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FORMULATION AND EVALUATION OF EFFERVESCENT GRANULE OF WHITE TEMU RHIZOME EXTRACT (*Curcuma zedoaria* (Christm.) Roscoe.) AS ANTIOXIDANT

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ABSTRACT

More than 9,606 plant species have medicinal properties, but only around 3−4% of these have been cultivated commercially and used in traditional medicine in Indonesia. One of the natural ingredients believed to have properties is the white temu rhizome. White Curcuma rhizomes are usually processed into food and drinks. White ginger rhizome has antioxidant activity. Antioxidants are secondary metabolites found in herbal plants and have pharmacological activities that can minimize free radicals. Several studies have shown that white ginger rhizomes have antioxidant activities that can remove free radicals. This research aims to formulate an effervescent granule preparation. for white temu rhizome extract (Curcuma zedoaria (Christm.) Roscoe) using the wet granulation method, which meets the requirements for the physical properties of granules and has antioxidant activity. Several formulae were selected from various combinations. Next, an evaluation was performed to determine the physical properties and activities of the formulated granules. The evaluation results showed that all formulations met the requirements of the physical properties of the granules. Qualitative antioxidant activity testing using TLC plates showed positive antioxidant results in the extract and effervescent granule preparation of white curcuma rhizome extract and in quantitative testing it was found that the IC50 value of white curcuma rhizome extract was in the strong category and in the effervescent granule preparation of white curcuma rhizome extract, the granules were found to be in the strong category.

Keywords: Effervescent Granule, Extracts, White Temu Rhizome (Curcuma zedoaria (Christm.) Roscoe), Antioxidants

INTRODUCTION

More than 9,606 species of medicinal plants can be found in Indonesia (Siregar *et al*., 2022), and only approximately 3–4% of these have been commercially cultivated and utilized in traditional medicine. The trend of utilizing herbal plants in traditional medicine is now very popular among Indonesian people (Khumaida *et al*., 2017; Elhassan *et al*., 2012). The use of herbal plants in traditional medicine is currently a very popular trend among Indonesians (Elhassan *et al*., 2012). Antioxidants are secondary metabolites found in herbal plants that have pharmacological activities and can be utilized for health. Reactive Oxygen Species or ROS are free radicals that can be minimized by antioxidants (Birben *et al*., 2012). Reactive compounds with unpaired electrons in their outer shells are defined as free radicals. Free radicals in the body can cause several degenerative diseases (Suena *et al*., 2021). Free radicals can be counteracted or mitigated by administering or consuming antioxidants (Suena *et al*., 2021).

Antioxidants are found in many types of plants, one of the plants that can be used as a natural antioxidant is white temu rhizome (Curcuma zedoaria (Christm.) Roscoe) which is

one type of the Zingiberaceae family. Based on the research conducted by Nahak and Sahu, white temu has antioxidant properties. Antioxidant activity test on white temu (Curcuma zedoaria (Christm.) Roscoe) with the DPPH method obtained an IC50 value of 6.54 µg/mL, which indicates that white temu has very strong antioxidant activity (Suena *et al*., 2021). Thus, white temu rhizome has the potential to be developed as an antioxidant.

White temu rhizomes are commonly processed into functional foods and beverages. White temu is a versatile spice that can be used in food and beverages, as well as in traditional medicine for various conditions, such as stomach pain, fever, red spots, and skin itching.

Along with the development of science and technology in the pharmaceutical field, the utilization of white temu rhizome (Curcuma zedoaria (Christm.) Roscoe) still needs to be developed, one of which can be made into a preparation that is easily accepted by the community, one of which can be made in the form of effervescent granules. Effervescent granules are coarse to very coarse powders in a dry mixture containing medicinal elements. In general, effervescent granules consist of citric acid, tartric acid, and sodium bicarbonate, which, when added to water, form foam owing to the reaction of acids and bases that liberate carbon dioxide. When put into water, the effervescent granules produce CO2, which aims to produce a solution quickly and simultaneously. Due to the presence of carbonate, which helps certain drugs taste better, effervescent granules can also produce a good taste in addition to a fast reaction (Sidoretno *et al*., 2022). Compared to other oral preparations, effervescent preparations also have several advantages, especially in terms of bioavailability. This form of medication eliminates the need for disintegration and dissolution of the drug prior to absorption, thus allowing for the rapid achievement of effective levels of the drug in the blood (Adepu & Ramakrishna, 2021).

The wet granulation method is commonly used to prepare effervescent granules. The wet granulation method can be defined as the process of mixing active substance particles and excipients into larger particles (aggregates) by adding the correct amount of binding liquid to create a moist mass that can be granulated. The wet granulation method is typically used when the active substance is resistant to moisture and heat (Sriwidodo *et al*., 2022).

Based on the background, the researchers are interested in formulating white temu rhizome extract *(Curcuma zedoaria* (Christm.) Roscoe) into an effervescent granule preparation, which is used as a health drink with antioxidant activity.

RESEARCH METHODS

Materials and tools

The tools used in this study include 12 and 18 mesh sieves, mortars and stampers, ovens, analytical scales (Mettler Toledo), chambers, KLT plates, capillary pipes, glassware commonly used in laboratories, filter paper, drop pipettes, spatulas, stopwatches, Granule Flow Tester, Tap density tester (TDT-3-H), Moisture Balance (Radwag®), pH meter (Mettler Toledo), UV light 254 nm and 365 nm, and UV-Vis spectrophotometry.

The materials used in this study include white temu rhizome extract (Curcuma zedoaria (Berg.)Roscoe) obtained from Lansida Herbal Yogyakarta, Citric Acid (Subur Kimia Jaya, Bandung), Tartric Acid (Subur Kimia Jaya, Bandung), Sodium Bicarbonate (Subur Kimia Jaya, Bandung), PVP (Dwi Lab, Bandung), Stevia, Xanthan Gum (Subur Kimia Jaya, Bandung), Maltodextrin (Subur Kimia Jaya, Bandung), Lactose (Dwi Lab, Bandung), and 96% ethanol v/v.

Research Procedure

1. Phytochemical Screening

   Phytochemical screening of extracts was carried out to determine the content of compounds contained in the extracts, including flavonoids, alkaloids, saponins, quinones, tannins, and steroids/triterpenoids (Pratama *et al*., 2022).

a. Flavonoids

0.1 grams extract was added 0.1 mg of Mg powder, 0.4 mL of amyl alcohol and 4 mL of 96% ethanol. The formation of a brick red or purple color indicates the presence of flavonoids.

b. Alkaloids

The extract (2 grams) was added to 10 mL of chloroform and filtered. The filtrate is added with 3 drops of the Dragendorff reagent were added to the filtrate. The color change to brick red or orange red indicates a positive alkaloid.

c. Saponins

0.1 grams extract was added to 10 mL of distilled water and shaken for 30 seconds. The formation of a stable foam indicates the presence of saponins.

d. Quinone

0.1 grams extract was added 1N NaOH. The formation of red color indicates positive quinone.

e. Tannins

0.1 grams extract was added 2 mL of $FeCl_3$ 1%. The formation of blackish green or blue color changes indicates positive tannins.

f. Steroid/Triterpenoid

0.1 grams extract was added 2 drops of anhydrous acetic acid and 1 drop of concentrated H_2SO_4. The formation of green color indicates positive steroid, while the formation of purple or red color indicates positive triterpenoid.

2. Preparation of effervescent granules

The preparation of effervescent granules of white temu rhizome extract was carried out by wet granulation method. The working steps are as follows:

a. The thick extract of white temu rhizome and other additional ingredients are weighted according to the formula to be made.
b. The thick extract of white temu rhizome that has been obtained from the extraction process with 96% ethanol is dried using maltodextrin and lactose by grinding until homogeneous, maltodextrin, and lactose are added until the extract looks dry.
c. The thick extract of white temu rhizome that has dried is then mixed using citric acid, tartrate acid, and sodium bicarbonate and then crushed until the mixture is completely homogeneous (mixture 1).
d. Then mixture 1 was added with PVP, Xanthan Gum and stevia (mixture 2).
e. Then, mixture 2 was sprayed little by little using 96% ethanol until the mass could be clenched.
f. Then, the clenchable mass was sieved using mesh 12, then dried in an oven at ±40°C, until the drying shrinkage rate was between 0.4−0.7%.
g. Then, the dried granule was sieved again using mesh 18, then the effervescent granule preparation of white temu rhizome extract (*Curcuma zedoaria* (Christm.) Roscoe) was stored in a desiccator which contained silica gel to avoid moisture absorption from the air before packaging.
h. After all effervescent granule formulas were made, then each formula was evaluated to determine the best formula.

3. Physical Properties evaluation of Effervescent Granule Preparations

a. Organoleptic

A sufficient amount of granules were taken, then observed directly with the parameters observed, namely the shape, smell, and color of the granules (Julianti *et al*., 2022).

b. Loss on Drying

Wet granules are weighed, then dried using an oven until a fixed weight is obtained. then the moisture content can be calculated (Sudarsono *et al*., 2021).

c. Angle of repose

The angle of repose was obtained by measuring the diameter and height of the granule (Sriwidodo *et al*., 2022).

d. Flow Tester

100 grams of granule is put into the funnel on the granule flow tester, open the bottom cover of the funnel and calculate the granule fall time using a stopwatch (Pratama *et al*., 2022).

e. Compressibility

This test is carried out using a 250 mL measuring cup then the entire granule is inserted into the measuring cup, the initial height of the granule is recorded. Then the measuring cup is tapped as much as 100−500 with an interval of 100 and recorded at each interval. After that, the weight of the granule is obtained after compressing and calculating the real density and compressible density.

f. Dissolve time

10 grams of dried granules were weighed, then put into a beaker glass and added with 250 mL water, then observed until the granules dissolved completely. The dissolving time is calculated using a stopwatch and record the results obtained.

g. Foam height of granules

A 250 mL beaker glass was filled with 150 mL of distilled water and then poured the granule. Stir slowly and record the time required by the whole granule to disperse homogeneously and cause foam.

4. Evaluation Antioxidant Activity

a. Thin Layer Chromatography (TLC)

Qualitative antioxidant activity testing was performed using thin-layer chromatography (TLC). The ethanol extract of white temu rhizome was dissolved in 96% ethanol and bottled on silica gel 60 F254 using a capillary tube. Silica gel 60 F254 was dotted and eluted using the appropriate eluent. The DPPH solution was sprayed, silica gel 60 F254 was left for a few minutes, the spots appeared, and the TLC profile was observed under visible light, UV light at 254 nm, and 365 nm (Sriwidodo *et al*., 2022).

b. The IC_{50} value of each intermediate product compared to ascorbic acid.

1. Preparation of DPPH Solution

Take 5 mg of DPPH dissolved using methanol p.a in a 50 mL volumetric flask, shake until homogeneous until a concentration of 100 µg/mL DPPH solution is obtained. Then store the DPPH solution in a dark container covered with aluminum foil and store at low temperature for immediate use.

2. Preparation of Blank Solution

1 mL of methanol p.a was put into a test tube, then the solution was added as much as 1 mL. Then 2 mL of methanol p.a was added and shaken until homogeneous. Then, the blank solution was incubated for 30 minutes at 37ºC. The absorbance of the blank solution was measured at the maximum wavelength of 517 nm.

3. DPPH Wavelength Optimization

DPPH solution with a concentration of 100 µg/mL is stored in a container that is protected from light by covering it with aluminum foil. DPPH solution must be made new for each test. Then this solution was determined the absorption spectrum using a UV-Vis spectrophotometer at a wavelength of 400−800 nm. The maximum wavelength of DPPH used is in the range of 515−520 nm.

4. Preparation of Test Solution

10 mg of extract was measured, then dissolved in 20 mL of methanol p.a to obtain a concentration of 500 µg/mL. A series of solutions with concentrations of 20, 30, 40, 50, 60, 70 µg/mL were then prepared.

5. Determination of Vitamin C Comparator Solution

10 mg of vitamin C was dissolved in 20 mL of methanol p.a in a 500 µg/mL volumetric flask. Then the solution was prepared in the concentration range of 1, 2, 3, 4, 5, 6 µg/mL.

6. Antioxidant Activity Testing of Extracts

   The absorbance of blank solution, each test solution and standard solution was measured, pipette 1 mL put into the tube, then add 2 mL methanol p.a. and 1.0 mL DPPH and shake well. After incubating at 37°C in the dark for 30 minutes, the absorbance at a wavelength of 519 nm was measured using a spectrophotometer.

7. Determination of % Inhibition and IC_{50} Value

   The antioxidant activity of the sample is determined by the amount of DPPH radical uptake inhibition through the calculation of percent inhibition (% inhibition).

RESULTS AND DISCUSSION

1. Phytochemical Screening Results

Table I. Phytochemical Screening Results

Compound	Sample
	Extract
Flavonoids	(+)
Alkaloids	(+)
Saponins	(+)
Quinone	(+)
Tannins	(+)
Steroids/Triterpenoids	(+)

Description: (+) contains the tested compound

White temu rhizome extract contains flavonoids, alkaloids, saponins, quinones, tannins, and steroids/triterpenoids. The results obtained in this study are in line with previous research, which showed that white temu rhizome extract contains flavonoids, alkaloids, saponins, quinones, tannins, and steroids/triterpenoids (Silalahi, 2018).

2. Physical Properties of Effervescent Granules

   The reparation of effervescent granules in this study was carried out by wet granulation method to avoid premature effervescent reaction. In the process of making effervescent granules, it was carried out at a room temperature of 25ºC with RH or room humidity of 20%.

Figure 1. The physical appearance of effervescent granule containing white temu rhizome extract

The formula used in this effervescent granule preparation consists of active substances and excipients (additional substances), namely white temu rhizome extract as an active substance, citric acid and tartrate acid as acid sources, sodium bicarbonate as a base source, PVP as a binder, lactose as a filler, stevia as a sweetener, xanthan gum as a suspending agent, maltodextrin as a solubility enhancer, and 96% ethanol as a solvent.

Organoleptic tests were conducted to determine the physical characteristics of the effervescent granule preparations made, the parameters observed consisted of shape, odor, color and taste. Effervescent granule preparations of white temu rhizome extract in the three formulas are generally in the form of granules with uniform size, have a

distinctive aroma like temu/turmeric extract. The brown color produced in the preparation comes from the color of the white temu rhizome extract and has a bitter taste that comes from white temu which has a distinctive bitter taste. The three formulas made did not show significant differences in terms of shape, aroma, and color.

Table II. Result of Organoleptic Test

	Organoleptic		
	Color	**Aroma**	**Shape**
Result	Brown	White temu aroma	Granule

Table III. Physical Properties Test Results

Test	**Result**			
	Flow Properties (s/100g)	**Angle of Repose (º)**	**Compressibility (%)**	***Loss on Drying (LOD)* (%)**
1	7.00	24.22	10.90	0.43
2	7.07	20.54	9.45	0.48
3	6.89	21.56	8.66	0.45
average	6.99±0.005	22.10±1.899	9.67±1.136	0.45 ± 0,002

Based on the Loss on Drying (LOD) test results 0.45 ± 0.002. The results of the evaluation of the water content obtained show that the three formulas meet the LOD requirements for granules, namely 0.4−0.7%. This is because during the drying process the granule preparation is in the oven at a drying temperature of ± 40°C for 24 hours, so that the granule preparation has a fairly low moisture content and dries evenly.

Flow rate testing on granule preparations aims to see whether the granules obtained can flow well, so that during the production process granules that have a good flow rate will easily flow into the die. The requirements for a good granule flow rate are in the range of 4−10 g/second (Sriwidodo *et al*., 2022).

The flow rate results obtained in effervescent granule preparations are 6.99 ± 0.005. From these results, it can be seen that formula meet the requirements of the flow time test, which is in the range of 4−10 g/sec. The difference in flow time can be influenced by the concentration of the acid source.

The rest angle value of the granule illustrates the flow properties of the granule. The results show that the three formulas have met the rest angle requirements because the rest angle values are >20° and <40° (Rusita & Regia, 2019; Indriastuti *et al*., 2023)

The real and compressible density test is carried out to determine the compressibility index value of the effervescent granule preparation. This evaluation is carried out by first weighing the granule preparation as much as 50 grams and putting it into a 250 mL measuring cup and then recording it for the initial volume. Furthermore, the measuring cup is inserted into the Tap Density Tester tool to be knocked 250 times then the volume of the granule is recorded again after knocking. This compressibility test is carried out to determine whether the granule preparation produced has good flow or not.

The compressibility test results obtained in effervescent granule 9.67±1.136. From the results obtained the formula, they meet the requirements because ≤ 20%, formula have a compressibility index in the excellent category. The size of the compressibility index is largely determined by how the granule preparation fills the space between particles and compresses more tightly during knocking.

Table IV. Result of Dissolve Time

Test	Result
I	4.07
2	4.15
3	4.19
average	4.14 ± 0.016

Description : Dissolving time < 5 minutes

The dissolving time test was carried out by dissolving 10 grams of effervescent granules from each formula into 250 mL of water. The dissolving time test was conducted to determine the time required for the granule to disperse in water. As for the end point of the dissolving time of the effervescent granule preparation, namely the shape of the granule preparation which turns into a smaller and dispersed powder. Granule preparations meet the requirements of the dissolving time test if the granule preparation can dissolve in less than five minutes (Yasmin *et al*., 2019; Pratama *et al*., 2023). The contact of water with effervescent granules causes a reaction between the acid source and the base source which produces CO_2 which causes the granules to disintegrate and dissolve. The test results of dissolving time obtained in effervescent granule preparations 4.14 ± 0.016. Citric acid, which has hygroscopic properties, will attract water more quickly for the carbonation reaction, so the carbonation reaction between carbonate with tartrate and citric acid can occur quickly when the concentration of citrate is increased. However, judging from the data above, it shows that the granule has a dissolving time of <5 minutes so it meets the requirements of the dissolving time test.

pH measurement effervescent granule preparations, namely to determine the quality of the preparation (Pratama *et al*., 2022). pH testing is carried out using a pH meter where the mechanism of action of the pH meter is to measure the activity of hydrogen ions by potentiometry. The pH test begins by preparing a solution of instant granule preparation, then the pH meter is calibrated first with a solution of pH 4, pH 7, and pH 10 then the electrode is inserted into the solution and wait until the pH value is read on the pH meter.

Table V. pH Result

Test	result
1	4.04
2	4.01
3	4.03
average	4.02 ± 0.019

The pH test results obtained in effervescent granule preparations 4.02 ± 0.019. pH granule is quite acidic because it has a pH of 4, so it does not meet the requirements (Indriastuti *et al*., 2023). This can occur because each formula uses 2 components, namely citric acid and tartric acid, which can cause the pH of the preparation to become acidic.

Table VI. Result of Foam

Test	Result
1	7.0
2	7.1
3	7.2
average	7.10 ± 0.047

Foam height was measured simultaneously when the effervescent granule preparation was dissolved in water. The average foam height obtained from effervescent granule preparations of white temu rhizome extract ranged from 6 to 7 cm. The foam height of the granule 7.10 ± 0.047. The foam height in effervescent granule preparations is influenced by the concentration of acids and

bases used; the higher the concentration of acids and bases, the more CO2 gas is produced. According to (Widyaningrum *et al*., 2015) foam in effervescent granule preparations consists of thousands of small bubbles that originate from liquids and are formed as a result of chemical reactions or mechanical treatments such as stirring. Foam is formed when bubbles grow and accumulate rapidly on the surface of the liquid.

3. Antioxidant Activity Testing Results

Antioxidant testing was carried out on effervescent granules that had been formulated after testing their physical properties.

Table VII. The IC_{50} Value of Each Intermediate Product Compared to Ascorbic Acid

Sample	IC_{50} µg/mL
Ascobic acid	8.14
White temu extract	53.04
Granule Effervescent	62.37

Based on the results of antioxidant activity testing obtained from the linear regression equation, the antioxidant activities of Ascobic acid was 8.14 µg/mL, temu putih extract was 53.04 µg/mL and effervescent granule preparation were 62.37 µg/mL. The antioxidant activity of the extracts and preparations is included in the strong category because it is in the range of 50–100 µg/mL. Ascobic acid, as a comparison, is included in the very strong category because it is <50 µg/mL, this is because Ascobic acid is a very pure compound. The antioxidant activity of the white temu extract and granule preparations did not show significant differences, indicating that the granule preparation formulation process did not affect the activity of the white temu extract used.

4. Thin Layer Chromatography

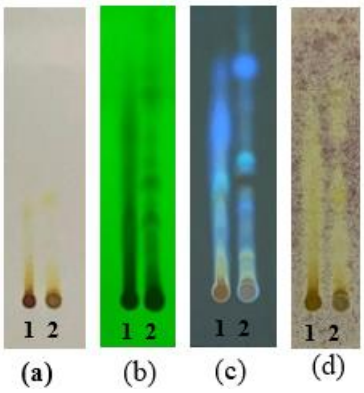

Figure 2. TLC result

Description: (1) White Temu Extract, (2) White Temu Effervescent Granule Formula III; (a) Visible light, (b) 254 nm light, (c) 366 nm UV light, (d) DPPH 0.2%.

On the TLC plate sprayed using 0.2% DPPH solution, a yellow spot is formed after spraying DPPH, this is due to the presence of compounds that can donate hydrogen atoms in the extract and granule preparation resulting in reduced DPPH molecules followed by a change in the color of the DPPH solution from purple to yellow which shows positive antioxidant activity (Yasmin *et al*., 2019). After testing the antioxidant activity of extracts

and granule preparations qualitatively, then proceed with testing the antioxidant content using the spectrophotometric method.

CONCLUSION

The evaluation results showed that all formulations met the requirements of the physical properties of the granules. Qualitative antioxidant activity testing using thin layer chromatography (TLC) showed positive results for antioxidants in extracts and effervescent granule preparations of white temu rhizome extract, with the IC50 value of white temu extract in the strong category range and in effervescent granule preparations of white temu extract obtained granules into the strong category.

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