond between the guar gum polymer and HPMC-K 15M. Another study reported something similar when tablets were formed using methacrylate polymer (Avbunudiogba et al., 2020). Tablet friability indicates the resistance of the tablet surface to impact during packaging. The value is good if the amount is below 0.8% (Syukri, 2018). The friability value decreases as the coating polymer concentration increases. This increase in concentration is thought to increase the thickness of the coating layer, thereby preventing the release of powder particles from the tablet surface. This finding is inversely proportional to the tablet's friability with a NaCMC matrix (Iswandana et al., 2018). Even though HPMC and NaCMC are hydrophilic polymers, the coating system will be more effective in reducing friability in tablets than the matrix system.

Disintegration time is required for a tablet to break completely into small particles or granules, as indicated by the hole in the tool basket passing through (Syukri, 2018); the disintegration time obtained ranged from 20.69 min to 27.36 min. Increasing the polymer concentration increases the tablet disintegration time with the exact estimation of the tablet's friability. Coated tablets must disintegrate within 60 min (Syukri, 2018). Several factors influenced the disintegration time, excipient usage, production tablet method, type and concentration of lubricant, machine compression during tabletting, as well as physicochemical properties of tablet ingredients (Nining et al., 2020).

Drug release kinetics

The purpose of sustained-release preparations is to slow the drug release rate in the digestive system and reduce the frequency of drug administration. The release rate of a dosage form regulates drug absorption from the sustained-release dosage form so that there is a constant rate to minimize

unexpected toxic peaks and subtherapeutic troughs in plasma levels, often occurring at various doses (Caldwell & Kaushal, 2017). For this purpose, it is necessary to characterize the drug release profile of the preparation using an in-vitro dissolution test (Al-Hashimi et al., 2018). Before testing, the maximum wavelength and calibration curve were determined to be used to measure dissolved drug levels spectrophotometrically. The maximum wavelength obtained is 270 nm with a calibration curve equation Y = 0.05970 µg/mL and 10.9 µg/mL. In the dissolution test, the solubility of the theophylline was measured at several time points for 8h or 480 min. A paddle-type tool was used with a speed setting of 60 rpm at 37°C with PBS pH 7.2 medium. Sampling was conducted at 15, 30, 60, 90, 120, 180, 240, 300, 360, 420, and 480 min.

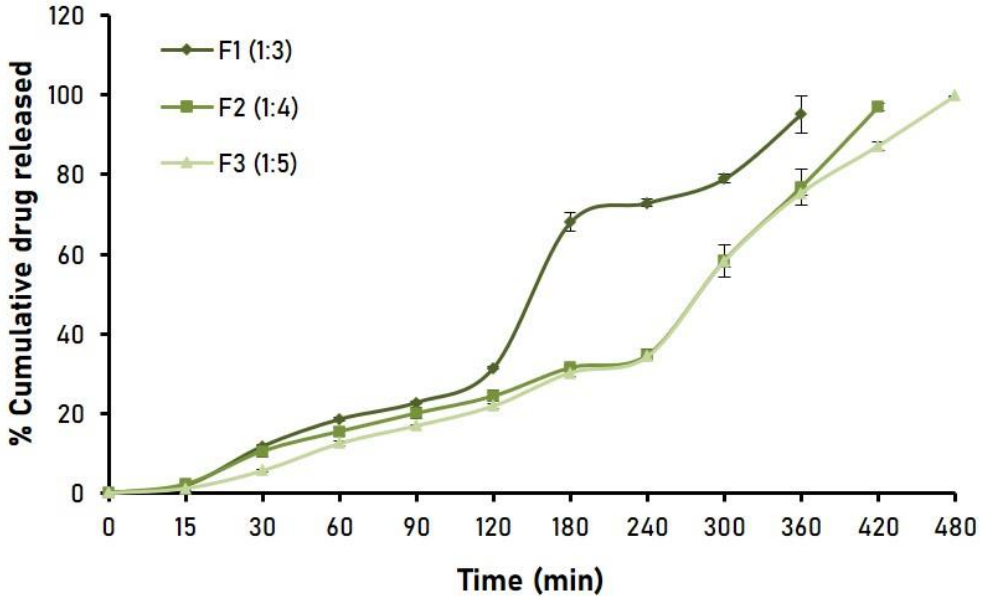

Figure 1. In-vitro dissolution profile of theophylline coated tablets in PBS 7,2

In Figure 1, the large amount of drug release in F1 began to occur significantly at 180 min (3h), which is very different from F2 and F3. Meanwhile, in F2 and F3, a significant difference in drug release occurred starting at 300 min. Regarding the shape of the curve, drug release in F2 and F3 shows almost the same shape. However, the F3 coating slightly inhibits drug release compared to F2, which is indicated by the position of the F3 curve below F2 on the graph. Theophylline is slightly soluble in water (Mohamed et al., 2013). Water-soluble drugs exhibit rapid release rates, usually through diffusion, whereas insoluble drugs are primarily released through gel erosion. In addition, water-soluble drugs tend to experience increased osmotic pressure, resulting in rapid diffusion—osmotic pressure applied to the sponge gel core causes polymer swelling (Mohamed et al., 2013). The results showed that increasing the concentration ratio of HPMC K15M to guar gum resulted in a decrease in theophylline dissolution. The mechanism for drug release from the preparation occurred through the process of developing the coating polymer (Singh et al., 2021). This event results in the formation of a gel around the tablet and inhibits the slow release of the drug. In this case, HPMC K15M is a polymer with high viscosity, which absorbs water significantly to form a gel. The dissolution medium penetrates the gel layer, and the drug molecules exit the system by diffusion. That can be seen from each formula in the dissolution rate data (Majumder et al., 2016).

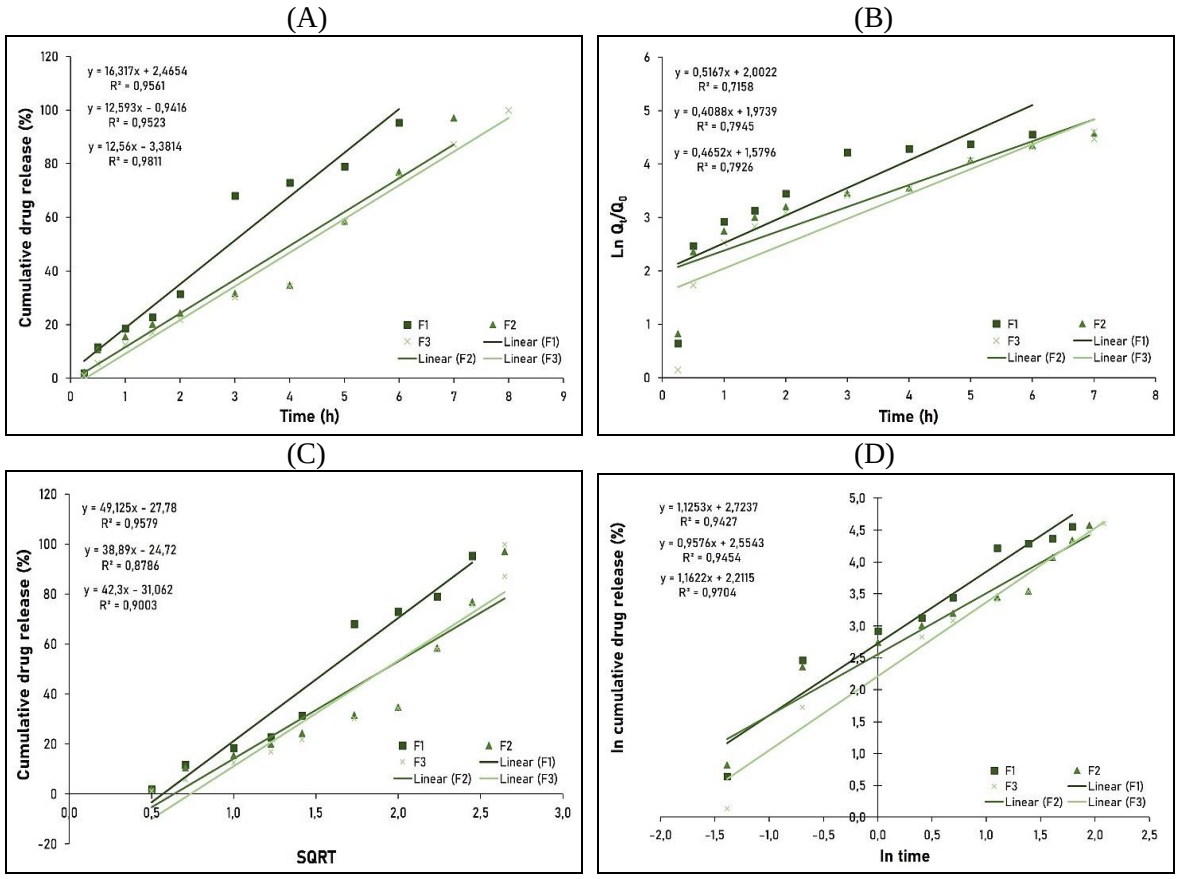

Figure 2. Comparative linear plots of (A) zero-order, (B) first-order, (C) Higuchi (SQRT), and (D) Korsmeyer-Peppas release kinetics model for F1-F3

Based on cumulative drug release data at 360 min, F3 (1:5) showed the most retarded release of up to 75.42% compared to F2 (1:4) and F1 (1:3), with drug release of 76.91% and 95.24%, respectively. These data show that increasing the HPMC K15M polymer by 1% in the preparation can hold the drug for 1.49–18.33%. That was also found in research on releasing salbutamol sulphate coated with various polymer concentrations. These differences cause the polymer thicknesslayer on the granules to vary and affect the drug release rate. Increasing the polymer's thickness will reduce the film layer's porosity, slowing drug release (Al-Hashimi et al., 2018). The physicochemical properties and the polymer amount used to coat the surface regulate the drug release rate. Moreover, it is regulated by changing the coating layer's thickness, tortuosity, and permeability (Seo et al., 2020).

Table 5. Estimated correlation coefficient and diffusion exponent values from theophylline dissolution data

Tablet	Zero-order		First-order		Higuchi		Korsmeyer-Peppas	
	r^2	K_0 (mol)	r^2	K_1 (h^{-1})	r^2	K_H	r^2	n
F1 (1:3)	0.9561	16.32	0.7158	0.52	0.9579*	49.12	0.9427	1.12
F2 (1:4)	0.9523*	12.59	0.7945	0.41	0.8786	38.89	0.9454	0.96
F3 (1:5)	0.9811*	12.56	0.7926	0.46	0.9003	42.30	0.9704	1.16

Table 5 and Figure 2A-2D show various release kinetic models to predict tablet drug release mechanisms and verify whether diffusion is Fickian or non-Fickian. The results with the highest linearity (r^2 closest to 1) show the behaviour of the zero-order kinetic model (Figure 2A) at F2 and F3 with rate constant (k) values of 12.59 and 12.56 mol, respectively. In general, these results do not show significant differences in slowdown rate. From the first to the 6h, the released drug concentration was almost similar between F2 and F3, but there was a significant difference at the 7h. A delivery system that follows zero-order kinetics will release the same amount of drug per unit of time and is the best release technique to achieve delayed effects (Rasul et al., 2020). F1 leads to two kinetic models with comparable correlation coefficients: the zero-order and the Higuchi models. That may imply that the viscosity of hydrated coatings may be the same despite differences in viscosity levels (Hirun, 2022). In the Kosrmayer-Peppas kinetic model (Table 5), relatively good linearity was also demonstrated in all three tablet formulas, and the release exponent (n) values were found to be in the range of 0.96–1.16, indicating a super-case II transport mechanism. It refers to the drug transport mechanism related to pressure and transition in hydrophilic glass polymers swelling in water or biological fluids (Solanki & Motiwale, 2020). The conclusive findings indicated that the tablet coating with the lowest concentration of film coating, F1 (1:3), adhered to the zero-order model, but the other two, F2 (1:4) and F3 (1:5), adhered to the Higuchi models.

CONCLUSION

Suitable quality theophylline tablets with HPMC K15M and guar gum coating have been successfully produced. Increasing the concentration ratio of HPMC K15M to the coating solution resulted in a decrease in the drug release rate. The maximum release is provided at F3 with a ratio of 1:5, which releases the drug for up to 480 min or 8h. The drug release kinetics formulations followed the Higuchi (F1) and zero-order kinetic model (F2 and F3).

ACKNOWLEDGEMENT

The authors thank Lemlitbang UHAMKA for grant support (298/F.03.07/2023) and the Faculty of Pharmacy and Science UHAMKA for the facilities provided until this research was completed.

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