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Original Article

EFFERVESCENT TABLET FORMULATION ETHANOL EXTRACTS 70% KELAKAI ROOT (*STENOCHLAENA PALUTRIS* (BURM. F.) BEDD.) WITH VARIATION CONCENTRATION OF GAS GENERATING AGENT

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ABSTRACT

Objective: The aim of this study is to determine the optimal formula of effervescent tablets 70% ethanol extract of Kelakai root (Stenochlaena palutris (Burm. f.) Bedd.) with variations concentration in gas generating agents and their effects on properties of the physical effervescent tablet.

Methods: Kelakai root was extracted with maceration using ethanol 70%, and total phenolic-flavonoids contents were determined. Effervescent tablets made for three formulas base on varying concentration gas generating agents. Effervescent tablets made by wet granulation. Evaluation physical properties of granules included flowability, tapped density, bulk density, and angle of repose. Evaluation physical properties of effervescent tablets included weight uniformity, thickness and diameter, friability, pH, hardness, effervescent time, and hedonic test.

Results: The extract had a total phenolic content of 625.35 µg GAE/mg extract, while the total flavonoid content was 735.24 µg QE/mg extract. The effervescent tablets have uniformity of sizes ranging from 1.29 to 1.3 cm and thickness from 0.49 to 0.5 cm, uniformity of weights with a coefficient of variation ranging from 1.04%-2.15%, fragility ranged from 0.03%-0.29%, tablet hardness ranged from 8.33-9 kg, and solubility ranged from 30-86 min. Statistical analysis showed that the p-value is>0.05, which means there are no significant differences between formulas by varying concentrations of citric acid and tartaric acid to influence the physical characteristics of effervescent tablets.

Conclusion: Formula III was the best formula because it meets the physical requirements and hedonice test of granules and tablets.

Keywords: Formulation, Effervescent tablet, Gas generating agent, Kelakai roots

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INTRODUCTION

Antioxidants are compounds that can inhibit or slow down the damage caused by the oxidation process. Most diseases originate from excessive oxidation reactions in the body. The body continuously produces radical compounds, which will cause the formation of free radicals in response to influences from outside the body. Antioxidants can inhibit oxidation by binding with free radicals and highly reactive molecules so that the cell which has damage can prevented [1]. One of the potential plants that have efficacy for health is Kelakai which contains active compounds that are nutritious for health. Kelakai is known to the people of Kalimantan as Pakis or Paku Haruan [2]. Kalakai contains very high Fe, which is useful for treating anemic disease [3]. Kelakai contains phenolics, flavonoids, alkaloids, and terpenoid that are effective as antioxidants. Kelakai roots have strong antioxidant activity with an IC_{50} value is 19.06 ppm [2].

One way to improve the potencies of Kelakai root is to formulate it into the effervescent tablet as an antioxidant. Effervescent has an advantage over other oral preparations because effervescent gives a fresh taste when used so that it will be liked by many consumers in consuming it. The other advantage from effervescent is an efficient, easy set-up solution containing an accurate dose so more easily absorbed by the body. The effervescent tablet is a tablet that contains an active substance with a mixture of acids and bases made by compression when dissolving in water will produce carbon dioxide. The gas generating agent is a component that can produce carbon dioxide gas to accelerate the disintegration of the effervescent tablet. One of the ingredients used as a gas-generating agent is sodium bicarbonate as a source of carbon dioxide in effervescent tablets [4]. Sodium bicarbonate is usually formulated in effervescent tablets with citric and/or tartaric acid. The combination use of citric acid and tartaric acid is preferred when citric acid using alone causes a sticky mixture so that it will be difficult to granulate. While if tartaric acid use alone, the powder will lose its strength and will clot [5]. Tablet effervescent also produces a delicacy because of carbonate that helps improve the taste of the Kelakai root extract [6].

This research aims to found the formulation of effervescent tablets of 70% ethanol extract of Kelakai root (Stenochlaena palutris (Burm. f.) Bedd.) as an antioxidant with varying amounts of gas generating agent and to determine the physical properties of the resulting effervescent tablets with weight uniformity test parameters, tablet hardness test, tablet friability test, and size uniformity test.

MATERIALS AND METHODS

Materials

The materials used in this research is Kelakai roots was collect from Liang Anggang Banjarbaru South Borneo, Indonesia. Ethanol 96% (Merck, Germany), Folin-ciocalteu (Merck, Germany), $AlCl_3$ (Merck, Germany), acetic acid glacial (Merck, Germany), quercetin (Sigma aldrich, USA), Na_2CO_3 (Merck, Germany), aquadest (Onemed, Indonesia), gallic acid (Sigma aldrich, USA) citric acid (Brataco), acid tartrate (Merck), Poly Vinyl Pirolidon (PVP) (Brataco, Indonesia), aerosil (Brataco, Indonesia), and aspartame (Brataco, Indonesia).

Preparation kelakai root extract

Kelakai roots were obtained from Liang Anggang, Banjarbaru, South Borneo. Determination has been done at the Faculty of Mathematics and Natural Sciences, Lambung Mangkurat University as (Stenochlaena palustri (Burm F.) Bedd.). Extraction of Kelakai roots by the maceration method. The powder was weighed with an analytic scale (Ohaus®) as much as 2500 g and then extracted using 70% ethanol solvent in a ratio of 1:10 for three days. The liquid extract was then separated from the residue using a paper filter then the maceration was carried out twice. The liquid extract collected was concentrated through a vacuum rotary evaporator (IKRF10®) at 60 °C until the concentrate extracts obtain. Finally, the concentrated extract store in a tight glass container and protect from

the light. The concentrated extract was added with aerosil in a ratio of 1:0.5 and ground until homogeneous [7].

The total phenolic contents

The total phenolic contents of the extract were determined by a colorimetric assay (Folin-Ciocalteu method) with a gallic acid standard solution. Exactly 0.5 ml of each appropriate dilutions of the extracts (50 ppm) and gallic acid standard in ethanol solutions (5, 10, 15, 25, and 30 ppm) was mixed with 1 ml of Folin-ciocalteu reagent (previously diluted with aquadest 1:10), 2 ml of 10% Na_2CO_3 was added after 5 min. All samples were analyzed in triplicate and the absorbance value was measured spectrophotometrically at 728 nm after allowed to stand in the dark for 70 min. Total phenolic levels were expressed as µg gallic acid equivalent in 1 mg of the extract [8].

The total flavonoid contents

The $AlCl_3$ colorimetric method was used to determine total flavonoid contents. Exactly 0.5 ml of the extracts (100 ppm) and the dilutions of the quercetin calibration curve (100, 200, 300, 400, and 500 ppm) were prepared in ethanol. Each of the dilutions was added to a tube containing 0.5 ml of 10% $AlCl_3.6H_2O$ solution and mixed with 4 ml of acetic acid glacial 5%. All samples were analyzed in triplicate and the absorbance was spectrophotometrically measured immediately at 415 nm after 20 min of incubation. Quercetin solitions were used to calculate the standard curve and the results were expressed as µg quercetin per 1 mg extract [9].

Formulation of the kelakai roots extract effervescent tablet

To find the best effervescent formulation, three different formulations design by varying the ratio of the acid-base compositions (table 1). Following the wet granulation method, the preparation of effervescent tablets consisting of two mixtures. The first mixture consists of a dry extract of Kelakai root, citric acid, tartaric acid, and aspartame. While the second mixture consists of PVP and sodium bicarbonate. The separation of this mixture aims to avoid premature reactions between the acid-base components. The first mixture was homogenized, while the second mixture sprays with 95% ethanol until it became a moist powder. The addition of ethanol aims to dissolve the binder. The second mixture was then sieved with sieve number 16 and dried in an oven (Thermo Scientific®) at 50 °C for 15 min. mixed all the mixture until homogeneous, then PEG 6000 was added as a lubricant. After being sifted with sieve number 16, the formed granules were dried in an oven (Thermo Scientific®) at 50 °C for 90 min. The resulting granule was sieved and finally tested for physical characteristics. Then it is printed with a manual tablet press [10, 11].

Table 1: Formulations of the kelakai roots extract effervescent tablet with various amount of acids-base

Composition	F1	F2	F3
Etanholic Kelakai roots*	170 mg	170 mg	170 mg
Citric acid**	9.1%	8.3%	7.7%
Tartrat acid**	18.2%	16.7%	15.4%
Sodium bicarbonatte**	22.7%	25%	26.9%
PVP	3%	3%	3%
PEG 6000	6%	6%	6%
Aspartam	15.5%	15.5%	15.5%
Aerocil	ad 100%	ad 100%	ad 100%
Desired tablet weight = 940 mg			

*The 70% ethanol extract of the root of Kelakai used as much as 170 mg based on a comparison using ascorbic acid, where 50 mg of ascorbic acid is equivalent to the IC_{50} of ascorbic acid of 5.64 ppm which can be used in calculating the dose of the 70% ethanol extract of the root of anchovies to make effervescent tablets [12]. **The ratio of citric acid: tartaric acid: sodium bicarbonate used in the formula is F1 (1:2:2.5); F2 (1:2:3); F3 (1:2:3.5).

Evaluation of the effervescent granules

Organoleptic test

The organoleptic test aims to see the occurrence of significant changes in the final preparation. The evaluation is to check the color and odor of the granules.

Angle of repose

The angle of repose is calculated by measuring the angle of the granule surface toward the plane surface. First, the granules of 50 g were weighted and flown slowly into a funnel fixed-to-a stand with the bottom layer covered. The cover then removes the granules that were allowed to drop on the graphical paper surface of the bottom most [10]. The repose angle (α) subsequently defined by measuring the height (h) and distance (d) of the formed granules then, involving the values into the equation:

$$\alpha = \text{Arc tan } (h/r) \quad \ldots\ldots (1)$$

Flowability study

Bulk density and tapped density

Two types of density are determined bulk density and tapped density. In a 100 ml measuring cylinder, 50 g of granules was weighted and put then the initial volume was measure. The measuring cylinder was tapped at the height of 2, 5 cm at 2-second intervals until no further change was noted in the volume [10]. From the equation below, bulk density and tapped density were calculated.

$$\text{Bulk Density} = \frac{\text{Granules weight}}{\text{Packing volume}} \ldots. (2)$$

$$\text{Tapped Density} = \frac{\text{Granules weight}}{\text{tapped volume of the packing}} \ldots\ldots. (3)$$

Carr's index for granules was measured to evaluate the bulk density and tapped density [10]. The values of Carr's index of ibuprofen granules were compared with references, as shown in table 2.

$$\text{Carr's index} = \frac{[(\text{Tapped density} - \text{Bulk Density}) \text{x } 100]}{\text{Tapped density}} \ldots\ldots. (4)$$

Hausner's ratio

The evaluation of these was conducted using a tap bulk density tester and determined using equations:

$$\text{Hausner s ratio} = \frac{\text{Tapped density}}{\text{Bulk density}} \ldots\ldots (5)$$

Evaluation of effervescent tablet

Organoleptic test

The organoleptic test aims to see the occurrence of significant changes in the effervescent tablet that has been formulating. The effervescent tablet formulation evaluated physically includes the color and odor of the effervescent tablet.

Weight variation

Twenty tablets were weighed discretely, and the tablet weight average was a check for the variation of the tablets. Herein, the deviation of the two tablets should have not more than the limit of the pharmacopeia requirements [10].

Thickness and diameter variation

Twenty tablets select randomly, and each tablet was measure for thickness and diameter using a digital caliper (Kenmaster).

Hardness

A tablet was selected and placed in the middle perpendicularly toward the hardness tester. The hardness level was scaled during the tablet breaking process mechanically [10]. The tablet hardness is measured in kg.

Friability

Weighed ten tablets that had been clean of dust (W_1), then put into a friability tester (CS-4 Revolution), set the speed to 25 rpm for four min. The tablets were removed and weighed again (W_2) [13]. The friability test has been done in triplicates.

Effervescent time

A tablet was randomly selected and put into a glass of 100 ml water. The dissolved tablet was subsequently evaluated using a stopwatch until a clear solution was obtained [10].

The sensory evaluation

The sensory evaluation was conducted by following a hedonic scale rating test using 15 panelists. Each panelist was asked to fill out questionnaires that required him/her to rate the color, taste, aroma, and texture. The responses included the following levels of preference: where scale 6 = really like, 5 = like, 4 = rather like, 3 = rather dislike, 2 = dislike, and 1 = really dislike [14].

Data analysis

All the experiments have been done three times, and the data were expressed as the mean value±SD. Statistical data analyzed by one-way analysis of variance (ANOVA) and P<0,05 considered to be significant with 95% confidence intervals.

RESULTS AND DISCUSSION

Extraction

A part of the preparation of herbal extract, the maceration was used as the primary extraction procedure owing to its simplicity and ability to yield alcoholic extract of the Kelakai roots. 70% alcohol is select as a solvent to obtain compounds such as essential oil, steroidal alkaloid, glycoside, tannin, and phenol. Kelakai roots extract was identified as brownish solutions with peculiar odor and bitter taste. In total, about 2.26% of the extract yielded from 2500 g Simplicia powder.

Determination of total flavonoid and polyphenol contents in Kelakai roots extract

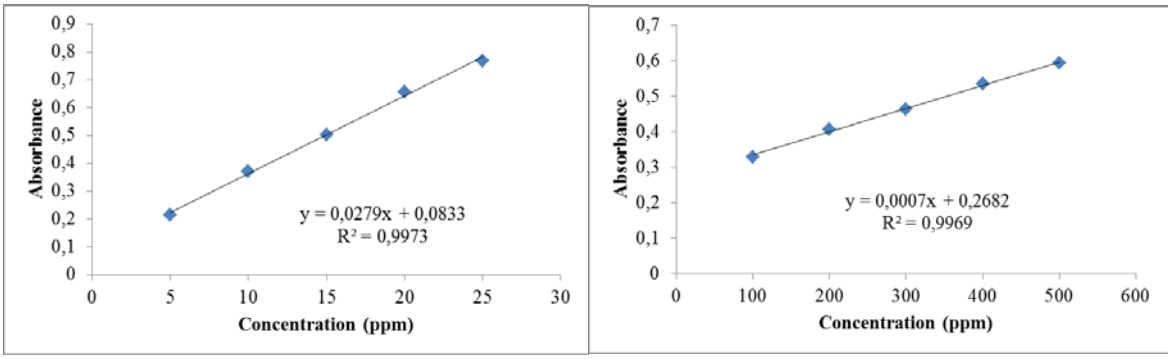

Fig. 1: Standard curve graph of (a) gallic acid and (b) quercetin

Phytochemical examination of the extracts of Kelakai roots revealed that the aqueous ethanolic extract is highly rich in flavonoid compounds as well as phenolic compounds. The total flavonoid content in the aqueous ethanolic extract of Kelakai roots was estimated as µg quercetin equivalent in 1 mg of extract, according to the method previously reported flavonoid and polyphenol contents in Kelakai roots extract. The calibration curve for quarcetin as a fig. 1 was performed at max 415 nm, quarcetin concentration range 100–500 ppm and the straight line equation obtained was y = 0.0007x+0.2682, r = 0.9969. The total flavonoid content was found to be 735.24±2.182 µg QE/mg Kelakai roots extract. Regarding the polyphenol content, it is expressed as µg gallic acid equivalent (GAE)/mg Kelakai roots extract. The quantitative determination was conducted using Folin-ciocalteau reagent according to the method previously reported. The calibration curve as a fig. 1. Was performed at max 728 nm, using gallic acid in the concentration range 5–30 ppm. The equation: y = 0.0279x+0.0833, r = 0.9973, was employed in calculating the Kelakai roots extract polyphenol content which was found to be 625.35±0.135 µg GAE/g extract. Phenols are the simplest bioactive phytochemicals possessing free radical scavenging ability due to the presence of hydroxyl groups. Flavonoids are a family of polyphenolics, which are synthesized by plants and can be categorized into different subclasses and each subclass comprises hundreds of different compounds [15]. It has been reported that phenolic compounds exhibit redox properties by acting as reducing agents, hydrogen donators and singlet oxygen quenchers. Strong relationship was observed between total phenolic content and antioxidant activity in many plant species. Phenolic compounds directly contribute to antioxidant action and act as free radical terminators [16].

Formulation of effervescent granule extract of Kelakai roots with a mixture of citric acid, tartaric acid, sodium bicarbonate, and other excipients of the three formulas is a modified obtained from the trial results. The effervescent granules of the extract of the root of Kelakai produced have a brown color, but after dissolving it will turn into a yellow solution with a dissolving time of 1 second (fig. 2). Manufacture of effervescent granules with wet granulation method has the advantage of making a simple, quick, and homogeneous granule produced [14]. Effervescent granules prepare by separating the acid and the alkali components to prevent reaction between acid-base components when mixed in wet conditions [17]. Citric acid and tartaric acid had functioned as a source of the acid, sodium bicarbonate as the alkali, PVP as the binder, aspartame as the sweetener, and aerosil as the filler. PVP as a binder in the wet granulation process can increase the solubility of drugs that are difficult to dissolve from solid dosage forms. The use of aspartame in formulas can enhance the taste and mask some of the unpleasant taste characteristics. PEG 6000 use as a lubricant, especially for soluble tablets. Where PEG 6000 has the advantage of increasing the flow rate, increasing the effectiveness of tablet binders, and providing plasticity to the granules [18]. Aerosil is a filler and acts as an adsorbent because it can absorb moisture, especially from the extract. The addition of 95% ethanol aims to dissolve the binder [11]. Physical characteristics of effervescent granules tested include organoleptic and flowability study. The results can be seen in table 2.

The granule flow time test aims to determine the time required for some granules to flow in a device. The granule flow time test obtained that 50 g of granules can flow entirely from the funnel between 7.1-7.27 s which the granule flow rate ranging from 6.88-7.05 g/s. All formulas have met the specified requirements, where the granule flow rate is 4-10 g/s it means the granules have good flowability. The flow properties can be seen in table 2. The formula I obtained better flow time and granule flow rate than formulas II and

III. The factor that affects the flow time of the granules is the tartaric acid used. Tartaric acid has a large density, which causes the granules containing more tartaric acid will flow easily because of the greater gravitational force. A large density indicates a huge molecular weight so that it will flow easily because of the greater gravitational force [19]. The flow time is influence by the shape, size, porosity, density, and friction between the granule particles. Stronger frictional forces between particles can cause a decrease in the mobility of the granules to flow so that the flow time will be lower [11]. Temperature and humidity are also effecting because if it is too high or too low it causes the granule flow rate to be slower [20].

Table 2: Physical properties of granul effervescent extract of Kelakai roots

Test parameter	Formulation		
	F1	F2	F3
Organoleptic:			
Color	Brownish	Brownish	Brownish
Smell	Distinctive smell	Distinctive smell	Distinctive smell
Forms	Granules	Granules	Granules
Taste	A little bitter	A little bitter	A little bitter
Bulk density (g/ml)*	0.54±0.00	0.51±0.00	0,52±0,00
Tapped density (g/ml)*	0.61±0.00	0.57±0.00	0,59±0,00
Granule flow time (s)*	7.10±0.26	7.23±0.11	7,27±0,06
Angle repose*	29.9 °±0.01	29.29 °±0.07	28,93 °±0,14
Carr's index*	11.59±1.66	10.00±1.62	11,61±0,87
Hausner index*	1.13±0.02	1.11±0.01	1,13±0,01
Flow propertys	Good	Good	Good

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

Carr's index or compressibility test aims to determine the decrease in granule volume when there is a knock or vibration. Carr's index of the effervescent granules ranges from 11.14-13.14%, which means granules have good flowability because of the requirements of the standard range from 11-15%. Carr's index of Formula II is 11.4%, while Formula I and Formula III have a higher compressibility value of 13.14%. The factor that affects the compressibility of the granules is the particle size because the difference in particle size in the granules will cause smaller particles to fill the cavity of the larger particles so that the volume of the granules will shrink [21]. Friction and attraction forces between particles are smaller in the presence of larger particle size so that the granules are denser and there is a volume change to be smaller during setting [22]. The combination of citric acid and tartaric acid causes high porosity value and large particle size because use a number 16 sieve. It can increase the volume of the particle cavity. The presence of large particle cavities causes high porosity value as well [11]. Smaller particles will form a mass with a greater density due to the reduction of cavities between particles. Compressibility is influence by particle size and particle shape. The smaller the percent compressibility, the better the flow rate. The larger the particle size causes the bulk density to decrease so that the larger particle size will have a better density [11]. Manual tapping can also affect the results of the compressibility test because the tapping is not uniform, both in time and pressure applied, so it is better to use tools such as a tap density tester.

Fig. 2: Effervescent granules of Kelakai root extract

The granule angle of the repose test aims to determine the flow behavior of the resulting granules. The granule angle of repose test results show that all formulas produce angles of repose ranging from 28.93°-29.29°. All formulas meet the requirements because the angle of repose of granules between in range 25-30° means granules has good flowability that can be seen in table 2. Formula I produces a larger angle repose than formula II and formula III. A higher concentration of citric acid and tartaric acid will result in a larger angle of repose, it happened because citric acid can absorb moisture in the air, and tartaric acid has hygroscopic properties that cause higher humidity. It can cause a greater cohesive force as well. A granule that is not cohesive will flow well, spreading to form a low heap so that the angle is smaller [11]. The less sodium bicarbonate content in the formula can cause the water content to be lower, so that the granules will flow and spread to form low heaps [23]. The angle repose is a measure of powder cohesiveness in which expressed forces of interaction between the particles exceed the gravitational attraction of the particles. A free-flowing powder will form a cone with a low angle of repose, whereas a cohesive powder will form a steep side. Some factors that affect the angle of repose are the size of particles and attraction and friction between the particles. The smaller the particle size, the higher the particle cohesiveness and will reduce the flow velocity so that the angle of repose formed is larger [24]. Differences in the concentration of citric acid and tartaric acid used can affect the effervescent granular flow characteristic. The higher the acid concentration used, the better the flow characteristic [22]. The flow time is influenced by the shape, size, porosity, density, and particle frictional forces and experimental conditions. Citric acid has a specific density value of 1.665 mg/ml, while tartaric acid has a specific density value of 1.7598 mg/ml [13]. Tartaric acid has a greater density than citric acid so that granules containing tartrate acid will have greater density. Large densities show large molecular weights that will flow more easily due to greater gravity [18]. The analysis statistic shows that the three effervescent granules formula has an average granule flow time which is not significantly different and less than 10 s. The result showed that citric acid, tartaric acid, and sodium bicarbonate in the formula have no significant effect on granule flow time.

Evaluation of effervescent tablet preparation

The organoleptic examination has been done to observe the color, aroma, shape, and taste of effervescent tablet preparations. Table 3 shows that the tablet shapes have a flat round shape, have a brown color, have a characteristic odor of Kelakai root extract, and have a bitter taste (fig. 3; table 3). The effervescent tablet of the Kelakai roots extract has a bitter taste because the aspartame as a sweetener cannot cover the taste of the Kelakai root extract with a 15% concentration.

Fig. 3: Kelakai roots extract effervescent tablet

The weight uniformity test aims to determine the uniformity of the weight of the effervescent tablet. The results of the uniformity of effervescent weight tablets meet the requirement because the effect of PVP concentration made the shape and size of the granules bigger. A lot of powder bound and the particle size of the granules was homogeneous. The results obtained indicate that the uniformity of tablet weights in all formulas meets the requirements in column A because no more than two tablets deviate 5% from the average weight, and in column B, there is not a single tablet that deviates more than 10% from the average weight average. The coefficient of variation (CV) meets the requirements because the results obtained in all formulas are not more than 6% [25]. The results can be seen in table 3.

The formula I obtained an average weight uniformity smaller than formula II and formula III. The formula I had the angle of repose is larger than formula II and formula III. Formula I had higher citric acid and tartaric acid content than formulas II and III. The higher concentration of citric acid and tartaric acid, the greater the angle of repose [11]. Formula I use a lower sodium bicarbonate content than formulas II and III. The lower concentration of sodium bicarbonate, the lower the water content, so the granules will flow and spread to form low piles [21]. Factors that affect weight uniformity are granule flow rate, granule angle of repose, granule moisture, and granule compressibility. The smaller the flow rate of the granules, the greater the angle of repose of the granules, this results in the compression power of the tablets getting smaller but the weight of the tablets produced is uniform. The uniformity of weight also influences by the flow properties of the tablet mass. Good flow properties cause the volume of material entering the compression chamber to be uniform so that the variation in tablet weight produced is not too large.

The data were then analyzed using Kruskal Wallis. The results of the Kruskal Wallis test obtained a sig value of 0.208 (>0.05), which means that there is no significant difference in the uniformity of tablet weight with variations in the gas generating agent in each formula. Based on the results of the Kruskal Wallis test, it concluded that there is no significant difference in the weight uniformity of effervescent tablets with the variation of the gas generating agent in each formula. The weight uniformity of effervescent tablets meets the requirements because there are no significant weight deviations, and the coefficient of variation obtain was not more than 6% so the variation of the gas generating agent in each formula has good weight uniformity and met the requirements.

Table 3: Tablets characteristics for in regards of acids-base amount variation.

Test parameter	F1	F2	F3
Organoleptic:			
Color	Brownish	Brownish	Brownish
Smell	Distinctive smell	Distinctive smell	Distinctive smell
Forms	Flat round	Flat round	Flat rounds
Taste	A bitter	A bitter	A little bitter
Weight (mg)±%CV	930±2.15	960±2.08	950±1,05
Weight uniformity (mg):			
Column A (5%)	893-987	893-987	893-987
ColumnB (10%)	846-1034	846-1034	846-1034
Thicknes (mm)±%CV	0.50±1.97	0.50±1.53	0,5±1,04
Diameter variation (mm)±%CV	1.30±0.53	1.29±0.31	1,29±0,36
Hardness (Kg)*	9±0.00	8.9±0.10	8,7±0,30
Friability (%)*	0.03±0.06	0.28±0.06	0,29±0,13
Effervescent time (min)*	86±5.8	42±1.00	30±3,00
pH*	6.54±0.01	6.58±0.00	6,62±0,01

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

The size uniformity test aims to determine the uniformity size of the effervescent tablet. The results of the size uniformity test met the requirements, with an average diameter of 1.29-1.3 cm and a thickness of 0.5 cm (table 3). Based on the results, the effervescent tablets have uniformity in size and meet the requirements because the effervescent tablets have a diameter of no more than three times or not less than 11/3 times the thickness of the tablets [25]. From the results, the value was not different between formula groups because the granules filled the same space. The results of the Kruskal Wallis test obtained a sig value of 0.346 (>0.05), which means that there is no significant difference in tablet size uniformity with variations in the gas generating agent in each formula. Based on statistical analysis with Kruskal Wallis, it concludes there is no significant difference in the uniformity of the effervescent tablet size with the variation of the gas generating agent in each formula.

The hardness test aims to determine the tablet's resistance to mechanical shock during packaging, storage, or transportation. The hardness requirements for an effervescent tablet range from 4-8 kg [26]. The results showed that formula I has a hardness of 9 kg, formula II has a hardness from 8.83 to 9 kg, and formula III has a hardness from 8.33 to 8.83 kg. All formulas do not meet the requirements for hardness, which is in the range of 3-5 kg. Formula I obtains a higher average hardness than formula II and formula III. The types of binders used, the nature of the active ingredient(s), and the composition of the ingredient(s) in the tablet will affect the hardness of the tablet; the tablet press speed, granulation flow, and air in the powder can also potentially affect tablet hardness. A hardness tablet could indicate excessive bonding potential between active ingredients and excipients, it can prevent the proper dissolution of the effervescent tablet needed for accurate dosage. The nature of the raw materials used can affect the hardness of the resulting tablet. The high concentration of citric acid and tartaric acid in the formula, the more hygroscopic the tablet is. It happens because citric acid can absorb moisture in the air, and tartaric acid has hygroscopic properties [11]. The less sodium bicarbonate concentration in the formula, the lower the water content [20]. It also appears because the time taken for the molding of the granules into tablets is too long causes the granules to become moist and affect the hardness of the resulting tablets. Stable tablet hardness can obtain by using an automatic mold using a machine. The binder concentration can also affect the hardness of the tablet. The greater concentration of the binder causes the effervescent tablet to be harder. The results of the Kruskal Wallis test obtained a sig value of 0.093 (>0.05), which means that there is no significant difference in tablet hardness with variations in the gas generating agent in each formula.

Based on the results of the Kruskal Wallis test, it can conclude that there is no significant difference in the hardness of effervescent tablets with variations in the gas generating agent in each formula.

The friability test aims to determine the tablet's ability to withstand shocks during the manufacturing process, packaging, transportation, and use by consumers [12]. Friability test of the effervescent tablet showed that percentage friability meets the requirements standard. Formula I have a small friability (0.03%) than formula II and III, respectively 0.28% and 0.29%. Based on the results, the effervescent tablet of the root extract of Kelakai has good friability meets the requirements because the effervescent tablet of the root of Kelakai loses less than 1% weight. The greater the hardness of the tablet, the smaller the brittleness [27], it's related to the results of the tablet hardness test, where formula I obtained a higher average hardness than formulas II and III. The percentage friability formula I is smaller than formula II and formula III. The analysis statistic with Kruskal Wallis obtained a sig value of 0.062 (>0.05), which means that there is no significant difference in tablet friability with variations in the gas generating agent in each formula. Based on the results of the Kruskal Wallis test, it concludes that there is no significant difference in the friability of effervescent tablets with variations concentrations of gas generating agents in each formula.

The effervescent time test aims to determine the time required for effervescent tablets to completely dissolve, which is mark by the cessation of the production of carbon dioxide (CO_2) gas in water. The requirement for dissolving time is less than 5 min to completely disintegrate and has an ideal dissolution time of 1-2 min. If the effervescent well dispersed in water within 5 min, then the formula meets the requirements for dissolving time. The results of the dissolution time test showed that the average dissolution time of effervescent tablets in 200 ml aquadest in formula I was 86 min, formula II was 42 min, and formula III was 30 min. Formula III produces a faster dissolution time than formula I and formula II. Solubility influence by structural features such as the ratio of polar groups to non-polar groups and molecules. The longer the chain of carbon atoms, the lower the polarity and causes the solubility in water to decrease, in this formula polarity of components sequentially is citric acid, tartaric acid, and sodium bicarbonate. Formulation III also has a higher sodium bicarbonate content than formula I and formula II, so the tablet dissolution time is faster because sodium bicarbonate is used as a carbon dioxide source in effervescent tablets [17]. The results of the dissolution time measurement showed that the effervescent tablet of the root of the Kelakai did not meet the requirements for the dissolution time of the effervescent tablet, which was 5 min. This is presumably due to the lower gas generating agent content in each formula, the greater the gas generating agent content, the more carbon dioxide (CO_2) gas is produced so that the required dissolution time is also faster. Where the gas generating agent functions as a disintegrant or crusher for effervescent tablets [23]. The use of aerosil is also thought to affect tablet dissolution time, where aerosil used as an adsorbent can absorb moisture so that it can affect the resulting tablet. The hardness of the resulting tablet *al.* so does not meet the requirements, so the harder the tablet, the longer the tablet will dissolve in water. The results of the Kruskal Wallis test obtained a sig value of 0.027 (<0.05), which means that there is a significant difference in tablet dissolution time with variations in the gas generating agent in each formula. Based on the results of the Kruskal Wallis test, it can be concluded that there is a significant difference in the dissolution time of effervescent tablets with variations in the gas generating agent in each formula. This can happen because the results of the effervescent tablet dissolving time test results in each formula are much different so there is a significant difference; the results obtained also do not meet the requirements for effervescent tablet dissolving time.

The pH test needs to be done because if the effervescent solution is too acidic, it can irritate the stomach, whereas if it has too much alkaline it will have a bitter taste and bad taste. The pH values of F I, F II, and F III of effervescent tablets in this study are qualified as good pH values, ranging from 6.54 to 6.62. The pH of the effervescent solution is said to be good if the pH is close to neutral i.e. 6-7 [24]. The statistical results show that the three formulas have different solution pH values not significant.

The tablet preference test aims to determine the response of respondent (fig. 4). The tablet preference test is carried out to assess the appearance of effervescent tablets by 15 respondents. Four aspects of the parameter assessment are texture, color, aroma, and taste. Texture and color assessment of tablets aims to determine the level of product acceptance through visuals. Based on the results, it concludes that formula I have a total score of 3.73, so that is included in the like category because the score was close to 4, formulas II and III obtain a total score of 3.6 so that it included in the like category because the score was close to 4. Formula I has a higher score than formula II and III, so the texture acceptance of effervescent tablets is more chosen by respondents in formula I. The color produced by the tablet is the original color of all the materials used, including additives to improve the color. Based on the results of data processing, it concluded that formula I have a total score of 3.07 so that it includes in the rather dislike category because the score was close to 3, formula II obtained a total score of 3.53 so is included in the like category because the score was close to 4, and formula III obtained a total score of 3.2 so that it included in the category disliked because the score is close to 3. Formula II has a higher score than formulas I and III so the color acceptance of effervescent tablets is more chose by respondents in formula II.

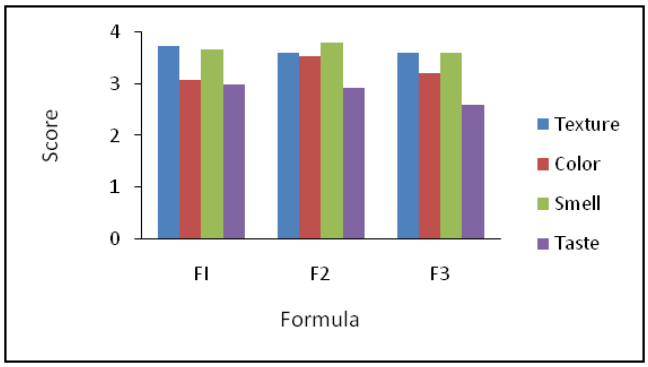

Fig. 4: Graph of sensory evaluations of kelakai roots effervescent tablet

The original aroma of the effervescent tablet comes from all the ingredients use without any additional components to improve the aroma. Based on the results of data processing, it can conclude that formula I obtain a total score of 3.67 so that it entered the like category because the score was close to 4, formula II has a total score of 3.8 it is included in the like category because the score is close to 4, and formula III has a total score of 3.6 so that it is included in the like category because the score was close to 4. Formula II has a higher score than formula I and III, which means the aroma acceptance of effervescent tablets is more chose by respondents in formula II.

The taste assessment aims to determine the level of acceptance of effervescent tablets. Based on the results, it's concluded that formula I is more disliked due to the acquisition of a score of 3, Formula II and III it's in the disliked category because the score is close to 3. The flavors acceptance score for formula I is higher than formula II and formula III so that the acceptance of tablet flavors is more chosen by respondents in formula I. The results obtained from each assessment parameter have different results because the tastes of each volunteer are different for the effervescent tablets produced. Preference test carried out by the four parameters including texture, color, aroma, and taste using the scale of five, namely very like is 5, liking is 4, disliking is 3, more dislike is 2, and very dislike is 1. So it can be concluded from the three formulas that formula I have the higher score on the texture and taste parameters, formula II has the higher score on the color and aroma parameters.

CONCLUSION

The formula optimum with the best physically characteristic effervescent tablet of Kelakai roots extract and has the highest degree of preference is formula III, whose composition of the mixture of citric acid, tartaric acid, and sodium bicarbonate is 1:2:3.5.

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All the authors have contributed equally.

CONFLICT OF INTERESTS

Authors declare no conflict of interest

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