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Instant Granules of Mangosteen Peel (Garcinia Mangostana L.) Ethanol Extract as Antioxidants

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Abstract: Free radicals in the air can trigger dangerous diseases, such as cancer and premature aging. To avoid this, antioxidant compounds are needed to donate electrons to free radicals, causing them to become more stable. A powerful antioxidant can be found in nature, including the mangosteen peel. This study aimed to find the best instant granule preparation formula from mangosteen peel extract (MPE) that can be practically consumed and the antioxidant stability during preparation. The wet granulation method was used to make instant granules, which have four formulas with varying amounts of xanthan gum as a suspending agent and maltodextrin as a solubility enhancer. The antioxidant activity was examined using the DPPH method. Based on the findings, formula 4 had the best properties with a drying shrinkage of 1.80%, a flow rate of 11.54 ± 1.56 g/s, repose's angle of 29.112 ± 0.45°, carr index of 14.043 ± 1.9%, and dispersion rate of 0.164 g/s. There is no residue in the solution. The shape and taste of this formula were most acceptable. The antioxidant activity of the extract and instant granules was not significantly different, with the IC50 of 34.64 µg/ml and 44.12 µg/ml, respectively. Based on the test result, it can be concluded that formula 4 with a concentration of xanthan gum 1% and 20% maltodextrin is a potent antioxidant supplement.

Introduction

Pollution and free radicals can both be harmful to the body. To deal with free radical-caused cell damage, an antioxidant is required, inhibiting oxidation by giving one or more electrons, making the substance more stable (1). The peel of the mangosteen fruit is one of the most plentiful sources of natural antioxidants, and Indonesia is one of the biggest producers of mangosteen (2, 3). Xanthones are the most potent antioxidant in mangosteen peel (4-5). The harsh flavor of the mangosteen rind, on the other hand, makes it less pleasant, and it is rarely consumed raw. The antioxidant chemicals it contains are also poorly soluble. It has been claimed that processing in the dosage form, including granules, can compensate for this shortage (6, 7).

Granulation is making granular material by developing grains or granules from a powdered or solid substance. The granulation procedure of the extracted material can boost solubility while masking the extract's disagreeable flavor (8, 9). The use of appropriate polymers facilitates this. Because of its high cohesive forces, xanthan is commonly utilized as a matrix in wet granulation techniques to sustain drug release (10). Aceclofenac was successfully administered to the colon in a targeted manner using xanthan gum-based tablets (11). According to a report, xanthan gum also generates a mixture with good physical properties that can be used in food formulas or supplements (12). With a gradual release, the tablet must disintegrate quickly to be absorbed and have an effect. Polymer combinations such as maltodextrin as the initial mixture with the extract might be used to address this issue. By employing maltodextrin as the main mixture, the solubility of sumac extract was reported to be dramatically enhanced from 3.5 percent to 25 percent (13). As a result, MPE's solubility and unpleasant taste were improved by producing it as instant granules with xanthan gum as a suspending agent and release-regulating matrix, and maltodextrin as a solubility enhancer. MPE's antioxidant stability during the preparation procedure was also assessed (8, 9).

Experimental Section

Tools

Analytical balance (Mettler Toledo), TLC plate GF254, Pycnometer (Pyrex), Moisture balance (OHAUS MB35), flow rate and angle of repose measuring device (ERWEKA GT), UV lamp 254 and 366 nm, water bath (Memmert), oven (Memmert), pH meter (Metler Toledo), rotary evaporator (BUCHI Rotavapor R-300), UV Spectrophotometer (TECAN M200 pro), HPLC Column (LiChroCART) and beaker (PYREX).

Ingredients

Mangosteen peel powder (*Garcinia mangostana* L.), 70% ethanol, toluene, ethyl acetate, chloroform, methanol (Merck), hydrochloric acid (HCl), aquadest, ammonia, amyl alcohol, ether, potassium hydroxide, gelatin solution, n-Hexane, Mayer's reagent, Dragendorf's reagent, Lieberman Buchard's reagent, Folin Ciocalteu's reagent, DPPH, NaOH and iron (III) chloride reagent. The formulation materials used are citric acid (PT.DWILAB), sodium citrate (PT.DWILAB), xanthan gum (PT.DWILAB), PVP K30 (PT.DWILAB), maltodextrin (PT.DWILAB), and sucrose (PT.DWILAB).

Extraction of Mangosteen Peel

Extraction was done by maceration using 70% ethanol reddest. The fine dry powder of the mangosteen peel (Garcinia mangostana L.) was weighed as much as 25 kg and soaked in 70% ethanol for 1 hour. The ethanol solvent was added again until all the simplicia powder was submerged. Then, it was allowed to stand for 4 x 24 hours while stirring occasionally. The macerate was collected every 24 hours. All collected macerate was then evaporated using a rotary evaporator at 30 rpm and a temperature of 40°C until a thick extract was obtained.

Phytochemical Screening and Standardization of Mangosteen Peel Extract

The secondary metabolite content of mangosteen peel extract was determined via phytochemical screening (MPE). Alkaloids, tannins, polyphenols, flavonoids, quinones, saponins, monoterpenes, sesquiterpenes, steroids, and triterpenoids were the phytochemicals screened. MPE quality was also determined through standardization. Organoleptic, ethanol-soluble extract, water-soluble extract, total ash, insoluble acid ash, and drying shrinkage were all inspections.

Instant Granule Formulation Optimization

A fluid bed spray dryer was used to produce instant granules. Maltodextrin was used to dry MPE, which was then combined with citric acid, sodium citrate, PVP, xanthan gum, and sucrose. The mixture was sprayed with 96 percent ethanol until granulated and passed through a 12 sieve. The granules were then dried for one hour in a 40°C oven. The granules were sieved one more with mesh 18. The optimized formulas can be seen in Table 1.

Table 1. Optimized formulas.

Composition (%)	F1 (%)	F2 (%)	F3 (%)	F4 (%)	Function
Mangosteen Peel Extract	1,2	1,2	1,2	1,2	Active substance
Citric Acid	0,5	0,5	0,5	0,5	Sour Flavor
Sodium Citrate	0,5	0,5	0,5	0,5	pH regulator
PVP K30	5	5	5	5	Fastener
Xanthan Gum	3	3	1	1	Suspending Agent
Maltodextrin	5	10	15	20	Solubility Enhancer
Sucrose	Ad 100	Ad 100	Ad 100	Ad 100	Sweeteners, Fillers

Physical Evaluation of Granule Preparations

Drying Loss (LOD)

A total of 1 gram of MPE's instant granules (MPEIG) was placed in a dish on a moisture balance device (Moisture Analyzer MA 50.R, Radwag, USA). The temperature was set at 105°C. Drying loss was recorded after the tool showed constant weight during heating.

Flow Rate and Angle of Rest

A total of 25 grams of MPEIG were weighed and placed in a funnel-shaped, closed-end device. The funnel was then kept at the height of 10 cm. The bottom where the granules dropped was marked with white paper. The granules were allowed to flow when the funnel lid was opened. The time when the granules traveled through the funnel was recorded. The height and diameter of the granules were also noted to calculate the angle of repose, flow rate, and angle of repose.

Compressibility Test

A total of 25 grams of MPEIG was put into a measuring cup contained in the volumenometer (Tapped Density Tester, Erweka SVM 221, Erweka). The final volume of the microcapsule determined the compressibility index of MPEIG after 500 beats.

Dispersion Rate and Sedimentation Volume

In 100 mL of distilled water, 5 grams of MPEIG were dissolved and agitated for 20 seconds. After 15 minutes, the sedimentation volume and solution's pH were measured.

Antioxidant Activity (IC50) using DPPH Method

MPE's and MPEIG's antioxidant activities were measured using the DPPH reagent. The sample and positive control (ascorbic acid) were generated in

quantities of up to 100 µL, with concentrations ranging from 10 to 50 ppm and 1 to 5 ppm, respectively. A 0.1 mL DPPH reagent (0.2 mg/mL in ethanol) was applied to the sample and positive control. The sample and positive control were left in the dark for 30 minutes (25°C), after which the absorbance was measured at a wavelength of 517 nm (Epoch™ Microplate Spectrophotometer, BioTek Instrument, Inc., Winooski, VT, USA). The IC50 value was calculated from the linear equation of %inhibition vs. concentrations.

Determination of α-mangosteen Level and Total Phenolic Content

The total phenolic content of MPE and MPEIG was calculated using gallic acid as the standard. The standard was created in various concentrations (200 – 600 ppm). 10 mg of MPE and 800 mg of MPEIG (containing 10 mg MPE) were dissolved in 10 mL of methanol to make the extract solution. In a dilution tube, 1 ml of the extract solution and each concentration of the standard solution were placed, followed by 5 mL of Folin-Ciocalteau reagent. After mixing the ingredients for 8 minutes, 4 mL of 1 percent NaOH was added. At a wavelength of 256 nm, the absorbance of the extract solution and the standard were measured (Epoch™ Microplate Spectrophotometer, BioTek Instrument, Inc., Winooski, VT, USA).

The α-mangosteen content was determined using high-performance liquid chromatography (HPLC) (Waters Alliance HPLC, Waters Corporation, USA). To generate the standard curve, the standard solution of α-mangosteen was formed into different concentrations ranging from 10 to 50 ppm. The extract solution (10 mg/mL in methanol) was filtered using a syringe filter before being placed in the HPLC sample tube. C18 was the column used. Methanol and aquadest were utilized in the mobile phase (95:5). The injection volume was set to 10 L, and the flow rate was set at 1 mL/min. The retention period of α-mangosteen was 10 minutes and was measured with a UV detector at a wavelength of 318 nm.

Results

Extract Properties

The extracted yield was 12.16 percent by weight (Simplicia 25 kg, extract weight 2,973 kg). In the simplicia sample, seven secondary metabolites were detected. According to the ethanol extraction method, MPE contains six secondary metabolites (see Table 2). MPE has been found to possess a high concentration of polyphenols, flavonoids, tannins, saponins, and quinones (14). As a result, MPE is recognized to have solid antioxidant capabilities (15, 16). The extract was a dark, thick liquid with a pungent stench and a bitter taste. The bitter taste and chelate are caused by the high tannin concentration (17). The extract properties can be seen in Table 2.

Table 2. Extract properties.

No.	Variable	Result
1.	Extract yield	12.16%
2.	Alkaloids	+
3.	Tannins	+
4.	Polyphenol	+
5.	Flavonoids	+
6.	Quinone	+
7.	Saponins	+
8.	Monoterpenes and Sesquiterpenes	-
9.	Steroids and Triterpenoids	-
10.	Organoleptic	Yellowish-brown color, bitter, typical mangosteen aroma
11.	Water content	7.83%
12.	Total ash content	0.248%
13.	Acid insoluble ash content	0.069%

Table 3. Instant granules properties.

No.	Variable	Result			
		F1	F2	F3	F4
1.	Organoleptic	Yellow, sweet, sticky	Yellow, sweet, sticky	Yellow, sweet, non-sticky	Yellow, sweet, non-sticky
2.	Loss on drying (%)	3.95 ± 0.003	3.91 ± 0.008	1.2 ± 0.005	1.8 ± 0.007
3.	Flow rate (g/s)	8.856 ± 0.234	9.02 ± 0.576	10.605 ± 0.917	11.541 ± 1.563
4.	Angle of rest (°)	27.685 ± 1.819	28.875 ± 0.398	26.839 ± 0.580	29.112 ± 0.453
5.	Carr's index	13.954 ± 0.676	14.894 ± 2.404	18.338 ± 1.919	14.043 ± 1.949
6.	Housner ratio	1.162 ± 0.009	1.176 ± 0.034	1.225 ± 0.029	1.164 ± 0.027
7.	Dispersed rate (s)	138	132	120	61
8.	Sedimentation volume	0	0	0	0
9.	pH	4.47 ± 0.03	4.42 ± 0.05	4.45 ± 0.01	4.38 ± 0.05

Instant Granules Characterization

According to the evaluation results, F1 and F2 exhibit similar qualities, notably yellow and sticky. This feature significantly diminishes its aesthetic value. Each formula's pH and sedimentation volume were not significantly different. F4, on the other hand, has the maximum flow rate, compressibility, and dispersion speed. Table 3 shows the physical properties of each formula.

Antioxidant Activity, α-mangosteen Level, and Total Polyphenols

MPE has a high level of antioxidant activity. The IC50 value increased after being transformed into an instant granule but did not differ statistically significantly. MPEIG had lower levels of α-mangosteen and total polyphenols, but they were still in the high range and not statistically different from MPE. IC50 value, α-mangosteen level, and total polyphenols of MPE and MPEIG can be seen in Table 4.

Discussion

The extraction process of mangosteen peel content was carried out using the maceration method to prevent damage to the thermolabile material (18). Based on the phytochemical screening process of mangosteen peel extract, mangosteen peel should contain terpenoids and steroids, but in this observation, it was not detected. This could happen because steroids/terpene groups are not soluble in ethanol and water (19, 20). The antioxidant activity of MPE results from its flavonoid and polyphenol content.

Standardization was done to assure the safety and quality of MPE. The relatively high water content can cause hydrolysis, making it susceptible to microbial activity and accelerating the growth of microorganisms (21). These can reduce the quality of traditional medicines and damage the compounds contained in the extract (22). Heavy metal contamination can also lead to an increase in the toxicity of the extract (23, 24). Based on the evaluation, MPE has low water content and heavy metal contaminants, so it is safe to be formulated into supplements.

Table 4. IC50 value, α-mangosteen level, and total polyphenols of mangosteen peel extract and its instant granule.

No.	Parameter	MPE	MPEIG
1.	IC50 value	34.636 g/mL	44.122 g/mL
2.	α-mangosteen level	29.766%	25.879%
3.	Total polyphenols	398.76 mg GAE/g	374.2 mg GAE/g

MPE was made into instant granules to mask the unpleasant taste and boost MPE solubility. According to the data, the formula with the highest maltodextrin content had the best dispersion velocity. Because of the low maltodextrin content and high xanthan gum content, the granules become sticky and sluggish to disperse. The high stickiness also causes the formula to flow slowly and compressibly. An excellent maltodextrin/xanthan gum ratio was 20:1 %w/w. This mixture's formula has an appealing appearance and taste, good compressibility, was easy to flow, and disperses swiftly.

MPEIG's antioxidant activity was slightly lower than MPE's, but not significantly, and it was still relatively robust. This could be because the wet granulation technique uses oven heating during drying. The amounts of α-mangosteen and polyphenols were reported to decrease after the samples were exposed to high temperatures. According to the data, the amounts of α-mangosteen and polyphenols reduced after the wet granulation process. As a result, dry granulation is advised when producing MPE granules.

Conclusion

The instant granules with the best properties were formula containing 1% xanthan gum and 20% maltodextrin with a drying shrinkage of 1.80%, a flow rate of 11.54 ± 1.56 g/s, repose's angle of 29.112 ± 0.45°, carr index of 14.043 ± 1.9%, and dispersion rate of 0.164 g/s. There is no residue in the solution. The shape and taste of this formula were most acceptable. The antioxidant activity of the extract and instant granules was not significantly different, with the IC50 of 34.64 µg/ml and 44.12 µg/ml, respectively. Based on the test result, it can be concluded that formula 4 with a concentration of xanthan gum 1% and 20% maltodextrin is a potent antioxidant supplement.

Declarations

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Conflict of Interest
The authors declare no conflicting interest.

Data Availability
The unpublished data is available upon request to the corresponding author.

Ethics Statement
Not applicable.

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