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Original Article

FORMULATION AND OPTIMIZATION OF EFFERVESCENT TABLET CONTAINING KAEMPFERIA GALANGA

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ABSTRACT

Objective: This study aims to optimise the formulation of effervescent tablets using ethanolic extract of *Kaempferia galanga* with citric and tartaric acids as sources of acids and to assess the physical properties of the tablet.

Methods: Effervescent tablets were formulated through dry granulation method and evaluated for organoleptic properties, flowability, angle of repose, compressibility index, moisture, hardness, friability, dissolution time, pH, weight uniformity and size uniformity. Data for optimization were analysed using Design Expert software, version 13.0. Simplex lattice design optimisation was used, with two independent variables, namely, concentrations of citric and tartrate acids. The tablets were then characterised.

Results: All five effervescent tablet formulas met the requirements in terms of weight uniformity and size uniformity. Only F1, F2, F3 and F4 satisfied the requirements for friability. Physical evaluation indicated that the hardness and dissolution time of the effervescent tablets also met the requirements. The combination of tartaric and citric acids affected the hardness, friability, size uniformity and dissolving time of *Kaempferia galanga* extract effervescent tablets, resulting in positive values for friability and dissolving time response values and negative values for hardness and size uniformity.

Conclusion: The optimal concentrations of citric and tartaric acids in effervescent tablets were 9.5% and 17.5%, respectively, with a desirability value of 0.789. Furthermore, the optimum formula can be developed at a later stage for stability tests and *in vivo* assays.

Keywords: Kaempferia galanga, Effervescent tablet, Simplex lattice design, Formulation, Optimisation

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INTRODUCTION

Kaempferia galanga is a plant that grows in tropical and subtropical areas, especially in tropical Asia, among others in China, Indonesia, Malaysia, Thailand, Taiwan and India [1]. Kaempferia galanga is abundant in flavonoids, alkaloids, glycosides, tannins and essential oils [2]. Kaempferia galanga has a chemical called *ethyl-p-methoxycinnamate*, which exerts many biological effects, including anti-cancer and anti-monoamine oxidase effects [3]. Moreover, *ethyl-p-methoxycinnamate* from Kaempferia galanga can reduce inflammation considerably [4].

Oral administration is the most expedient method of administering medications and has been effective over the years; it has also been associated with high patient compliance. However, oral route has severe effects on individuals who have difficulty taking this dosage form, such as those who experience nausea and swallowing difficulties when taking the drug orally, as well as sluggish absorption and prolonged onset of action [5]. Among other oral dosage forms, an effervescent tablet is one of the best alternatives to overcome this disadvantage because it is immediately dissolved and/or dispersed in water before administration, thereby reducing the risk of irritation caused by direct contact with the digestive tract [6]. CO₂ in the composition facilitates the entry of active ingredients into paracellular pathways, helps with absorption and provides a pleasant taste, which is better than other oral dosage forms [7].

Citric and tartaric acids are two acid sources most frequently employed in the manufacture of effervescent tablets [8]. Basic ingredients are derived from sodium bicarbonate and are utilised to mask the astringent flavor of *Kaempferia galanga* extract [9]. Utilising citric and tartaric acids helps ensure the success of the preparation of effervescent tablets. The use of a single acidic substance presents difficulties. The ratio of citric acid to tartaric acid significantly affects the physical properties of effervescent tablets [8]. The combination of citric and tartaric acids can strengthen the bonds between particles in effervescent tablets, thereby increasing hardness, shock and friction resistance during compression, packaging and distribution. This is accomplished when citric acid and tartaric acid are combined [10]. Citric acid has several advantages over other acid sources; in particular, citric acid is highly soluble in water and can impart a sour flavor to effervescent tablets, whereas tartaric acid is also highly soluble in water compared with other types of acids. When only citric acid is present, the mixture becomes sticky and difficult to granulate, whereas tartaric acid alone causes particles to readily agglomerate. The combination of citric and tartaric acids can alter the physical properties of the resultant granules because of their unique characteristics [11, 12]. Additional lubricants may then be required. PEG 6000 is soluble in water and was used as a lubricant in this study [11].

This work proposes information to optimize the formulation of effervescent tablets containing *Kaempferia galanga* rhizome extract.

MATERIALS AND METHODS

Material

Kaempferia galanga was obtained from Balai Besar Penelitian dan Pengembangan Tanaman Obat dan Obat Tradisional (Indonesia) and identified by a botanist from the Balai Besar Penelitian dan Pengembangan Tanaman Obat dan Obat Tradisional, Kementerian Kesehatan Republik Indonesia with specimen voucher number of YK.01.03/2/892/2021. Citric acid, tartaric acid, sodium bicarbonate, povidone k-30 (PVP), polyethylene glycol 6000 (PEG 6000), lactose and aspartame were obtained from Merck (Germany). Flavouring and colouring agents were obtained from Suburb Kimia Jaya Company (Indonesia).

Tablet formulation

Five tablet formulations of *Kaempferia galanga* extract, namely, F1, F2, F3, F4 and F5, were determined with different proportions of

citric acid and tartrate acid as well as other ingredients to a total weight of 3000 mg (table 1). The formulation study was conducted

in the Pharmaceutical Laboratory at the Faculty of Pharmacy, Universitas Muhammadiyah Surakarta, Indonesia.

Table 1: Formulations of Kaempferia	galanga effervescent tablet (% w/w)
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Composition	Formula (% w/w)				
-	Ι	II	III	IV	V
Extract	5	5	5	5	5
Lactose	40	40	40	40	40
Citric Acid	27	18	13.5	9	0
Tartaric Acid	0	9	13.5	18	27
Bicarbonat Natrium	15	15	15	15	15
Polyvinylpyrrolidone (PVP)	1	1	1	1	1
PEG 6000	5	5	5	5	5
Aspartam	5	5	5	5	5
Flavor	2	2	2	2	2

Tablet preparation

For each formulation, 200 tablets were prepared using wet granulation procedure [13] with slight modifications. An acid-based solution was prepared by mixing citric acid, tartaric acid, lactose, polyvinylpyrrolidone (PVP) and flavouring and colouring compounds. The mixture was ground with a mortar and pestle and mixed with 96% ethanol added dropwise to form a hard mass. Granules were passed though a 60 mesh and dried in a climate chamber (Memmert ICH110) at 65 °C with 25% RH (Relative Humidity) for 24 h. An alkaline-based solution was prepared by mixing dry extract, sodium bicarbonate, aspartame, polyvinylpyrrolidone, flavouring, colouring and lactose. The mixture was ground with a mortar and pestle and added with 96% ethanol dropwise to form a hard mass. Granules were passed through a 60 mesh and then dried.

Measurement of effervescent granules

Test of time flow

About 100 g of granules were placed in a flow ability tester. The mass was allowed to circulate, and a digital stopwatch was used to record the time. The acceptable discharge rate must not exceed 10 g per second [14].

Test for angle of repose

About 100 g of the granule mass was placed on the flow ability instrument. The mass was allowed to circulate freely. The angle of repose and the height and circumference of the powder mound were determined. Angle reposes of 30 to 40 indicate adequate flow properties [14].

Test of compressibility

The sample was poured in a 100 ml measuring cup attached to the bulk density tester to record initial volume. The instrument was turned on, and a rhythm was played. Final volume was recorded. If the compressibility index falls between 11% and 15%, this indicates that the material has excellent compression characteristics [14].

Moisture test

Moisture content was measured using moisture balance analyser. The optimal moisture content of granules for the production of effervescent tablets is between 2% and 4% [7].

Measurement of effervescent tablets

Organoleptic tablet

Test size, shape, colour, presence or absence of odor, flavor, surface shape, consistency and physical defects were observed visually on effervescent tablets [15].

Test for weight uniformity

Twenty tablets were weighed individually by using an analytical balance. No more than two tablets should weight with 5% deviation from the mean, and none of the tablets should weight with 10% deviation from the mean [7].

Tablet hardness

Firmness was evaluated using a firmness tester. The optimal hardness ranges between 4 and 10 kg/cm² [11].

Tablet friability

Twenty tablets were tested in a friabilator at 25 rpm for 4 min. Tablet specifications that are still acceptable are less than 1% [16].

Dissolve time test

An effervescent tablet was placed in a beaker glass containing 1000 ml of distilled water. The time required for the tablet to completely dissolve was recorded. The optimal dissolution duration is between 60 and 120 sec [17].

Tablet pH test

The pH of the effervescent solution was determined using a pH meter by dissolving one tablet in 200 ml of distilled water in a glass beaker [18].

Size uniformity

Diameter and thickness of a tablet were determined. The diameter must not be more than three times its thickness or less than one-third of it [19].

Optimisation formulas

Optimisation was carried out with Design Expert software version 13 with Simplex Lattice Design (SLD) by encoding the results of flowability, angle of repose, compressibility index, moisture, hardness, friability, dissolution time, pH, weight uniformity and size uniformity. The optimum formula obtained was tested again for physical properties, and the results were compared with the point prediction results of Simplex Lattice Design. Results were verified by one sample T-test.

RESULTS AND DISCUSSION

Kaempferia galanga is a botanical species that thrives in tropical and subtropical areas, particularly in tropical Asia, encompassing China, Indonesia, Malaysia, Thailand, Taiwan and India [2, 20, 21]. It has white rhizome and a very subtle flavor. Plants, including Kaempferia galanga, belonging to the Zingiberaceae family exhibit a range of biological activities, including antioxidant, antibacteria, anti-inflammatory, analgesic, gastritis relieving, dyspepsia relieving and anticancer [20, 22-25]. In the present study, we extracted samples through maceration with 96% ethanol, and the extraction efficiency was 12.21%. Dried Kaempferia galanga had no discernible odor and was dark brown, as determined by organoleptic analysis. Another study that used maceration achieved a yield of 13.12% when employing n-hexane as solvent and a yield of 5.52% when employing ethyl acetate as solvent [23]. Yield analysis is crucial because it helps determine the efficacy of the extraction procedure, where a higher yield value corresponds to a greater production of compound components [26].

Effervescent granul assessment

Effervescent tablets are pharmaceutical preparations consisting of alkaline and acidic components, which undergo a chemical reaction

to release carbon dioxide gas. When added to a liquid solution, effervescence aids in dissolving the tablets [11]. Acidifying agents, namely, citric acid and tartaric acid, were used in various combinations in the present study, and their effect on effervescent tablets containing *Kaempferia galanga* extract as the active constituent was investigated. Flow rate, angle of repose, compressibility and moisture content were determined.

Flow rate test was conducted to determine the quality of effervescent powder because it affects tablet compression; a high flow rate enables the powder to flow quickly, resulting in uniform sizes [27]. Flow rate test was conducted by observing the duration and velocity of the flow of effervescent powder. A decent flow rate has a minimum flow rate of 10 g/sec. F1, F2, F3, F4 and F5 had a satisfactory flow rate and met the requirement of flow rate of less than 10 sec for 100 g of powder (table 2).

Parameter	FI	FII	FIII	FIV	FV
Flowability (g/s)*	06:04:40±00:32:30	05:17:00±00:07:00	05:18:20±00:13:26	05:36:20±00:09:49	06:15:00±00:10:32
Angle of repose*	30.02±0.75	29.30±0.56	29.01±0.20	28.58±0.19	29.23±0.29
Compressibility index (°)*	3.14±1.31	2.34±1.23	2.76±1.81	3.88±1.79	6.09±0.10
Moisture (%)*	1.54±0.89	1.50 ± 0.87	1.43±0.83	1.46±0.84	1.30±0.75
Hardness (Kg)*	8.044±1.022	5.821±0.442	5.581±0.812	9.167±0.384	5.369±0.516
Friability (%)*	0.081±0.077	0.102±0.035	0.201±0.171	0.157±0.245	1.530±0.523
Dissolving time (sec)*	03:47:49±00:04:53	03:02:04±00:35:38	03:00:38±00:00:32	02:51:17±00:09:18	02:31:17±00:08:18
pH*	4.45±0.02	4.18±0.01	4.14±0.02	3.87±0.02	3.78±0.03
Average weight (g)*	3.359±0.008	3.286±0.029	3.294±0.081	3.162±0.112	3.293±0.029
Average size (mm)*	0.891±0.008	0.914±0.007	0.901±0.005	0.866±0.007	0.908±0.006

*Result are expressed as a mean±SD, n=3

The effervescent powder had an excellent flow rate due to consistent particle size. In the present study, the effervescent powder was sieved with a 40-mesh sieve to increase particle size uniformity and enhance the resultant flow rate. The incorporation of 1% polyvinylpyrrolidone as a binder in the formulation increased the particle size, thereby reducing cohesive forces and enhancing fluidity [18]. Powder flow rate depends on the degree of repose angle and compressibility; a small degree of repose angle indicates a high powder flow rate. A high compressibility value indicates a high powder flow rate, the lower the compressibility value. In previous experiments, acid optimisation was conducted in effervescent tablets from extracts with a flow rate of 5 sec for 50 g granules. The resulting flow rate falls into the category of 'good flow rate.'

In this study, the angle of repose test was used to characterise the flow rate of effervescent powders. Powders with a more significant value for the angle 0of repose have a low flow rate capability than powders with a smaller value [19]. A suitable angle of repose is between 25° to 45°. Table 2 shows the testing results for the angle of repose for effervescent powder for each formula, with the angle of repose for F1 as 30.02°, F2 being 29.30°, F3 being 29.01°, F4 being 28.58° and F5 being 29.23°. The maximum value of the silent angle was observed at F1, which supported a previous finding [28] that optimised the acid combination formula; F1 had the most excellent angle of repose in F1, as well as a higher citric acid content than other formulations. Citric acid can absorb moisture from the air, increase humidity and cause enormous cohesive forces. Noncohesive granules will disperse to form low piles and a small angle. A combination of citric acid and tartaric acid will decrease the cohesiveness of particles, thereby increasing their angle of repose.

Compressibility test is used to evaluate the properties of effervescent powders that are stable and compact when subjected to pressure during tablet printing. A compressibility value of 20% indicates good compressibility; the lower the powder's compressibility value is, the more excellent its flowability will be [28]. Table 2 shows the compressibility data and indicates that each formula satisfies the requirements for good compressibility, with values of 3.14% for F1, 2.34% for F2, 2.76% for F3, 3.88% for F4 and 6.09% for F5. The finest formula was F2 because it had the lowest compressibility value of 2.34%; the lower the compressibility value is, the more excellent the powder's flowability will be. Previous research also produced effervescent tablet formulations from extracts with compressibility values of 4% to 9%; these results demonstrated that the powder possessed excellent compressibility [8]. Angle of repose, shape, density, and granular size can affect compressibility value. Powders with smaller particle sizes are denser than powders with larger particle sizes [29]. Powders with uniform granule shapes and sizes will be simpler to compress, allowing for the production of effective effervescent tablets.

Moisture content test is performed to determine the moisture content of effervescent powder following drying. Powders with a high moisture content increase the risk of powder adhering to the punch or tablet printer. Furthermore, a higher moisture content of the powder indicates a greater risk of an early effervescent reaction, resulting in less stable tablets. Hence, 5% is an acceptable moisture level for effervescent tablets [16]. Table 2 present the moisture content data, which indicate that each formula met the requirements, with values of 1.54% for F1, 1.50% for F2, 1.42% for F3, 1.46% for F4 and 1.29% for F5. All formulas met the requirements for moisture content, but F5 was considered the best because its moisture content was significantly lower than the 5% limit.

Effervescent tablet assessment

Tablets were prepared through dry granulation, where effervescent powder was separated between acidic and alkaline mixtures. A thick extract was dried and mixed with maltodextrin at a ratio of 1:3. The dry extract was combined with the alkaline portion and placed in a particular container, and the acidic mixture was placed in another specific container. The mixtures were dried in a climatic chamber at $60 \,^{\circ}$ C for 48 h. The two parts were combined (acid and alkaline) and added with PEG 6000. The sample was sieved through a mesh 40 until a ready-to-print mixture was produced. Physical tests of granule powder and tablets were conducted in triplicate. Organoleptic properties, tablet hardness, tablet friability, tablet dissolution time test, pH, weight uniformity and size uniformity. Evaluation was carried out to ensure that the tablets comply with the standard tablet requirements.

Organoleptic tests involve observing the tablet's shape, colour, flavor and odour [15]. All effervescent tablets of *Kaempferia galanga* extract have identical physical characteristics, including a flat, round shape, yellow-white spots and a sour and distinct aroma. The resultant tablet has a rounded, flat form because of the round shape of the tablet punch. The yellow hue with white patches is derived from the Kaempferia galanga extract, while the combination of additional ingredients produces colouring and white shade. In the effervescent tablet formulation, sour taste is caused by other components, particularly lemon flavor, which is used to mask the taste of the extract and has a distinct fragrance due to the aroma of the extract. Previous research optimised effervescent tablet formulations to produce tablets with uniform physical characteristics, namely, brownish and yellowish colour due to the colour of the quote and additives used [32]. In this regard, we studied the formulation of brown effervescent tablets from sections with white granules induced by the quotes and additives in the preparation mixture.

Hardness test aims to characterise the strength or resistance of tablets to impact or mechanical stress during production and drug

distribution. The required tablet hardness is between 4 and 9 kg/cm² based on United States Pharmacopeia (USP) [16]. The hardness values of F1, F2, F3, F4 and F5 are 8, 5,8, 5,5, 9 and 5,3 kg (table 2), which satisfied the requirement. Binders also affect tablet hardness. PVP at 1% was used as the binder in the formulation; in general, the concentration of PVP used ranges from 0.5% to 5%. When combined with hygroscopic powder or high moisture content, PVP will increase the tablet hardness due to increased bonding power between particles. During testing, the same concentration of polyvinylpyrrolidone was added to each formula and affected the hardness of the tablet. Compressive pressure exerted during printing also influences tablet hardness; the greater the pressure exerted during printing is, the harder the tablet will be. The effect of citric acid and tartaric acid concentrations on tablet hardness was evaluated. Citric acid is more influential in determining tablet hardness than tartaric acid. Citric acid bound to one water molecule will be stronger than tartaric acid; therefore, citric acid can be used to produce tablets with high hardness. Citric acid and tartaric acid affect the hardness of tablets. According to the test results, F1, with the highest citric acid content, produces tablets with a hardness of 8 kg, which falls within the required range. These results are consistent with previous research [31] on optimising acids in effervescent tablets with a hardness value of 8 kg in F5, which has a higher citric acid concentration than the other formulations.

Friability test determines the resistance of a tablet to mechanical disturbances to maintain its shape. The acceptable friability is less than 1%. In table 2, F1 has a friability value of 0.08%, F2 has a friability value of 0.10%, F3 has a friability value of 0.20%, F4 has a friability value of 0.15% and F5 has a friability value of 1.53%. Hence, F1, F2, F3 and F4 meet the requirements for tablet friability, while F5 does not meet the requirements for tablet friability. F5, which had the lowest moisture content (1.29%), produced tablets with a higher friability value than the other formulas. The friability value of F5 is high at 1.53% (table 2). The tablet's friability will increase if it is moist because of the weak bonding power between tablet particles. Citric acid and tartaric acid have opposing effects on tablet friability, with the latter having a more significant effect than the interaction of citric acid and tartaric acid. According to research findings, F5 contained more tartaric acid than the other formulations. A previous study on the effervescent tablet formulation of a combination of citric acid and tartaric acid with the lowest moisture content at F1 (1.03%) produced tablets with a high friability of 0.98%, which is still within the acceptable range for good tablet friability [8].

Tablet dissolution time test determines how long a tablet should be dissolved in a solution. The optimal dissolution time for effervescent tablets is under 5 sec. According to the test results in table 2, the dissolution times for F1 to F5 are 3.47, 3.02, 3.00, 2.51 and 2.31 sec, respectively. All the test results satisfy the criterion of less than 5 sec. However, the best formula was F5 because the resulting dissolution time was faster than the other formulas at 02.31 sec; the quicker an effervescent tablet dissolves, the better its effect will be. This finding is due to the acid source; tartaric acid has more hygroscopic properties than citric acid, allowing it to absorb water more readily and react quicker than the other formulas [33]. The disintegrating time of effervescent tablets is also affected by the fragility of the tablets; in the present study, F5 had a high friability

value of 1.53%, thereby accelerating the process of tablet solubility. The hydrophilic nature of PVP as a binder facilitates the entrance of water into the tablet pores, and the tablet dissolving process begins with the entry of water into the tablet pores. The entrance of water into the pores of the tablet causes an effervescent reaction between the acid and carbonate, which releases carbon dioxide for the dissolution of effervescent tablets [31]. According to previous research, the formulation of effervescent tablets from extracts on F4 has the lowest friability value and produces the quickest dissolution time than the other formulations.

The acidity of Kaempferia galanga effervescent tablet solution was determined by measuring its pH. If the pH of the effervescent solution is too acidic, then it can cause gastric irritation; if it is too alkaline, then it can cause a bitter and unpleasant taste. The pH of effervescent tablets was determined using a pH meter. F1 to F2 had pH values of 4.45, 4.18, 4.14, 3.87 and 3.78, respectively. The pH of the solution decreased due to the pH of the effervescent tablet as a result of 27% acid content. The addition of acid, specifically citric acid and tartaric acid enhances the acidity of the effervescent tablet solution, thereby decreasing its pH. The increase in the acid's H+ions is responsible for decreased pH (table 2). By contrast, an increase in H+ion production results in a decrease in pH value. Previous study [33] reported that the addition of 35% acid resulted in a pH of 4, which was lower than the addition of 15% acid (pH of 5.91). Effervescent has adequate solubility at pH between 5 to 7 because it is unstable at pH greater than 8. The required pH for effervescent is 6. The pH of the effervescent must be acidic because sodium bicarbonate necessitates an acidic reagent. In the presence of the acid developer's hydrogen ions, sodium bicarbonate reacts to liberate carbon dioxide [16].

The Indonesian Pharmacopoeia requires tablets with an average weight>300 mg to have 5%-10% weight deviation. Weight uniformity indicates the uniformity of the tablet's active ingredient content. All formulations had an acceptable CV (>5%).

Size uniformity influences the quality and aesthetics of the tablet; therefore, the uniformity of tablet size should not exceed three times the size nor fall below one-third the size of the tablet. The size uniformity of the effervescent tablets satisfies the requirements and is directly proportional to the tablet weight uniformity test, as the punch heavily influences it and dies moulds on the tablet press, not by a mixture of acidic or wet formulations.

Characterization of an optimized effervescent tablet

A linear model was developed based on data analysis and processing with Design Expert software version 13 to compute the Simplex Lattice Design (SLD) equation for each response.

Determining the optimal formula aims to produce the optimal formula based on response data from the preparation parameters. The value A represents the proportion of citric acid, while the value B represents the proportion of tartaric acid. A positive value for each component indicates a synergistic effect, in which the response value will increase if the component is increased. The negative value indicates an antagonistic or opposing relationship between the components and the response. The magnitude of the number or value indicates the magnitude of the influence of the components on the response [33].

Table 3: Projected model equations for effervescent tablet responses using the simplex lattice design method

Chart	Parameter	Equality	Model
А	Hardness	Y = 8.23 (A)+5.56 (B)+24.99 (A)(B)	linear
В	Friability	Y = 0.187 (A)+1.37 (B) – 2.93 (A)(B)	linear
С	Dissolving time	Y = 3.43 (A) + 2.30 (B)	linear

According to the equation in table 3, the responses to the tablet hardness test are positively correlated; that is, if the components of citric acid and tartaric acid are increased, then the hardness value of the effervescent tablet increases, meaning that the resulting tablet will be hard. Tartaric acid has a greater influence on hardness (+5.56) than

citric acid (+8.23). The linear graph (fig. 1) shows that the higher the composition of tartaric acid added to the formula is, the harder the resulting tablet will be. A previous work [8] stated that if tartaric acid is used as the sole acid, then the resulting powder easily loses its strength and clumps, thereby increasing hardness when printed.

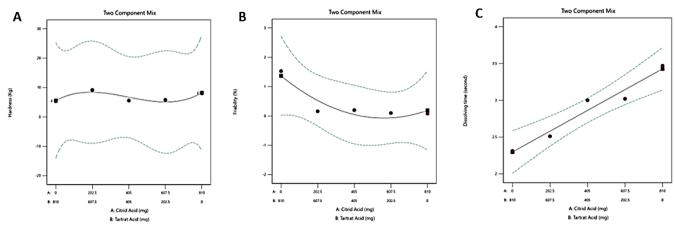


Fig. 1: Plot of citric acid and tartrat acid concentration on the (A) Hardness, (B) Friability, and (C) dissolving time

The graph depicts the correlation between the quantity of citric acid and tartaric acid and the fragility of effervescent tablets (fig. 1). The higher coefficient of citric acid than tartaric acid leads to fragile tablets. Based on the response equation for the tablet friability test, it has a negative effect; when citric acid and tartaric acid components are reduced, the tablet friability value will also decrease. The value of tartaric acid (+1.37) had a greater influence on tablet friability than citric acid (+0.187). Ref. [11] reported that the increase in the proportion of citric acid is due to the influence of the high hygroscopicity of citric acid. An increase in the concentrations of citric acid and tartaric acid has a beneficial effect on the response of the dissolving time test [31], so the response value of the tablet dissolution time will also increase (table 3). The value of citric acid is greater (+3.43) than tartaric acid (+2.30) and is reinforced by the linear graph (fig. 1c). The concentration of citric acid is higher than tartaric acid, and the use of citric acid leads to increased tablet solubility.

The one-sample T-test findings (table 4) indicate that, at a 95% confidence level, no statistically significant difference was found between the anticipated and experimental outcomes (p>0.05).

Table 4: Optimum formula verification

Parameter	Predictions	Optimum formulas	Sig. 2-tailed	Interpretation
Hardness (Kg)*	8	6.527±0.866	0.000	Significantly different
Friability (%)*	0.285	0.077±0.105	0.473	Not significantly different
Dissolving time (s)*	02:69:60	02:36:06±00:06:05	0.180	Not significantly different

*Result are expressed as a mean±SD, n=3

The optimal formula is a formula whose results fall within the parameter limits. It should have a desirability value close to number one. According to the simplex lattice design method expert software design, the optimal formulas for citric acid and tartaric acid are 9.5% and 17.5%, respectively, with a desirability value of 0.789. Fig. 2 displays the results of the optimal formula prediction.

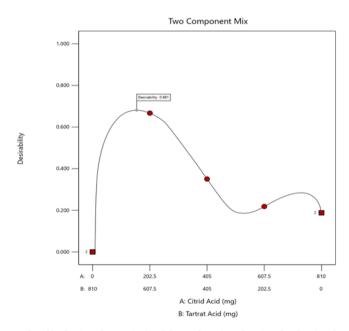


Fig. 2: Contour plot displaying the optimized formula using the simplex lattice design method

CONCLUSION

The presence of both citric acid and tartaric acid affects the physical assessment of tablet hardness but has no impact on tablet friability or dissolving time. The simplex lattice design approach was utilized to determine the most optimum concentrations of citric acid and tartaric acid in the effervescent tablets of *Kaempferia galanga* extract. The optimal concentration of citric acid was found to be 9.5%, while the optimal concentration of tartaric acid was determined to be 17.5%. The desirability value associated with these concentrations is 0.789. Moreover, the ideal formula can be formulated in a subsequent phase for stability tests and *in vivo* experiments.

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AUTHORS CONTRIBUTIONS

Tri B Julianti-Designed the study, Literature review, method selection, Collected samples, writing the original draft, and Editing; Mohd. F. A. Bakar-Review-Designed the study, compilation of data, and supervision; Erindyah R Wikantyasning-Designed the study, Review, editing, compilation of data, and supervision.

CONFLICT OF INTERESTS

The authors declare no conflict of interest.

REFERENCES

- Preetha TS, Krishnan PN, Thankappan C, Preetha S, Suvarna Preetha T, Sudarsanan Hemanthakumar A. A comprehensive review of Kaempferia galanga L. (Zingiberaceae): a high sought medicinal plant in tropical Asia. J Med Plants Stud. 2016;4(3):270-6.
- Abu Bakar FI, Abu Bakar MF, Rahmat A, Abdullah N, Sabran SF, Endrini S. Anti-gout potential of Malaysian Medicinal Plants. Front Pharmacol. 2018;9:261. doi: 10.3389/fphar.2018.00261, PMID 29628890.
- Cahyawati PN. Analgesic and anti-inflammatory effects of Kaempferia galanga. Wicaksana J Lingkung Pembang. 2020;4(1):15-9.
- Riasari H, Rachmaniar R, Wahyuni S. Evaluation patch of rhizoma extract kencur (*Kaempferia galanga* L.) as antiinflammatory with enhancer. IJPST. 2019;6(2):59. doi: 10.24198/ijpst.v6i2.18932.
- Ghourichay MP, Kiaie SH, Nokhodchi A, Javadzadeh Y. Formulation and quality control of orally disintegrating tablets (ODTs): recent advances and perspectives. BioMed Res Int. 2021;2021:6618934. doi: 10.1155/2021/6618934, PMID 34977245.
- Alemanni M, DE Salvo R, Moroni B, Ehret A. A real-world evidence study evaluating geffer effervescent granules for the symptomatic relief of digestive symptoms. SAGE Open Med. 2022;10:20503121221088815. doi: 10.1177/20503121221088815, PMID 35371486.
- Surini S, Wardani MR, Sagita E. Evaluating of effervescent tablets containing grape seed (*Vitis vinifera* L.) extract as a nutraceutical. Int J App Pharm. 2017;9:150-3. doi: 10.22159/ijap.2017.v9s1.76_83.
- 8. Syahrina D, Noval N. Optimization of the combination of citric acid and tartric acid as an acidifying agent in purple sweet potato extract effervescent tablets (*Ipomoea batatas* L.). J Surya Med. 2021;7(1):156-72.
- 9. Lobubun NA, Chabib L. Effervescent granule formulation of acetone extract of kencur rhizome (*Kaempferia galanga* L.) with varying polyvinyl pyrrolidone concentrations. J of Pharm and Health Res. 2022;3(3):139-49.

- Sofyah TM, Tukiran T, Sutoyo S. Antioxidant of effervescent tablet formulated from a combination of secang wood and red ginger extracts. J I Dasar. 2022;23(2):121. doi: 10.19184/jid.v23i2.28136.
- Taymouri S, Mostafavi A, Javanmardi M. Formulation and optimization of effervescent tablet containing bismuth subcitrate. J Rep Pharma Sci. 2019;8(2):236-44. doi: 10.4103/jrptps.JRPTPS_11_19.
- Almatroodi SA, Alsahli MA, Almatroudi A, Verma AK, Aloliqi A, Allemailem KS. Potential therapeutic targets of quercetin a plant flavonol and its role in the therapy of various types of cancer through the modulation of various cell signaling pathways. Molecules. 2021;26(5)1315. doi: 10.3390/molecules26051315, PMID 33804548.
- Rukaya BE, Syuhada S, Veronika DY. Formula optimization and physical stability evaluation of effervescent tablet preparations of aqueous extract of moringa leaves (*Moringa oleifera* L.). JB. 2022;2(3):28-37. doi: 10.57174/jborn.v2i3.62.
- Aulifa DL, Wibowo DP, Safitri N, Budiman A. Formulation of effervescent granules from red ginger (*Zingiberis Officinale* Roscoe Var. Rubrum) extract and its antioxidant activity. Int J Appl Pharm. 2022;14(1):112-5.
- Forestryana D, Abdurrahman, Ramadhan H. Effervescent tablet formulation ethanol extracts 70% kelakai root (*Stenochlaena Palutris* (Burm. F.) Bedd.) with variation concentration of gas generating agent. Int J Appl Pharm. 2022;14Special Issue 2:10-6. doi: 10.22159/ijap.2022.v14s2.44740.
- Aklima A, Baral PK, Amin MT, Emon TI, Hossain MS. Formulation and quality optimization of effervescent tablet of glipizide: an approach to comfort anti-diabetic medication. MHS. 2020;3(2):14. doi: 10.30560/mhs.v3n2p14.
- Sopyan I, Wahyuningrum R, Insan Sunan KS. An experimental design in the optimization of various tablet excipient formulations=a concise review. Int J Appl Pharm. 2022;14(1):28-32. doi: 10.22159/ijap.2022v14i1.43380.
- Wati S, Saryanti D. Effervescent granule formulation of bitter melon extract (*Momordica charantia* L.) with gelatin as a wet granulation binder. J Nutraceuticals Herb Med. 2019;2(1):20-8. doi: 10.23917/jnhm.v2i1.8052.
- Tanjung YP, Puspitasari I. Formulation and physical evaluation of noni fruit extract effervescent tablets (*Morinda citrifolia* L.). J Unpad Farmaka. 2019;17(1):1-14.
- Wang SY, Zhao H, XU HT, Han XD, WU YS, XU FF. *Kaempferia galanga* I: progresses in phytochemistry, pharmacology toxicology and ethnomedicinal uses. Front Pharmacol. 2021;12:675350. doi: 10.3389/fphar.2021.675350, PMID 34737693.
- 21. Silalahi M. *Kaempferia galanga* and bioactivity. J Pendidik Inform Sains. 2019;8(1):127.
- 22. Muharrami LK, Munawaroh F, Ersam T, Santoso M. Phytochemical screening of ethanolic extract: a preliminary test on five medicinal plants on Bangkalan. J Pena Sains. 2020;7(2):96-102. doi: 10.21107/jps.v7i2.8722.
- 23. Dwita LP, Hikmawanti NP, Yeni S, Supandi. Extract fractions and ethyl-p-methoxycinnamate isolate from *Kaempferia galanga* elicit anti-inflammatory activity by limiting leukotriene B4 (LTB4) production. J Tradit Complement Med. 2021;11(6):563-9. doi: 10.1016/j.jtcme.2021.06.004, PMID 34765520.
- Andriyono RI. Kaempferia galanga L. as anti-inflammatory and analgesic. J Kesehat. 2019;10(3):495.
- Julianti TB, Bakar MF, Wikantyasning ER. Phytochemical antioxidant analysis and *in vitro* xanthine oxidase inhibitory activity of *Kaempferia parviflora* and *Kaempferia galanga*. Trop J Nat. Prod Res. 2022;6(12):1981-5.
- Raina AP, Abraham Z, Sivaraj N. Diversity analysis of *Kaempferia* galanga L. Germplasm from South India using DIVA-GIS approach. Ind Crops Prod. 2015;69:433-9. doi: 10.1016/j.indcrop.2015.02.052.
- 27. Apsari PA, Sari DN, Kusuma AP, Indrati O. Effervescent tablet formulation melinjo seed extract (gnetum gnemon l.) using peg 6000 as lubricant and citric acid tartaric acids as acid sources. Eksakta: J Sci Data Anal. 2018;18(1):30-41. doi: 10.20885/Eksakta.vol18.iss1.art4.
- 28. Syaputri FN, Saila SZ, Tugon TD, R AP, Lestari D. Formulation and test of physical characteristics of effervescent granule preparations

from ethanol extract of red betel leaves (*Piper crocatum* ruiz) as antidiabetic. J Ilmu Kefarmasian. 2023;4(1):191-8.

- Lynatra C, Wardiyah W, Elisya Y. Formulation of effervescent tablet of temulawak extract (*Curcuma xanthorrhiza* Roxb.) with variation of stevia as sweetener. SANITAS. 2018;9(2):72-82. doi: 10.36525/sanitas.2018.9.
- Anesakirani A, Pramono YB, Nurwantoro. Physical and organoleptic characteristics of jackfruit fruit effervescent tablets (*Artocarpus heterophyllus* Lamk.). J Teknol Pangan. 2018;2(1):59-63.
- 31. Taymouri S, Mostafavi A, Mahmoodi H. Formulation design and optimization of taste masked effervescent tablet containing methocarbamol. Iran J Pharm Sci. 2021;17(4):1-14.
- 32. Herlina KN, Kuswardhani N, Belgis M, Tiara A. Characterization of physical and chemical properties of effervescent tablets temulawak (*Curcuma zanthorrhiza*) in the various proportion of

sodium bicarbonate and tartaric acid. E3S Web Conf. 2020;142:7. doi: 10.1051/e3sconf/202014203006.

- Violalita F, BR. The effect acid addition on characteristic effervescent tablet of tamarillo. International Journal on Advanced Science Engineering and Information Technology. 2015;5:3. doi: 10.18517/ijaseit.5.3.528.
- Asyhari HF, Cabral KB, Wikantyasning ER. Optimization of soursop (Annona muricata L.) leaf extract in nanoemulgel and antiacnes activity test against Propionibacterium acres staphylococcus aureus staphylococcus epidermidis bacteria. Pharmacon. 2023;20(2):216-25. doi: 10.23917/pharmacon.v20i2.23308.
- Noval N, Kuncahyo I, Pratama AF, Nabillah S, Hatmayana R. Formulation of effervescent tablets from ethanol extract of bundung plant (*Actionoscirpus grossus*) as an antioxidant. J Surya Med. 2021;7(1):128-39.