Jurnal Teknologi Industri Pertanian, 36 (1): 1-11, April 2026 *Available online on*
ISSN: 0216-3160 E-ISSN 2252 3901 *https://journal.ipb.ac.id/index.php/jurnaltin*

Research Paper

OPEN ACCESS

Check for updates

FORMULATION OF KONJAC GLUCOMANNAN AND CARRAGEENAN-BASED HARD CAPSULE

Winda Herman [1,2,)*], Titi Candra Sunarti[1)], Sapta Raharja[1)], Khaswar Syamsu[1)]

[1)]Agroindustrial Engineering Study Program, Faculty of Agricultural Engineering & Technology, IPB University
Kampus IPB Darmaga, Bogor 16680, West Java, Indonesia
[2)]Industrial Engineering Study Program of Institut Teknologi Perkebunan Pelalawan Indonesia
Email: winda@itp2i-yap.ac.id

Article Info

Received: October 11, 2024
Revised: December 20, 2025
Accepted: January 10, 2026
Published: April 2026

Keywords:

carrageenan, formula optimization, hard capsule, konjac glucomannan

ABSTRACT. Commercial hard capsules are primarily manufactured from bovine or porcine gelatine, which often restricts consumer choice owing to religious concerns and vegetarian lifestyles. Konjac glucomannan demonstrates superiority as a gelling and film-forming material, making it a highly potential gelatin substitute in the manufacture of hard capsules. The objectives of this study was to design and determine the optimum conditions for a hard capsule formula based on konjac glucomannan and carrageenan. This study was employed response surface methodology (RSM). The independent variables analyzed were the ratios of konjac glucomannan (2.5%, 3%, and 3.5%; X1), carrageenan (1.5%, 2.0%, and 2.5%; X2), and glycerol (0, 0.125%, and 0.250%; X3). The dependent response variables analysed were capsule moisture content and disintegration time. The moisture content ranged from 5.6% to 15.9%, indicating that higher ratios of konjac glucomannan and glycerol resulted in higher capsule moisture content. Capsule disintegration time ranged from 10.12 to 24.25 min, indicating that a higher glycerol ratio accelerated the hard capsule destruction time. The capsule moisture content and disintegration time were significantly influenced by the raw material used and the resulting capsule specifications.

INTRODUCTION

The term capsule originates from the Latin term “capsula, ” which means small container. Capsules are defined as solid preparations in which the drug or active compound is enclosed within a soluble hard or soft shell. Hard capsules are typically filled with powders or granules, whereas soft capsules (also known as soft gels) are generally filled with liquids. Hard capsules consist of two distinct parts: the body and cap. This design allows them to be filled manually during prescription services at pharmacies, a flexibility that constitutes a major advantage over other dosage forms. In contrast, soft capsules are formed, filled, and sealed using a single machine process, which consequently yields greater content uniformity and homogeneity and often facilitates better drug dissolution because the drug is frequently already in solution form (Ministry of Health, 2020).

In the pharmaceutical field, hard capsules are important packaging materials that provide comfort during drug consumption. They serve as practical containers to maintain the stability of the active ingredients against the influence of light, moisture, and oxygen, thereby ensuring a long shelf life (Chen *et al.*, 2016). According to data from Future Market Insights (2022), the global market value of hard capsules was US$1.7 billion in 2021 and are projected to continue growing to around US$3.2 billion by 2032. Commercial hard capsules are generally made from gelatin, derived from pigs or cows (Gelatin Representatives of the World, 2021). However, gelatin-based hard capsules often influence consumer preferences owing to religious issues and the rise of vegetarianism globally, as these populations do not consume animal products (Karim and Bhat, 2009). To capture and serve these market segments, there is an evident need to develop alternative plant-derived

 DOI: https://doi.org/10.24961/j.tek.ind.pert.2026.36.1.1

ingredients as substitutes for gelatin in the manufacture of hard capsules.

Hydroxypropyl methylcellulose (HPMC), derived from plant materials, has been successfully used to replace animal gelatin in the manufacturing of hard capsules. HPMC capsules have a low moisture content (4–6%) and are therefore unlikely to become brittle when exposed to low humidity (Chen *et al.,* 2016). Furthermore, HPMC capsules are known to be chemically stable and do not interact with medications (Jones *et al.,* 2012). To date, commercial hard capsules made from cellulose include DRcaps®, enTRinsic™, Vcap®, and Bio-VXR®, all of which claim to protect acid-labile drugs from harsh stomach conditions (Vattanagijyingyong *et al.,* 2022). However, the search for other alternative materials with similar properties to gelatin and offering greater production potential must continue.

Konjac glucomannan is a suitable alternative material for manufacturing biopolymer-based packaging films because of its safe, edible, and annually renewable characteristics. However, the search for other alternative materials that exhibit similar properties to gelatin and offer greater production potential must continue (Rachmawati, 2018). Carrageenan is frequently used as a constituent material in the manufacture of drug delivery matrices (Sedayu *et al.,* 2019). Even when used in small amounts, delivery systems containing carrageenan offer several significant advantages over systems without it (Gu *et al.,* 2021). Furthermore, combining carrageenan with konjac glucomannan, locus bean gum, and other polysaccharides can notably improve the hardness, smoothness, elasticity, and transparency of the resulting gel (Dong *et al.,* 2021). The manufacture of hard capsules often involves the addition of plasticizers to form a composite film. The addition of glycerin (glycerol) to the konjac glucomannan hard capsule composition is vital, as it causes the resulting biopolymer to be more flexible and soft than formulations without it (Rachmawati, 2018).

Previous research by Chen *et al.* (2016) demonstrated that hard capsules were manufactured using oxidized konjac glucomannan and carrageenan; however, the resulting capsule films exhibited a relatively high moisture content of 12%. Similarly, Rachmawati (2018) reported the use of konjac glucomannan, agar, and glycerin in hard capsule production. However, the resulting hard capsules were imperfect, displaying non uniform thickness and persistent air bubbles on the capsule surface.

Based on the above description, this study aimed to develop hard capsules by combining konjac glucomannan and carrageenan with an added plasticizer, followed by optimization using response surface methodology (RSM). The variables investigated were the composition ratios of konjac glucomannan, carrageenan, and glycerin, based on the response variables of moisture content and disintegration. Therefore, the primary purpose of this study was to design optimum formula conditions for konjac glucomannan- and carrageenan-based hard capsules by analyzing the characteristics and performance of the resulting product.

RESEARCH METHODS

Time and Place of Research

This research was conducted at the Laboratories of Process Technology and Bioindustry, Division of Agroindustrial Engineering and Technology, Faculty of Agricultural Engineering and Technology, IPB University, and PT Kapsulindo Nusantara.

Tools and Materials

The raw materials utilized were konjac glucomannan (90% purity), obtained from CV. Tri Mitra Agro; semi-refined kappa carrageenan (PT Indo Chem); glycerol (Pro Analysis Merck); demineralized water (PT Barataco); soya lecithin from Buanachem Bandung; HCl (Pro Analysis Merck); H_2SO_4 (Pro Analysis Merck); and erythromycin stearate (Erysanbe brand). The equipment utilized included beakers, measuring cylinders, micropipettes, Petri dishes, stirring rods, a thermometer, a pH meter, a digital scale, a hot plate magnetic stirrer, a drying oven, and dipping pins.

Research Procedure

This research was conducted in two main stages: formulation of model materials for hard capsule production through optimization and validation of the final product based on the optimum conditions obtained, and evaluation of drug release (dissolution) from hard capsule products prepared under these optimum conditions.

Raw Material Characterization

The characterization of konjac glucomannan and carrageenan raw materials includes moisture and ash contents (AOAC 2005)**,** pH, and 1% viscosity.

 DOI: https://doi.org/10.24961/j.tek.ind.pert.2026.36.1.1

Hard Capsule Production

Hard capsules were produced by preparing a gel solution comprising 2.5% (w/v) konjac glucomannan, 1.5% (w/v) carrageenan, and 0.25% (w/v) glycerol. The process began with mixing konjac glucomannan flour with 50 mL of aquadest. This mixture was then stirred at 1200 rpm for 4 h at room temperature to break down the glucomannan flour crystals. Once the glucomannan colloidal solution was formed, carrageenan, glycerol, and another 50 mL of aquadest were added. The solution was stirred again at 80°C for 30 min. Molding was performed by dipping a pen into the gel solution, which was then dried for 2 h. After drying, separation from the dipping pen was carried out, followed by cutting according to size, combining the hard capsule parts, and finally placing the assembled capsules into plastic clips and storing them at room temperature of 27°C and a relative humidity (RH) of ± 51%.

Experimental Design

The optimum conditions of the formulation process were determined using the response surface methodology (RSM), specifically the Box–Behnken design (BBD) model, implemented via the Design Expert 13.0 program. The BBD design consisted of three independent variables (X): KGM, carrageenan, and glycerol, as shown in Table 1. The following sections detail the variables and their respective levels assigned for the formulation process using the BBD model.

Based on RSM, the Box–Behnken design utilized 15 testing points involving three factors. All testing points were experimentally conducted in the laboratory to determine the observed responses (Y), specifically the capsule moisture content and capsule disintegration (Ministry of Health, 2020), for each treatment variation provided by RSM. From all these experimental results, RSM ultimately provides the optimum conditions for the process. The recommended optimum condition was then validated to verify the goodness of fit of the design.

Capsule Moisture Content (AOAC, 2005)

Moisture content was determined by weighing a 1 g sample of the capsule shell, which was then placed in an oven. Drying was conducted at 105°C for 3 h. The dried hard capsule was then cooled in a desiccator containing silica gel as the absorbent. After cooling, the capsule shell was weighed again. Moisture content was determined using the following equation:

$$Moisture\ content = \frac{X - Y}{X} \times 100\%$$

where X and Y are the initial and final weights of the hard capsules, respectively.

Disintegration

Disintegration testing was performed according to the method specified by the Ministry of Health (2020). Capsules were placed in a medium of distilled water at 37°C and stirred at a speed of 100 rpm. The capsules were observed to disintegrate within 30 min.

Hard Capsule Specification

Capsule specifications were measured for both the capsule formulation and the validated best-recommended capsule. These measurements included capsule weight, determined using an analytical balance; length and diameter of the body and cap, measured using a caliper; and capsule thickness, measured using a screw micrometer (Amalina *et al.*, 2020).

Dissolution of Erythromycin Stearate in Capsules

Dissolution of erythromycin stearate in capsules was carried out in vitro using 0.2 g of erythromycin stearate. The capsules were immersed in a dissolution medium resembling gastric conditions, prepared with 900 mL of 0.1 M HCl solution at a temperature of 37°C and stirred at 100 rpm. Capsule rupture time and drug release were observed simultaneously from 1 to 15 min

Table 1. Variables and levels that RSM assigns to the formulation of hard capsules

Variabel Factor (%)	Level			References
	Minimum Limit	Center Point	Maximum Limit	
Konjac Glucomannan	2.5	3.0	3.5	Chen *et al.*, 2016
Carrageenan	1.5	2.0	2.5	Chen *et al.*, 2016
Glycerol	0	0.125	0.250	Chen *et al.*, 2016; Rachmawati, 2018

 DOI: https://doi.org/10.24961/j.tek.ind.pert.2026.36.1.1

Furthermore, dissolution testing was continued by collecting samples that dissolved in the medium after 20, 25, 30, 45, 60, 75, 90, and 120 min.

The samples were filtered using filter paper to remove any undissolved erythromycin stearate. Next, 2 mL of the sample solution was diluted with 2 mL of the dissolution medium, and then 4 mL of 75% (v/v) sulfuric acid was added; this triggers a reaction that produces a yellow-green color. The dissolved erythromycin stearate content was subsequently determined by measuring the absorption at a wavelength of 482 nm using a UV spectrophotometer (Chen *et al.*, 2016).

Modelling the Dissolution Kinetics of Erythromycin Stearate

Kinetics modelling was performed using the Ddsolver add-in software in Microsoft Excel. DDsolver is an additional menu integrated into Excel software that can be utilized for statistical and kinetic modelling (Citrariana *et al.*, 2020). The analysis utilized frequently employed drug release kinetics models, namely zero-order, first-order, Higuchi, Korsmeyer Peppas, and Hixson Crowell, and applied a nonlinear regression approach according to the equation listed in Table 2.

RESULT AND DISCUSSION

Raw Material Characterization

The quality characteristics of the konjac glucomannan and carrageenan used in this study are presented in Table 3.

As shown in Table 3, the moisture contents of both raw materials satisfied the specified standard (below 12%). A lower moisture content in the raw material generally indicates better quality. However, the ash content of carrageenan was observed to be extremely high at 16%, whereas that of glucomannan was less than 2.0%. This significant difference affected the quality of the resulting hard capsules. During hard capsule manufacturing, the initially clear konjac glucomannan solution became cloudy after the addition of carrageenan. This phenomenon is similar to that observed in gelatin-based capsules: Febriana et al. (2021) reported that a high ash content in gelatin reduces clarity, resulting in cloudy gelatin. Similarly, when high-ash gelatin is used as the raw material for capsule shells, the resulting capsules are not clear.

The pH value of KGM was measured at pH 6.17, which is lower than the neutral pH standard for carrageenan. However, KGM was still able to form a gel solution. According to Wang and Andi (2013), combining xanthan gum with KGM can form a gel at any pH, even though xanthan itself does not form a gel; the greatest synergy is observed at pH 5 with a 2:3 ratio of the two ingredients. Regarding viscosity, both KGM and carrageenan met the standard. However, KGM exhibited a significantly greater viscosity (37,000 cPs) than carrageenan (10.230 cPs). Consequently, the preparation of hard capsule solutions utilizing KGM necessitated a heating process at a stable temperature of 80°C. This is supported by Rachmawati (2018), who stated that the viscosity of KGM solution increases as its heating increases.

Table 2. Dissolution kinetic model equations in DDSolver Program (Siswanto *et al.*, 2016)

Model	Zero order	First order	Higuchi	Korsmeyer-P	Hixson Crowell
Equations	F = K0*t	F =100*[1-Exp(-k1*t)]	F = kH * t 0,5	F =Kkp*tn	F =100*[1-(1-kHC*t)3]

Notes : F = Amount of drug dissolved in % ; t = disolution time

Table 3. Characteristics of konjac glucomannan and kappa carrageenan

Spesification	Konjac Glucomannan (KGM)	Kappa Carrageenan	KGM Technology Standard	Standard SNI 83911:2017 for Refined Carrageenan
Moisture Content (%)	11	6.7	<12	<12
Ash Content (%)	<2.0	16	2,16	15-40
pH	6,17	7,1	7	-
Viscosity 1% (cPs)	37.000	10.230	>36.000	>5

 DOI: https://doi.org/10.24961/j.tek.ind.pert.2026.36.1.1

Formula Optimization in The Manufacture of Hard Capsules

Based on the formula recommendations from RSM, 15 experiments were conducted. All BBD-recommended formulas successfully formed hard capsules, as illustrated in Figure 1, with the detailed specification analysis results presented in Table 3. The hard capsule combination of KGM and carrageenan exhibited a slightly cloudy color and contained spots caused by KGM granules that had not dissolved completely. Additionally, air bubbles were trapped in the hard capsule solution during molding, resulting in a rough surface. This finding aligns with Fahrullah and Ervandi (2022), who observed that whey films containing 3% KGM showed trapped air bubbles and the presence of granules due to incomplete mixing of KGM with the whey matrix. They noted that these surface bubbles could be removed via a vacuum process. Furthermore, Wang and Andi (2013) highlighted the unique requirement for forming a fully soluble glucomannan gel, stating that the formation of a thermoreversible gel necessitated a heating process at 85°C and a pH of 9–10.

Based on the results of the design of variables and levels provided to the formulation process with the BBD model, 15 formulas were generated, as detailed in Table 4. Each of these formulas was subsequently analyzed for moisture content and capsule disintegration.

Moisture Content

Moisture content is a crucial parameter for meeting commercial standards in hard capsule production because it is directly related to capsule durability. Capsule moisture content also significantly influences microbial activity and capsule brittleness. When the moisture content in a hard capsule is too high, it causes the capsule to become mushy and easily susceptible to mold growth during storage. This finding aligns with the research of Junianto et al. (2013), who stated that high capsule moisture content, especially if it exceeds 20–60%, can potentially promote the growth of mold and mildew. Conversely, hard capsules that are too dry easily become brittle or break.

In this study, hard capsules were produced with a moisture content ranging from 5.6% to 15.9%. The measured moisture content value is still considered low compared to the gelatin capsule standard of 13-16% (Ministry of Health, 2020). However, this range is regarded as relatively high for capsules derived from vegetable materials, as hydroxypropyl methylcellulose (HPMC) typically exhibits a much lower moisture content ranging from 4% to 6% (Chen *et al.*, 2016). The moisture content of hard capsules is known to be affected by drying time, drying temperature, and the viscosity of the raw materials (Junianto *et al.*, 2013).

Figure 1. Hard capsule produced from mixture of konjac glucomannan and carrageenan

Table 4. Response optimization results of Box-Behnken designs on RSM for hard capsule formulation

Run	Factor			Responses	
	Glucomannan (%)	Carrageenan (%)	Glycerol (%)	Moisture Content (%)	Disintegration Time (min)
1	3	1.5	0.25	12.1	10.12
2	3	2.5	0	10.4	17.06
3	3	2	0.125	8.8	10.17
4	2.5	2	0	5.6	18.36
5	3	2	0.125	7.6	10.55
6	3.5	2	0.25	14.5	19.09
7	3	2	0.125	8.2	12.05
8	3.5	2	0	9.1	22.42
9	3	1.5	0	8.5	14.59
10	3	2.5	0.25	15.9	14.03
11	2.5	2.5	0.125	11.6	15.48
12	2.5	2	0.25	9.9	16.17
13	3.5	1.5	0.125	13.5	18.13
14	2.5	1.5	0.125	6	16.44
15	3.5	2.5	0.125	10.6	24.25
Ministry of Health (2020)				13-16	< 30

 DOI: https://doi.org/10.24961/j.tek.ind.pert.2026.36.1.1

This relationship was further investigated by Fatnasari *et al.* (2018), who found that the moisture content of the edible film increased as the concentration of glycerol in the edible film formulation increased. In this study, because the hard capsules were dried using the same time and temperature (2 h at 29°C), the resulting capsule moisture content was predominantly influenced only by the ratio of the raw materials, as presented in Figure 2.

The optimization process for the desired moisture content response aimed to produce a minimum capsule moisture content of less than 16%. Ultilizing RSM, the interactions between ingredients were observed (Figure 2). Figure 2A illustrates the interaction between KGM and carrageenan, where increasing the ratio of KGM led to higher moisture content (ranging from 5.6% in formula 4–14.5% in formula 6). Similarly, the interaction between KGM and glycerol (Figure 2B) showed that a greater combined ratio of these two ingredients was correlated with higher moisture content (ranging from 6% in formula 14–13.5% in formula 13). Furthermore, the interaction between carrageenan and glycerol (Figure 2C) also indicated that a greater ratio of these components resulted in the highest moisture content (15.9% in formula 10). Overall, the results of this study consistently demonstrated that the greater the ratio of glucomannan and glycerol used in the formulation, the higher the resulting capsule moisture content.

Based on the RSM analysis, the results for the moisture content response indicated a significant response model. The lack of fit was found to be non-significant, with a p-value greater than 0.05 (specifically, 0.4464), thereby meeting the statistical requirements. Furthermore, the model exhibited strong statistical reliability: the R2 value was 0.9821, the VIF showed a value of 1, and the adequate precision was 18.7443. Both the adjusted R^2 (0.9498) and predicted R2 (0.7935) met the requirements, with a small difference of 0.1563. As affirmed by Ahmad *et al.* (2020), a correlation coefficient (R^2) value closer to 1 demonstrates a very good correlation between the experimental and predicted response values. Specifically, the R2 value of 0.9821 indicates that 98.21% of the response variation is explained by the factors, with only 1.79% attributable to other factors.

Disintegration Time

Hard capsules as packaging serve as a drug delivery system to the target site of action, providing a comfortable feeling in the oral cavity and thus helping to mask bitterness when the drug is consumed. Disintegration testing aims to characterize the time required for hard capsules to break down when subjected to the digestive system. In this study, hard capsules with disintegration times ranging from 10.12 to 24.25 min were successfully produced. The variations in capsule disintegration times observed in this study can be attributed to differences in the ratio of components used in the manufacturing of hard capsules. This observation is consistent with the study by Said *et al.* (2014), who reported that variations in capsule disintegration times were due to differences in the capsule shell. Consequently, the disintegration behavior of the capsules in this study can be understood by examining the interaction of the ratio of raw materials used, as presented in Figure 3. The optimization process for the desired disintegration response aimed to achieve the minimum possible hard capsule disintegration time. Utilizing RSM, the interaction between ingredients was observed, specifically in Figure 3A, which illustrates the relationship between KGM and carrageenan. Here, the lowest disintegration time was observed in formula 7 (12.05 min), and the highest disintegration time was observed in formula 15 (24.25 min). This trend leads to the conclusion that the lower the ratio of KGM used, the faster the capsule disintegration will be.

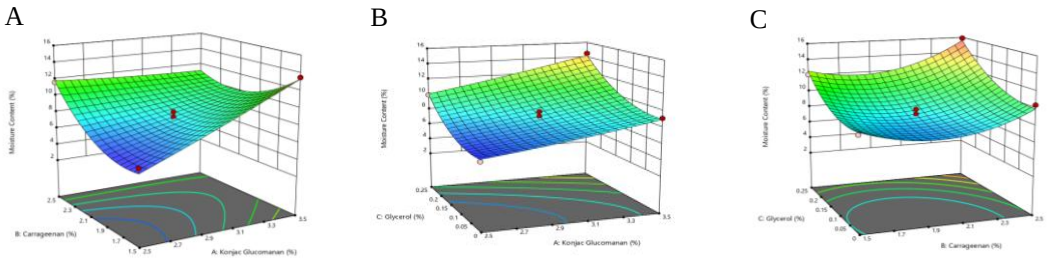

Figure 2. 3D surface response graph of moisture content of hard capsules produced from several concentration of (A) konjac glucomannan and carrageenan, (B) konjac glucomannan and glycerol (C) carrageenan and glycerol

 DOI: https://doi.org/10.24961/j.tek.ind.pert.2026.36.1.1

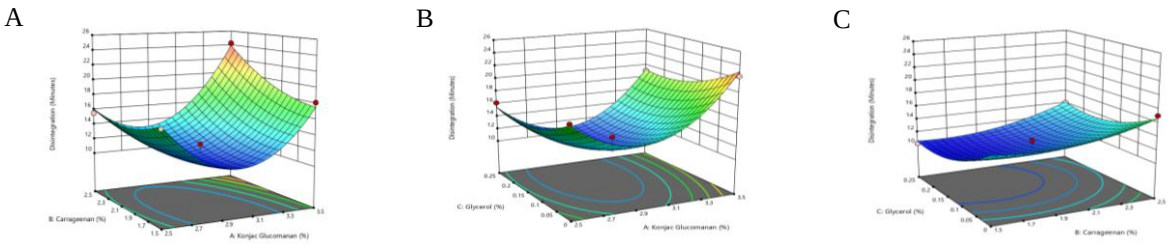

Figure 3. 3D surface response graph of disintegration time of hard capsules produced from several concentration of (A) konjac glucomannan and carrageenan, (B) konjac glucomannan and glycerol (C) carrageenan and glycerol

Figure 3B shows the interaction between KGM and glycerol, where the lowest disintegration time was observed in formula 7 (12.05 min) and the highest in formula 8 (24.42 min). This indicates that the lower the ratio of KGM used, the faster the disintegration will be. Furthermore, Figure 4C depicts the interaction between carrageenan and glycerol, showing the lowest disintegration time in formula 1 (10.12 min) and the highest in formula 2 (17.06 min). This pattern suggests that the higher the ratio of glycerol used, the faster the disintegration will be. Overall, the results of this study conclude that the greater the ratio of glycerol utilized in the formulation, the faster the hard capsule disintegration will occur.

Based on the RSM analysis, the results for the disintegration response indicated a significant response model. The lack of fit was found to be non-significant, as evidenced by a p-value greater than 0.05 (specifically 0.618); thus, it met the statistical requirements. The model demonstrated strong statistical reliability: the R2 value was 0.9833, the VIF was 1, and the adequate precision was 18.0428. Both the adjusted R^2 (0.9534) and the predicted R2 (0.8422) met the requirements, with a small difference of 0.1112. As highlighted by Ahmad *et al*. (2020), an R^2 value closer to 1 signifies a very good correlation between the experimental and predicted response values. The R2 value of 0.9833 specifically indicates that 98.33% of the response variation is explained by the formulation factors, leaving only 1.67% attributable to other factors.

Model Validation

Validation was conducted to ensure the suitability between the predicted results of the response variables and the actual conditions after testing. The validation process was performed according to the optimization solution provided by the Design Expert 13 software, which specified a ratio of konjac glucomannan (2.84%), carrageenan (1.81%), and glycerol (0.11%).

The software prediction for this optimized formula was a moisture content of 7.22% and a disintegration time of 10.77 min, yielding a desirability level of 0.910. This indicates that the formula is expected to produce a product with characteristics that match the target specifications with 91% confidence. Following the analysis stage (as shown in Table 5), RSM provided confidence intervals and prediction intervals to estimate the responses at a 95% confidence level (Table 6).

The validation results presented in Table 6 show that the response values were a capsule moisture content of 7.23% (with a standard deviation of 0.66) and a disintegration time of 10.35 min (with a standard deviation of 0.91). These actual response values were obtained from three repetitions and fell within the range of the e of the 95% prediction interval (PI). The measured capsule moisture content of 7.23% was significantly lower than the hard capsule film moisture content reported by Chen et al. (2016), which was 12%. Furthermore, this result met the quality standards for capsule shells, which specify a maximum moisture content of not more than 10% (BPOM, 2019). The capsule disintegration time also met pharmacopoeia standards, specifically requiring the time to be less than 30 min (Ministry of Health, 2020). Since the response validation results successfully met all required standards, it was concluded that konjac glucomannan and carrageenan can be successfully applied as raw materials in the manufacture of hard capsules.

Hard Capsule Specification

The specifications of the hard capsules produced based on the recommendations of the design expert 13.0 software program are presented in Table 7. The recommended capsule specifications are consistent with the findings of similar research, although the thickness and weight of the capsules remain comparatively low when measured against commercial capsule standards.

 DOI: https://doi.org/10.24961/j.tek.ind.pert.2026.36.1.1

Table 5. Model validation actual response values from the optimization of hard capsule formula

Repetition	Actual		Prediction	
	Moisture content (%)	Disintegration Tine (min)	Moisture content (%)	Disintegration Time (min)
1	7.6	11.02		
2	6.8	10.47	7.22	10.77
3	7.3	9.56		

Table 6. Confirmation validation results from the optimization of hard capsule formula

Parameter	Predicted Mean	Predicted Median	Std Dev	N	SE Pred	95% PI low	Data Mean	95% PI High
Moisture content	7.22	7.22	0.66	3	0.52	5.86	7.23	8.58
Disintegration Time	10.76	10.76	0.91	3	0.72	8.90	10.35	12.63

Table 7. Capsules specification produced from optimized formula

Specifications	Research Results	Validation Results	Commercial Capsule *
Length (cm)			
Body	1.733 - 2.103	1.681	1.793 - 1.895
Cap	0.818 - 1.068	1.054	1.021 - 1.123
Diameter (cm)			
Body	0.686 - 0.791	0.699	0.728 - 0.740
Cap	0.689 - 0.803	0.703	0.758 - 0.770
Thickness (mm)			
Body	0.054 - 0.068	0.059	0.101 - 0.107
Cap	0.056 - 0.070	0.061	0.104 - 0.110
Weight (g)	0.038 - 0.097	0.040	0.086 - 0.106

*(Amalina *et al.,* 2020)

The observed non-uniform capsule thickness in this study can be attributed to the manual capsule molding technique, in which the rotation of the mold significantly affects the adhesion of the solution to the capsule form. This observation is consistent with the research by Suptijah *et al.* (2012), who reported that irregular mold rotation techniques and manual manufacturing processes can result in uneven capsule shell thickness.

The specification of hard capsules produced in this study directly affects the performance of the drug delivery system. In particular, a low capsule thickness accelerates the disintegration time of the capsule, allowing the drug to be released in a short period. Factors that fundamentally affect the drug delivery system include capsule size and polymer characteristics, such as hydrophobicity or hydrophilicity (Bansal *et al.,* 2011).

Dissolution of Erythromycin Stearate in Capsules

An in vitro dissolution test was conducted to determine the time required for the capsule to release the drug in a 0.1 M HCl solution. The dissolution process begins with the entry of the medium solution into the capsule surface, which leads to swelling and pore formation. Once the capsule shell degrades, the medium interact with the active substance, resulting in a gradual release and substance, resulting in the gradual release and subsequent absorption of the active substance. The capsule dissolution process is illustrated in Figure 5. The test results showed that the capsule rupture time ranged from 2 to 7 min, and 80% of the drug was released within 6–12 min. This drug release ability of 6–12 min was faster than that reported by Chen *et al.* (2016), where their 80% DO capsules released erythromycin stearate (80%) within 30–45 min and had a rupture time ranging from 5–10 min. Furthermore, the results met the standard of the Chinese pharmacopoeia (2010) for gastric soluble erythromycin stearate capsules, which mandates that 75% of the drug must be released within 45 min and the capsule rupture time should be 5–10 min. Therefore, the capsules recommended in this study successfully met the pharmacopoeial standard.

The percent dissolution of erythromycin stearate was measured as follows: 19.25% dissolved at 20 min, 28.90% at 30 min, 32.68% at 45 min, 35.38% at 60 min, 38.54% at 75 min, 43.90% at 90 min, 49.19% at 105 min, and 57.02% dissolved at 120 min. Dissolution of erythromycin stearate using capsules in this study was still low compared with the required standard. Based on the Indonesian pharmacopoeia (Ministry of Health,

2020), the dissolution tolerance for erythromycin stearate must be not less than 75% of the labeled amount dissolved within 120 min. In contrast, erythromycin stearate without the capsule shell dissolved at 79.61% within 120 min.

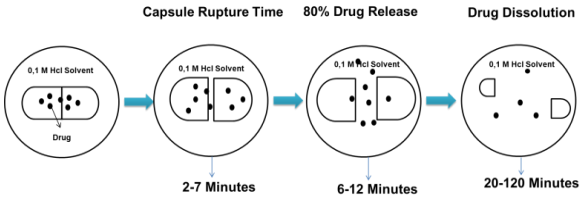

Figure 5. Capsule dissolution process (Chen *et al.* 2016)

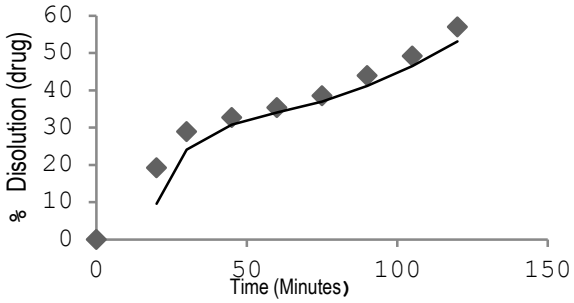

Figure 6. Dissolution of erithromycin stearate in recommended capsules

Modelling the Dissolution Kinetics of Erythromycin Stearate

Modelling drug dissolution kinetics was conducted to describe the drug release rate and determine the release model obtained from the dissolution results. This analysis was performed using the dissolution results. This analysis was performed using the DDSolver program with a nonlinear regression approach, applying the equations listed in Table 8.The best dissolution kinetics model based on the dependent approach is determined by evaluating several statistical criteria, including the smallest MSE and AIC, and the largest adjusted R^2 (Rsqr adj) and model selection criterion (MSC) (Citrariana *et al.*, 2020). The values for Rsqr adj, AIC, MSC, and MSE are presented in Table 9.

The kinetic models generated above indicate that the Higuchi kinetics model best describes the dissolution of erythromycin stearate compared to the other models. The Higuchi model was selected because it yielded the largest Rsqr adj and MSC values, as well as the smallest AIC and MSE values among all the tested kinetic models. Dissolution kinetic model is illustrated in Figure 7.

CONCLUSIONS AND RECOMMENDATIONS

Conclusions

Hydrocolloids sourced from vegetables, namely, konjac glucomannan and carrageenan, were successfully applied in the manufacture of vegetable hard capsules, demonstrating their potential as gelatin substitutes. The optimization results recommended a ratio of konjac glucomannan, carrageenan, and glycerol of 2.84, 1.81, and 0.11%, respectively, which achieved a high desirability level of 0.910% (equivalent to 91%). Validation conducted using this accurate response ratio yielded a capsule moisture content of 7.23% and a disintegration time of 10.35 min. These results successfully met the 91% confidence interval. The physical characteristics of the resulting capsules showed a relatively thin thickness compared to those of standard gelatin capsules.

Table 8. Dissolution kinetics model equations in the DDSolver program

Model	Zero order	First order	Higuchi	Korsmeyer-P	Hixson-Crowell
Equations	$F = K_0*t$	$F = 100*[1-Exp(-k_1*t)]$	$F = k_H * t^{0,5}$	$F = K_{kp}*t^n$	$F = 100*[1-(1-k_{HC}*t)^3]$

Note: F= amount of drug dissolved in (%), and t = amount of substance dissolved in time (min).

Table 9. Kinetic model of erythromycin stearate dissolution by using recommended hard capsules

Model	Average			
	Rsqr adj	AIC	MSC	MSE
Zero order	0.8105±0.02	56.5859±1.81	0.7499±0.16	54.5431±10.76
First order	0.9137±0.00	495388±1.15	1.5329±0.02	24.7330±3.15
Higuchi	0.9757±0.01	36.1497±8.01	3.0206±0.84	7.0532±5.41
Korsmeyer-Peppas	0.9750±0.01	37.4312±7.52	2.8782±0.78	7.2644±5.37
Hixson-Crowell	0.8872±0.00	51.9483±1.24	1.2652±0.08	32.3488±4.28

Notes: Rsqr adj: coefficient of determination, MSE: Mean Square Error, AIC: Akaike Information Criterion and MSC: Model Selection Criterion

Recommendations

Further research is necessary to address several areas, including investigating methods to increase the temperature and pH of glucomannan solutions to successfully produce thermoreversible gels, applying vacuum treatment to the solution during the molding process to effectively remove air bubbles from the capsule surface, and identifying alternative gelling agents with characteristics that more closely match those of KGM.

REFERENCES

Ahmad A, Rehman MU, Wali AF, El-Serehy HA, Al-Misned FA, Maodaa SN, Aljawdah HM, Mir TM, Ahmad P. 2020. Box–behnken response surface design of polysaccharide extraction from rhododendron arboreum and the evaluation of its antioxidant potential. *Molecules*. 25(17). https://doi.org/10.3390/molecules25173835

Amalina N, Anggraeni Y, and Dhilasari EM. 2020. Formulasi cangkang kapsul dengan kombinasi kappa karagenan dan iota karagenan. *Pharmaceutical and Biomedical Sciences Journal*. 2(1): 1–10.

Bansal V, Sharma PK, Sharma N, Pal OP, Malviya R. 2011. Applications of chitosan and chitosan derivatives in drug delivery. *Journal of Carbohydrate Chemistry*. 11(7): 849–865. https://doi.org/10.1080/07328309208018274

BPOM. 2019. Badan Pengawas Obat dan Makanan Republik Indonesia Nomor 32 Tahun 2019 Tentang Persyaratan Keamanan dan Mutu Obat Tradisional. *Jakarta: BPOM RI*, 1–37.

Chen Y, Zhao H, Liu X, Li Z, Liu B, Wu J, Shi M, Norde W, Li Y. 2016. TEMPO-oxidized Konjac glucomannan as appliance for the preparation of hard capsules. *Carbohydrate Polymers*. 143: 262–269. https://doi.org/10.1016/j.carbpol.2016.01.072

Citrariana S, Lukitaningsih E, and Nugroho AK. 2020. Studi Perbandingan disolusi in-vitro pada formula tablet levofloksasin immediate-release menggunakan variasi kadar disintegran sodium starch glycolate. *Majalah Farmaseutik*. 16(1): 83. https://doi.org/10.22146/farmaseutik.v16i1.48941

Dong Y, Wei Z, and Xue C. 2021. Recent advances in carrageenan-based delivery systems for bioactive ingredients: A review. *Trends in Food Science and Technology*. 112: 348–361. https://doi.org/10.1016/j.tifs.2021.04.012

Fahrullah F and Ervandi M. 2022. Karakterisasi mikrostruktur film whey dengan penambahan konjac glucomannan. *Agrointek : Jurnal Teknologi Industri Pertanian*. 16(3): 403–411. https://doi.org/10.21107/agrointek.v16i3.12303

Fatnasari. 2018. Pengaruh konsentrasi gliserol terhadap karakteristik edible film pati ubi jala*r (Ipomoea batatas L .). Agrotech*. 5(1): 27–35.

Febriana LG, Stannia PHN, Fitriani AN, Putriana NA. 2021. Potensi gelatin dari tulang ikan sebagai alternatif cangkang kapsul berbahan halal: karakteristik dan pra formulasi. *Majalah Farmasetika*. 6(3): 223. https://doi.org/10.24198/mfarmasetika.v6i3.33183

Future Market Insights. 2021. *Hard-gelatin-capsules-market*. https://www.futuremarketinsights.com/reports/hard-gelatin-capsules-market

Gelatin Representatives of the Word. 2021. *Gelatin*. https://www.gelatininfo.com/grow.html

Gu Mc, Clements DJ, Li J, Su Y, Yang Y, Li J. 2021. Formulation of alginate/carrageenan microgels to encapsulate, protect and release immunoglobulins: Egg Yolk IgY. *Food Hydrocolloids*, 112(September 2020), 106349. https://doi.org/10.1016/j.foodhyd.2020.106349

Jones BE, Basit AW, and Tuleu C. 2012. The disintegration behaviour of capsules in fed subjects: A comparison of hypromellose (carrageenan) capsules and standard gelatin capsules. *International Journal of Pharmaceutics*. 424 (1–2): 40–43. https://doi.org/10.1016/j.ijpharm. 2011.12.034

Junianto, Kiki H, and Ine M. 2013. Karakteristik cangkang kapsul yang terbuat dari gelatin tulang ikan. *Jurnal Akuatika*. 4(1): 46–54.

Karim AA and Bhat R. 2009. Fish gelatin: properties, challenges, and prospects as an alternative to mammalian gelatins. *Food Hydrocolloids*. 23 (3):563–576. https://doi.org/10.1016/j.foodhyd.2008.07 .002

Kemenkes RI. 2020. Farmakope Indonesia edisi IV. In *Departemen Kesehatan Republik Indonesia*.

Rachmawati W. 2018. *Konjac Glucomannan-Agar-Gliserin for Biopolimer of Hard Capsule*. 5(1): 45-53.

Said MI, Triatmojo S, Erwanto Y, Fudholi A. 2014. Aplikasi gelatin kulit kambing bligon sebagai bahan dasar dalam formula terhadap sifat-sifat cangkang kapsul obat. *Jurnal Ilmu dan Industri Peternakan*. 150–157.

Sedayu BB, Cran MJ, and Bigger SW. 2019. A review of property enhancement techniques for carrageenan-based films and coatings. *Carbohydrate Polymers*. 216*:* 287–302. https://doi.org/10.1016/j.carbpol.2019.04.021

Siswanto A, Hapsari I, Zulaikha YU, Rosmawati E. 2016. Pemodelan pelepasan in vitrotablet floatingteofilin dengan program ddsolver. *Pharmacy*. 17(2): 5–9.

Suptijah P, Suseno SH, and Kurniawati. 2012. Aplikasi karagenan sebagai cangkang kapsul keras alternatif pengganti kapsul gelatin application of carrageenan as hard capsule for gelatin capsule subtitute. *Journal of Public Health and Pharmacy*. 15(3): 223–231.

Wang W and Andi J. 2013. Introduction of konjac. *Technical Article.* 9–11. http://www.cybercolloids.net/sites/default/files/private/downloads/ Introduction to Konjac.pdf

Vattanagijyingyong Y, Kulvanich P, and Chatchawalsaisin J. 2022. Fabrication of delayed release hard capsule shells from zein/methacrylic acid copolymer blends. *European Journal of Pharmaceutical Sciences*. 171: 106124. https://doi.org/10.1016/j.ejps.2022.106124