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Design of Robusta Coffee Extract and Kelulut Honey Effervescent Granules with Different Sweeteners

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Abstract
The primary challenge in pharmaceutical preparation is the low stability of most active substances. Effervescent granules serve as a strategic solution, enhancing the chemical stability of robusta coffee (*Coffea canephora*) and kelulut honey (*Heterotrigona itama*) while providing rapid solubility and masking unpleasant tastes to improve patient adherence. Robusta coffee beans and kelulut honey are antioxidant-rich. This study created effervescent granules from a 70% ethanol extract of robusta coffee seeds and kelulut honey with stevia, mannitol, and lactose to achieve stable physicochemical properties and to increase the taste acceptability of the preparation. The research had five stages: extraction with 70% ethanol, design using the Simplex Lattice Design method, physicochemical properties evaluation of the optimum formula, real-time physical stability, and DPPH in vitro testing. The optimal formulation had 3.70%:7.29%:9.00% (stevia: mannitol: lactose). The brown mixture tasted sweet-sour and smelled like coffee. Physical evaluations revealed a moisture content of 2.53±0.10%, a pH of 6.16±0.07, and a flow rate of 10.81±0.07 seconds. While the raw extract combination showed an IC50 of 7.707 μg/mL, the optimized granules recorded 33.982 μg/mL, indicating strong antioxidant activity. In conclusion, the formulation successfully provides a stable, fast-dispersing, and palatable delivery system for natural antioxidants, offering significant potential for nutraceutical applications.

Keywords: Antioxidant, Robusta Coffee Beans, Effervescent Granules, Kelulut Honey, Simplex Lattice Design, Variations of Sweeteners

Desain Granul Effervescent Ekstrak Kopi Robusta dan Madu Kelulut dengan Variasi Pemanis

Abstrak
Tantangan utama dalam sediaan farmasi adalah rendahnya stabilitas sebagian besar zat aktif. Granul *effervescent* dikembangkan sebagai solusi strategis untuk meningkatkan stabilitas kimia kopi robusta (*Coffea canephora*) dan madu kelulut (*Heterotrigona itama*), memberikan kelarutan cepat, serta menutupi rasa tidak enak guna meningkatkan kepatuhan pasien. Biji kopi robusta dan madu kelulut kaya akan antioksidan. Studi ini bertujuan memformulasikan granul *effervescent* dari ekstrak etanol 70% biji kopi robusta dan madu kelulut dengan stevia, manitol, dan laktosa untuk mencapai sifat fisikokimia yang stabil dan untuk meningkatkan daya terima rasa dari sediaan. Penelitian ini terdiri dari lima tahap: ekstraksi dengan etanol 70%, desain menggunakan metode *Simplex Lattice Design* dengan pemanis yang berbeda, evaluasi sifat fisikokimia dari formula optimum, stabilitas fisik real-time, dan pengujian DPPH secara *in vitro*. Formulasi granul *effervescent* optimal yaitu variasi 3,70%:7,29%:9,00% (stevia:mannitol:laktosa). Sediaan berwarna coklat dengan rasa asam manis dan aroma khas kopi. Evaluasi fisik menunjukkan kadar lembab 2,53±0,10%, pH 6,16±0,07, dan laju alir 10,81±0,07 detik. Meskipun kombinasi ekstrak murni memiliki nilai IC50 sebesar 7,707 μg/mL, granul yang dioptimasi mencatat nilai 33,982 μg/mL, yang menunjukkan aktivitas antioksidan kuat. Kesimpulannya, formulasi ini berhasil menyediakan sistem penghantaran antioksidan alami yang stabil dan enak dikonsumsi dengan potensi signifikan untuk aplikasi nutrasetika.

Kata Kunci: Antioksidan, Biji Kopi Robusta, Granul *Effervescent*, Madu Kelulut, *Simplex Lattice Design*, Variasi Pemanis

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1. Introduction

Hippocrates (460-370 BCE) and Paracelsus (1493-1541 CE) influenced pharmacy formulation, composition, and manufacturing processes.[1] Pharmaceutical preparations in natural medicine have advanced. Indonesia, a biodiversity-rich nation, has been using natural materials in medicine since the 1900s, promising growth for the natural-based pharmaceutical business. Oral natural medicine preparations including solutions are popular due to their ease of administration and long-lasting effects.[2-4] The primary concern regarding these liquid preparations is the low stability of most pharmacological active ingredients in aqueous environments.[5] Effervescent granules can increase active pharmaceutical ingredient stability, are user-friendly, taste well, and improve patient adherence[6,7], and are suitable for acid-stable substances like phenolic acids and amino acids.[8,9]

Drug preparation involves evaluating materials and adding excipients in accordance with GMP and CPOTB.[1,3,10] To improve taste, stevia, mannitol, and lactose can be added. In limited amounts, stevia is needed due to its high sweetness[11], and FDA says it affects antioxidant activity at 1-4% concentrations.[12] The 50:50 ratio of mannitol and lactose at 8% affects active substance release.[13-15] Coffee, a bitter natural ingredient beverage, is often sweetened or enhanced with honey.[16]

The robusta coffee bean (*Coffea canephora*) is empirically used to relieve exercise pain, while kelulut honey (*Heterotrigona itama*) used as a wound ointment. The combination of coffee and honey has been proven to significantly enhance power output and endurance during physical training.[17] Kelulut honey has a sour taste; thus, sweetness must be added.[18,19] Robusta coffee bean extract, rich in phenolic and flavonoid components, exhibits high antioxidant capabilities, as verified by its IC50 value of 8.98 μg/mL.[20] At 10% concentration, kelulut honey has the maximum antioxidant capacity with the IC50 value of 14.29-90.63 μg/mL.[21] These two elements potentially prevent degenerative illnesses from free radicals.[22]

The effervescent form is crucial for these specific ingredients to mask the inherent bitterness of robusta coffee and the sharp sourness of kelulut honey, which would otherwise be unpalatable in standard liquid preparations. The optimization of sweeteners was considered to balance the high intensity of sweetness with the physicochemical integrity of the granules, specifically regarding their impact on moisture content, flow characteristics, and the release profile of antioxidant compounds.

Therefore, this study which are developed in effervescent granules preparations and observe the effect of variation in the concentration of the sweeteners on the physical stability and antioxidant activity to expand the inventory of natural ingredient medicines with antioxidant activity by contributing to the discovery of these ingredients.

2. Materials and Methods

2.1. Instruments and Methods

The Instruments and apparatus comprise climatic chamber (Memmert®), oven (Memmert®), rotary evaporator (IKA®), UV-Vis spectrophotometer (Shimadzu® 2450), analytical balance (Shimadzu AUY220®), grinder, moisture analyzer (Kern DLB®), sonicator (Branson® 1510), Thermo Scientific 4642090), pH meter (HANNA®), maceration container, mesh 16 and 20, micropipettes (10-100 μL and 100-1000 μL), glassware (Iwaki Pyrex®), aluminum foil, glass bottles, glass funnels (Pyrex®), parchment paper, glass bowls, spatula, and scoop.

2.2. Materials

The materials comprise aquadest, citric acid (Chemipan), tartaric acid (Vinicas), DPPH (Sigma Aldrich), 70% ethanol (Smart-Lab), FG lactose (Leprino-Foods), FG mannitol (Leprino-Foods), PA methanol (Smart-Lab), sodium bicarbonate (AHDD), PVP K-30 (Smart-Lab), robusta coffee simplicia (PT. Juragan Muda Indonesia), FG stevia (CV. Subur Kimia Jaya), and kelulut honey (Madu Syaiful).

2.3. Methods

2.3.1. Collection of Samples

Mature robusta coffee cherries were selected manually harvested fresh from Sungai Kakap District, Kubu Raya Regency, West Kalimantan, Indonesia, with red coloration serving as the indicator of full maturity.[23] Plant authentication was verified at the Faculty of Mathematics and Natural Sciences, Universitas Tanjungpura (Report No. 146/LB/FMIPA/UNTAN/2024). Kelulut honey samples obtained from local producers in Kubu Raya Regency were adapted to SNI 8664:2018 requirements, stored in food-grade containers, shaded from direct sunlight, below 28°C, and without metal tools.[24]

2.3.2. Extraction and Characterization

Robusta coffee samples were dried for 24 hours at 60-70°C, and clean seed samples were ground in a grinder.[23] A total of 500 grams of robusta coffee bean simplicia powder was macerated in 1 liter of 70% ethanol for 3×24 hours. Maceration results were filtered and heated at 50°C in a rotary evaporator, producing a dry robusta coffee extract.

Standardization was done on robusta coffee extract and raw materials of Kelulut honey. Parameter test for extract and raw materials consist of two parameters that are the specific parameter and the non-specific parameter. The specific parameter consists organoleptic assessments (color, odor, taste, texture, and consistency), yield percentage, and phytochemical screening. The non-specific parameter consists of moisture content and specific gravity.

2.3.3. Design of Effervescent Granules

The formulation was executed based on the research of Syahrina[24] and Ansel[25], incorporating a composition of diverse sweeteners including stevia, mannitol, and lactose, as per the formula derived from Design-Expert software version 13.0 (Stat-Ease, Inc., Minneapolis, MN, USA) subsequently followed by granulation via the wet granulation technique. The formulation was executed in 14 runs.

The manufacturing process took place in a controlled temperature and humidity environment. Granule production involved the separate granulation of acid and alkali in a 1:1 ratio. After being sieving with sieve No.16, the granules were dehydrated in a 50°C oven for 24 hours. The dried grains then sifted with sieve no.20, the acid and basic granules are blended until uniform. Granules were measured to determine manufacturing weight reduction.[25]

2.3.4. Design Verification

The design was verified through moisture content test, acidity level, and preparation flow rate measurements. To test moisture content, 1 gram of granules were weighed and analyzed at 105°C using a moisture analyzer. Less than 5% moisture is acceptable. Acidity was measured with a calibrated pH meter submerged in distilled water. The flow rate was determined by measuring the time required for 10 grams of granules to leave a funnel using a stopwatch. A good flow rate test requires 10 grams of granules to flow from the funnel in 1 second.[7,26]

$$\text{Flow Rate} = \frac{\text{granule weight}}{\text{time (second)}}$$

Design Expert software was used to find the best formula after collecting response values. Formulating the optimal formula was like developing the optimization formula with the ideal stevia, mannitol, and lactose concentration ratios. The best formula was then tested.

2.3.5. Organoleptic Test

Organoleptic evaluations of effervescent granules encompass visual assessments of color, aroma, and texture, in addition to the gustatory experience of the granules.[7,26]

2.3.6. Bulk and Tapped Density Test

A sample weighing 25 grams (M) was deposited into a 100 mL measuring cylinder. The visible volume (V0) was measured to the nearest scale increment. Tapped density was determined by tapping the cylinder 30, 500, and 1250 times, followed by the measurement of the observable volume (Vf).[7,26]

$$\text{Bulk Density} = \frac{M}{V0}$$

$$\text{Tapped Density} = \frac{M}{Vf}$$

Each sampling difference must not exceed 2 mL. If there is a discrepancy, the process should be repeated until the difference is no greater than 2 mL.[26]

2.3.7. Carr's Index and Hausner Ratio Test

25 grams of granules were transferred into a 100mL measuring cylinder, ensuring that no compaction occurs. The surface of the powder was smoothed without compression. The initial bulk volume (V0) was measured to the nearest scale increment, and the bulk density (g/mL) was calculated using the formula m/V0. Subsequently, the tapped volume (Vf) was determined after subjecting the measuring cylinder to 1,250 taps. The resulting volumetric data were used to calculate Carr's Index and the Hausner Ratio, which were then evaluated against the flow characteristics standards specified in Table 1.[26]

$$\text{Carr's Index} = \frac{V0\text{-}Vf}{V0} \times 100\%$$

$$\text{Hausner Ratio} = \frac{V0}{Vf}$$

2.3.8. Angle of Repose Test

The test was performed by introducing 10 grams of precisely measured grains into the funnel. The base radius (R) and the height (H) of the granule pile were measured to calculate the angle of repose (θ) is as follows.

$$\theta = \tan^{-1}\frac{H}{R}$$

2.3.9. Time of Disperse and Foam Height

The dispersion test involved weighing 5 grams of granules in a 250 mL beaker filled with 100 mL of distilled water. The grains were mixed gently, and the duration

Table 1. Correlation Between Carr's Index, Hausner Ratio, and Angle of Repose to Flow Characteristics [7,26]

Hausner Ratio	Carr's Index (%)	Angle of Repose (degrees)	Flowability
1.00-1.11	1-10	25-30	Excellent
1.12-1.18	11-15	31-35	Good
1.19-1.25	16-20	36-40	Fair
1.26-1.34	21-25	41-45	Passable
1.35-1.45	26-31	46-55	Poor
1.46-1.59	32-37	56-65	Very poor
>1.60	>38	>66	Very very poor

necessary for complete dispersion and foam production was documented, along with the foam height generated. The stipulated dispersion time for effervescent granules is 5 minutes.[24]

2.3.10. Real-Time Physical Stability Test

Evaluations were performed on the effervescent granule formulations throughout a 28-day storage duration at a temperature of 30±2°C/65±5%RH. Assessments were conducted on days 0, 7, 14, 21, and 28 covering parameters such as moisture content, degree of acidity, flow rate, tapped density, bulk density, Carr's Index, Hausner Ratio, angle of repose, dispersion time, and foam height.[26]

2.3.11. Antioxidant Activity Test

Antioxidant activity was assessed using the DPPH radical scavenging method according to the SNI 8623:2018 standard.22 A series of concentrations for the raw materials with 1:1 solution of robusta coffee extract and kelulut honey (25, 5, 1, 0.5, and 0.25 µg/mL) and the optimal granule formula (100, 50, 25, 10, 5, and 5 µg/mL) were prepared using methanol p.a. The mixtures were incubated for 30 minutes at room temperature in dark containers with a 0.1 mM DPPH stock solution at 1:1 volume ratio. Absorbance was measured using a UV-Vis spectrophotometer at a wavelength of 515.2 nm. The percentage of inhibition was calculated using the following formula.

A linear regression between %inhibition and sample concentration yield the equation y = bx + a, was utilized to compute the IC50 value.[27]

3. Results

3.1. Characterization of Samples

The characterization results of the raw materials indicate a yield of robusta coffee extract at 27.514%, exhibiting a dry consistency, brown-black hue, bitter flavor, distinctive coffee scent, and a viscous texture. Kelulut honey possesses a liquid fluidity, a brownish-black hue, a sweet-sour flavor, a distinctive honey fragrance, and a velvety texture. Both exhibit positivity for phenolic and flavonoid chemicals. The moisture percentage of robusta coffee extract is 1.98±0.24%, while that of kelulut honey is 11.28±1.55%. Their actual densities are 0.9992 grams/cm³ and 1.34406 grams/cm³, respectively.

3.2. Effervescent Granules Optimization

The optimization outcomes shown by the Design Expert software reveal a ratio of stevia, mannitol, and lactose at 3.70%, 7.29%, and 9.00%, respectively, with a desirability score of 0.952. The results regarding moisture content, degree of acidity, and flow rate are presented in Table 2.

Table 3 displays the results of the statistical analysis for each response. The data processing findings yielded the significant value (p-value), the adequacy of repeated observations (lack of fit), and the signal-to-noise ratio (adequate precision). Each response possesses a distinct model to evaluate the relationship between factors and responses, characterized by a non-significant lack of fit value and a significant model as established by the ANOVA test. All three replies exhibit satisfactory lack of fit and appropriate precision values, signifying that the model is applicable. The formulas for moisture content (Y1), degree of acidity (Y2), and flow rate (Y3) are as follows.

$$Y1 = -0.0233(A) + 3.81(B) + 2.72(C) - 1.91(AB) + 3.53(AC) - 2.26(BC) + 11.87(ABC)$$

$$Y2 = +13.72(A) + 7.25(B) + 6.13(C) - 14.25(AB) - 8.14(AC) - 2.37(BC)$$

$$Y3 = +11.83(A) + 10.82(B) + 10.87(C) - 1.49(AB) - 1.45(AC) - 0.044(BC) + 1.39(ABC)$$

Contour plots and prediction graphs paired with actual responses for moisture content, degree of acidity, and flow rate are presented in Figure 1.

3.3. Models Verification

The actual response data acquired is subsequently compared to the expected values. The predicted data for moisture content, degree of acidity, and flow rate

Table 2 Response Evaluation Results

Run	Factor (%)			Response		
	Stevia (A)	Mannitol (B)	Lactose (C)	Moisture Content (%)	pH	Flow Rate (second)
1	1.50	8.00	10.50	3.27	6.69	10.82
2	2.75	1.00	16.25	2.74	6.25	10.83
3	3.50	7.50	9.00	2.64	6.05	10.79
4	2.80	5.00	12.20	2.78	5.83	10.83
5	3.50	7.50	9.00	2.45	6.19	10.80
6	1.50	4.50	14.00	2.74	6.22	10.85
7	2.80	5.00	12.20	2.74	6.00	10.83
8	3.15	6.25	10.60	2.89	6.32	10.80
9	1.50	3.33	15.17	2.45	5.69	10.83
10	2.78	3.00	14.23	2.74	5.68	10.85
11	4.00	3.00	13.00	2.65	6.32	10.88
12	4.00	1.00	15.00	2.65	6.63	10.85
13	2.75	1.00	16.25	2.78	6.28	10.82
14	1.50	1.00	17.50	2.74	6.23	10.87

were calculated to be 2.45%, 6.19, and 10.79 seconds, respectively. The actual average data collected were 2.53%, 6.16 seconds, and 10.81 seconds, with corresponding standard error values of 0.098, 0.205, and 0.011, respectively.

3.4. Physical Stability of Granules

Data indicates that the granules remain stable during storage for 28 days at a temperature of 30±2°C/65±5%RH. However, there is a reduction in flowability, an increase in acidity and moisture content during storage. The preparation exhibits a brown hue accompanied by a distinctive coffee fragrance. The outcomes are illustrated in Figure 2.

3.5. Antioxidant Activity

The IC50 value indicates that the antioxidant activity of the raw materials, comprising robusta coffee

Table 3. Statistic Response Analysis with ANOVA

Factor		Moisture Content (Y1)	pH (Y2)	Flow Rate (Y3)	Criteria
Source Model		Special Cubic	Quadratic	Special Cubic	
	p-value	0.0093	0.0405	0.0038	<0.05
A-Stevia	Coefficient	-0.0233	0.0038	+11.83	
B-Mannitol	Coefficient	+3.81	<0.05	+10.82	
C-Lactose	Coefficient	+2.72	+13.72	+10.87	
AB	Coefficient	-1.91	+7.25	-1.49	
	p-value	0.5531	+6.13	0.0040	
AC	Coefficient	+3.53	-14.25	-1.45	
	p-value	0.2982	0.0399	0.0052	
BC	Coefficient	-2.26	0.0040	-0.0440	
	p-value	0.0070	-8.14	0.5458	
ABC	Coefficient	+11.87	0.2223	+1.39	
	p-value	0.0142	0.0052	0.0135	
Lack of Fit	p-value	0.3188	-2.37	0.1319	>0.05
Adeq Precision	Adequate signal	10.3596	0.0180	10.8254	>4.0000
Range		Minimize	In range	Minimize	
Lower Limits		2.45	5.61	10.79	
Upper Limits		3.27	6.69	10.88	
Importance		++++	++	+++++	

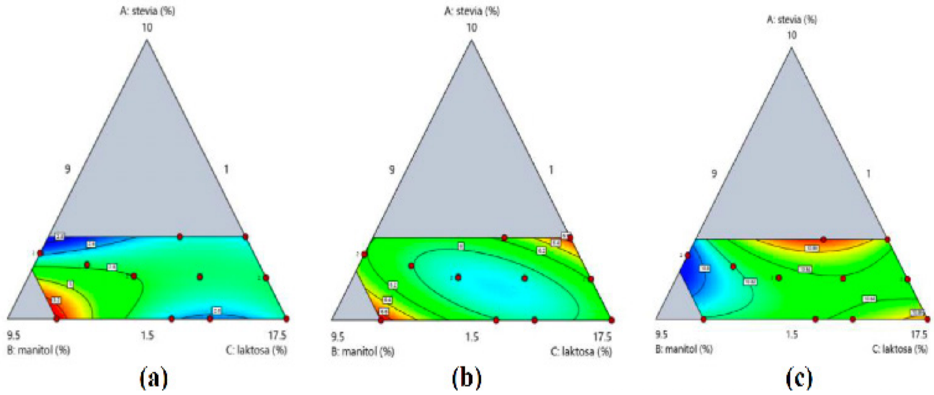

Figure 1 (a) Moisture Content Response Contour; (b) Degree of Acidity Response Contour; (c) Flow Rate Contour Response; The regions shaded in red signify the highest response values, however the regions shaded in blue denote the lowest response values in the 14-run formula.

extract and kelulut honey, along with the appropriate effervescent granule formulation, is classified as strong presented in Figure 3. The IC50 of the raw substance is 7.707 µg/mL, while the IC50 of the optimal formulation, which had 3.70%:7.29%:9.00% (stevia: mannitol:lactose), is 33.982 µg/mL.

4. Discussion

The characterization results of the raw materials in this investigation conform to the recognized criteria. The 70% ethanol solvent yields 27.514%, surpassing that of 96% ethanol. Consistent with prior studies, the yield percentages of 96% and 70% ethanol extracts from the same plant genus via the maceration method were 24.48% and 11.15%, respectively.[28] The tube test was positive for the presence of phenols and flavonoids, which is in accordance with previous research.[29] The moisture content of robusta coffee extract at 1.98%±0.24 signifies that the extract qualifies as a dry extract, as its moisture percentage is below 5%. Furthermore, kelulut honey complies with the SNI 8664-2018 standard, which stipulates a moisture level of less than 27%.[24]

Formula verification showed how sweetener components affect moisture content, acidity level, and flow rate. Larger coefficients with positive values indicate a direct relationship and high influence on the response, while negative coefficients indicate an inverse relationship.[30] The interaction of materials, such as mannitol, can lead to an elevation in moisture

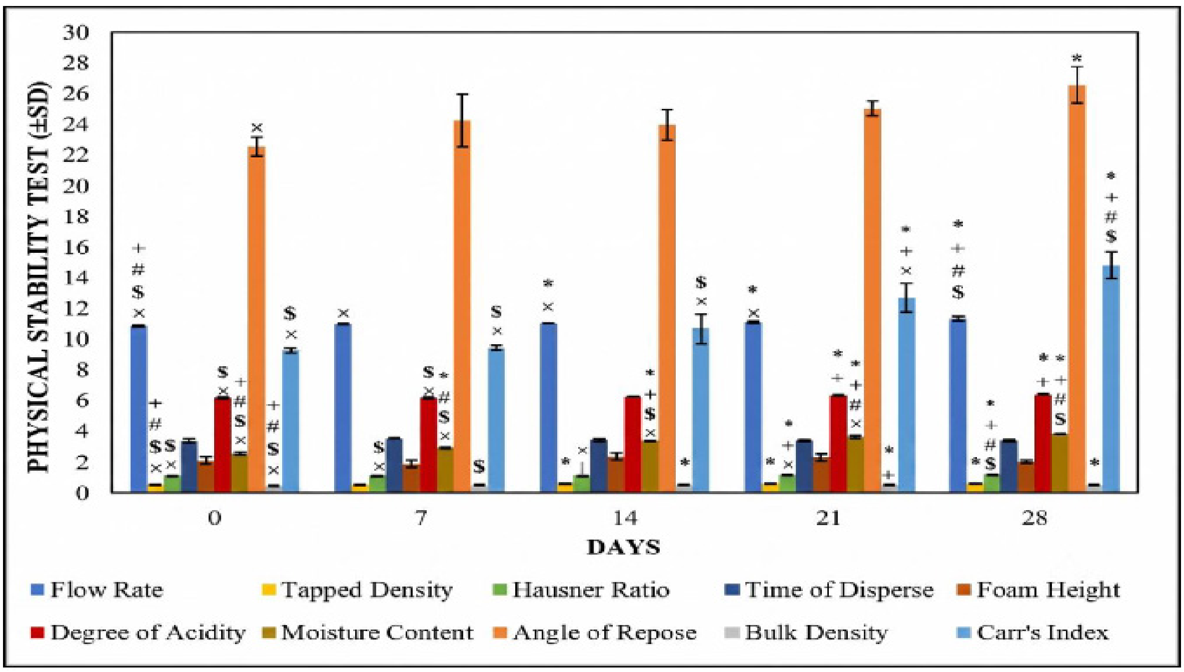

Figure 2 Results of Real-Time Physical Stability Test; *= Significantly different from day 0 (p<0.05); += Significantly different from day 7 (p<0.05); #= Significantly different from day 14 (p<0.05); $= Significantly different from day 21 (p<0.05); ×= Significantly different from day 28 (p<0.05)

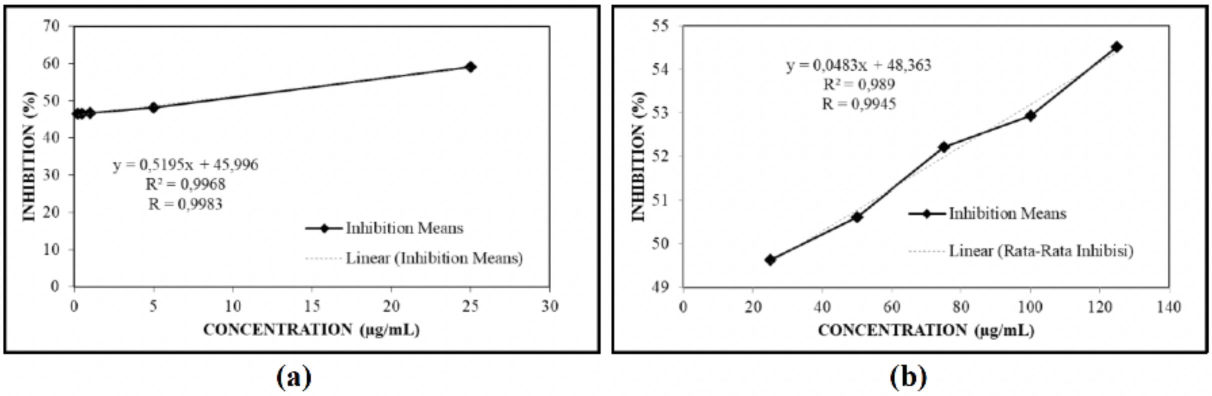

Figure 3. Linear Regression Equation for %Inhibition; (a) Combination of 70% Ethanol Extract of Robusta Coffee and Kelulut Honey in a 1:1 Ratio and; (b) Optimal Formula of Effervescent Granules

content, pH, and flow rate. The granule testing room's conditions cause the hygroscopic citric acid to release water, making mannitol unstable and the granules more humid even though the material is relatively non-hygroscopic and easily dried.[31] Furthermore, lactose and stevia have carbohydrate structures with hydroxyl groups, which form hydrogen bonds with water molecules to increase their hydration capacity and affect the preparation's moisture content.[32]

As preparation water content increases, pH becomes more basic. According to Nuraziz[33] and Hendyana[34], stevia sweeteners contain compounds that can contribute H+ ions, such as organic acids and minerals like potassium and cinnamic acid, which lowers the pH of the preparation. If moisture content rises, granules will stick to each other, slowing flow.[35,36] Lactose has a specific gravity of 1.545 g/cm³, stevia 1.0042-1.0068 g/cm³, and mannitol 1.514 g/cm³, affecting the value.[31,35] A substance flows better with a higher specific gravity because it increases molecular weight. Because lactose absorbs more water, the lactose-mannitol ratio is crucial to flow rate. Because mannitol has smaller particles than lactose, higher concentrations produce smaller granules.[31]

Formula optimization was done using Design Expert to adjust response values to the good category based on observational data of three responses. The formulation consisting of 3.70% stevia, 7.29% mannitol, and 9.00% lactose was selected as the optimal formula due to its superior desirability score of 0.952, which indicates the highest success in achieving minimized moisture content and optimized flow rate among the 14 runs. A desirability value near 1.0 indicates the program's ability to improve products. As the error percentage in the three responses is <5%, the proposed model is acceptable.

The physical stability test showed increased flow, moisture, and acidity. The observed reduction in flowability and enhancement of moisture content during the 28-day storage period are primarily attributed to the hygroscopic nature of citric acid, which facilitates moisture absorption and leads to the formation of stronger inter-particle liquid bridges. This increased moisture triggers minor CO_2 release, subsequently reducing H^+ ion activity and causing a gradual increment in the pH of the preparation.[36] Due to citric acid's hygroscopicity[37] and increased moisture content, acid components may decompose and decreasing flow rate.

Days 7, 14, and 21 have stable angle of repose data because it does not vary significantly. The preparation rests at a stable angle. Granule shape, particle size, and moisture affect the value.[36] The attractive force, frictional force, and particle size affect the repose angle. Small particles have high cohesiveness and are hard to flow.[37] Storage increases angle of repose in proportion to moisture and flow rate. The lactose-mannitol ratio serves as a critical factor for flowability; lactose, with a higher specific gravity compared to mannitol, enhances the molecular weight and ease of flow, whereas higher concentrations of mannitol result in smaller particle sizes that increase cohesiveness and impede the flow rate. According to Figure 2, the true density of the preparation on day 0 differs significantly from days 7, 14, 21, and 28 with a significance value of <0.05. Days 7, 14, 21, and 28 show little variation, indicating a stable preparation. Real and tapped density tests simulate powder sedimentation during storage and transport. Bulk density is more accurate than true density for packaging.[32,37]

On day 0, the Carr's Index value of the preparation differed significantly from days 21 and 28 (sig. value <0.05). On day 0, the Hausner Ratio of the preparation differed significantly from days 21 and 28 (sig. value <0.05). The formulation is stable on day 14 because it only changes on day 28. Sweetener is the critical point that raises compressibility index and Hausner

Ratio.[32] The increased moisture content during storage increases particle size and voids. Lower compression resistance makes particles more compressible.[31] Due to its high specific gravity, citric acid improves flow. After reconstitution, granules characteristics are evaluated to determine how acid and base ratios affect dispersion. According to reconstitution results, the preparation produced a brown coffee liquid with a sweet-sour taste, a slight bitter aftertaste, and the robusta coffee aroma. Figure 2 shows a dispersion time of 3.37±0.14 minutes to 3.53±0.02 minutes. The obtained dispersion time is within the allowed range of <5 minutes.[37]

The analysis showed that the data is normally distributed and homogeneous with a sig. value of 0.073 for dispersion time and 0.642 for foam height. A Post Hoc test was performed to find significant differences in each test point's average value. Figure 2 shows that day 0 preparation dispersion time and foam height were not significantly different from other days with a sig. value >0.05. The value shows that citric, tartaric, and sodium bicarbonate are stable from 0 to 28 days. After testing the stability of the effervescent granule preparation, the content must be tested for antioxidant activity using the DPPH radical scavenging method.

The DPPH radical scavenging reaction method was chosen because it effectively screens small amounts of antioxidant molecules visually. When antioxidant compounds donate electrons to the DPPH radical, DPPH turns from purple to yellow.[39,40] The combination of raw materials exhibited superior antioxidant potency with an IC50 value of 7.707 µg/mL, which is stronger than the individual values reported in prior research, specifically 8.98 µg/mL for robusta coffee extract and 14.29–90.63 µg/mL for kelulut honey. Although the final effervescent preparation showed a decrease in activity with an IC50 of 33.982 µg/mL suggests a partial degradation of thermosensitive polyphenols during the wet granulation and drying processes, which is consistent with previous findings regarding the impact of thermal processing on natural antioxidants.[20]

The compounds, especially chlorogenic acid, a polyphenol and flavonoid, and the drying method during granule preparation can cause this. Number and position of phenolic hydrogens in chlorogenic acid and flavonoids affect quenching activity. Thus, phenolic compounds with more hydroxyl groups have higher antioxidant activity. With one carboxyl group, three hydroxyl groups, and a phenolic group with two hydroxyl groups, chlorogenic acid is expected to be a major antioxidant.[39,40] Heating accelerates the initiation reaction, reducing antioxidant activity. Heating also damages bioactive components, reducing free radical scavenging. Raw materials and effervescent granule preparations have strong antioxidant activity, according to results.

Chlorogenic acid and flavonoids may be important because their hydroxyl groups can transfer electrons to free radicals and form complexes with metals, inhibiting lipid peroxidation and inflammation-induced tissue damage. NRF2, which inhibits NF-kB in ROS-induced inflammation, is synthesized by chlorogenic acid.[40] This study aimed to determine the optimal combination of sweeteners for an effervescent granule formula, as well as to assess its preparation, stability, and antioxidant activity using the DPPH method. Although there are limitations to this study, it also opens avenues for further research, including the exploration of antioxidant activity through alternative methods and the execution of preclinical and clinical trials.

5. Conclusion

This study found that the optimal formula of effervescent granules contained variations of 3.70%, 7.29%, and 9.00% for stevia, mannitol, and lactose sweeteners. The optimal formula is brown, smells like coffee, and tastes sweet-sour. The formula has a moisture content of 2.53±0.10%, a degree of acidity of 6.16±0.07, and a flow rate of 10.81±0.07 seconds. For 28 days, the formulation's contact angle, dispersion time, and foam height remain stable. Storage decreased flowability, increased pH, and increased moisture content. The active substance, 70% ethanol extract of robusta coffee and kelulut honey, has an IC50 of 7.707 µg/mL, and the optimal effervescent granule preparation has 33.982 µg/mL, which is very strong.

Conflict of Interest

The authors declare that they have no conflicts of interest.

References

References must be numbered in order of appearance in Author 1, A.B.; Author 2, C.D. Title of the article. Journal Name. Year, Volume, page range.

1. Jamróz W. Printing techniques: recent developments in pharmaceutical technology. Acta Pol Pharm. 2017;74(3):753–763.
2. Wikantika K, Ghazali MF, Dwivany FM, Novianti C, Yayusman LF, Sutanto A. Integrated Studies of Banana on Remote Sensing, Biogeography, and Biodiversity: An Indonesian Perspective. Diversity. 2022;14(4):1–20.
3. Saptaningtyas AI, Indrahti S. Dari industri jamu tradisional ke industri jamu modern: perkembangan industri jamu sido muncul dalam mempertahankan eksistensi perusahaan tahun 1951-2000. Histotriografi. 2020;1(2):172–80.
4. Lodhi VD, Jadon AS, Sen J, Jain PK, Thakur BS, Khare

B, et al. Effervescent Tablets: Everything You Need To Know. Asian J Dent Health Sci. 2022;2(4):1–8.
5. Fickri DZ. Formulasi dan uji stabilitas sediaan sirup anti alergi dengan bahan aktif chlorpheniramin maleat (CTM). J Pharm Care Anwar Med. 2019;1(1):16–24.
6. Egeten KR, Yamlean PVY, Supriati HS. Formulasi dan pengujian sediaan granul effervescent sari buah nanas (Ananas comosus L. (Merr.)). J Ilm Farm. 2016;5(3):116–121.
7. Patel SG, Siddaiah M. Formulation and evaluation of effervescent tablets: a review. J Drug Deliv Ther. 2018;8(6):296–303.
8. Sari AM, Rosamah E, Suwinarti W, Kusuma IW, Arung, ET. Aktivitas antioksidan dan antibakteri dari ekstrak bee pollen lebah kelulut (Tetragonula sarawaknensis). J Ris Ind Has Hutan. 2021;13(2):123–132.
9. Muslimin I. Pengaruh tingkatan suhu penyangraian (Roasting) terhadap karakteristik aroma kopi arabika. Jasathp J Sains Dan Teknol Has Pertan. 2021;1(1):33–40.
10. Piekara A, Krzywonos M, Szymańska A. Sweetening Agents and Sweeteners in Dietary Supplements for Children-Analysis of the Polish Market. Nutrients. 2020;12(8):1–9.
11. Center for Food Safety and Applied Nutrition (US). Aspartame and other sweeteners in food [Internet]. Silver Spring (MD): U.S. Food and Drug Administration; 2025 Feb 27 [cited 2025 Jul 7]. Available from: https://www.fda.gov/food/food-additives-petitions/aspartame-and-other-sweeteners-food.
12. Ulfa RA, Saepuloh A, Cahyanto T, Darniwa AV, Adawiyah A. Pengaruh jenis pemanis terhadap pH dan aktivitas antioksidan sirup pucuk mangga (Mangifera indica). Teknol Pangan Media Inf Dan Komun Ilm Teknol Pertan. 2022;13(1):76–83.
13. Rustiani E, Hidayat N. Pengembangan Granul Instan Herbal Kombinasi Ekstrak Brokoli dan Herba Pegagan dengan Variasi Jenis Pemanis. Pros Semin Nas Sains Dan Terap. 2023;1(1):65–65.
14. Pratama R, Saputro MR, Sani AR, Robiatul RS, Mulki MA. Pengaruh eksipien terhadap sifat fisik granul effervescent: Review. J Ilmu Farm Dan Kesehat. 2024;2(1):137–154.
15. Hidayati DN, Marwan LS, Murfrod. Formulasi tablet hisap ekstrak etanolik daun kemangi (*Ocimum sanctum* L.) dengan variasi pemanis manitol dan laktosa. J Ilmu Farm Dan Farm Klin. 2015;12(1):11–19.
16. Furqan M, Nurman S. Ekstrak polar kopi hijau arabika (*Coffea arabica* L.) sebagai antihiperglikemi pada mencit (*Mus musculus*). J Healthc Technol Med. 2020;6(2):1325–1331.
17. Febriani S, Pradana AK, Manggabarani S. Pengaruh pemberian kopi dengan kombinasi gula aren dan madu terhadap endurance dan power. J Pangan Kesehat Dan Gizi Univ Binawan. 2021;2(1):62–71.
18. Afriliah N, Taurina W, Andrie M. Karakterisasi simplisia madu kelulut (*Heterotrigona itama*) sebagai bahan baku sediaan obat penyembuh luka. Maj Farm Dan Farmakol. 2022;26(3):104–10.
19. Yusuf DPM, Kawareng AT, Indriyanti N. Skrining fitokimia dan uji aktivitas antioksidan ekstrak etanol propolis lebah kelulut (*Heterotrigona itama*). Proceeding Mulawarman Pharm Conf. 2021;14:237–241.
20. Latief M, Muhaimin MM , Heriyanti HH, Tarigan IL, Sutrisno SS. Determination antioxidant activity of *Coffea arabica*, *Coffea canephora*, Coffea liberica and sunscreens cream formulation for sun protection factor (SPF). Pharmacogn J. 2022;14(2):335–342.
21. Shamsudin S, Selamat J, Sanny M, A.R. SB, Jambari NN, Khatib A. A comparative characterization of physicochemical and antioxidants properties of processed *Heterotrigona itama* honey from different origins and classification by chemometrics analysis. Molecules. 2019;24(21):1–20.
22. SNI 8664-2024 Madu - BBPSIK Jogjakarta [Internet]. 2023 [quoted July 7 2024]. Available at: https://drive.google.com/drive/folders/1ATG-ycurpNEUpE2rJiKshVxOCO-dwGwD.
23. Haryanto B, Thohar A, Basri H, Widodo D, Wibowo NS, Juniawan. Pelatihan Budidaya berkelanjutan (Good Agricultural Practices-GAP) dan Pascapanen (Post-Harvest) Kopi Robusta. II. Jakarta: Badan Penyuluhan dan Pengembangan SDM Pertanian, Kementerian Pertanian, Republik Indonesia dan SCOPI, GCP, dan ICCRI; 2019.
24. Syahrina D, Noval N. Optimasi Kombinasi Asam Sitrat dan Asam Tartrat sebagai Zat Pengasam pada Tablet Effervescent Ekstrak Ubi Jalar Ungu (Ipomoea batatas L). J Surya Med. 2021;7(1):156–72.
25. Ansel HC, Allen Jr LV. Pharmaceutical dosage forms and drug delivery systems. 10th ed. Philadelphia (PA): Lippincott Williams & Wilkins; 2014.
26. Rani KC, Parfati N, Muarofah D, Sacharia SN. Formulasi granul effervescent herba meniran (Phyllanthus niruri L.) dengan variasi suspending agent xanthan gum, CMC-Na, dan kombinasi CMC-Na-mikrokristalin selulosa RC-591. J Sains Farm Klin. 2020;7(1):39.
27. Saehu A, Suryani BN, Noviyanto ABF. Uji Aktivitas Antioksidan dari Formulasi Sabun Mandi Cair Ekstrak Etanol Biji Kopi Robusta (Coffea canephora). J Pendidik Biol. 2022;7(2):124–135.
28. Zulfaidah NT, Kurniawati E, Putri GH, Widiani F. The Effect of Variation in Solvent Concentration on Caffeine Content in Green Arabica Coffee Bean Extract (Coffea arabica) using UV-Vis Spectrophotometry. J Food Pharm Sci. 2024;12(3):266–272.
29. Fatmawati S, Sjahid LR, Utami NM, Kartini. Total Phenolic, Total Flavonoid Content and in vitro Sun Protection Factor test of Arabica Coffee Leaves Extract (*Coffea arabica* L). J Pharm Policy Pract. 2021;14(1):57–66.
30. Kumar S, Ashish B. Formulation by Design Approach for Fizzy Granules Using Statistical Optimization Methodologies. Asian J Pharm. 2015;9(4):S59–S67.
31. Sulistiani ND, Anam C, Yudhistira B. Karakteristik tablet effervescent labu siam (Sechium edule Sw.) dan ekstrak secang (Caesalpinia sappan L.) dengan filler laktosa-manitol. J Teknol Has Pertan. 2018;11(2):99–109.
32. Sadovnikova A, Garcia SC, Hovey RC. A Comparative Review of the Cell Biology, Biochemistry, and Genetics of Lactose Synthesis. J Mammary Gland Biol Neoplasia. 2021;26(2):181–96.
33. Nuraziz CE, Khairi AN. Effect of Adding Stevia Sweetener (Stevia rebaudianna) and Arabic Gum Filler on the Physicochemical Properties of Chayote Squash (Sechium edule) Powder Drink. AgriTECH.

2024;44(2):161–72.
34. Hedyana V, Wachid M, Harini N. Pengaruh penambahan serbuk daun stevia dan pektin daun cincau hijau terhadap sifat fisik, kimia, dan organoleptik selai buah naga merah. Food Technol Halal Sci J. 2021;4(1):66–81.
35. Widyasanti A, Klarasitadewi A. Pengaruh rasio bahan-pelarut dan lama terhadap karakteristik fisikokimia ekstrak cair daun stevia (*Stevia rebaudiana Berton*i). J Agroindustri. 2022;12(2):86–95.
36. Rani KC, Parfati N, Jayani NIE, Kurniawan IMA, Kristiani NPW. The development of moringa leaves effervescent granules with effervescent agent of citric acid and sodium bicarbonate. Pharmaciana. 2020;11(2):225–38
37. Rashati D. Pengaruh variasi konsentrasi asam basa terhadap sifat fisik dan stabilitas granul effervescent ekstrak daun katuk (*Sauropus androgynus* (L) Merr.). J Ilm Farm Akad Farm Jember. 2024;7(2):107–15.
38. Vanhere KG, Derle DV, Khatale SB, Nangude SL. A Comprehensive Review on Effervescent Tablets. J Drug Deliv Ther. 2023;13(7):141–50.
39. Fahlefi MIR, Yunita MN, Choirunnisa IR, Zhafira FA, Rahma RA. Effect of *Coffea canephora* Bean Extract on Lead Acetate-Induced Rat. J Farm Dan Ilmu Kefarmasian. 2024;1(1):97–104.
40. Wijianto B, Pratiwi L, Hermawati E. Evaluation of Physicochemical and Antioxidant Properties of Kelulut (*Heterotrigona itama*) Honey and Forest Honey Authentic to West Borneo. NanoBioScience. 2025;14(1):1–8.