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Optimization of Sucrose and Propylene Glycol Concentration in the Formulation of Chewable Gummy Tablets of Moringa Leaf Extract (*Moringa oleifera L.*)

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Abstract

Background: Moringa leaves extract is promising to develop into nutraceutical products, especially a chewable gummy. The desirable characteristics of chewable gummies are soft, elastic, springy, and flexible. Gelatin is a widely used gelling agent that maintains gel structure during storage. The other ingredients determining the chewable gel structure are filler and plasticizer. This study aimed to assess the effect of sucrose and propylene glycol concentration on Moringa leaves extract-based chewable gummy. **Methods:** The pour method conducted the preparation of chewable gummy tablets. Factorial design study (22) was applied to analyze the effect of two factors herein, filler and plasticizer. Two concentration levels in each element, herein sucrose (30% and 35% concentration) and propylene glycol (2% and 4% concentration), on the physical characteristics of the gummy tablet. **Results:** The results of the factorial analysis showed that the increase in sucrose concentration would produce a longer dispersion time and lower swelling ratio. The increase in propylene glycol decreases the syneresis potency. The alteration of physical characteristics during 14 days of storage, particularly in dispersion time, swelling ratio, and syneresis percentage. **Conclusions:** Based on the results of feasible design space, sucrose concentration (30-35%) and propylene glycol concentration (2-4%) optimized in this study produce the desirable characteristics of chewable gummy.

Keywords: Chewable Gummy; *Moringa oleifera*; Propylene Glycol; Sucrose

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Introduction

The Moringa plant (*Moringa oleifera*) is a plant that belongs to the Moringaceae family. Moringa plants contain nutrients and bioactive compounds that are beneficial to human health. Moringa leaves are widely used by tropical countries such as Indonesia, the Philippines, and India as food support because of the content of antioxidants and amino acids (Ferreira et al., 2008). Previous studies have shown that the ethanol extract of Moringa leaves has a high antioxidant content. The content of flavonoid and phenolic compounds in the 70% ethanol extract of Moringa leaves is 16.33 mg/g and 28.56 mg GAE/g (Sohaimy et al., 2015). The main flavonoid constituents in moringa leaf extract are quercetin, kaempferol, and kaempferol glycosides. (Coppin et al., 2013). The antioxidant activity of 70% ethanol extract of Moringa leaves also showed moderate antioxidant activity with IC50 value = 44.10 ± 0.05 µg/ml (Sohaimy et al., 2015). Based on these data,

potential development of nutraceutical products based on Moringa leaf extract is carried out. Several nutraceutical products based on moringa leaves have been developed, including herbal teas and effervescent tablets (Eo et al., 2018; Murdiana et al., 2018). Products that have been designed are proven to have antioxidant and antibacterial activity (Eo et al., 2018).

Chewable gummy is a nutraceutical product as a form of innovation for delivery via the oral route. Chewable gummy can be applied as a drug delivery system in the pharmaceutical and food industries. Chewable gummy can be used in children and older people who experience dysphagia, accelerating drug release because the active ingredients are dispersed in a soft matrix, able to cover the taste and senses of the less acceptable active ingredients (Dille et al., 2018). Chewable gummy is a tablet with a gel base. Chewable gummy is not compressed in the manufacturing process but uses molds made of silicone or metal to form chewable gummy (Matulyte, Marksa, et al., 2021). The main components of chewable gummies include gelling agents, water, sucrose, corn syrup, or other fillers.

Chewable gummy tablets based on gelatin as the primary gelling agent have been developed extensively and are proven to have a fast disintegration time, an elastic structure, and are stable in storage. (Dille et al., 2018). Previous studies have shown that the form and elasticity of chewable gummies are determined by the type of gelling agent used and the concentration of sucrose. The concentration of gelling agent and sucrose significantly impacts the chewable gummy mass's viscosity, rheology, and water activity (Čižauskaite et al., 2019). Plasticizers such as glycerin and propylene glycol are commonly used in chewable gummy formulations to increase the elasticity of the chewable gummy mass. Glycerin can prevent water loss and sucrose crystallization in chewable gummies during storage (Matulyte, Marksa, et al., 2021).

Previous research has developed a chewable gummy for Moringa with a gelatin gelling agent. The optimal concentration of gelatin in the Moringa extract chewable gummy formula is 10% because this concentration produces a chewable gummy that does not show syneresis during storage (Rani et al., 2021). The preparation's soft texture during storage limits this study's results. Therefore, the gelatin-based chewable gummy texture in this study needs further optimization to produce a chewable gummy with a firm texture but still elastic and not easily sticky. The approach that can be taken to improve the chewable gummy texture is to optimize the concentration of other three-dimensional structural components, namely fillers, and plasticizers. Sucrose is a filler commonly used to form chewable gummies because sucrose can increase the strength of gelatin molecular networks due to hydrogen bonds with water and gelatin. Gelatin holds bound water more efficiently when combined with sucrose and water (Burey et al., 2009). Using sucrose at concentrations that are too high can have a negative impact because sucrose is hygroscopic and causes structural changes to become softer during storage (Chabib et al., 2014).

Sucrose concentrations > 50% in chewable gummy preparations are not recommended because of their low nutritional value and the risk of triggering cardiovascular disease. In previous studies, it was known that the results of the chewable gummy organoleptic test showed that panelists preferred the use of a sucrose concentration of 25-35% in terms of aroma, color, taste, and texture. The second factor to be optimized is the concentration of propylene glycol as a plasticizer. The plasticizer can affect the bonding microstructure of the gelling agent and form a barrier to prevent water loss from the chewable gummy structure. This causes the texture of the chewable gummy to be maintained as the initial condition in storage (Čižauskaite et al., 2019). Previous research stated that using propylene glycol up to a concentration of 4% could increase the chewable gummy's elasticity through decreasing intermolecular forces (Čižauskaite et al., 2019; Matulyte et al., 2021). Future studies need to optimize the concentration of sucrose and propylene glycol as fillers and plasticizers to obtain a chewable gummy with adequate physical characteristics during storage.

This research will optimize the chewable gummy formula with the active ingredients of Moringa leaf extract on a gelatin basis, sucrose as a filler, and propylene glycol as a

plasticizer. This study uses a factorial design to optimize the concentration of components forming the three-dimensional structure of the chewable gummy, namely fillers, and plasticizers. Optimization was carried out through a 2^2-factorial design, namely two factors (sucrose and propylene glycol) and two concentration levels for each factor, 25% and 35% for sucrose, while propylene glycol at 2% and 4%. The optimal sucrose and propylene glycol concentration was determined by factorial analysis using Minitab 19 software.

Methods

The chewable gummy formulation with the active ingredient of 70% ethanol extract from Moringa leaves was carried out using heat and congealing (Kadhim & Ali, 2019). The concentration of Moringa leaf extract used in each formula is 2%. This study optimized four recipes with a factorial design of 2^2. The variation in the concentration of sucrose used in this study was 30% and 35%, while the variation in the concentration of propylene glycol was 2% and 4%.

Material

The plant material used in this study was Moringa leaf powder with a degree of fineness that could pass through the No. Sieve. Mesh 500. Moringa leaf powder obtained from KWT Sri Rejeki, Bojonegoro. Additional ingredients used in the formulation include gelatin (Gurotrade World Commerce SL, America), mannitol (Qingdao Bright Moon Seaweed Group Co. Ltd, Qingdao-China), citric acid (PT. RZBC IMP & EXP. Co. LTD, Shandong- China), sucrose (PT. Sugar Group Companies, Mataram-Indonesia), propylene glycol (PT. Dow, Singapore Private Limited), sodium benzoate (Emerald Kalama Chemical, B.V, Rotterdam-Netherlands), melon flavor (KH. Roberts, Buroh Lane-Singapore), *aqua purificata*.

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Procedure

Making Chewable Gummy Moringa Leaf Extract

Chewable gummy moringa leaf extract was manufactured using 70% ethanol extract of Moringa leaves with a concentration of 2%. This study had four optimized formula combinations, as shown in Table 1. The planned chewable gummy weight was 3 grams. According to the planned formula, each material was weighed with the Ohaus Scout Pro SPS202F digital balance.

The manufacturing process begins with dispersing the Moringa leaf extract in 5 ml of aqua purificata. Sucrose was then dissolved in aqua purificata while heating at 80°C. Gelatin and mannitol were added to the sucrose solution while maintaining temperature. Propylene glycol is added slowly with continuous stirring until a homogeneous mass mixture is formed. Citric acid and sodium benzoate were each dissolved in 5 ml of aqua purificata, then added to the mixture. The melon flavor is added while continuing to stir. After that, the previously dispersed ethanol extract was added when the mass of the mixture reached 60°C. The chewable gummy mass mixture is poured slowly into the silicone mold, waiting for it to solidify at room temperature for 15 minutes. The next stage was when the chewable gummy mass began to solidify. The preparations in the mold were stored in the refrigerator chiller (Panasonic, Indonesia) for 15 minutes. Chewable gummy in the mold is then stored at room temperature for 24 hours, after which the preparation is released from the mold and packaged in a plastic bag (Čižauskaite et al., 2019). The next stage was to evaluate the physical characteristics of the chewable gummy of Moringa leaf extract.

Table 1. Chewable Gummy Formula of Moringa Leaf Extract with Various Concentrations of Sucrose and Propylene Glycol

Formula	Percentage (%)			
	Formula 1	**Formula 2**	**Formula 3**	**Formula 4**
Moringa leaf extract	2	2	2	2
gelatin	10	10	10	10
sucrose	30	30	35	35
Propylene Glycol	2	4	2	4
mannitol	10	10	10	10
Citric acid	1	1	1	1
Sodium benzoate	0,5	0,5	0,5	0,5
Melon flavor	2	2	2	2
Aqua purificata	42,5	40,5	37,5	35,5,
Total	**100**	**100**	**100**	**100**

Evaluation of Chewable Gummy Physical Characteristics of Moringa Leaf Extract

Evaluation of the physical characteristics of the chewable gummy of Moringa leaf extract included physical observations, weight variation, chewable gummy dimensions, disintegration time, swelling index, and syneresis. Texture analysis, including chewiness, gumminess, and hardness, was carried out on the optimum formula obtained in this study.

Physical Observation

The four chewable gummy formulas for Moringa leaf extract were subjected to physical observations, including color, taste, shape, texture, and smell. Observation of the texture of the preparation was carried out qualitatively by gently pressing the surface of the chewable gummy using both fingers. When pressed using both fingers, the chewable gummy's elasticity and stickiness were recorded as the texture of the chewable gummy (Prakash et al., 2014).

Weight Diversity

Determination of the variety of chewable gummy weights was carried out by taking as many as 20 dosage units from each formula. The chewable gummy was weighed with the Ohaus Pioneer Soehnle (Darmstadt, Germany) analytical balance, and then calculating an average of 20 gummies was The test results were declared eligible if there was not one preparation whose weight deviated more than 7.5% from the average weight of the chewable gummy. If one tablet unit is outside the range, the test is repeated with an additional 20 chewable gummy tablets. Chewable gummy tablets are declared eligible if no single unit deviates more than 10% from the average weight of chewable gummy (Davydova, 2018). This weight diversity test aims to ensure the homogeneity of the resulting chewable gummy moringa leaf extract.

Chewable Gummy Dimensions

The evaluation of chewable gummy dimensions aims to determine the uniformity of the size of chewable gummy preparations. Parameters observed included the length, width, and thickness of 10 units of chewable gummy. The dimensions of the chewable gummy were measured using Kenmaster® calipers (Indonesia). Evaluation results are declared eligible if the standard deviation of the measurements of each dimension is not more than 5% (York et al., 2001). The results of measuring the dimensions of the chewable gummy can be used as information to determine the dimensions of the primary packaging used.

Time is destroyed

Evaluation of the disintegration time of the chewable gummy was carried out to predict the speed of release of the active ingredient of Moringa leaf extract from the chewable

gummy. This evaluation can provide an overview of the process of absorption of active ingredients by the body. The test was carried out by placing the chewable gummy in a beaker glass containing 100 ml of *aqua purificata* at 37° C., measured with a ThermoPro® digital thermometer (Shanghai, China). Disintegration was observed until the chewable gummy preparation was completely crushed or dispersed using a digital stopwatch Q&Q HS43 (Čižauskaite et al., 2019). The maximum acceptable disintegration time for chewable gummy is 15 minutes (Dille et al., 2018).

Swelling Ratio

The chewable gummy development index was measured by weighing the initial weight of the chewable gummy (Wd). The swelling index determines the absorption capacity of the liquid in the chewable gummy structure. In the next stage, the chewable gummy preparation was soaked in 100 ml of aqua purificata for 10 seconds at controlled room temperature (25-30°C). A chewable gummy that has been soaked is then removed and cleaned using filter paper to absorb water adhering to the surface of the chewable gummy(Kowalski et al., 2019).

$$\text{Swelling Ratio} = \frac{Ws-Wd}{Wd} x100\%$$

Index:

Ws = weight of chewable gummy after soaking

Wo = weight of chewable gummy before soaking

Syneresis

Syneresis is a condition where water molecules are released from the gel structure (Febriani et al., 2020). Syneresis occurs due to contraction or shrinkage of the gel structure (Kadhim & Ali, 2019). The high percentage of chewable gummy syneresis indicated that the preparation's texture softened faster, and the instability of the preparation was poor. The measurement of the syneresis percentage of the preparation was carried out at controlled room temperature by attaching filter paper to the surface of the chewable gummy. The difference in weight of chewable gummy before and after contact with a filter paper is calculated as the percentage of syneresis according to the following equation:

$$\text{Syneresis Percentage} = \frac{A-B}{A} \text{ x } 100\%$$

Index:

A = Initial weight of chewable gummy preparation

B = The final Weight of the chewable gummy preparation

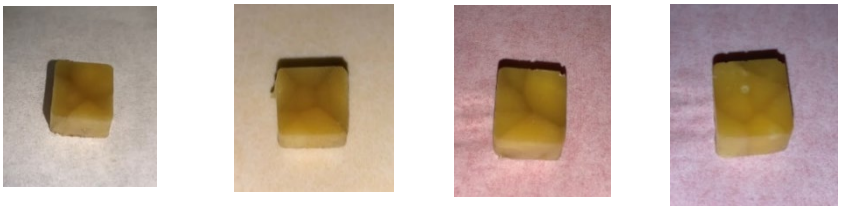
Data analysis

Data analysis on the physical characteristics of chewable gummy preparations was carried out through an experimental analysis of 2^2 factorial designs using Minitab® 19 software. The results were analyzed on Pareto charts, main effect charts, and contour plots (Budi et al., 2011). The graph shows the effect of the filler components sucrose and propylene glycol as plasticizers on the physical characteristics of chewable gummy tablets, including variations in weight, disintegration time, swelling index, and syneresis.

Result

Physical Observation Evaluation of Chewable Gummy Moringa Leaf Extract

Observing the chewable gummy's shape, color, smell, taste, and texture. Physical observation test is one of the factors that must be considered in product development because panelists will assess a new food product for the first time and its visual appearance (Figure 1). The four formulations are square in shape, yellow in color, smell of melon, sweet in taste, have a chewy, elastic texture, and are not sticky when pressed with a finger.



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

Figure 1. Chewable gummy tablets of Moringa leaf extract (a) Formula 1, (b) Formula 2, (c) Formula 3, and (d) Formula *4*

Evaluation of Weight Diversity

Weights that vary and show large deviations indicate the inhomogeneity of the active ingredient content. Determination of the variety of dosage weights is carried out by weighing 20 dosage units one by one and then calculating the average dosage weight, as well as determining the deviation of the weight of each dosage unit from the average Weight (Davydova, 2018).

Table 1. Average weight of chewable gummy moringa leaf extract

Average ± SD			
Formula 1	**Formula 2**	**Formula 3**	**Formula 4**
2,81±0,01	2,84±0,06	2,87±0,05	2,86±0,06

The four chewable gummy formulas of Moringa leaf extract with gelatin as a carrier in this study fulfilled the requirements for the diversity of the weight of chewable gummy preparations. This was because all chewable gummy units did not deviate by more than 7.5% in weight from the average chewable gummy weight of Moringa leaf extract. This condition indicates that the active ingredient of Moringa leaf extract is distributed evenly in each chewable gummy preparation unit.

Evaluation of Chewable Gummy Dimensions

Evaluation of the uniformity of the dimensions of the chewable gummy was carried out by measuring the length, width, and thickness of the chewable gummy using a digital vernier caliper. Evaluating the dimensions of these tablets provides information regarding the uniformity of dosage sizes and the dimensions of primary packaging materials required for packaging preparations during storage. The data is the average of the dimensions of 10 chewable gummy units. The results obtained showed compliance with the dimensional specifications of the chewable gummy of Moringa leaf extract because the coefficient of variation of the ten dosage units tested was <5.0%.

Table 2. Average dimensions of chewable gummy moringa leaf extract

Parameter	Formula 1	Formula 2	Formula 3	Formula 4
Length (cm)	1,48±0,01	1,48±0,01	1,48±0,01	1,49±0,01
Width(cm)	1,48±0,00	1,48±0,00	1,48±0,01	1,48±0,01
Thickness (cm)	0,97±0,02	0,98±0,00	0,98±0,01	0,98±0,01

Time is Destroyed

Evaluation of disintegration time is used to predict the speed of disintegration of chewable gummy in aqueous media while ensuring the release of the active ingredient of Moringa leaf extract from the gel matrix (Matulyte, Marksa, et al., 2021). The faster the chewable gummy disintegrates in the media, the faster the drug release begins. The disintegration times of the four chewable gummy formulas of Moringa leaf extract with varying concentrations of sucrose and propylene glycol are shown in Figure 2. The results showed that the disintegration times of the four formulas were in the range of 3.95 -6.06 minutes. The disintegration time indicated by the four formulas met the ideal disintegration time requirements for chewable gummy preparations, namely <15 minutes.

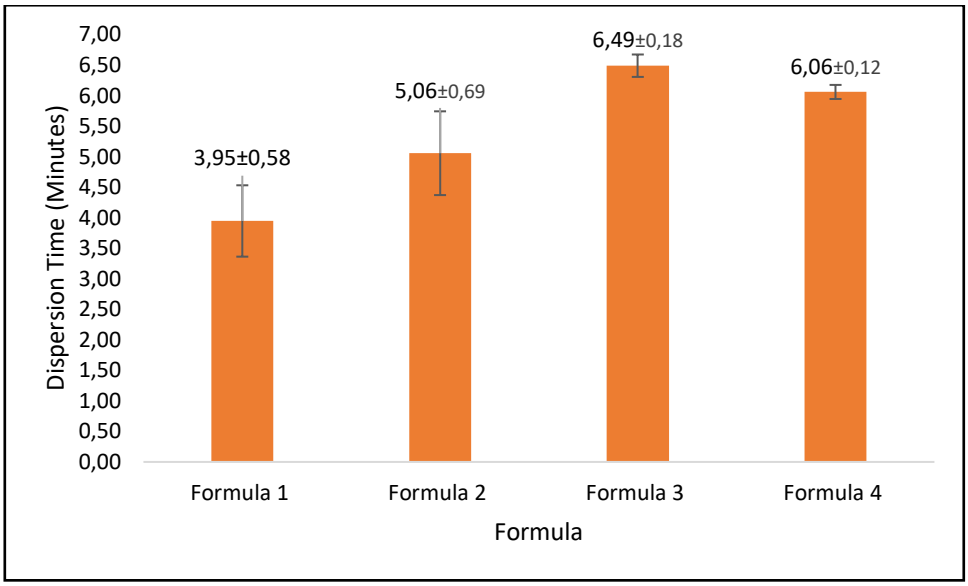


Figure 2. Disintegration time of the four chewable gummy formulas of Moringa leaf extract. Results are the mean of three replicates ± SD.

Swelling Ratio

The swelling index was evaluated to determine the ability of the chewable gummy gel matrix to swell in water (H. E. Park et al., 2020). Swelling index related to syneresis parameter and chewable gummy disintegration time (Figure 3). The smallest development index was shown by formula 4, 0.43 ± 0.08%, while the largest development index was shown by formula 1, 0.75 ± 0.32%.

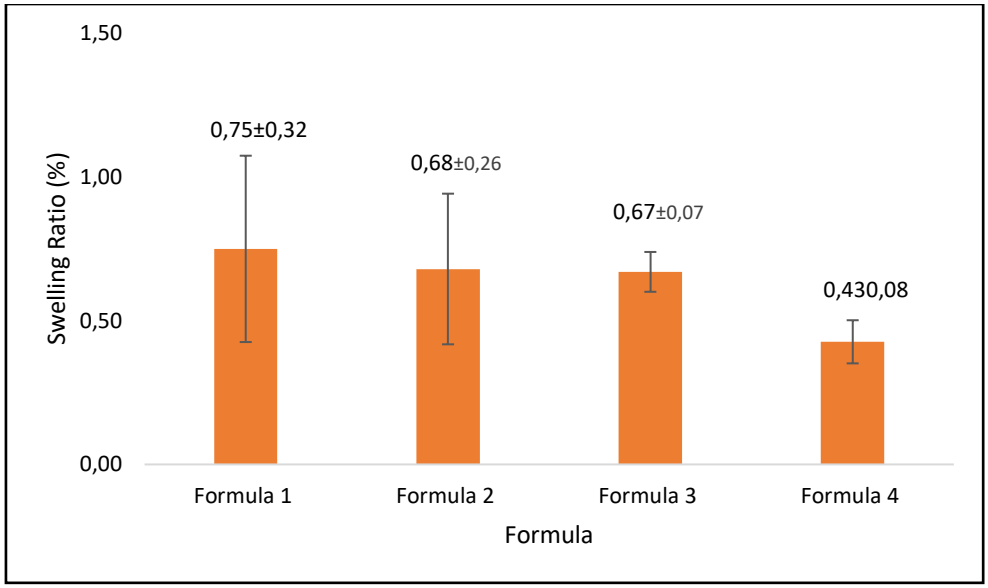


Figure 3. Development index of the four chewable gummy formulas of Moringa leaf extract. Results are the mean of three replicates ± SD.

Syneresis

The syneresis of chewable gummy preparations was evaluated by measuring the loss of chewable gummy weight during storage compared to the initial weight. Syneresis can predict the strength of the gel network formed in holding water molecules. The high syneresis percentage of chewable gummy preparations indicates the low strength of the gel-forming polymer network. This condition indicates the instability of the preparation in long-term storage because the preparation will soften easily (Prakash et al., 2014).

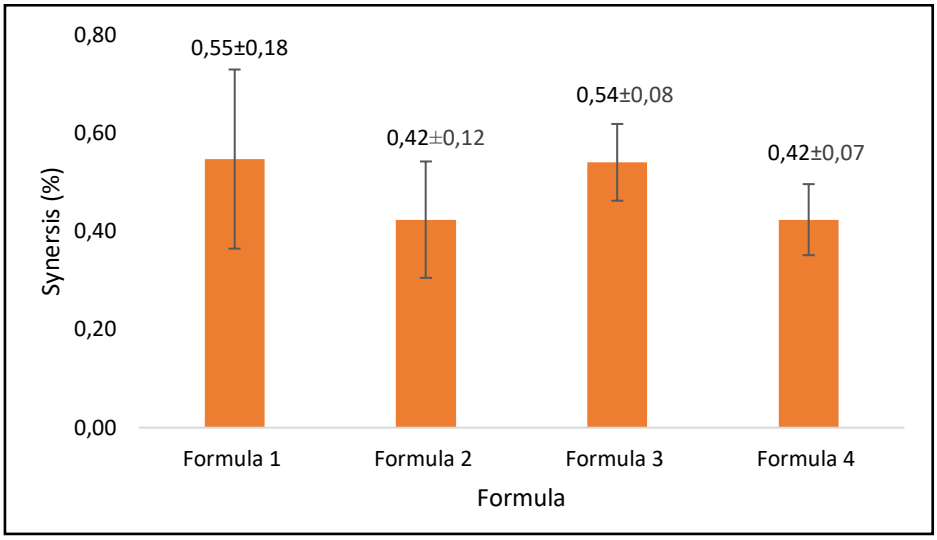


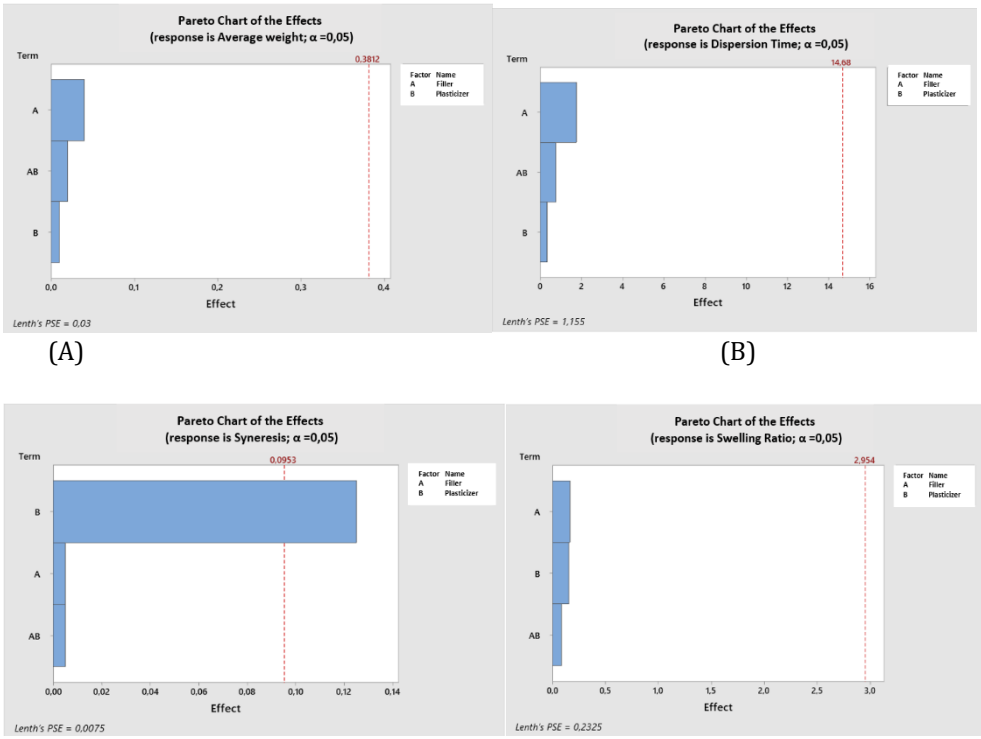
Figure 4. Syneresis percentage of the four chewable gummy formulas of Moringa leaf extract. Results are the mean of three replicates ± SD.

Factorial Design Analysis Effect of Variation of Sucrose and Propylene Glycol Concentrations on the Physical Characteristics of Chewable Gummy

The effect of variations in sucrose concentration (30% and 35%) and plasticizer concentration (2% and 4%) on the physical characteristics of chewable gummy preparations were performed using Minitab® 19 software. Pareto charts performed analysis, main effect plots, and contour plots. The three graphs provide information on the effect of sucrose as a filler and propylene glycol as a plasticizer in each formula on weight variation, disintegration time, swelling index, and syneresis.

The Pareto chart provides information to determine the factors that influence the physical characteristics of chewable gummy preparations due to variations in sucrose concentration as a filler and propylene glycol as a plasticizer (Figure 5).

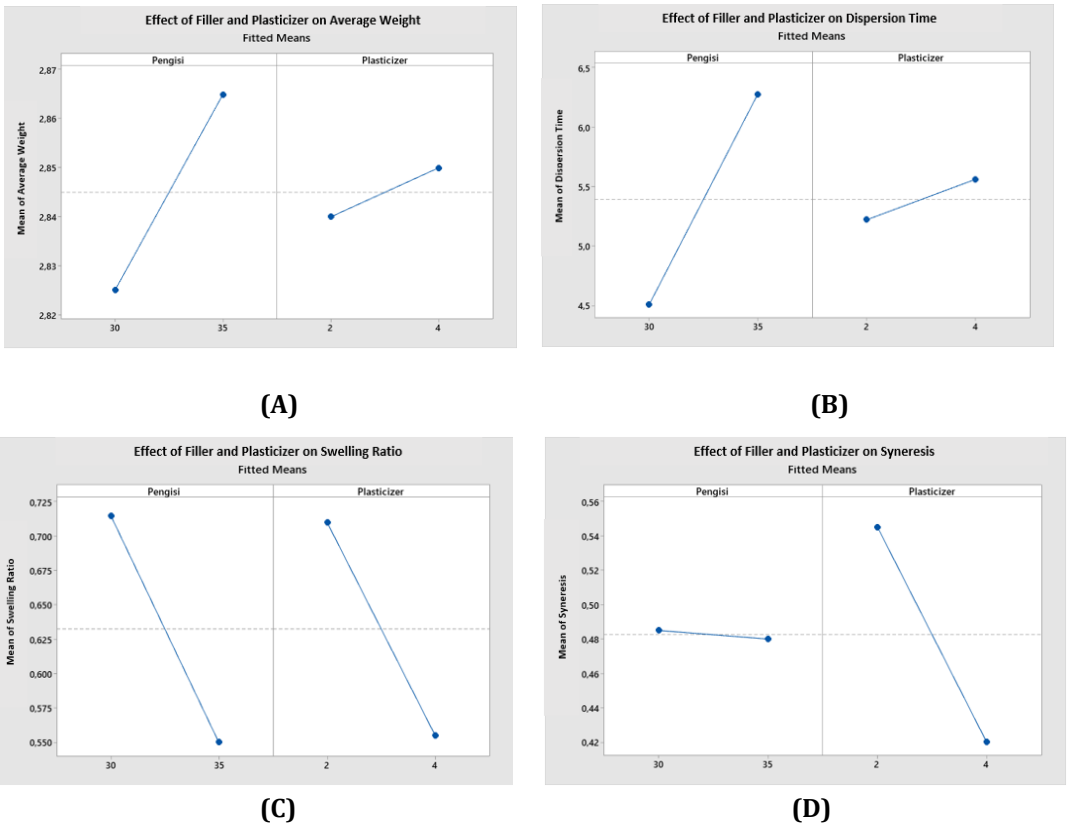
Based on the Pareto chart, increasing sucrose concentration increases the average tablet weight, disintegration time, and swelling index. Meanwhile, syneresis is more influenced by the concentration of propylene glycol as a plasticizer in the formula. The main effects plot graphic is used to support the analysis of the results based on the Pareto chart. Based on the analysis of the main effect plot, it can be seen that the profile of the effect of different concentrations of sucrose and propylene glycol on the characteristics of chewable gummy. The results of the main effects plot showed an increase in sucrose concentration as a filler from 30% to 35%, increased variation in weight and disintegration time, decreased swelling index, and did not affect syneresis. While increasing the concentration of propylene glycol as a plasticizer from 2% to 4% increased the variation in weight and disintegration time and decreased swelling and syneresis indices (Figure 6).



(A) (B)

(C) (D)

Figure 5. Pareto chart of the effect of varying concentrations of sucrose and propylene glycol on (A) weight average; (B) disintegration time; (C) development index; (D) syneresis



(A) **(B)**

(C) **(D)**

Figure 6. Graph of the main effects plot of the influence of variations in the concentration of sucrose and propylene glycol on (A) the average Weight; (B) disintegration time; (C) development index; (D) syneresis

Contour plot analysis aims to determine the effect of the concentration of the independent variables (sucrose and propylene glycol) on the dependent variables,

including the average tablet weight, disintegration time, swelling index, and syneresis (Figure 7). The colors on the graphs show the parameter values resulting from changes in the concentrations of sucrose as a filler and propylene glycol as a plasticizer. Increasing the sucrose concentration up to 35% and 4% propylene glycol concentration increased the average weight of the chewable gummy and extended the disintegration time but decreased the percentage of swelling and syneresis indices with values of 0.45% and 0.42%, respectively. Chewable gummies with lower concentrations of sucrose and propylene glycol showed faster disintegration time (< 4 minutes), but the swelling and syneresis indices increased, namely > 0.75% and > 0.54%.

Based on the results of the contour plot, the optimum concentration of sucrose and propylene glycol. The optimum area is obtained through a feasible design space graph through the overlay results and determining the desired preparation specifications. The workable design space graph shows that the use of sucrose with a concentration range of 30% - 35% and propylene glycol with a concentration range of 2% -4% can produce chewable gummy moringa leaf extract with an average weight between 2.77-3.00 grams, disintegration time ≤ 15 minutes, development index < 1%, and syneresis percentage < 1%. The feasible design space graph is shown in Figure 8.

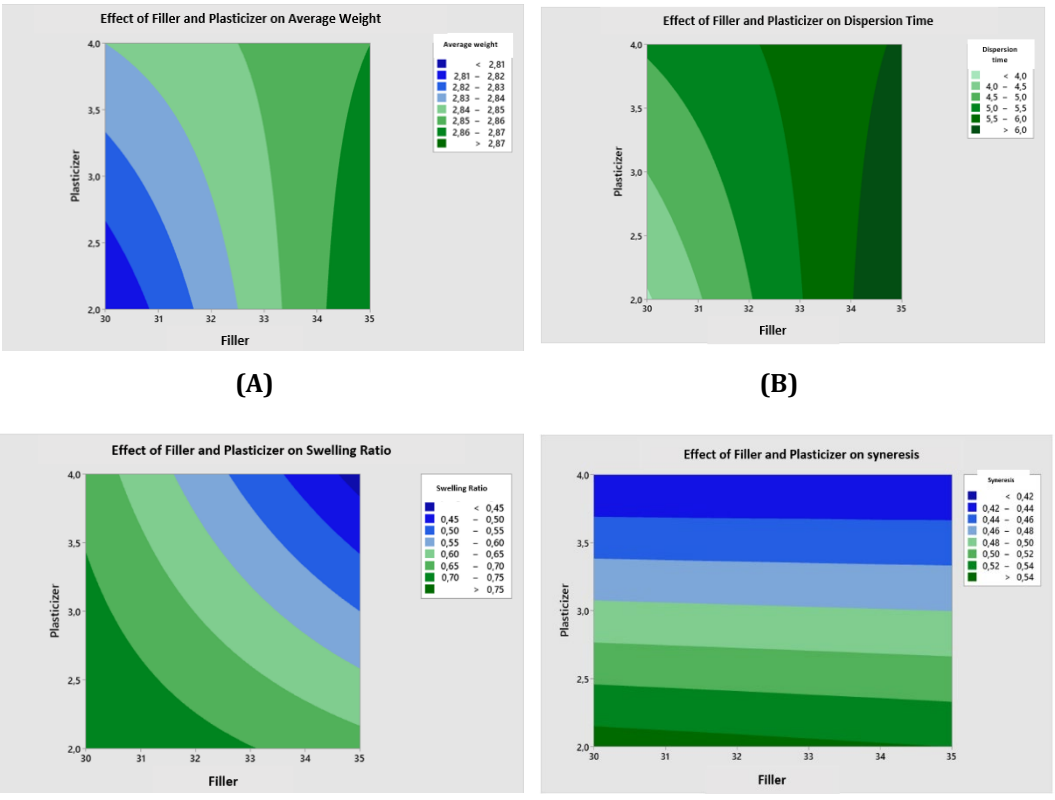


Figure 7. Contour plot of the effect of varying concentrations of sucrose and propylene glycol on (A) weight average; (B) disintegration time; (C) development index; (D) syneresis

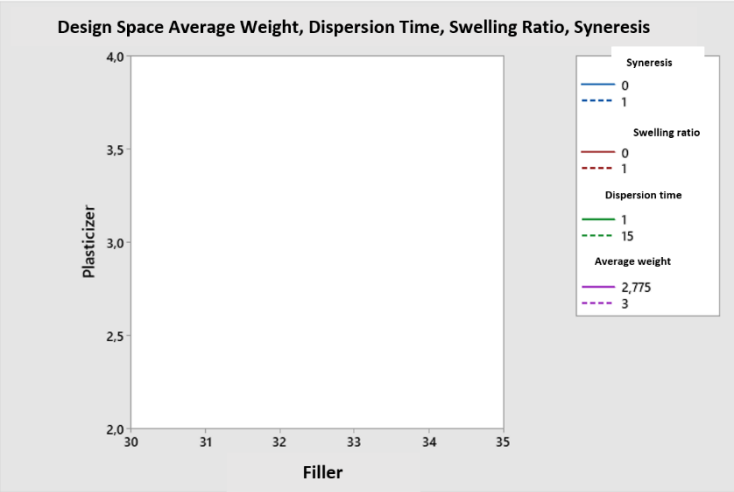


Figure 8. Graph of feasible design space for various concentrations of sucrose and propylene glycol

Discussion

Optimization of the concentration of sucrose as a filler and propylene glycol as a plasticizer is necessary to obtain a strong and elastic chewable gummy texture. Using plasticizers in previous studies can avoid the crystallization of sucrose on the surface of the chewable gummy. Besides that the resulting chewable gummy is elastic, shiny, and transparent. Variations in the weight of the chewable gummy were also observed to be minimal with plasticizers (Matulyte, Marksa, et al., 2021). The concentration of sucrose as a filler also determines the texture and stability of the chewable gummy. The interaction between gelatin, sucrose, and plasticizer has a role in controlling the moisture content and water activity on the surface of the chewable gummy (Čižauskaite et al., 2019). In this study, optimization was carried out based on the factorial design with two factors, namely sucrose and propylene glycol, and two levels for each factor, namely 30% and 35% for sucrose and 2% and 4% for propylene glycol. The factorial design is aimed at seeing the relationship between two or more variables on the physical characteristics of the chewable gummy, as well as knowing the effects of concentration and interaction of the two factors (Koteswari et al., 2016). The influence of the two variables on the physical characteristics of the preparation was observed by evaluating the physical characteristics, including the variety of weights, dimensions, disintegration time, swelling ratio, and syneresis.

The physical observation evaluation of the chewable gummy was carried out by observing the shape, color, smell, taste, and texture using the five senses (Feris et al., 2015). Consumers' qualitative acceptance of tastes and preferences can support product development and marketing (Muzamir Mahat et al., 2020). The results of physical observations of the chewable gummy of Moringa leaf extract showed that the chewable gummy had a square shape, light yellow color, melon smell, and sweet taste. The surface of the chewable gummy was slightly cloudy and did not show any sucrose crystallization on the surface. The turbidity that appears on the surface of the chewable gummy is thought to be due to the interaction between the extract and gelatin. The interaction of extracts and gelatin in previous studies can affect the texture of the chewable gummy, including color (Čižauskaite et al., 2019). The use of polyol group compounds, including propylene glycol, has a significant impact as a humectant and prevents moisture loss in chewable gummies (Matulyte, Marksa, et al., 2021). This causes the chewable gummy's surface in this study not to show sucrose crystallization. All of the chewable gummy formulas in this study showed an elastic texture, but formulas 3 and 4, with a 35% sucrose concentration, produced a firmer chewable gummy structure. Increasing the concentration of sucrose can increase the strength of the polymer network so that the texture of the chewable gummy becomes stronger (Čižauskaite et al., 2019).

The weight variation test was carried out to detect deviations in the weight of each unit of chewable gummy preparation. A large deviation in weight indicates that the homogeneity of the weight and content of the active ingredient in the preparation is not properly guaranteed during the manufacturing process. The results of evaluating the diversity of the weight of chewable gummy tablets of Moringa leaf extract in this study showed results that met the requirements. The weight range of the chewable gummy tablets of the four formulas is within the range of 2.77-3.00 grams. In addition, there was no chewable gummy unit whose weight deviated by more than 7.5% from the average weight in each formula (Davydova, 2018). Based on the experimental analysis of the factorial design, the difference in the concentration of sucrose as a filler has more effect on the weight of the chewable gummy than the difference in the concentration of propylene glycol. Increasing the sucrose concentration increased the average weight of chewable gummy in formula three and formula 4. Storage in the freezer after the preparations had solidified also positively minimized variations in weight. This is because the freezing process can avoid the release of water molecules from the chewable gummy while avoiding the absorption of environmental moisture (Matulyte, Mataraite et al., 2021).

The uniformity of the size of the chewable gummy affects the uniformity of the contents and dimensions of the primary packaging required for packaging. The homogeneity of the chewable gummy size increases patient acceptance of the preparation (Kadhim & Ali, 2019). The results of observing the dimensions of the chewable gummy (length, width, and thickness) show that the four formulas meet the dimensional specifications because the coefficient of variation in the length, width, and thickness of the chewable gummy is not more than 5.0% (Augsburger & Hoag, 2008).

The disintegration time test of chewable gummy aims to predict the speed of the chewable gummy matrix to be dispersed in aqueous media. In addition, the disintegration time test also plays a role in predicting the release rate of the active ingredients until they are ready to be absorbed into the systemic circulation (Matulyte, Marksa, et al., 2021) and the chewable gummy disintegration time of the four formulas met the requirements, namely no more than 15 minutes (Rustiani & Andini, 2019). Analysis of the Pareto chart and main effect plot shows that sucrose concentration has more influence on the disintegration time of the chewable gummy. Increasing the sucrose concentration from 30% to 35% causes an increase in disintegration time. The interaction between gelatin and sucrose increases with increasing sucrose concentration, narrowing the space between the particles. This condition is due to the increased rigidity of the gel structure (Čižauskaite et al., 2019). The narrower space between particles causes it to be difficult for water molecules to enter the chewable gummy structure, so the disintegration time becomes longer.

Evaluation of the swelling index of the chewable gummy was carried out to predict the ability of the chewable gummy to expand when in contact with aqueous media (H. Park et al., 2010). The swelling capacity of the chewable gummy in this study decreased with increasing concentrations of sucrose and propylene glycol. The Pareto chart analysis and the main effect plot show that changes in sucrose concentration have more impact on the swelling index. Increasing the concentration of sucrose as a filler from 30% to 35% can reduce the swelling power of the preparation. The increased sucrose concentration causes the distance between the gel matrices to become narrower and the water molecules that encourage the practice to swell less. This has an impact on decreasing the development index of chewable gummy preparations.

A syneresis is an event where water comes out of the gel structure because the gel structure shrinks (Kadhim & Ali, 2019). Syneresis can also occur when the chewable gummy matrix absorbs moisture from the environment so that the number of adsorbed water molecules exceeds the ability of the gel matrix to hold water molecules. The syneresis test was carried out to determine the ability of the chewable gummy matrix to retain water contained in the preparation structure. Based on the analysis of Pareto charts, main effects plots, and contour plots, differences in propylene glycol concentrations have

more effect on chewable gummy syneresis than sucrose concentrations. Increasing the concentration of propylene glycol as a plasticizer can increase the elasticity of the chewable gummy and prevent loss of mass, including water molecules trapped in the structure of the chewable gummy (Matulyte, Marksa, et al., 2021).

An experimental analysis of 2^2 factorial designs was carried out to see the relationship between the two variables, namely the concentration of fillers and plasticizers, and to determine the interaction effect of the two factors. The results of the Pareto chart analysis showed that changes in sucrose concentration significantly impacted the average weight, disintegration time, and swelling index. Meanwhile, the difference in the concentration of propylene glycol as a plasticizer significantly impacts the syneresis potential of chewable gummy. The results of the main effects plot analysis also show similar results. Increasing sucrose concentration as a filler increases the average weight and disintegration time and decreases the swelling index. Increasing the concentration of propylene glycol as a plasticizer decreases the swelling and syneresis indices. Contour plots show color gradations that indicate differences in dependent variables due to changes in the concentration of sucrose and propylene glycol (Koteswari et al., 2016).

The results of the contour plot analysis showed that using a concentration of 35% sucrose and 4% propylene glycol produced a chewable gummy weighing > 2.77 grams, a longer disintegration time of > 6 minutes, but a lower swelling and syneresis index. Meanwhile, the use of 30% sucrose and 2% propylene glycol resulted in a chewable gummy with lower weight (< 2.81 gram) and faster disintegration time (< 4 minutes) but higher swelling and syneresis indices. The results of the overlay contour plot show the feasible design space. Feasible design space is an area of optimum concentration of independent variables to produce physical characteristics that meet specifications. The feasible design space graph shows the limits of each sucrose and propylene glycol concentration to produce physical characteristics of chewable gummy preparations that meet the requirements. The results showed that the concentration range of 30-35% sucrose as a filler and 2-4% propylene glycol as a plasticizer could produce an average tablet weight between 2.77-3.00 grams, disintegration time < 15 minutes, swelling index < 1%, and syneresis < 1%. However, from the graphs, the optimum areas for sucrose and propylene glycol concentrations have not been obtained because the tested concentration ranges provide results that meet the requirements. Further research requires optimization with a wider concentration range of sucrose and propylene glycol. Based on the results of further evaluation regarding the physical characteristics of the chewable gummy preparation, it is known that the optimum concentration of sucrose is 30% and 4% propylene glycol. This concentration produced a chewable gummy with a swelling index below 1% and did not show syneresis during storage.

Conclusions

The concentration of sucrose as a filler and propylene glycol as a plasticizer is essential in forming a chewable gummy structure. Based on the results of factorial analysis, increasing the concentration of sucrose will impact increasing the average weight, disintegration time, and decreasing the swelling index. Meanwhile, increasing the concentration of propylene glycol as a plasticizer significantly reduced the percentage of syneresis in the preparation. This study did not obtain the optimum concentration of sucrose and propylene glycol because the concentration ranges used were 30-35% for sucrose and 2-4% for propylene glycol to produce physical characteristics that met the requirements.

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Declaration statement

The authors reported no potential conflict of interest

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