International Journal of Pharmaceutical and Bio-Medical Science

ISSN(print): 2767-827X, ISSN(online): 2767-830X

Volume 03 Issue 09 September 2023

Page No: 454-459

DOI: https://doi.org/10.47191/ijpbms/v3-i9-03, Impact Factor: 6.858

Determination of Specific and Non-Specific Parameters of Cempedak Leaf Simplisia (*Artocarpus Integer*)

Anna Khumaira Sari[1], Muhammad Ikhwan Rizki[2], Nabila Hadiah Akbar[1], Maulida Amaliya[1], Fadlilaturrahmah[2], Normaidah[1]

[1]Pharmacist Profession Education Program, Faculty of Mathematics and Natural Sciences, Lambung Mangkurat University Banjarbaru, South Kalimantan, Indonesia

[2]Study Program of Pharmacy, Faculty of Mathematics and Natural Sciences, Lambung Mangkurat University Banjarbaru, South Kalimantan, Indonesia

ABSTRACT

Cempedak (Artocarpus integer (Thunb.) Merr.) is a plant with the genus Artocarpus that grows in Kalimantan and has properties as antimalarial, antidiabetic, abdominal pain and anticancer. This study aims to determine the specific and non-specific parameters of simplisia. The method used refers to the Indonesian Herbal Pharmacopoeia and General Standard Parameters of Extracts. Samples came from the South Kalimantan Province and Central Kalimantan Province. The results of the organoleptic test of simplisia are in the form of powder, light green in color, smelling typical of leaves and tasteless. Microscopic results show epidermis, sclerenchyma, xylem, phloem, air cavities, chlorophyll and stomata. The results of each test have a range, namely ethanol soluble juice content 17.80% - 25.40%, water soluble juice content 15.27% - 19.33%, total ash content 8.07% - 10.25%, acid insoluble ash content 2.32% - 3.82%, Pb metal contamination <0.001 - 0.004 mg/kg and Cd 0.160 - 0.178 mg/kg. A. integer leaf simplisia contains alkaloid, flavonoid, saponin, tannin, glycoside, phenolic and anthraquinone compounds which are confirmed on the KLT profile with the same compound content. Total phenol content was 18.88% - 20.29% b/w EAG. The test results of specific and non-specific parameters of A. integer leaf simplisia from two different places have met the requirements set by the Indonesian Herbal Pharmacopoeia and BPOM RI.

KEYWORDS: *Artocarpus integer,* Folin-Ciocalteu, Simplisia

ARTICLE DETAILS

Published On:
07 September 2023

Available on:
https://ijpbms.com/

INTRODUCTION

The World Health Organization (WHO) explains that 80% of the world's population use herbal medicine as their main health treatment (Alam & Mishra, 2017)[1]. Scientific research on medicinal plants with clinical trials and less standardized raw materials for traditional medicines is one of the reasons for the low utilization of medicinal plants used by the industry (Sutrisina, 2016) [2]. Cempedak (*Artocarpus integer* (Thunb.) Merr.) is one of Indonesia's native plants that grows abundantly, one of which is in the forests of Kalimantan with an altitude of about 1000 m above sea level (Agus *et al.*, 2014)[3]. Cempedak leaf are widely used by the people of South Kalimantan Province and Central Kalimantan Province as traditional medicine. Empirically, cempedak leaf are used as antimalarial, antidiabetic, stomach pain and anticancer (Rizki *et al.*, 2021) [4].

The raw materials of Traditional medicine must be guaranteed for efficacy and safety that meet the quality standards of medicinal products and ingredients (Sutomo *et al.*, 2021) [5]. WHO explained that standardization is important because the process involves physicochemical evaluation of medicinal raw materials such as the selection and manufacture of raw materials, safety assessment, efficacy and stability maintenance (Kunle *et al.*, 2012)[6]. There are two quality parameters of simplisia and extracts, specific parameters and non-specific parameters (Wigati & Rahardian, 2018)[7]. Specific parameters aim at qualitative aspects of the content of chemical compounds and quantitative aspects of the levels of chemical compounds that directly responsible for their pharmacological activity (Husni *et al.*, 2020)[8]. Non-specific parameters aim to have consistent safety and good efficacy for consumers by maintaining the compound content, safety and stability of the extract (Sutomo *et al.*, 2017) [9].

MATERIAL AND METHOD

A. The production of cempedak *A. integer* (Thunb.) Merr. leaf simplisia powder

The leaf of *A. integer* were determined at Kebun Raya Banua, Banjarbaru, South Kalimantan. Fresh leaf of *A. integer* (Thunb.) Merr. which have been collected were then wet sorted to separate impurities or foreign materials contained in the leaf, then knitted to facilitate the drying process. The leaf of A. integer were dried at 50ºC until the dry simplisia results were obtained and then powdered with a blender and mashed with a sieve no. 20. The results of the simplisia powder obtained were then weighed (Depkes RI, 2008) [10].

B. The determination of simplisia specific parameters

1. Organoleptic

Organoleptic examination of simplicia includes shape, color, smell and taste(Kotagiri *et al*., 2021) [11].

2. Microscopic test

This microscopic test was carried out using 10x magnification (Handayani *et al*., 2018) [12].

3. Ethanol and water soluble contents

The simplisia weighed as much as 5 g. Extraction using 96% ethanol solvent and 100 mL saturated chloroform solvent respectively then left for 18 hours. The filtrate was filtered quickly, Filtrate was taken as much as 20 mL and evaporated to dry at 105ºC until a fixed weight is obtained, then the percentage to the initial powder weight %b/b is calculate (Depkes RI, 2008) [10].

5. Phytochemical screening

The phytochemical screening carried out included Phenolic identification (Ulfah *et al*., 2020)[13], Flavonoid identification (Depkes RI, 2008)[10], Alkaloid, Steroid and tannin identification (Riduana *et al*., 2021)[14], Saponin identification (Indriyanti *et al*., 2018) [15].

6. Chromatogram pattern

The sample were dripped into the GF_{254} TLC plate and eluted using the mobile phase n-hexane : ethyl acetate with a ratio of 4:6 (v/v) and 3:7 (v/v) respectively. UV lamps of 254 and 366 nm were used for spot observation (Arifin *et al*., 2006) [16].

7. The determination of total phenol content

1 mL of gallic acid with concentrations of 10 ppm, 20 ppm, 30 ppm, 40 ppm, 50 ppm and samples with a concentration of 100 ppm. The solution was reacted with 2.5 mL of 5% Folin-Ciocalteau reagent, then allowed to stand for 3 minutes, added 2 mL of 1 M Na_2CO_3 and shaken until homogeneous, then allowed to stand for the operating time. The absorbance of the test solution was measured using the maximum wavelength obtained. Measure with uv visible spectrophotometry instrument (Marsella, 2018 [17]; Sami *et al*., 2020 [18]) .

C. The determination of simplisia non-specific parameters

1. Drying shrinkage

The leaf simplisia of *A. integer* (Thunb.) Merr. 1 g was weighed and put into a covered porcelain crucible which had previously been tarred and heated at 105ºC for 30 minutes. The simplicia in the crucible is flattened and put in the oven. Open the lid on the crucible and heat it with an oven temperature of 105ºC until a constant weight is obtained (Depkes RI, 2008) [10].

2. Total ash content and acid-insoluble ash content

Simplisia was weighed as much as 2 g, then put into a silicate crucible. Heat to 800ºC, cool and weigh. For acid insoluble ash content, the ash obtained was boiled using 25 mL of HCl for 5 minutes. The ash was collected and filtered with ash-free filter paper, then washed with hot water. Ashing was carried out in a crucible to a fixed weight. Calculated as follows: Total ash content = $\frac{W2-W0}{W1}$ x 100%

Explanation :
W0=the weight of empty crucible (g)
W1=the weight of early simplisia (g)
W2=weight of crucible +the ash of simplisia (g)
(Erawati & Fernando, 2018) [19]

3. Pb and Cd metal contamination

Pb and Cd levels were analyzed by weighing a sample of 50 mg and ignited in a furnace at 450ºC for 18 hours. The ash that has been obtained, then cooled and added with 5 mL of HCl, then evaporated. The evaporated sample was added with HNO_3 0.1 M as much as 1 mL, then put the test solution into a 5 mL measuring flask and added HNO_3 0.1 M until the limit mark (Rizki, 2020) [20]. Analysis of sample solutions and standard curves using *Atomic Absorption Spectroscopy* (AAS) with wavelengths of 271.0 nm and 288.8 nm to analyze Pb and Cd, respectively (Hanwar *et al*., 2017) [21].

RESULT

A. The specific parameters of simplisia

Determination result of simplisia specific parameters

Table 1. Determination results of simplisia specific parameters

Region	Simplisia yield	Organoleptic	Microscopic test	Ethanol soluble content ± SD (%)	Water soluble content ± SD (%)	Phenol content Mean (%b/b EAG) ± SD
South Kalimantan Province	42 ± 0,42	Powder, light green in color,	Upper epidermal cells, sclerenchyma, xylem, phloem, air cavities, lower	17,80 ± 0,17	15,27 ± 0,25	18,88 ± 0,78

		smelling typical of leaf, and tasteless	epidermis, chlorophyll and stomata			
Central Kalimantan Province	40,59 ± 0,81	Powder, light green in color, smelling typical of leaf, and tasteless	Upper epidermal cells, sclerenchyma, xylem, phloem, air cavities, lower epidermis.	25,40 ± 0,44	19,33 ± 0,21	20,29 ± 0,32

Phytochemical screening

Phytochemical screening results showed that both samples contained flavonoids, alkaloids, saponins, tannins, glycosides, phenolics and anthraquinones.The results of phytochemical screening from the two different places showed the same phytochemical compound content or no difference in compound content from the two places.

Chromatogram pattern

Table 2. Determination results of chromatogram pattern

Mobile phase	n-hexane : ethyl acetate (3:7) v/v at UV lamp 254 nm		n-hexane : ethyl acetate (3:7) v/v on the H_2SO_4 spot viewer		phase n-hexane : ethyl acetate (4:6) v/v at UV lamp 254 nm.		n-hexane : ethyl acetate (4:6) v/v on the H_2SO_4 spot viewer	
Sample	1	2	1	2	1	2	1	2
Spot1	Rf_1=0,22	Rf_1=0,24	Rf_1=0,22	Rf_1=0,24	Rf_1=0,18	Rf_1=0,18	Rf_1=0,18	Rf_1=0,18
Spot2	Rf_2=0,31	Rf_2=0,31	Rf_2=0,31	Rf_2=0,31	Rf_2=0,35	Rf_2=0,36	Rf_2=0,35	Rf_2=0,36
Spot3	Rf_3=0,85	Rf_3=0,87	Rf_3=0,85	Rf_3=0,87	Rf_3=0,85	Rf_3=0,87	Rf_3=0,80	Rf_3=0,80

1 : South Kalimantan Province; 2: Central Kalimantan Province

B. The non-specific parameters of simplisia

Table 3. The determination result of non-specific parameters

Sample	Drying shrinkage	Total ash content	The acid-insoluble ash content	Heavy metal	
	Mean ± SD (%)	Mean ± SD (%)	Mean ± SD (%)	Pb(mg/kg)	Cd(mg/kg)
1.	4,10 ± 0,20	8,07 ± 0,06	3,82% ± 0,13	<0,001	0,160
2.	5,07 ± 0,23	10,25 ± 0,13	2,32% ± 0,08	0,004	0,178

1 : South Kalimantan Province; 2: Central Kalimantan Province

DISCUSSION

The determination results stated that the specimen of the plant was a Cempedak plant (*Artocarpus integer* (Thunb.) Merr.) from the Moraceae family and the genus Artocarpus with specimen number 050/27-LIT/KRB.

A. The specific parameters of simplisia

The results of transversal microscopic tests showed that both samples have the same results, there are upper epidermal cells, sclerenchyma, xylem, phloem, air cavities and lower epidermis. The epidermis is the outermost tissue that has a function in protecting the tissue from the external environment located below. Sclerenchyma function is to strengthen plant tissue (Rohmawati *et al.*, 2022) [22]. Xylem can transport water and minerals from the roots to the leaf. Phloem is a vascular network that transports photosynthetic products from the leaf to the rest of the plant (Nurza, 2019) [23].

The results of the longitudinal section microscopic test showed that both samples had the same results, the presence of epidermal cells, chlorophyll and stomata. The type of stomata present in the *A. integer* (Thunb.) Merr. leaf sample is the anisocytic type. Anisocytic stomata type is a type of stomata found in the Moraceae family (Advinda, 2018[24]; Utami *et al*., 2018[25]).

The requirement for ethanol soluble content is more than 6.7% (Depkes RI, 2008)[10], it can be concluded that the ethanol soluble content of *A. integer* (Thunb.) Merr. leaf met the requirements (Sadik & Anwar, 2022) [26]. According to Maryam *et al* (2020), the sum of the ethanol and water soluble content should not exceed 100%, it can be concluded that the sum of the ethanol and water soluble content has met the requirements.The results showed that leaf samples contain more semi-polar - non-polar chemical compounds that are soluble in ethanol solvents than polar chemical compounds that are soluble in water solvents (Maryam *et al*., 2020) [27].

Chemical compounds that are suspected to be dissolved in polar solvents are tannins, saponins, quaternary alkaloids, carotenoids, amino acids and sugars. Chemical compounds that are suspected to be soluble in semi-polar - non-polar solvents are alkaloids, terpenoids, phenolics, aglycones, glycosides, lipids, volatile oils and waxes (Khotimah, 2016)[28]. Phytochemical screening results showed that both samples contained flavonoids, alkaloids, saponins, tannins, glycosides, phenolics and anthraquinones.The results of phytochemical screening from the two different places

showed the same phytochemical compound content or no difference in compound content from the two places.

The results of the chromatogram pattern on the plate show Rf values that are not much different indicating that the two samples have almost the same chromatogram profile and qualitatively show the chemical compounds contained in the sample. The resulting chromatogram profile confirms the results of phytochemical screening previously carried out that both samples contain the same chemical compounds (Maryam *et al*., 2020)[27].

Determination of total phenol content the results of the operating time at 45 minutes are similar to the results of research by Candra *et al.*, 2021.The standard curve equation of gallic acid obtained in this study is y = 0.028x + 0.127 with a correlation coefficient (r) value of 0.997. It is concluded that this value can be used for the determination of total phenolic content (Yulianis *et al*., 2020[29]; Suharyanto & Prima, 2020[30]).

Testing data on total phenol levels using *independent samples T-test* on spss got a sig value. (2-tailed) of 0.044 which means there is a significant difference between the total phenol content of South Kalimantan Province and Central Kalimantan Province. Factors that can affect the results of total phenol content in extracts are the growing environment, altitude, air humidity, temperature, pH, light intensity, nutrients and soil quality where plants grew. These factors greatly affect the content of compounds contained in plant samples, one of which is phenolic compounds (Bata *et al.*, 2018) [31]. South Kalimantan Province when viewed from the state of the place is in a garden far from where people live with an average temperature around 18.1ºC - 33.3ºC and humidity of 72% - 94%, while Central Kalimantan Province is close to where people live or settlements with an average temperature around 26.8ºC and humidity of 86%. (BPS, 2018[32]; BPS, 2019[33]).

B. The non-specific parameters of simplisia

The requirement for drying shrinkage value in simplisia is that it should not be more than 10% (BPOM, 2014) [34], the smaller the water content reduces the possibility of simplisia being overgrown by mold. Chemical compounds that may be lost during the sample drying process are essential oils, volatile compounds and water. (Sutomo *et al*., 2021) [5].

The requirement for total ash content according to the applicable standard parameters is no more than 16.6%, so it can be concluded that the total ash content of *A. integer* (Thunb.) Merr. leaf simplisia powder has met the requirements (Hidayati *et al.*, 2018) [35], the higher the ash content obtained, the higher the content of inorganic compounds (minerals) in the sample, the smaller the total ash content value, the better the purity (Arimpi & Pandia, 2019)[36]. The difference in results is influenced by the place where the plants grew, soil conditions and contamination from impurities (Rizki, 2020)[20]. The value of acid insoluble ash content illustrated the level of contamination of minerals or metals that are insoluble in acid, the smaller the value of acid insoluble ash content, the lower the level of contamination (Erjon *et al*., 2017)[37]

Based on the Limitation of metal contamination data, according to the Head of the Food and Drug Administration Regulation No. 12 of 2014 concerning Quality Requirements for Traditional Medicines is not more than 10 mg / kg for Pb and is not more than 3 mg / kg for Cd, so it can be concluded that both samples have met the requirements set (Rizki, 2020) [20]. The difference in results is due to the different places where the plants grew. The place where *A. integer* plants grew in Central Kalimantan Province is close to settlements or people's homes while the place where *A. integer* plants grew in South Kalimantan Province is in a garden far from people's homes. Lead metal (Pb) can come from dust and polluted air (Kusuma & Andriani, 2019) [38]. Pollution from vehicle gases is one of the causes of Pb metal contamination because as much as 70% of the lead (Pb) contained in gasoline will be released through vehicle's exhaust in the form of emissions used by local residents (Yulius & Afdal, 2014) [39]. Cd metal can come from industrial waste, agricultural waste or household waste. Cadmium (Cd) metal from agricultural waste can come from the use of inorganic phosphate fertilizers or pesticides (Sutrisno & Kuntyastuti, 2015)[40]. Cd metal contaminates plants, one of which is through water which will be absorbed by plant roots (Munadi & Hamid, 2022) [41]. Pb and Cd metal contaminants are toxic with a long half-life when exposed to humans (Kusuma & Andriani, 2019[38]; Ikhsan *et al*., 2020[42]) .

CONCLUSION

Test results of specific parameters and non-specific of of *A. integer* (Thunb.) Merr. leaf simplisia met the standard requirements.

ACKNOWLEDGMENT

We would like to thank Lambung Mangkurat University for funding this research through the mandatory lecturer program from LPPM (Institute for Research and Community Service).

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