Journal Homepage: -www.journalijar.com

INTERNATIONAL JOURNAL OF ADVANCED RESEARCH (IJAR)

Article DOI:10.21474/IJAR01/13473
DOI URL: http://dx.doi.org/10.21474/IJAR01/13473

RESEARCH ARTICLE

DEVELOPMENT OF EFFERVESCENT TABLETS BASED ON RED GINGER (ZINGIBER OFFICINALE ROSC. VAR. RUBRUM) AND ROSELLA FLOWER (HIBISCUS SABDARIFFA L.)

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Manuscript Info

Manuscript History
Received: 28 July 2021
Final Accepted: 31 August 2021
Published: September 2021

Key words:-
Covid-19, Effervescent Tablet,Ginger Extract, Rosella Extract, Tablet Quality

Abstract

The COVID-19 virus is still spreading throughout the world, and many efforts are being made to combat the outbreak and develop vaccines. Several traditional plants such as ginger and rosella can increase endurance and ward off various diseases. In this research, effervescent tablets made from ginger and rosella have been developed. Five formulations of effervescent tablets with different concentrations of acid and base mixtures have been made to test their physical properties, both granules, and effervescent tablets. The granule physical properties test results showed that the variation of the mixture of acids and bases had no significant effect on the physical properties of the granules. The physical quality of the granule is following the applicable requirements. The same thing was also found in the weight uniformity test. In contrast, in the brittleness and hardness test, tablet formulation 5 (an acid mixture consisting only of tartaric acid) showed the best results. From the dissolution time test, it was found that the use of a mixture of citric acid and tartrate was able to accelerate the dissolving time compared to the use of one type of acid. From the test results, it can be concluded that formulation five tablets show the best quality of tablets. Further studies need to be done regarding the application of ginger and roselle effervescent tablets to increase the body's immunity from COVID-19.

Introduction:-

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), better known as COVID-19, has been designated by WHO as a pandemic since March 11, 2020, and is still spreading its spread until now. This virus can easily be spread by human-to-human transmission of droplets, especially in people who are close to each other. Until now, it is still unclear what causes this virus (Rahman et al., 2021). **Coronavirus** is a human or mammalian-transmitted, positive, unsegmented RNA virus that belongs to the Coronaviridae family. This virus attacks the respiratory tract and generally does not cause severe effects. However, two types of coronavirus have caused thousands of fatalities, namely SARS-CoV and Middle East Respiratory Syndrome (MERS-CoV) (Huang et al., 2020; Zhu et al., 2020).When someone is infected with coronavirus, the most common characteristics include fever,

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dry cough, and shortness of breath. COVID-19 is different from the previous coronavirus, where the virus is straightforward to spread. Even though a vaccine has been found for COVID-19 and has begun to be distributed throughout the country, much research is being carried out to overcome this outbreak, considering that COVID-19 has become a severe problem for almost all countries worldwide (Chen et al., 2020; Zhou et al., 2020).

Apart from vaccines, various ways to treat or prevent COVID-19 are still being investigated by researchers now, utilizing traditional plants. Red ginger (Zingiber officinale Rosc.) It is a medicinal plant that grows in Indonesia, both as a side plant and in particular areas. Ginger is rich in oleoresin (gingerol, shogaol) and has been widely used as traditional medicine, flavoring agent, and antimicrobial agent (Ghafoor et al., 2020; Kizhakkayil and Sasikumar, 2011). Regarding COVID-19, several studies have revealed that ginger contains compounds that can inhibit the replication rate of this virus (Amin and Jha, 2020; Goswami et al., 2020). In several countries such as the United States, United Kingdom, and Nigeria, ginger has been applied to sufferers of COVID-19. It has been proven that consuming ginger can accelerate the healing of sufferers (Orisakwe et al., 2020).

One of the herbal plants often used as medicine is roselle, which Indonesian people generally consume in tea. Rosella has the potential as a source of functional food, antioxidants, antibacterial, anti-inflammatory, anti-cancer, natural dyes and is used in the health sector (Nurnasari and Khuluq, 2018). Rosella flowers contain essential compounds such as anthocyanins, flavonoids, and polyphenols, which according to several studies, can protect the heart, fight cancer, and treat carcinoma (Formagio et al., 2015). Rosella flowers have been used in various countries, such as in Egypt to treat heart and nerve diseases, in North Africa to treat sore throats and dry coughs, and in China and Iran to treat high blood pressure (Da-Costa-Rocha et al., 2014).

It can be said that both ginger and roselle flowers can be used as other alternatives to maintain the body's immunity due to the increasing spread of COVID-19. So far, the two plants are generally consumed by brewing. However, recently there are beverage preparations in the form of effervescent, namely in tablets that dissolve quickly and are more practical for consumption(Kartikasari et al., 2015).Effervescent tablets are made by pressing the active ingredients with a mixture of citric acid and bases such as sodium carbonate. Combining these mixtures is believed to maintain medicinal quality, increase drug solubility, and be more attractive for consumption because it helps improve the taste of certain drugs(Mahdiyyah et al., 2020).

Several studies have studied the manufacture of ginger effervescent tablets (Aghazadeh et al., 2019; Giyatmi and Lingga, 2019; Kholidah and Khumaidi, 2014)and roselle (Aprilianto, 2011; Asiani et al., 2012), with a mixture of different acids and bases. No literature discusses the manufacture of effervescent tablets using ginger and rosella flowers as far as the author's search. Therefore, in this study, effervescent tablets made from red ginger and rosella flowers were carried out. The acid mixture used is citric acid and tartaric acid, while the base used is sodium bicarbonate. A total of 5 effervescent tablet formulations with varying concentrations of acid and base were prepared and then tested the physical properties of the granules, and effervescent tablets were. Granule physical properties test includes moisture content test, Carr's index test, and angle of repose test. The physical properties test for effervescent tablets includes weight uniformity test, brittleness test, hardness test, and dissolving time test.

Materials and Methods:-

The materials used in this study were fresh red ginger rhizome (Zingiber officinale Rosc. Var. Rubrum) and red roselle flower (Hibiscus Sabdariffa L) obtained from Karanganyar Regency, starch Manihot, 96% ethanol, filler agent (dextrin), effervescent agent. (citric acid, tartaric acid, and sodium bicarbonate diluted using 96 percent ethanol), Polyvinyl Pyrrolidine (PVP) binding agent, and Polyethylene Glycol (PEG) 6000 lubricating agent. The tools needed include an analytical balance, oven, stopwatch, mesh sieves no 12, 16, and 40, blender, rotary evaporator, single punch tablet printing machine (Atelier TDP-5), LABINDIA Tablet Hardness Tester type TH 1050 M, Benchtop Tablet Friability Tester Instrument CS-4, mortar and pestle, drying cabinet, Mettler Toledo moisture analyzer, Tapped density tester SVM Erweka, filter paper, plastic container, porcelain cup, and glass beaker.

Preparation of ginger and rosella extracts

Fresh red ginger rhizome is washed, then sorted, and weighed. The rhizomes are sliced 1-3 mm thick, then dried in a drying cabinet at a temperature of ± 40 ° C. Dry red ginger rhizome is brittle when broken and weighed until the weight remains. The ginger rhizome is then powdered in a blender and stored in a plastic container with a lid. The same procedure is also carried out to obtain roselle pollen.

The extract was made by maceration using 96% ethanol as a solvent. A total of 1.5 kg of dry ginger or roselle powder is macerated with 75% solvent (11.25 liters) of 96% ethanol, then put in a tightly closed vessel and left at room temperature for five days protected from light while frequently stirring. After five days, the maceration results are filtered and squeezed. The waste is added with 25% parts (3.75 liters) of 96% ethanol until 100% (15 liters) are obtained into a closed vessel, left in a cool place, protected from light for two days, and filtered. The macerate was combined and then evaporated using a rotary evaporator at a temperature of ± 40 ° C to obtain an ethanol extract of 252.7 g. The extract was concentrated again by evaporation in a water bath to obtain a thick ethanol extract of 204.4 g. A total of 200 g of thick red ginger or rosella extract is dried by adding little by little Manihot starch with a ratio of 1: 3, then crushed until homogeneous. The fine extract was sieved with a No.40 mesh sieve and then dried in a drying cabinet at a temperature of ± 40ºC to obtain dry extracts of red ginger rhizome and roselle flowers.

Preparation of effervescent granules

The preparation of effervescent granules uses the wet granulation method by making acid and alkaline granules separately. Table 1 shows five effervescent tablet formulations with varying acid and base weights. Several dry extracts of red ginger and roselle flower were mixed homogeneously with citric acid and tartaric acid for acid granules. Then the wet granule is made using PVP, which has been dissolved with ethanol. Several dextrins are combined homogeneously with sodium bicarbonate to make alkaline granules, and then PVP, which has been dissolved in ethanol, is added to make a wet granule. The mixture of each formulation was granulated until the same mass was obtained, then sieved using a mesh No. sieve. 12 and dried in a drying cabinet with a temperature of 40-60 ° C for ± 1-2 hours until the appropriate material moisture content is obtained. The dry granules were sieved again using a No. mesh sieve. 16. The dry granules that have been obtained are then tested for their physical properties. The effervescent granules obtained were then compressed utilizing a tablet printing machine by mixing the acid granules, alkaline granules, ginger and roselle extracts, and PEG. After that, the effervescent tablets were tested for the quality of their physical properties.

Table 1:- Effervescent tablet formulation

Component	Formula (mg)				
	I	**II**	**III**	**IV**	**V**
Red Ginger Extract	0.15	0.15	0.15	0.15	0.15
Rosella Extract	0.15	0.15	0.15	0.15	0.15
PVP	10.2	10.2	10.2	10.2	10.2
Dextrin	1111	1111	1111	1111	1111
Effervescent mix					
• Tartaric Acid	-	172	347	526	708
• Citric Acid	682	516	347	175	-
• Sodium Bicarbonate	818	812	806	799	792

Extract antioxidant activity test using DPPH method with UV-Vis Spectrophotometer

The basic idea behind this antioxidant activity test method is to quantify antioxidant activity by measuring DPPH radical capture by a compound with an antioxidant activity using UV-Vis spectrophotometry to determine the value of free radical scavenging activity expressed as the IC50 value (Inhibitory Concentration). The IC50 value is defined as the concentration of the test compound that can reduce free radicals by 50%. The smaller the IC50 value, the higher the free radical scavenging activity. The formula calculates attenuation to DPPH:

$$\%Inhibition = \frac{(ControlAbs\ .-SampleAbs\ .)}{ControlAbsorbance} \times 100\% \text{(Eq. 1)}$$

Test the Physical Properties of the Granules

Test Moisture Content

Moisture content is an important quality parameter for dry products because it will determine the durability and shelf life of the product. Hygroscopic granules produce poor granule flow so that the uniformity of tablets is also not good. In this test, a moisture balance tool is used. The tool is inserted into an aluminum plate, then weighed ± 1 gram in a cup, then the percentage of the water content of the granule will be obtained. Water content was measured three times and averaged.

Test Carr's index

Carr's index test results are said to be good if Carr's index value is <20%, or it can be said to have good flow properties. The smaller the% Carr's index, the better the flow properties. A total of ± 30 grams of granules were weighed and put in a 50 ml measuring cup, then the volume (V1) and bulk density were measured, according to equation (2). The measuring cup containing granules was placed on a tapping device, tapped 300 times. The experiment was repeated three times with different granules, then the volume (V2) and tapped density were measured, according to equation (3). Carr's index is calculated using equation (4).

$$Bulkdensity = \frac{m}{V_1} \quad \text{(Eq. 2)}$$

$$Tappeddensity = \frac{m}{V_2} \quad \text{(Eq. 3)}$$

$$Carr'sindex = \frac{Tappeddens\ .-Bulkdens\ .}{Tappeddensity} x\ 100\% \quad \text{(Eq. 4)}$$

Test the angle of rest

If the angle of rest formed is ≤ 30 °, it indicates that the granule can flow freely, and if the angle formed is ≥ 40 °, it indicates that the granule has poor flowability(Kholidah and Khumaidi, 2014).Several granules are inserted into the flow funnel with the bottom closed then flattened, after which the powder holder at the bottom of the funnel is opened, let the powder flow on the table covered with paper. The pile of powder formed is measured for height and radius. The angle of rest is calculated based on equation (5). α is the angle of repose, h is the height of the pile of powder (cm), and r is the powder's radius.

$$Tan\alpha = \frac{h}{r} \quad \text{(Eq. 5)}$$

Test of physical properties of effervescent tablets

Weight uniformity test

Uniformity of weight is one factor that determines the uniformity of the active substance in tablets, affecting the uniformity of the therapeutic effect. The weight uniformity test needs to be done to determine whether, in one tablet printing, the weight of each tablet is more or less the same. In each test, ten tablets of each formulation were taken as samples. The results obtained should not be more than two tablets, with each weight deviating from the average weight of the tablet.

Brittleness test

The brittleness of the tablet describes the strength of the tablet surface against abrasion on the tablet surface. The fragility of the tablets was carried out by freeing ten tablets of dust and then weighed and put into the friability tester. The tool is run for 4 minutes at a speed of 25 rpm. After that, the tablet is dust-free again and weighed. This test is carried out three times for each formulation. Equation (6) shows the fragility calculation formula. $W_i$is the initial weight, while $W_f$is the final weight. The fragility of a tablet is said to be good if the value is <1%.

$$Brittleness = \frac{W_i - W_f}{W_i} \times 100\% \quad \text{(Eq. 6)}$$

Hardness Test

Tablet hardness is a parameter that describes the resistance of tablets against mechanical stress. The tablet is inserted into the Hardness tester. Then the tool is turned on until the hardness number or value is obtained. The experiment was repeated ten times for each formulation.

Dissolve Time Test

The dissolution time test aims to check whether the tablets dissolve quickly according to resin requirements. The dissolving time of an excellent effervescent tablet will disintegrate and dissolve quickly in 1-2 minutes or less than 5 minutes. An effervescent tablet is put into the water with a volume of 250 ml. The dissolving time is calculated with a stopwatch starting from immersing the tablet until all the tablets are crushed and dissolved.

Results and Discussion:-

Extract antioxidant activity

Tabel 2:- The results of the evaluation of the physical properties of the Extract's Antioxidant Activity

Extract	%Inhibition	IC 50 (%)
Red Ginger Extract	73,171	0,061
Roselle Extract	51,220	0,082
Mix Red Ginger and Rosella Extract	80,488	0,042

Table 2 shows the results of the antioxidant activity test of the extract, which shows that the free radical scavenging effect of the extract preparations shows that the mixture of ginger extract and rosella extract has greater inhibitory power against free radicals, which is 80.488% with an IC 50 value of 0.042 where the results of the mixture of extracts are classified as having good active antioxidants. This is by the research results by Philip Molyneux (2004), which states that the level of the antioxidant power of test compounds using the DPPH method can be classified based on the IC50 value, where the smaller the IC50 value, the higher the free radical scavenging activity(Molyneux, 2004).

Granule physical properties

Table 3:- Evaluation results of granule physical properties test

Formulation	Flow Rate (gr sec^{-1})	Silent Angle (^{o})	*Moisture Content* (%)	*Tapped Density* (gr mL^{-1})	*Bulk Density* (gr mL^{-1})	*Carrs Index*
I	14,19	9,84	3.09	0,57	0,64	10,98
II	18,49	9,92	3.25	0,50	0,61	9,91
III	19,04	10,10	3.45	0,59	0,57	8,79
IV	14,24	10,22	3.36	0,83	0,54	7,67
V	14,63	10,20	3.29	0,57	0,57	7,69

Table 3 shows the granule physical properties test results, including the moisture content test, Carr's index test, and the angle of repose test. It can be seen that the granules in formulation 1 have the lowest water content of 3.09%, while the most significant water content is obtained in formulation 3, which is 3.45%. A good moisture content value for effervescent granules should be below 0.5% (Giyatmi and Lingga, 2019; Patel and Siddaiah, 2018).Thus, the water content in this study is still too high. This can be due to the less long drying process (1-2 hours) and the low drying temperature (40-60°C) in this study, so there is still water in the granules. In Carr's index test, it can be observed that the lowest and highest Carr's index values are found in formulations 2 and 1, respectively, with a range between 7 to 11.36. Granules are said to have a suitable flow type if Carr's index value is between 5-15% (Kartikasari et al., 2015; Nurahmanto et al., 2017).

Meanwhile, in the angle of repose test, it was found that the angle of repose value for the five granule formulations was not much different, with a range between 9.7 to 10.57 degrees. This indicates that the effect of acid concentration has little effect on the angle of rest or flow properties of the granules. It can also be observed that the granules in formulation 5 (the highest tartaric acid concentration) have the most excellent angle of repose. This can be due to the greater cohesion force between tartaric acid particles, resulting in a larger angle of rest (Kartikasari et al., 2015). Granules have a good flow when the angle of rest is less than 30 degrees (Giyatmi and Lingga, 2019; Patel and Siddaiah, 2018). From the granule physical properties test, it can be concluded that the differences in the composition of citric acid, tartaric acid, and sodium bicarbonate do not have a significant effect on the physical properties of the granules.

Evaluation of ginger and rosella extract effervescent tablets

The physical appearance of effervescent tablets

Evaluation of the physical appearance of the tablets was carried out by observing the shape, color, odor, surface of the tablet, and whether there was any damage to the tablet. The evaluation of the physical appearance of the effervescent tablets of ginger and roselle extract formulas I, II, III, IV, and V are the same, namely tablets are round flat, yellowish pink, odorless, sour taste, with smooth surface, and no defects on the tablet.

Figure 1:- Ginger and rosella extract effervescent tablet.

Weight uniformity

The weight uniformity test needs to be done to determine tablets' level of weight uniformity in one tablet printing. The results of the weight uniformity test are shown in Table 3. It can be observed that there is not a single tablet whose weight deviates more than 5% and 10% of their respective mean weights so that it qualifies as an effervescent tablet that is fit for consumption (Kholidah and Khumaidi, 2014; Patel and Siddaiah, 2018). Fine granule flow properties also influence good weight diversity results. Due to the granules' excellent flow properties, the granules' ability to fill the die will be more constant, and the resulting weight will also be more uniform.

Tablet fragility

This test is intended to prevent crushed tablets during the packaging, distribution, and storage processes. The brittleness of the tablet describes the strength of the tablet surface against abrasion on the tablet surface. The good friability value is less than 1% which means the tablet is mechanically stable (Kartikasari et al., 2015; Patel and Siddaiah, 2018). In this study, ten tablets were taken for each formulation and carried out three times for brittleness testing, then weighed. Obtained the average value of the fragility of formula 1 of 1.03%: 1.09%: 0.93%. In formula 2 there is a result of 0.5%: 0.7%: 0.85%, formula 3 has a result of 0.98%: 0.99%: 0.90%. In formula 4 the results are 0.88%: 0.84%: 0.85%, and in formula 5 the results are 0.93%: 0.74%: 0.75%. It can be concluded that the average value of the friability test is below <1%, with formulation 5 showing the best results. Besides, it can be seen that formulation 1 (containing only citric acid) has the highest percentage value of friability. In contrast, the lowest percentage value of friability is obtained in formulation 5 (containing only tartaric acid). This indicates that the concentration of citric acid can affect the fragility of the tablets (Giyatmi and Lingga, 2019).

Tablet Hardness

Tablet hardness test is intended to see the resistance of tablets against loads or mechanical stress, for example, shock or impact. The hardness of the tablet can be influenced by several factors, including the pressure during tableting, the physical properties of the material being compressed, and the amount and type of material used (Aprilianto, 2011). Good hardness for effervescent tablets is 4-8 kg/cm^2(Kartikasari et al., 2015; Kholidah and Khumaidi, 2014). In formulation 1, the hardness of the tablets obtained an average of 4.7 kg.cm^{-2}, formula 2 with an average of 5.23 kg.cm^{-2}, formula 3 with an average of 4.6 kg.cm^{-2}, formula 4 with an average of 4.6 kg.cm^{-2}, and formula 5 with an average of 7.23 kg.cm^{-2}. From the results obtained, it can be concluded that all formulations meet the criteria in the tablet hardness test, with formulation 5 showing the best hardness value.

Dissolving Time

The dissolving time test is a test that is performed to determine whether the granule can dissolve and for how long the granule can dissolve. A reasonable dissolving time requirement for effervescent tablets is around 1-2 minutes (Kartikasari et al., 2015; Kholidah and Khumaidi, 2014). The results of the dissolution time test can be seen in Table 4. It can be observed that formula 1 has the longest dissolving time. The variation of citric acid and tartaric acid resulted in a faster dissolving time of effervescent tablets. According to the test results, the interaction between citric acid and tartaric acid can enhance the solubility time, indicating that formulas 2, 3, and 4 have a superior solubility time than formulas 1 and 5. Because citric acid is hygroscopic, it might increase the amount of water in the powder, causing it to dissolve quickly. The tartaric acid with a higher concentration will have a greater density. The molecular weight will also be more excellent and make it easier for the powder to flow (Giyatmi and Lingga, 2019; Kholidah and Khumaidi, 2014).

Table 4:- Solubility test results.

Formula	Time
1	108 seconds

2	30 seconds
3	46 seconds
4	43 seconds
5	58 seconds

Conclusion:-

In this study, effervescent tablets from ginger and roselle extracts have been successfully prepared with different formulations. Several tests regarding the physical properties of granules and effervescent tablets have been carried out. The results show that the ratio of citric acid to tartaric acid and sodium bicarbonate affects the physical properties of the granules, such as moisture content, angle of rest, and Carr's Index. Variations in acid and base concentrations did not influence weight uniformity in the weight uniformity test. Formulation 5 (just tartaric acid as an acid combination) performed best in both the brittleness and hardness tests. Citric acid and tartaric acid, at various doses, accelerated the dissolving time in the solubility test. Formula 5 is the best overall, according to test findings of the physical qualities of granules and effervescent tablets. It can be concluded that effervescent tablets from ginger and rosella extract can be made/formulated easily. However, further research is still needed regarding the effects of ginger-rosella effervescent tablets on endurance.

Acknowledgments:-

This research was funded by the Ministry of Research and Technology / National Research and Innovation Agency and the Ministry of Finance Education Fund Management Institute in 2020.

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