Indonesian Journal of Pharmaceutics
IdJP
ISSN : 2597-8748

Vol 4, Issue 3, 2023 (276-285)
http://journal.unpad.ac.id/idjp

Tableting Turmeric Rhizome (Curcuma domestica Val.) and Mangosteen Peel (Garcinia mangostana L.) Extract as Antioxidant Supplement

Amalia Reyhani, Sriwidodo Sriwidodo*, Anis Yohana Chaerunisa, Abd. Kakhar Umar, Evi Sylvia Nurrasjid, Mas Rahman Roestan

Department of Pharmaceutics and Pharmaceutical Technology, Faculty of Pharmacy, Universitas Padjadjaran, Sumedang 45363, Indonesia.

Submitted : 02/06/2022, Revised : 03/08/2022,, Accepted : 08/06/ 2023, Published : 16/08/2023

Abstract

Free radicals are unstable molecules that lose electrons in their outer orbitals. These compounds can be toxins for the human body and cause various degenerative diseases. To avoid this, we need antioxidants. Examples of common sources of antioxidants are turmeric (Curcuma domestica Val.) and mangosteen rind (Garcinia mangostana L.). Both of these plants have very strong antioxidant activity but have a less favorable taste for consumption. This study aimed to obtain tablets containing turmeric rhizome and mangosteen rind extract that can cover the taste with a variety of binders. Subsequently, we observed the antioxidant activity of two extracts before and after preparation. The tableting method was wet granulation and the characterization included the physical properties of the tablets. The levels of curcumin, alpha mangosteen, and total polyphenols were also checked. The antioxidant activity was measured using the DPPH method. Based on the characterization results, NaCMC 5% was the best binder for preparing tablets containing turmeric rhizome and mangosteen rind extract with a flow rate of 11.434 g/s, repose's angle of 29.39^{o}, loss on drying of 2.65%, carr's index of 15.22, hardness of 43N, friability of 0.926%, and disintegration time of 16.44 minutes. The antioxidant test result showed that the combination of turmeric extract and mangosteen rind extract with a ratio of 1:2 had the best antioxidant activity with an IC_{50} value of 31.01 µg/ml, alpha mangosteen level of 29.77%, and curcumin level of 27.22%. The antioxidant activity of the preparation was not changed significantly after tableting. Based on the findings, it can be concluded that the tablet formulation of turmeric rhizome and mangosteen rind extract using 5% NaCMC can be potentially used as an antioxidant supplement.

Keywords: Free radicals, Antioxidants, Turmeric Rhizome, Mangosteen rind, Tablets.

*Corresponding author,
e-mail : sriwidodo@unpad.ac.id (S. Sriwidodo)

https://doi.org/10.24198/idjp.v4i3.39667

1. Introduction

Free radicals are highly reactive chemical molecules and are said to be the cause of premature aging, cancer, liver, lung, kidney, rheumatism, diabetes, cataracts, and narrowing of blood vessels or atherosclerosis. Free radicals are relatively unstable molecules because atoms in their outer orbits have one or more unpaired electrons and are destructive or damaging to other cells (Khaira, 2010). To counteract free radicals, an antioxidant is needed to inhibit the oxidation. Antioxidants donate one or more electrons so that the radical compound will become stable, and unreactive, and break the chain reaction (Kosasih et al., 2004).

One of the highest antioxidant sources is turmeric. The active substances contained in turmeric are 3-5% essential oils which include curcumin, bisdemethoxycurcumin, desmethoxy curcumin, sesquiterpenes and monoterpenes of essential oils such as ar-turmerone (31.1%), arcurcumin (63%), kurlon (10, 6%), and turmerone (10%), resin, starch, and cellulose. These various compounds are responsible for the ability of turmeric to provide anti-inflammatory, antimicrobial, antifungal, and antioxidant effects (Pranata, 2014). Mangosteen rind is also a well-known source of antioxidants. It contains xanthones which include mangosteen, alpha-mangosteen, mangostinon A and B, flavonoids, and mangosterol. These xanthones have high antioxidant activity (Rezki et al., 2017).

The combination of two or more types of antioxidants allows it to produce higher antioxidant activity (Wicaksono & Ulfah, 2017). The combination of plants to increase their antioxidant potential has been carried out by several studies, but so far there is no reported study on the antioxidant effectivity of turmeric rhizome and mangosteen rind extract combination in tablets form. In addition, the combination of these two extracts can produce higher activity at lower doses. Extracts of turmeric rhizome and mangosteen rind have a bitter taste and are rarely ingested raw, so in this study, we formulate them into tablets. The tablets were optimized and characterized by studying the impact of several binders on their physicochemical properties including the antioxidant stability of the extracts during manufacturing.

2. Method

2.1 Materials

Turmeric rhizome (Curcuma domestica Val.) and mangosteen rind simplicia (Garcinia mangostana L.), 96% ethanol, toluene, ethyl acetate, formic acid (Merck), chloroform, methanol (Merck), amprotab (Bratachem), Na-CMC (Bratachem), Magnesium Stearate (Bratachem), PVP K30 (Quadran), Talcum, Starch (Bratachem), and Lactose (Bratachem).

2.2 Extraction of turmeric (Curcuma domestica Val.) and mangosteen (Garcinia mangostana L.)

The turmeric rhizome was extracted using 96% ethanol for 24 hours with a ratio of 1:10. After a day, the macerate and pulp were separated. The macerate was filtered and the volume was calculated. The dregs obtained were then macerated 2 times using 96% ethanol as solvent. The mangosteen rind was extracted by maceration using 70% ethanol redest. 25 kg was weighed and put into the macerator then soaked using 70% ethanol redest for 1 hour, then allowed to stand for 4 x 24 hours while stirring occasionally. For every 24 hours, the macerate was collected and filtered using filter paper and the solvent was replaced with a new one. The filtrates of each extract were then evaporated using a rotary evaporator at 30 rpm and a temperature of <400C (Idawati, et al, 2019; Cahya & Prabowo, 2019).

2.3 Phytochemical screening of turmeric extract (Curcuma domestica Val.) and mangosteen extract (Garcinia mangostana L.)

The phytochemical screening was done including alkaloids, tannins, saponins, flavonoids, polyphenols, quinone,

monoterpene and sesquiterpene, steroid, and triterpenoid. Parameter examination of turmeric extract (Curcuma domestica Val.) and mangosteen extract (Garcinia mangostana L.) included organoleptic, drying shrinkage, water-soluble level, ethanol soluble level, total ash content, acid Insoluble Ash Content, and specific gravity.

2.4 Testing the antioxidant activity of turmeric extract (Curcuma domestica Val.), mangosteen extract (Garcinia mangostana L.), and tablet preparation

The antioxidant activity was measured using the DPPH method. Sample solutions as much as 0.01 mL; 0.02 mL; 0.03 mL; 0.04 mL and 0.05 mL and the standard solution (0.01 mL, 0.02 mL, 0.03 mL, and 0.04 mL) were added with 0.05 mL of 0.2 mL of DPPH solution. Ethanol (95%) was then added to the sample and standard solutions to reach a volume of 1 mL. The mixtures were homogenized and allowed to stand for 30 minutes in dark conditions and not exposed to direct light. The measurements were made for 6 replication. If the result was positive, the color of the solution would change from purple to yellow. The absorbance value was read at the maximum wavelength (λ), where the blank used was 1 mL ethanol without the addition of sample solution (Suryadi, 2013). Afterward, the %inhibition was calculated using the formula:

$$\%Inhibition = \frac{DPPH\ absorbance - sample\ absorbance}{DPPH\ absorbance}\ x\ 100\% \quad \text{(Eq. 1)}$$

The %inhibition value at various sample concentrations was used to make a linear regression equation with the extract concentration as the X axis and %inhibition as the Y axis. The IC_{50} value was obtained by inputting the 50% as the inhibition value to the equation (Suryadi, 2013).

2.5 Determination of total polyphenols of mangosteen and turmeric extract and tablet preparation

A total of 1 ml of the test solution and each variation in the concentration of the comparison solution were put into a test tube. Then 5 ml of aqueous Folin-Ciocalteau reagent was added (7.5% in water). After that, the solution mixture was allowed to stand for 8 minutes, and added 4 ml of 1% NaOH, incubated for 1 hour. The measurements were performed by using spectrophotometry at the maximum wavelength. Blank measurements were also carried out in the same way without the test solution. Finally, a calibration curve was made and the total phenol content was calculated (Depkes RI, 2017).

2.6 Determination of -mangostin content from mangosteen extract (Garcinia mangostana L.) and tablet preparation

The levels of α-mangostin in the extract were tested using HPLC. The separation was carried out at 25ºC on a Lichrocart column (5 m, 4 mm × 250 mm). This method used acetonitrile (solvent A) and 0.2% formic acid in water (solvent B). This method used a gradual linear gradient. The injection volume and flow rate were 20 L and 1 mL/min. UV wavelength was set at 240 nm. α-mangostin calibration curves were performed at different concentrations of 15, 30, 60, 120, and 240 g/mL. The absorbance was entered into a linear regression equation to calculate the levels of α-mangostin in the mangosteen rind extract (Ghasemzadeh et al., 2018).

2.7 Determination of curcumin content from turmeric extract (Curcuma domestica Val.) and tablet preparation

The curcuminoid level was measured using spectrophotometry. Preparation of the test solution was carried out by weighing 10 mg of extract and dissolving them in 10 ml of ethanol P. The filtered solution was put into a

10 ml volumetric flask and added ethanol P to the limit mark. The standard solution was made by weighing 10 mg of curcumin, put into a 10 ml volumetric flask, added by ethanol P to the mark, and then diluting to create 100, 60, 40, 20, 10, and 2 ppm of standard solution. The concentration measurement was carried out by pipetting separately 2 mL of the test solution, each series of standard solution, and blank solution into the microtube. The absorption of these preparations was observed at a wavelength of 420 nm (Depkes RI, 2008).

2.8 The combination tablet formulation of turmeric extract (Curcuma domestica Val.) and mangosteen extract (Garcinia mangostana L.)

Optimization was done by making 3 variations of the formula based on the type of binder. The binders used were Na CMC, PVP, and starch. The three binders are commonly used binders in tablet manufacturing and are considered to have good binding capacity to form granules. The procedure used for this optimization was the wet granulation method because this method can provide good stability and evenly distributed granules. The optimized formulas can be seen in Table 1.

Table 1. Formula optimization.

Component	F1 (%)	F2 (%)	F3 (%)	Function
Mangosteen extract	34.2	34.2	34.2	Active ingredient
Turmeric extract	17.11	17.11	17.11	Active ingredient
Amilum	5	5	5	Adsorbant
Amprotab	5	5	5	Disintegrant
Na CMC	5	-	-	Binder
PVP	-	5	-	Binder
Amilum paste	-	-	5	Binder
Mg stearate	2	2	2	Lubricant
Talk	2	2	2	Glidant
Lactose	Ad 100	Ad 100	Ad 100	Filler

2.9 Evaluation of granules and tablet preparations containing extracts of turmeric (Curcuma domestica Val.) and extracts of mangosteen (Garcinia mangostana L.)

Evaluation of the granules including LOD, flow test, angle of repose, and compressibility. Evaluation of the tablets including organoleptic, hardness test, size and weight uniformity, friability, and disintegration time.

3. Result

3.1 Extraction of turmeric (Curcuma domestica Val.) and mangosteen (Garcinia mangostana L.)

Based on the calculation, the yield percentage of each extract was high (>10%). Mangosteen rind extract has a yield of 14.3% while turmeric rhizome extract has a yield of 12.16%.

3.2 Phytochemical screening of turmeric extract (Curcuma domestica Val.) and mangosteen extract (Garcinia mangostana L.)

The secondary metabolite content of each extract was quite varied. Turmeric rhizome extract contains all tested metabolites except steroids. Meanwhile, mangosteen rind extract does not contain terpenes, triterpenoids, and steroids. The metabolite content of each extract can be seen in Table 2.

Table 2. Secondary metabolites of turmeric rhizome and mangosteen rind.

Metabolites	Turmeric rhizome	Mangosteen rind
Alkaloid	+	+
Polyphenol	+	+
Tannin	+	+
Flavonoid	+	+
Monoterpene dan sesquiterpene	+	-
Steroid	-	-
Triterpenoid	+	-
Quinone	+	+
Saponin	+	+

3.3 Parameter examination of turmeric extract (Curcuma domestica Val.) and mangosteen extract (Garcinia mangostana L.)

Based on standardization results, turmeric rhizome, and mangosteen rind extract are very safe for consumption or use as medicine. Specific and non-specific parameters indicate values below the allowable limit. The standardization results for the two extracts can be seen in Tables 3 and 4.

Table 3. Standardization results of turmeric rhizome extract.

Parameter	Results	Requirements
Organoleptic	Thick, yellow in color, and has a characteristic smell	Thick extract; yellow; characteristic odor; slightly bitter taste.
Yield	14,3%	> 11,0%
Drying shrinkage	9,84%	< 10%
Total ash content	0,28%	< 0,4%
Acid insoluble ash content	0,08%	< 0,1%
Water content	8,2%	< 10%
Specific gravity	0,879%	< 1%

Table 4. Standardization results of mangosteen rind extract.

Parameter	Results	Requirements
Organoleptic	Thick, brown in color, smells and tastes slightly bitter	
Yield	12,60%	> 8,2%
Drying shrinkage	8,49%	<10%
Total ash content	0,244%	< 4,4%
Acid Insoluble Ash Content,	0,069%	< 0,2%
Specific gravity	0,81%	<1%
Water content	7,83%	< 10,8%

3.4 Curcumin content from turmeric extract (Curcuma domestica Val.) and tablet preparation

The linear equation of standard curcumin can be seen in Figure 1. From the linear equation, the curcumin content in the turmeric rhizome extract was calculated and the curcumin content was 27.22%. These results meet the requirements for the level of curcumin contained in turmeric extract in the Indonesian Herbal Pharmacopoeia, which is not less than 3.82%.

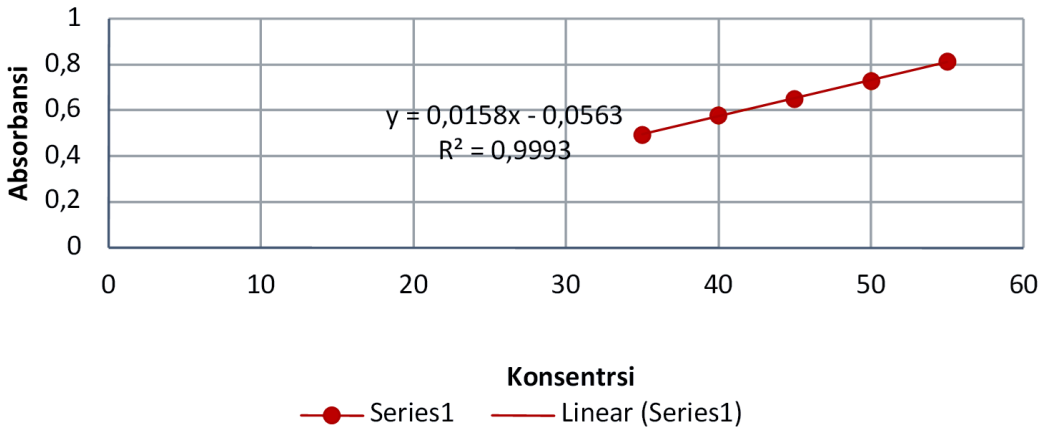

Figure 1. Standard curve of turmeric extract.

3.5 Alpha mangosteen content from mangosteen extract (Garcinia mangostana L.) and tablet preparation

The linear equation of the standard alpha-mangosteen can be seen in Figure 2. From this test, a standard curve was obtained to get a linear equation that would be used to calculate the levels of alpha-mangosteen in the extract. The concentration variation was then plotted with the AUC (Area Under Curve) in a curve, where the x value was the concentration variation and y was the AUC value. The observation was performed at a wavelength of 318 nm.

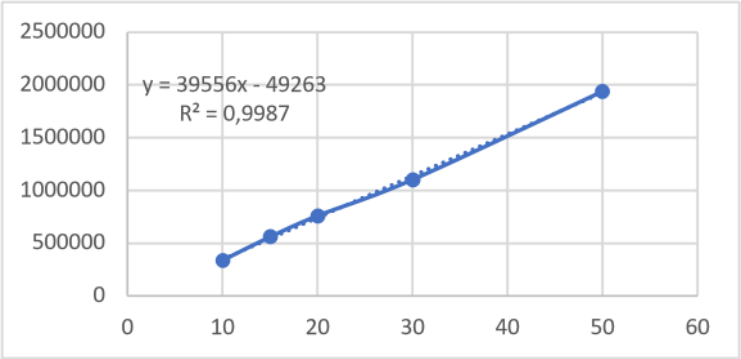

Figure 2. Standard curve of alpha mangosteen.

Based on the test result, the level of alpha-mangosteen in the mangosteen rind extract was 29.766%, where the content met the requirements in the Indonesian herbal pharmacopeia (not less than 10.60%).

3.6 Evaluation of Combination Tablets of Turmeric Rhizome Extract and Mangosteen Peel Extract

3.6.1 Granules Evaluation

Based on the evaluation results, the formula containing 5% Na-CMC has good physical properties with a loss on drying value of 2.65%, flowability of 11.434%, repose's angle of 29.39°, and carr's index of 15.217. This value indicates that the tablet has good flowability and compressibility (<30° and >15). The value of a loss on drying, flowability, angle of repose, and Carr's index of each formula can be seen in Figure 3.

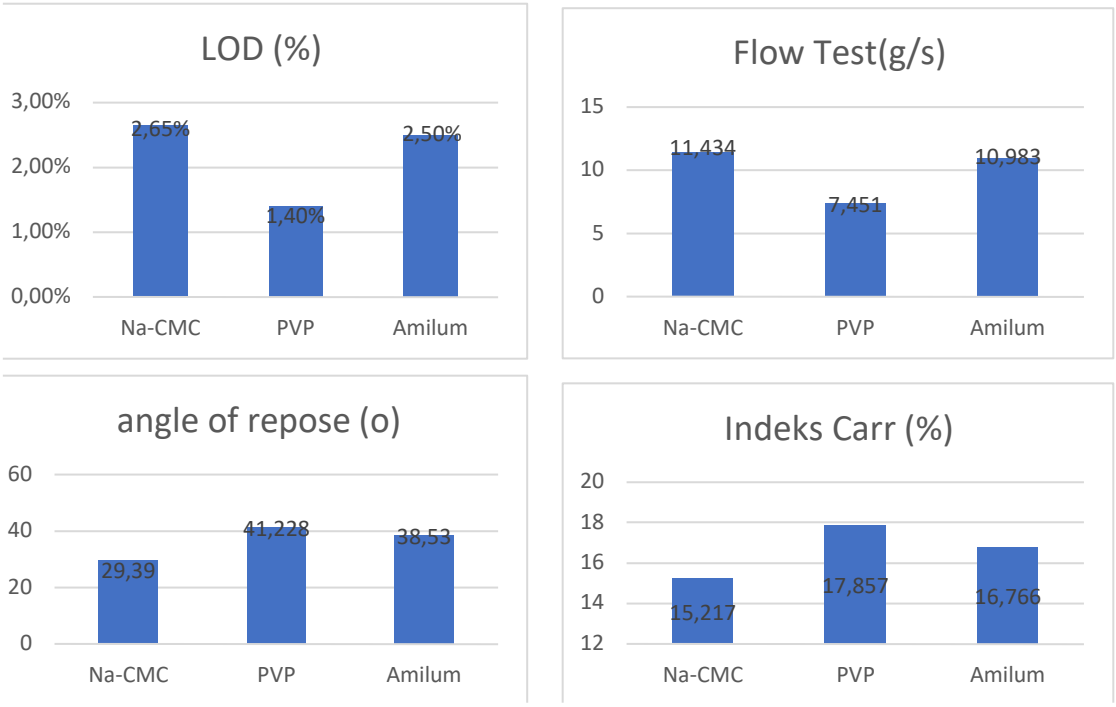

Figure 3. Loss on drying, flowability, angle of repose, and index carr properties of the tablets.

3.6.2 Tablet Evaluation

The tablets of all formulas have the same color, which was yellowish brown with shiny characteristics. The uniform color was only found in formulas using Na-CMC as a binder. Na-CMC also managed to maintain a round tablet shape and prevent cracking and brittleness. The thickness and diameter of the tablet can be seen in Figure 4.

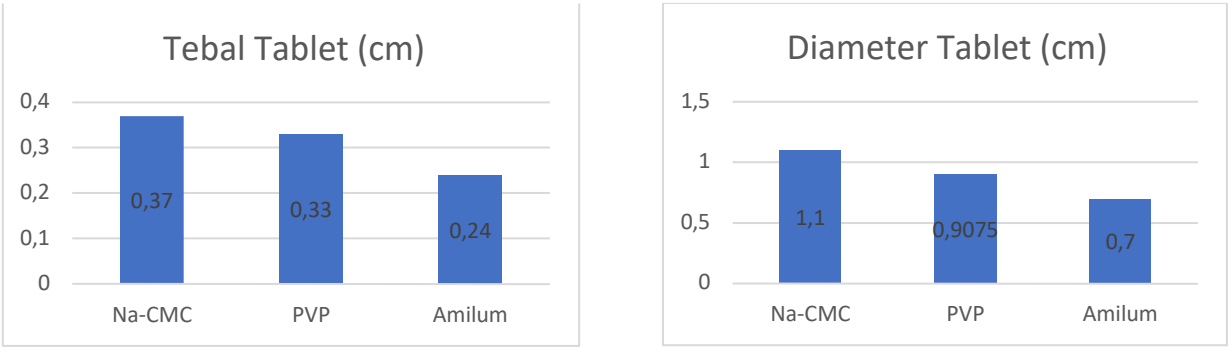

Figure 4. Thickness and diameter of the tablets.

Good hardness, uniformity of weight, friability, and disintegration time were owned by tablets containing Na-CMC as a binder. Tablets with PVP as a binder had the worst characteristics. The low hardness and friability made the tablets brittle. The physical properties of each formula can be seen in Figure 5.

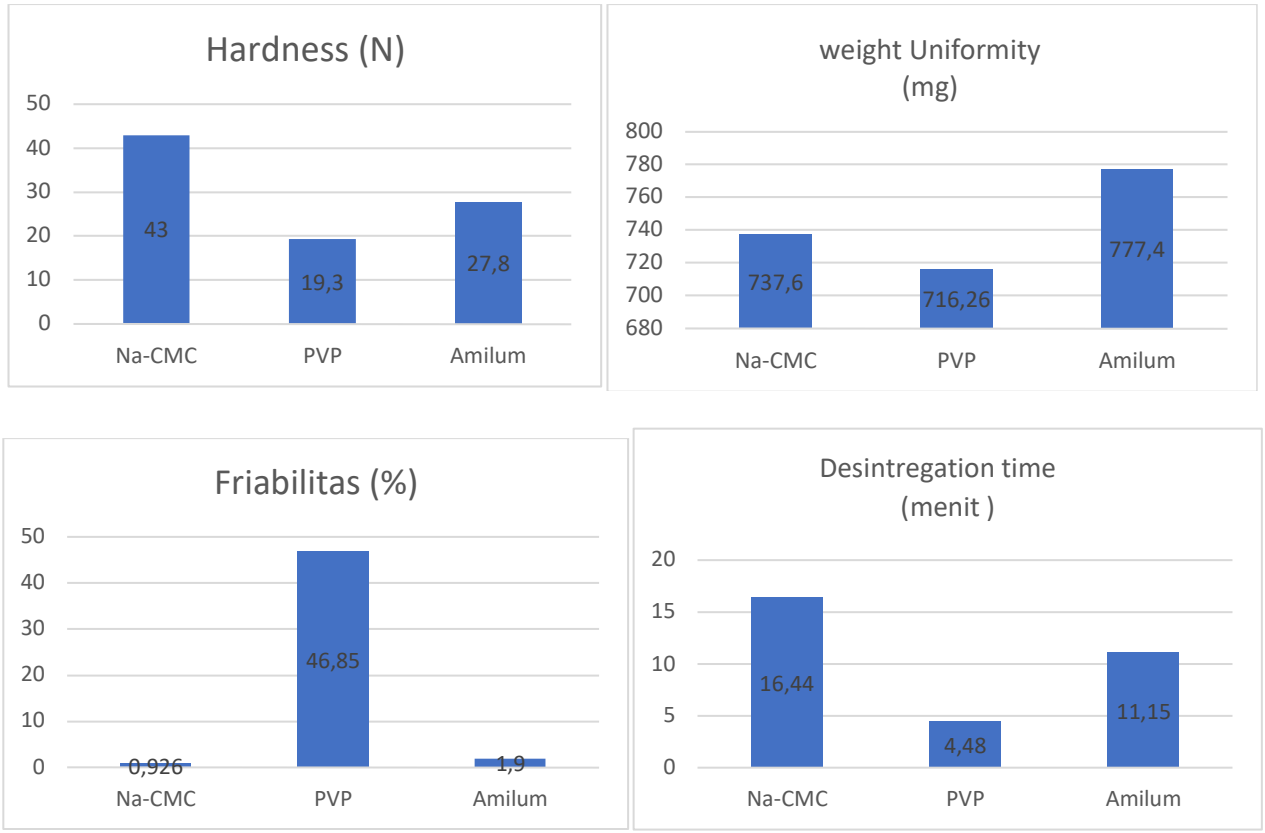

Figure 5. Hardness, weight uniformity, friability, and disintegration time of the tablets.

3.7 Antioxidant activity of turmeric extract (Curcuma domestica Val.), mangosteen extract (Garcinia mangostana L.), and tablet preparation

Based on the measurement results, the IC_{50} values of the two extracts and their tablet form were classified as strong antioxidants. The IC_{50} value of each sample can be seen in Table 5.

Table 5. IC_{50} value of the samples.

Sample	IC_{50} (µg/ml)
Ascorbic acid	1.81
Turmeric rhizome extract	37.551
Mangosteen rind extract	34.298
Combination of turmeric and mangosteen extract	31.01
Turmeric rhizome extract tablet	53.4
Mangosteen rind extract tablet	47.17
Combination of turmeric rhizome and mangosteen rind extract tablet	41.23

3.8 Total polyphenols of the extracts and tablets

The total phenolic content of each extract showed a decrease in levels after being made into tablets. However, when combined

into one tablet, the IC_{50} value is higher than the single tablet form. The total phenolic content of each sample can be seen in Table 6.

Table 6. Polyphenols content of the samples.

Sample	Content (%)
Tumeric rhizome extract	30.99
Mangosteen rind extract	39.87
Turmeric rhizome extract tablet	23.68
Mangosteen rind extract tablet	34.736
Combination of turmeric and mangosteen extract Tablet	37.84

4. Discussion

Based on the test, all parameters and physicochemical screening for both of the extracts are already following the requirements. Likewise, the curcumin, alpha-mangosteen, and total polyphenols were in the range of the requirements.

The method used for making the tablet was wet granulation. The optimization was carried out to see which binder gives the best tablet properties. Three binders were compared, including Na-CMC, PVP, and starch. Based on the test results, Na-CMC was the only binder that fits all ranges of requirements, while the other two binders produced brittle tablets. The chemical evaluations revealed that the tablets contained 37.84% total polyphenols, this value was greater than the total polyphenols in the tablet of each extract. The IC_{50} test was also carried out. The smaller the value, the stronger the antioxidant activity. If the IC_{50} value is below 50 g/ml, it belongs to the very strong antioxidants. The IC_{50} value of the α-mangostin extract tablet was 53.4 g/ml and the IC_{50} value of the turmeric extract tablet was 47.17 g/ml. The tablet containing these two extracts had a lower IC_{50} value which was 41.23 g/ml. Based on the findings, tablets containing both extracts had the greatest antioxidant activity compared to their single dosage form. When compared to the extract's IC_{50} value, the tablet form has a higher value. However, this value was not significantly different. The increase can occur due to several factors, including the unstable nature of mangosteen at temperatures above 40^{o}C due to the manufacturing method used was wet granulation and there was a heating stage. Besides, the time between extract testing and tablet preparation was fairly far enough away, so that during storage there might be a degradation.

5. Conclusion

Tablets containing turmeric rhizome and mangosteen rind extract with strong antioxidant activity have been successfully obtained through wet granulation using Na-CMC as a binder. The combination of these two extracts has the optimal effectivity at the ratio of 1:2. There was an increase in the IC_{50} value of the extracts after the tableting process. The heating process in the wet granulation process might affect the antioxidant stability of the extracts. However, the differences were not significant and the IC_{50} value of the tablets was still within the very strong range category. Based on the findings, it can be concluded that the tablet formulation of turmeric rhizome and mangosteen rind extract using 5% NaCMC is potentially used as an antioxidant supplement.

6. Acknowledgments

This work was supported by research grants from the Ministry of Research and Technology/National Research and Innovation Agency (1827/UN6.3.1/LT/2020).

References

1. Cahya, D. and Prabowo, H. 2019. Standarisasi Spesifik Dan Non-Spesifik Simplisia Dan Ekstrak Etanol Rimpang Kunyit (Curcuma domestica Val.). Jurnal Farmasi Udayana.
2. Depkes RI. 2008. Farmakope Hebal Indonesia. Jakarta: Departemen Kesehatan Republik Indonesia
3. Depkes RI. 2017. Farmakope Hebal Indonesia Edisi II. Jakarta: Departemen Kesehatan Republik Indonesia
4. Ghasemzadeh, A., Jaafar, H. Z., Baghdadi, A., & Tayebi-Meigooni, A. 2018. Alpha-Mangostin-Rich Extracts from Mangosteen Pericarp: Optimization of Green
5. Extraction Protocol and Evaluation of Biological Activity. Molecules. 23, 1–16
6. Gloria Murtini, Y. E. 2018. Teknologi Sediaan Solid, Kementrian Kesehatan Republik Indonesia.
7. Idawati, S., Hakim, A., & Andayani, Y. 2019. Pengaruh Metode Isolasi a- mangostin dari Kulit Buah Manggis (Garcinia mangostana L.) terhadap Rendemen α-mangostin. Jurnal Penelitian Pendidikan IPA (JPPIPA). 5(2), 144–148.
8. Kosasih, E., Setiabudhi, T., & Heryanto, H. (2004). Peranan Antioksidan pada Lanjut Usia. Pusat Kajian Nasional Masalah Lanjut Usia.
9. Melannisa, R., Da'I, M., & Rahmi, T. R. 2011. Uji Aktivitas Penangkap Radikal Bebas dan Penetapan Kadar Fenolik Total Ekstrak Etanol Tiga Rimpang Genus Curcuma dan Rimpang Temu Kunci. Pharmacon. 12(1): 40-43.
10. Rezki, A. P., Gonggo, S. T., & Sabang, S. M. 2017. Analisis Kadar Flavonoid dan Fenolat Pada Kulit Buah Manggis (Garcininia mangostanaL.). Journal Akademika Kimia. 6(4), 196–199.
11. Suryadi N.S, J. 2013. Daya Antioksidan Ekstrak Etanol Kulit Buah Manggis (Garcinia mangostana L.) Pengeringan Matahari Langsung dan Freeze Drying. Jurnal Ilmiah Mahasiswa Universitas Surabaya. 2(1), 1–19.
12. Weecharangsan, W., Opanasopit, P., Sukma, M., Ngawhirunpat, T., Sotanaphun, U., & Siripong, P. (2006). Antioxidative and neuroprotective activities of extracts from the fruit hull of mangosteen (Garcinia mangostana Linn.). Med Princ Pract, 15(4), 281– 287.
13. Wicaksono, I., & Ulfah, M. 2017. Aktivitas Antioksidan Kombinasi Ekstrak Etanol Daun Sirsak (Annona muricata L.) dan Daun Jambu Biji (Psidium guajava L.) dengan Metode DPPH (2,2-difenil-1-pikrilhidrazil). Inovasi Teknik Kimia. 2(1), 44-48.