ISSN: 2085-675X (Print)
ISSN: 2354-8770 (Electronic)

Jurnal Kefarmasian Indonesia
Available online at https://jkefarind.com/index.php/jki
Original Research Article
JKI

The Characterization of Instant Granule Melinjo Peel (*Gnetum gnemon* Linn.) as Alternative Treatment for Hyperuricemia

Firdha Senja Maelaningsih*, Diah Permata Sari, Andriyani Rahmah Fahriati, Teungku Raviola Saputra, Andika Al Ansori

Department of Pharmacy, STIKes Widya Dharma Husada Tangerang, South Tangerang, Indonesia

ARTICLE INFO

Article history:
Received 23 September 2024
Revised 21 January 2025
Accepted 19 February 2025
Published online 28 February 2025

*Corresponding author.
E-mail: *firdhasenja@wdh.ac.id*
DOI: https://doi.org/10.22435/jki.v15i1.6690

Citation: Maelaningsih FS, Sari DP, Fahriati AR, Saputra TR, Al Ansori A. The Characterization of Instant Granule Melinjo Peel (*Gnetum gnemon* Linn.) as Alternative Treatment for Hyperuricemia. Jurnal Kefarmasian Indonesia. 2025;15(1):80-86.

ABSTRACT

Hyperuricemia is a non-communicable disease characterized by high levels of purine in the blood. One of the foods high in purine is melinjo chips. Instant granules from melinjo peel extract with a concentration of 450 mg have been proven to be effective as an anti-hyperuricemia treatment. To ensure the quality of the instant granule preparation, a quality evaluation was conducted to establish it as a new alternative in hyperuricemia therapy. The study aimed to assess the quality of the instant granule preparation of melinjo peel extract, including physical evaluation (particle size, loss on drying, and pH), characterization with Scanning Electron Microscope (SEM) and Fourier Transform Infrared Spectroscopy (FT-IR), and specific microbial tests. The test results revealed that the particle size of the instant granules was classified as coarse particles, the Loss on Drying results showed 1.29% granule loss, and the pH evaluation indicated that the granules had a pH of 7.78. Based on the SEM characterization, the granules exhibited non-clumping and heterogeneous morphology. FTIR analysis showed the presence of quercetin in the instant granules of melinjo peel. Specific microbial testing indicated the absence of E. Coli in the preparation. Therefore, it is concluded that the instant granule preparation of melinjo peel has characteristics that make it suitable for development as an instant nutraceutical granule preparation for anti-hyperuricemia treatment.

Keywords: *Gnetum gnemon* peel; Hyperuricemia; Instant granule; Quality evaluation

INTRODUCTION

Gout or hyperuricemia occurs due to high levels of purine in the blood. Hyperuricemia or gout is a non-communicable disease but if not treated immediately it has the potential to become gout arthritis. Potential complications include the risk of kidney stones and increased risk of mortality due to cardiovascular disorders.[1] The prevalence of hyperuricemia globally is 2.6% to 36%, but in each country the prevalence varies. This is influenced by the environment, diet, and genetics.[2] The prevalence of hyperuricemia in Indonesia is 15%.[3]

Many people do not routinely check their uric acid levels, so they find out too late that they have hyperuricemia. Hyperuricemia is greatly influenced by lifestyle, namely diet and exercise habits.[1] From a health perspective, the shift in modern lifestyle is currently one of the biggest risk factors. Research shows that there is a relationship between lifestyle and uric acid levels in the body, including consuming foods high in purines.[4]

ISSN: 2085-675X (Print)
ISSN: 2354-8770 (Electronic)

The antioxidant activity of the melinjo plant in almost all parts of the plant, starting from the extract of the roots, leaves, seeds, and stems of melinjo, can ward off free radicals. Melinjo extract has a protein content of 9-10% which has the potential as an antioxidant to ward off free radicals, the main cause of cancer. [5]From this study, it can be seen that the melinjo plant has great potential as a nutraceutical product that is beneficial for public health, including preventing and treating diseases.[6]

Excessive consumption of melinjo seeds or processed melinjo seeds can cause hyperuricemia because they contain high levels of purine.[7] However, several studies have shown that melinjo peel can reduce uric acid levels. Melinjo peel has been proven effective in various pharmacological activities, such as antioxidants, antimicrobials, anti-hypercholesterolemia, and anti-hyperuricemia. The study results indicated antioxidant activity, total phenols, and antimicrobial properties with an extraction temperature treatment of 60°C.[8]

Based on in vivo research, melinjo peel extract was given to mice as test animals after a high-cholesterol diet via a tube for 14 days. The LPL enzyme activity increased after being given melinjo peel extract because it contained flavonoids.[1] In vivo anti hyperuricemia testing stated that the ethanol extract of melinjo was more effective at a dose of 450 mg/kgBW compared to allopurinol 90 mg/kgBW, reducing uric acid levels by 50% and 54%. According to Sari et al. (2019), an ethanol extract of melinjo peel with a dose of 13 mg/kgBW can reduce uric acid levels by up to 31.25.[9]

In 2022, our research team conducted a study on the formulation of instant granules from melinjo peel extract. The best formula (Formula 1), contains 450 mg of extract and 1 g of PVP (Polyvinylpyrrolidone). The instant granule formula has undergone several evaluations, including flow time, angle of repose, compressibility index, moisture content, dissolution time, and analysis of melinjo peel extract levels. The results of the physical evaluation of the formula are positive.[10]

The researchers developed an instant granule preparation formula from melinjo peel extract, based on its antihyperuricemic activity tested in vivo. To ensure the quality of the nutraceutical preparation, it is essential to conduct quality evaluation tests to maintain consistent properties and characteristics during manufacturing, storage, and patient use. This research is an important step in developing a new alternative for high-quality hyperuricemia therapy. After identifying the best formula, further tests were conducted, including physical characterization, microbiology, and accelerated stability tests, to ensure that the instant granule preparation of melinjo peel meets the highest quality standards. The reason for choosing instant granule preparations is that they are the easiest to apply to the community, and no study has been conducted on the formulation of instant granule preparations from melinjo peel extract.

METHODS

This research is an experimental study. The methods used in this study are physical evaluation (particle size, loss on drying, pH testing), characterization with Scanning Electron Microscope (SEM) and Fourier Transform Infrared Spectroscopy (FTIR), and specific microbial tests on instant granule preparations.

Equipment and materials

The study utilized the following tools: a sieving shaker, moisture content analyzer, pH meter, Scanning Electron Microscopy (FE-SEM FEI INSPECT F50), and Fourier Transform Infrared Spectroscopy (FT/IR-6100 type A). The materials used included instant granules of Melinjo peel, distilled water, pH 4 and 7 buffers, KBr, quercetin, and Mac Conkey Agar (MCA) medium.

ISSN: 2085-675X (Print)
ISSN: 2354-8770 (Electronic)

Physical evaluation of instant granules

Particle size

Weighed the granules used in the test, placed them into the sieving shaker, and started sieving for 10 minutes. Weighed the granules trapped in each sieve and calculated the percentage of fractions using the following formula[11] :

$$\%\ fraction = \frac{granule\ weight}{total\ weight} x100\%$$

Loss on drying (LoD)

Weighed 10 grams of instant granules, tested on a moisture content analyzer, test was done for 10 minutes.[12]

pH Testing

Weighed 5 g of instant granules, dissolved in 100 mL of distilled water. The instant granule solution was measured with a pH meter that had been calibrated using pH 4 and 7 buffers.[13]

Characterization of instant granule

Scanning electron microscopy (SEM)

This test aims to see the morphology formed in instant granules. The sample was coated with gold-palladium for 10 seconds, the sample was tested with SEM. The expected result is the absence of pores in instant granules.[14]

Fourier Transform Infrared Spectroscopy (FT-IR)

This test aims to determine the structure of the functional groups of a compound. Instant granule and quercetin samples were each ground with KBr and compressed to make pellets then scanned in the range of 400-4000 cm^{-1}.[15]

Specific microbial testing

The specific microbial testing involves checking for the presence of E. coli bacteria. Bacterial isolation is performed by streaking the inoculum on a petri dish containing MacConkey Agar (MCA) medium using the streak plate method. The inoculum is aseptically streaked on the MCA using a round one needle, and then the petri dish is inverted and incubated at 37°C for 48 hours. A negative result is indicated if the MCA turns brick red, and positive if it turns pink, and bacterial colonies grow around the MCA.[16]

RESULTS AND DISCUSSION

Instant granules of melinjo peel extract that have been made using the wet granulation method and a dose of 0.45 grams which have antihyperuricemic activity, were tested for the quality of the instant granule preparation consisting of physical evaluation (particle size, loss on drying, pH test), characterization with SEM and FTIR, and specific microbial testing.

Physical evaluation of instant granules

Particle size

The purpose of the test was to determine the particle size of instant granules of melinjo peel extract to ensure that the granules have the appropriate size [17]. The test was carried out using a sieving shaker with sieves arranged in sequential order, starting from the top with sizes 12, 14, 16, 18, 20, and a collection pan. Based on Table 1, the particles from the instant granules of melinjo peel extract are distributed across several particle size ranges, with more particles in mesh numbers 16 and 20. This indicates that the particle size range of the granules is 850 µm - 1.18 mm, categorizing the instant granules of melinjo peel extract as coarse powder.[18]

Table 1. Particle size of instant granule

Sieve number	Sieve size	Granule weight	%Fraction
12	1.7 mm	2.9	6.35
14	1.4 mm	7.1	15.54
16	1.18 mm	11.9	26.04
18	1 mm	3.0	6.56
20	850 µm	12.1	26.48

Loss on drying (LOD)

The Loss on Drying (LOD) test measures the moisture content of granules by comparing their wet weight with their weight after drying. The aim is to determine the percentage of moisture in the granules.[19] In a LOD test with 3 repetitions, the average value obtained was 1.29% (refer to table 2). The requirement for LOD value is 1 - 2%. Therefore, the instant

ISSN: 2085-675X (Print)
ISSN: 2354-8770 (Electronic)

granules of melinjo peel extract have a good LOD value as they meet the requirements.[20]

Table 2. LOD and pH testing of instant granule

Repetition of-	LOD	pH
1	1.26%	7.80
2	1.22%	7.75
3	1.38%	7.80
Average	1.29%	7.78

pH testing

The pH test measures the granules' acidity level when they are turned into a solution. This test is essential for assessing the quality of the granule preparation. The results of the pH test on the instant granule solution are presented in Table 2, showing a value of 7.78. Based on the pH value, it can be inferred that the instant granule preparation of melinjo peel extract is close to neutral. If the pH of the granule preparation is too acidic, it may cause stomach irritation, while if the pH is too alkaline, it will result in a bitter taste.[21]

Characterization of instant granule

Scanning electron microscope (SEM)

Testing using SEM was carried out to see the morphology of the instant granules of melinjo peel extract (Figure 1). The results of the characterization test of the instant granule preparation using SEM with a magnification of 500x, 1000x, 2000x, and 5000x had an irregular or heterogeneous shape, were hollow, and did not clump together. The irregular or heterogeneous shape indicates that quercetin in the instant granules of melinjo peel extract was not found on every surface of the granule.[22]

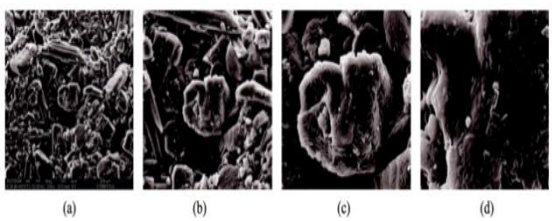

Figure 1. Result of *Scanning Electron Microscopy* (SEM) testing of instant granule with magnification 500x (a), 1000x (b), 2000x (c), 5000x (d).

Fourier transform infrared spectroscopy (FT-IR)

The results of the characterization of instant granule preparations using FTIR compared to quercetin compounds (Figure 2) indicate that the preparation still contains flavonoid compounds that act as anti hyperuricemia. At a wave number of 3400 cm^{-1} indicates the OH stretching functional group, at a wave number of 1550 - 1650 cm^{-1} indicates the presence of a C-C stretching bond, a wave number of 1670 cm^{-1} indicates the carbonyl group C = O stretching, and wave numbers 650 and 1000 cm^{-1} indicate the presence of an aromatic group or ring.[23]

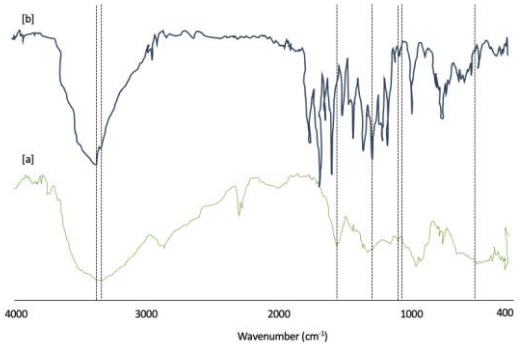

Figure 2. Result of FTIR testing; (a) instant granule; (b) quercetin

Specific microbial testing

The results of the 24 and 48-hour incubation test, with three repetitions and 2 dilutions (see Table 3), indicated that the sample preparation did not contain E. coli bacteria. This was evident from the lack of brick red colonies after the suspension was plated on MCA media.[24]

Table 3. Result of specific microbial testing

Sample	Incubation time (hour)	
	24	48
Sample dilution 10^{-1}	-	-
Sample dilution 10^{-2}	-	-
Positive control (*E. coli* bacteria)	+	+
Negative control	-	-

ISSN: 2085-675X (Print)
ISSN: 2354-8770 (Electronic)

CONCLUSION

Characterization tests of instant granules of melinjo peel have been carried out including physical evaluation (particle size, loss on drying, and pH), SEM and FTIR characterization, and specific microbial testing.

Based on particle size testing, it showed that the particle size ranged from 850 µm to 1.18 mm, including coarse particles. The LOD value met the requirements, being below 1-2%. The pH testing indicated safety, approaching a neutral level. The SEM characterization results showed irregular or heterogeneous shapes, hollow, and no clumping, suggesting the presence of quercetin, although not on every surface. The quercetin compound in the instant granule preparation was confirmed by the FTIR test. Specific Microbial Testing revealed no E. coli bacterial contamination in the instant granule preparation of melinjo peel. Therefore, it is concluded that the instant granule preparation of melinjo peel has characteristics that make it suitable for development as an instant nutraceutical granule preparation for anti-hyperuricemia treatment.

Conflict of Interest

The authors declare no conflict of interest.

Authors' Declaration

The authors hereby declare that the work presented in this article is original and that any liability for claims relating to the content of this article will be borne by them.

Acknowledgments

The authors would like to express their gratitude to the Ministry of Research, Technology, and Higher Education for providing funding for this research. The authors would also like to thank STIKes Widya Dharma Husada Tangerang, Universitas Indonesia, and Universitas Islam Negeri Jakarta for their support and for making this research possible.

REFERENCES

1. Rendra VD, Sakdiah, Zanaria TM. Hubungan konsumsi emping melinjo (Gnetum gnemon L) Aceh terhadap kadar asam urat pada mencit (Mus musculus L). Jurnal Kedokteran Syiah Kuala. 2023 Mar;23(1):24–8. Doi: 10.24815/jks.v23i1.28008
2. Dehlin M, Jacobsson L, Roddy E. Global epidemiology of gout: prevalence, incidence, treatment patterns and risk factors. Vol. 16, Nature Reviews Rheumatology. Nature Research; 2020. p. 380–90. Doi: https://doi.org/10.1038/s41584-020-0441-1
3. Santoso BN, Suwangto EG, Iryaningrum MR. The Association Between Knowledge About Gout Arthritis with NSAID and Allopurinol Consumption in Rumah Susun Penjaringan. Review of Primary Care Practice and Education (Kajian Praktik dan Pendidikan Layanan Primer). 2021 Apr 13;4(1):18. Doi:https://doi.org/10.22146/rpcpe.58359
4. Wijayanti L, Wahyudi A, Septianingrum Y. The Correlation Between Lifestyle and Increased Uric Acid Levels In The Elderly. Nurse and Holistic Care. 2021 Sep 8;1(2):48–55. Doi:https://doi.org/10.33086/nhc.v1i2.2212
5. Sari M, Rahmawati SI, Izzati FN, Bustanussalam, Putra MY. Antioxidant Activity of Ethanolic Extract of Peel and Seed Melinjo (Gnetum gnemon) Based on Color Variations. In: Proceedings of the 1st International Conference for Health Research–BRIN (ICHR 2022). Dordrecht: Atlantis Press International BV; 2023. p. 255–65. Doi: 10.2991/978-94-6463-112-8_25
6. Hasby Puarada S, Nadia R, Gurning S, Harahap WU. Pemanfaatan Limbah Kulit Buah Melinjo (Gnetum gnemon L) Menjadi Produk Olahan Keripik Kulit Buah Melinjo. Jurnal Pengabdian kepada Masyarakat. 2020 Dec

ISSN: 2085-675X (Print)
ISSN: 2354-8770 (Electronic)

1;11(4):567–72. Doi:https://doi.org/10.26877/e-dimas.v11i4.6464
7. Hasan AEZ, Husnawati, Puspita CA, Setiyono A. Efektivitas Ekstrak Kulit Melinjo (Gnetum gnemon) sebagai Penurun Kadar Asam Urat pada Tikus Putih (Rattus norvegicus) Hiperurisemia. Current Biochemistry. 2020 Jan 6;7(1):21–8. Doi: https://doi.org/10.29244/cb.7.1.3
8. Angel V, Parhusip AJN. Karakterisasi Ekstrak Kulit Melinjo (Gnetum gnemon L.) Merah Sebagai Komponen Antibakteri. FaST - Jurnal Sains dan Teknologi (Journal of Science and Technology). 2024 May 31;8(1):59. Doi: http://dx.doi.org/10.19166/jstfast.v8i1.7598
9. Sari NK, Soemardji AA, Fidrianny I. Kajian Pengaruh Ekstrak Daun dan Kulit Buah Melinjo pada Tikus Jantan Hiperurisemia Biji Melinjo (Gnetum Gnemon L.). Journal of Medicine and Health. 2019;2(4):956–64. Doi: https://doi.org/10.28932/jmh.v2i4.1840
10. Sari DP, Fahriati AR, Maelaningsih FS. Formulation of Instant Granules from Ethanolic Extract of Melinjo Peel (Gnetum gnemon L) Extract as Anti-Hyperuricemia. Jurnal Kefarmasian Indonesia. 2023 Aug 31;13(2):140–9. Doi:https://doi.org/10.22435/jki.v13i2.6290
11. Julianti TB, Mentari IA, Wikantyasning ER, Azzahra S, Hairunisa I. Formulasi dan Uji Antioksidan Formula Granul Effervescent Ekstrak Kulit Buah Pulasan (Nephelium mutabile Blume). Jurnal Pharmascience. 2022 Oct 1;9(2):285–99. Doi: http://dx.doi.org/10.20527/jps.v9i2.13717
12. Kalalo T, Yamlean PVY, Citraningtyas G. Pengaruh Penggunaan Pati Kulit Nanas (Ananas comosus (L.) Merr.) sebagai Bahan Pengikat pada Granul CTM. PHARMACON. 2019 Feb 28;8(1):203. Doi: https://doi.org/10.35799/pha.8.2019.29255
13. Putriana NA, Mardawati E, Wardhana YW, Afifah N, Wulandari A, Wira DW, et al. Formulation and Evaluation of instant granules from Ketapang Badak fruit (Ficus lyrata Warb) using wet granulation method as an antioxidant supplement. Indonesian Journal of Pharmaceutics. 2022 Jan 28;3(3):116. Doi:https://doi.org/10.24198/idjp.v3i3.37062
14. Mentor S, Cummings F, Fisher D. Preparation of biological monolayers for producing high-resolution scanning electron micrographs. PLoS One. 2022 Jul 8;17(7):e0266943. Doi: https://doi.org/10.1371/journal.pone.0266943
15. Nurfitriyana, Fithri NA, Yanuarti R. Analisis Interaksi Kimia Fourier Transform Infrared (FTIR) Tablet Gastrorentif Ekstrak Daun Petai (Parkia speciosa Hassk) dengan Polimer HPMC-K4M dan Kitosan. 2022 Aug;03(02):27–33. Doi: https://doi.org/10.62702/ion.v3i2.69
16. Damayanti T, Purwantisari S. Deteksi Escherichia coli Dalam Sampel Obat Tradisional Jenis Jamu Bubuk di Balai Besar Pengawasan Obat dan Makanan (BBPOM) Semarang. Jurnal Akademika Biologi. 2020 Jul;9(2):15–9. Retrieved from: https://ejournal3.undip.ac.id/index.php/biologi/article/view/29308.
17. Imtihani HN, Alfreeda S, Arif JRA. Pengaruh Variasi Disintegran Avicel PH-102 dan Primogel terhadap Karakteristik Co-Processed Excipient. Jurnal Ilmiah Medicamento. 2023 Mar 30;9(1):9–15. Doi: https://doi.org/10.36733/medicamento.v9i1.4635
18. Pramesti N, Novidahlia N, Siti Nurlaela R, Pangan JT, Fakultas G, Pangan I, et al. Penggunaan Ekstrak dan Perisa Jahe terhadap Potensi Kegumpalan pada Serbuk Pemanis Intensitas Tinggi. 2024;3(4). Doi:

ISSN: 2085-675X (Print)
ISSN: 2354-8770 (Electronic)

https://doi.org/10.30997/karimahtauhid.v3i4.13015

19. Fatmawati A, Elvana, Elvana A. Optimasi Formula pada Granul Paracetamol dengan Variasi Komposisi Bahan Pengisi Laktosa dan Avicel PH 101 Serta Evaluasi Parameter Kadar Lembab Moisture Content dan Loss on Drying. Indonesian Pharmacy and Natural Medicine Journal. 2020;4(1):25–32. Doi: http://dx.doi.org/10.21927/inpharnmed.v4i1.1806
20. Utami SM, Ismaya NA, Ratnaningtyas TO, Yunarto N. Formulasi Sediaan Minuman Serbuk Fungsional Kombinasi Biji Jagung (Zea mays L.) dan Madu. Jurnal Kefarmasian Indonesia. 2022 Aug 26;109–17. Doi: https://doi.org/10.22435/jki.v0i0.5536
21. Pratama R, Roni A, Fajarwati K. Uji Sifat Fisik Granul Instan Ekstrak Pegagan (Centella asiatica) Menggunakan Metode Fluid Bed Dryer. Journal of Pharmacopolium. 2022 Dec;5(3):299–304. Doi: https://doi.org/10.36465/jop.v5i3.1062
22. Solikhati A, Rahmawati RP, Kurnia SD. Analisis Mutu Fisik Granul Ekstrak Kulit Manggis dengan Metode Granulasi Basah. Indonesia Jurnal Farmasi. 2022;7(1):1–9. Doi:https://doi.org/10.26751/ijf.v7i1.1421
23. Parhi B, Bharatiya D, Swain SK. Application of quercetin flavonoid based hybrid nanocomposites: A review. Saudi Pharmaceutical Journal. 2020 Dec 1;28(12):1719–32. Doi:https://doi.org/10.1016/j.jsps.2020.10.017
24. Arifin KZ, Sulistyani N. Uji Kandungan Bakteri Escherichia coli Dalam Produk Obat Tradisional yang Dijual di Pasar Beringharjo. Jurnal Fitofarmaka Indonesia. 2023;10(1):11–6.Doi:https://doi.org/10.33096/jffi.v10i1.883