Clinical and Pharmaceutical Sciences Journal

Research article

The Effect of Starch-Lactose Filler Ratio on the Quality Characteristics of Meniran Herbal Powder Capsule

Joko Kawiyanto[1*], Alifah Asri Elina[2], Jessica Herlin Labella Sasongko[3]

[1]Diploma Pharmacy, Politeknik Katolik Mangunwijaya, Jl.Gajah Mada No 91, Semarang, Indonesia
[2]PT Jamu Borobudur, Jl. Hasanudin No. 1, Semarang, Indonesia
[3]Faculty of Pharmacy, Universitas Gadjah Mada, Yogyakarta, Indonesia

*Corresponding Author: jokoka2@gmail.com

Received: 17 November 2024 | Revision: 15 January 2025 | Accepted: 21 January 2025

Abstract

The empirical utilization of medicinal plants by Indonesians has long been known as "jamu". Meniran (*Phyllanthus niruri* Linn) is a plant containing *phyllantin* and h*ypophyllantin* which have immunostimulant activity and potential for development into traditional medicine. This study aims to determine the influence of the starch-lactose filler ratio in the formulation of meniran extract herbal powder for the development of traditional medicine capsule preparations. The research was conducted experimentally using four meniran herbal powder formulas with variations in the starch-lactose filler ratio: 100%:0 (M1); 73%:27% (M2); 50%:50% (M3); and 27%:73% (M4). Based on the physicochemical properties of the powder, the most optimum formula was selected and evaluated for the quality of meniran extract capsule based on the requirements of the Indonesian Food and Drug Agency, including organoleptic tests, flowability, loss on drying, and disintegration time. The results of this study show that variations in the starch-lactose filler ratio affect the moisture content of meniran herbal powder. Formula M2 with a starch:lactose filler ratio of 73:27 exhibited flowability that meets the requirements for development into traditional medicine capsules.

Keywords: Herbal powder, lactose, meniran; *Phyllanthus niruri* L; starch

Introduction

The use of plants as medicinal ingredients has long been known by Indonesians, especially in the form of "jamu". One type of plant known for its many benefits is meniran (*Phyllanthus niruri* Linn), which contains saponins, flavonoids, polyphenols, *phyllantin*, *hypophyllantin*, and potassium salts. These compounds interact with each other to enhance their antioxidant activity [1]. Antioxidants play a role in maintaining the balance of reactive oxygen species levels due to exposure to UV radiation, psycho-emotional stress, unhealthy environments, air pollution, contaminated food, and other negative factors [2]. The components *phyllantin* and *hypophyllantin* in meniran have also been found to have immunostimulant activity [3].

The use of plant extracts for medicinal purposes is limited by unpleasant taste characteristics, distinctive odor, and poor bioavailability. Therefore, traditional medicines have been developed in capsule form to mask the bitter taste of herbal medicine, making it easier for consumption by the public, and improving dosing accuracy to achieve the desired therapeutic outcomes [4]. The powdered plant extract to be formulated into capsules needs to be mixed with additional materials that serve as fillers-binders, disintegrants, lubricants, and adsorbents [5]. The addition of these materials is known to enhance the physicochemical properties of the extract powder for formulation into final dosage forms. Capsule formulations are chosen because they have advantages such as masking unpleasant odor and taste, ease of consumption, ease of preparation, and stability during storage [6]. Farida *et al* [7], compared the use of lactose and starch as filler materials in the capsule formulations of raw materials from ginger, turmeric, and meniran herbs. The study results showed that both lactose and starch produced satisfactory capsule disintegration indices, flow times, uniformity of capsule weight, and capsule disintegration times.

This study aims to determine the influence of the concentration ratio of starch-lactose as filler materials on the powder of meniran extract jamu. This research is also beneficial for developing meniran herbal capsule formulations that meet the quality requirements of traditional medicine.

Materials and Methods

This study is an experimental research to observe the cause-effect relationship between the independent variable (starch-lactose concentration ratio) and the dependent variables (organoleptic tests, flowability, loss on drying, and disintegration time). The relationship between the independent variable and the dependent variable is influenced by controlled variables (temperature, humidity, and equipment used).

Materials

The tools used in this study are an analytical balance with a precision of 0.001 grams, flowability tester, moisture analyzer, disintegration tester, stopwatch, and manual capsule filling device with 100 holes. The active ingredient used in this study is meniran extract (Borobudur Extraction Center), and other additional ingredients include starch (Ubon Sunflower Company Limited), lactose (Glanbia, USA), magnesium stearate (FACI Asia Pacific Pte Ltd), aerosil (Wacker Chemicals China Co. Ltd), and size 0 hard gelatin capsule (Capsugel Indonesia).

Methods

Meniran herbal capsule formulation

Formula optimization was determined the most optimal ratio of the combination of amylum and lactose. Each formula can be seen in Table 1. Materials are weighed using analytical balances.

Table 1. Meniran herbal powder formula

Formula	Function	M1(%)	M2(%)	M3(%)	M4 (%)
Meniran Extract	Active ingredients	60	60	60	60
Starch	Filler	37	27	18.5	10
Lactose	Filler	-	10	18.5	27
Magnesium stearate	Lubricant	2	2	2	2
Aerosil	Adsorbent	1	1	1	1
Total		100	100	100	100

. The evaluation was carried out by observing the physical appearance of the powder after being exposed to the effect of air humidity of 40 – 50% [8], [9] for 3 days. Drying loss testing was also carried out with a moisture analyzer before and after meniran herbal powder was exposed to the air. Loss on drying (LOD) test is carried out using a moisture analyzer at a temperature of 105oC. The required LOD value for meniran herbs is ≤ 10% [10]. Capsule filling was carried out using a formula that has met the parameters of physical appearance and water content is re-made and then inserted into the capsule shell using a capsule filling tool. Formula optimization was determined using the most optimal ratio of the combination of amylum and lactose. The evaluation was carried out by observing the physical appearance of the powder after being exposed to the effect of air humidity of 40 – 50% [8], [9] for 3 days. Drying loss testing was also carried out with a moisture analyzer before and after meniran herbal powder was exposed to the air.

Physical properties testing

Organoleptic test was carried out with the five senses based on the physical appearance of meniran herbal powder. Loss on drying (LOD) was carried out using a moisture analyzer. Flowability test was carried out using a flowability tester. A good flow rate is >10 grams/second [11]. Disintegration time was performed using a disintegration tester. A good disintegration time value for traditional medicine capsules is ≤30 minutes [10].

Results and Discussion

Meniran herbal powder formulation

Meniran herbal powder consists of active ingredients and additives. The active ingredient used is meniran extract, comprising 60% of the composition. Based on Wahjuni *et al.*'s research in 2017 [12], it is known that 30% meniran

extract is capable of providing immunomodulatory effects. Therefore, the formula in this study serves as the development of traditional medicine from meniran extract to enhance immune function.

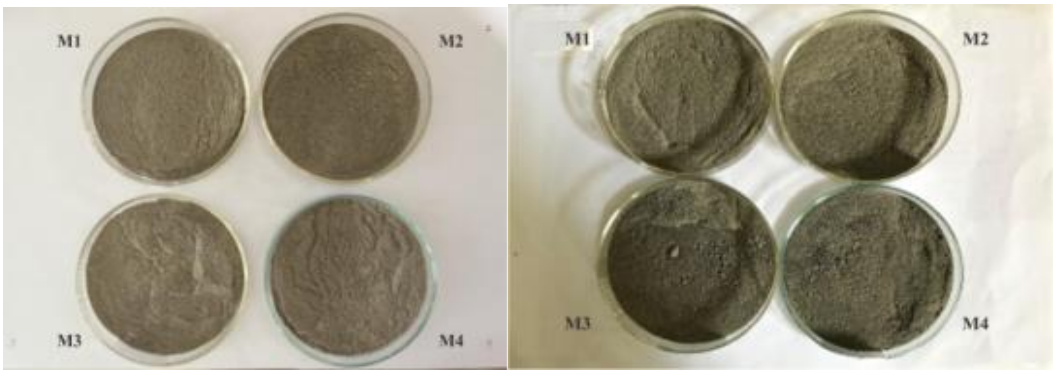
As additives, lactose is used as a filler to achieve the desired capsule weight. Lactose is known for its good flow properties and can be formulated into granules beneficial in the capsule pre-formulation process [13]. Starch is also added as a filler and disintegrant at certain concentrations [14]. Economical price, support for active ingredient release, and inert nature are factors in the selection of filler materials [15].

Aerosil is used as an adsorbent to protect beneficial substances from moisture impact, enhance the homogeneity of material mixtures, and prevent moisture due to reactions between substances. Aerosil has small particles that result in a large surface area. Aerosil's small particles result in a large surface area, enhancing moisture absorption capacity. [16].

Additionally, to improve the flow properties of plant extracts, which generally do not flow well and are hygroscopic, magnesium stearate is added as a lubricant. Flow property characteristics can affect production efficiency, especially in the powder-filling process from the hopper in capsule-filling machines [13]. The meniran extract capsule formulation in this study uses four formulas made with variations in the combination ratio of starch-lactose, namely 100%:0 (MI); 73%:27% (M2); 50%:50% (M3); and 27%:73% (M4). Subsequently, the herbal powder is evaluated based on physicochemical characteristics to determine the formulation to be encapsulated in size 0 capsules and undergo further quality evaluation.

Physicochemical characteristic evaluation of meniran herbal powder

The resulting M1, M2, M3, and M4 meniran herbal powders can be observed in Figure 1. The whole formula can be made into a homogeneous herbal powder, has a characteristic meniran odor, and appearing grayish. This shows that the addition of lactose as a filler does not affect the visual physical parameters of meniran herbal powder. The hygroscopicity of the powder is tested as a result of exposure to air humidity at room temperature. The results of exposure can be observed in Figure 1. The shape of M3 and M4 powders has changed to become somewhat lumpy. The hygroscopicity of M3 and M4 indicates the effect of lactose concentration on the formula. The higher the concentration of lactose used, the more hygroscopic the powder produced. This is by research by Jin *et al.(*2021) [9] which shows that the use of lactose in red ginger extract powder produces a hygroscopic powder. The most optimal addition of lactose is shown in the M2 formula, which is as much as 10%. In M1 and M2 the powder does not change shape after exposure. The ability of the M1 and M2 formulas to cope with air humidity without changing their physical appearance indicates a controlled hygroscopic nature. This is an important aspect in the processing, manufacturing, and packaging process of pharmaceutical preparations [17].



A B

Figure 1. Appearance of meniran herbal powder before and after exposure to air humidity
(A: before exposure, B: after exposure, left to right from top to bottom: M1, M2, M3, M4)

The optimization results of the meniran herbal powder formula are presented in Table 2. In formula M1, without the addition of lactose filler, it shows the highest drying loss value compared to the other three formulas. The more lactose used, the lower the drying loss value. This may occur due to the high moisture content of lactose, which results in a high water-binding capacity [18]. The drying loss values of all four formulas before and after exposure meet the requirements for good powder moisture content. Based on the evaluation results of the physicochemical characteristics of meniran herbal powder, formula M1 and M2 are selected to be encapsulated into herbal capsules and undergo further quality evaluation.

Table 2. Physicochemical characteristic evaluation of meniran herbal powder before and after exposure to air humidity

Parameters	Before exposed				After exposed			
	M1	M2	M3	M4	M1	M2	M3	M4
Form	Powder	Powder	Powder	Powder	Powder	Powder	Slightly clumping	Slightly clumping
Color	Grey	Grey	Grey	Grey	Grey	Grey	Grey	Grey
Odor	Scent of meniran	Scent of meniran	Scent of meniran	Scent of meniran	Scent of meniran	Scent of meniran	Scent of meniran	Scent of meniran
Loss on Drying (%)	7.03	5.35	4.35	3.36	8.71	7.27	6.69	5.25

Quality evaluation of meniran herbal capsule

The quality of meniran herbal capsules from the selected formula is presented in Table 3. The reproducibility of the formula can yield powder with an appropriate physical appearance, which is gray, homogeneous, and has a characteristic meniran odor. The results from each formula meet the quality requirements for traditional medicine as good capsule formulations with moisture content not exceeding 10% [19]. The addition of lactose results in a decrease in drying loss value by the moisture characteristics of lactose.

Table 3. Data of Quality of meniran herbs capsules

Parameters	M1	M2
Form	Powder	Powder
Color	Grey	Grey
Loss on Drying (%)	7.01	5.24
Flow rate (g/s)	10	10
Disintegeration time (minute)	21	20

Flow properties are not affected by the addition of lactose and exhibit flow properties that meet the requirements. This research is consistent with the study by Syukri *et al*., 2018 [20], which found that adding lactose filler provides better flow rates compared to adding starch filler in the formulation of dew fruit extract tablets. Aerosil, besides serving as an adsorbent, at concentrations of 0.1 - 1.0%, can also be used as a glidant to improve flow properties by reducing particle friction [14]. Additionally, magnesium stearate is used in the formula at concentrations of 0.25 - 5.0%, which serves as a lubricant but has less effective anti-adherent and glidant effects [21]. Therefore, aerosil is combined with magnesium stearate to enhance their potential.

The results of the disintegration time test on meniran herbal capsules M2 show lower values compared to M1. The disintegration time of both formulas meets the quality requirements for good traditional medicine capsule formulations, which is ≤30 minutes. Good capsule disintegration time indicates that capsule formulations can disintegrate quickly after ingestion, thus providing pharmacological effects promptly [22].

Conclusion

From this research, we can infer that changes in the ratio of starch-lactose fillers influence the moisture absorption of meniran herbal powder. Among the two formulations studied, M2, with a ratio of starch-lactose fillers at 73:27, generates meniran herbal powder with satisfactory flowability, lower moisture loss during drying, and quicker disintegration compared to formulations lacking lactose fillers.

Acknowledgment

The author would like to thank the Director of Politeknik Katolik Mangunwijaya, the Director of PT Industri Jamu Borobudur, the Faculty of Pharmacy Universitas Gadjah Mada and all parties who supported and contributed to the preparation of this research.

Declaration

Author contribution	:	Joko Kawiyanto proposing the topic and research methodologies, Alifa drafting the proposal and performing analysis, Jessica Herlin Label presenting the data and discussion.
Funding statement	:	No funding is available for this research.
Conflict of interest	:	We declare that there is no competing interests.
Ethics Declaration	:	As the authors, we confirm that this work has been written based on ethical research principles in compliance with our university's regulations and that the permission was obtained from the relevant institution during data collection. We fully support CliPs commitment to upholding high standards of professional practicing honesty in all academic and professional activities.
Additional information	:	No additional information is available for this paper.

References

[1] R. Marisi Tambunan, G. F. Swandiny, and S. Zaidan, "Uji Aktivitas Antioksidan dari Ekstrak Etanol 70% Herba Meniran (Phyllanthus niruri L.) Terstandar," *J. Ilmu Kefarmasian*, vol. 12, no. 2, pp. 60–64, 2019.

[2] A. Yashin, Y. Yashin, X. Xia, and B. Nemzer, "Antioxidant activity of spices and their impact on human health: A review," *Antioxidants*, vol. 6, no. 3, pp. 1–18, 2017, doi: 10.3390/antiox6030070.

[3] P. G. R. W. Perdana, "REVIEW: Aktivitas Imunomodulator Ekstrak Herba Meniran (Phyllanthus niruri L.)," vol. IX, no. 1, pp. 50–54, 2022.

[4] M. A. Archer *et al.*, "Formulation and evaluation of capsules containing extracts of Cassia sieberiana for improved therapeutic outcome," *Sci. African*, vol. 10, p. e00609, 2020, doi: 10.1016/j.sciaf.2020.e00609.

[5] S. Esmaeili, L. Dayani, A. Taheri, and B. Zolfaghari, "Phytochemical standardization, formulation and evaluation of oral hard gelatin capsules from Pinus eldarica bark extract," *Avicenna J. Phytomedicine*, vol. 11, no. 2, pp. 168–179, 2021, doi: 10.22038/AJP.2020.16716.

[6] F. Wulandari, F. Widyawati, K. Rizaldi, and F. Syaputri, "Formulasi Dan Evaluasi Fisik Sediaan Kapsul Ekstrak Daun Cincau Hijau (Cyclea barbata Miers) Sebagai Anti Inflamasi," *J. Ilm. As-Syifaa*, vol. 12, pp. 150–157, Jan. 2021, doi: 10.33096/ja.v12i2.638.

[7] S. Farida, T. Mana, and T. Dewi, "Karakteristi Mutu Kapsul Ramuan Kebugaran Untuk Saintifikasi Jamu," *J. Tumbuh. Obat Indones.*, vol. 12, pp. 25–32, Aug. 2019, doi: 10.22435/jtoi.v12i1.1078.

[8] S. K. Niazi, *Handbook of Preformulation: Chemical, Biological, and Botanical Drugs, Second Edition (2nd ed.).* INFORMA HEALTH CARE, 2019.

[9] S. Jin *et al.*, "Improved Hygroscopicity and Bioavailability of Solid Dispersion of Red Ginseng Extract with Silicon Dioxide.," *Pharmaceutics*, vol. 13, no. 7, Jul. 2021, doi: 10.3390/pharmaceutics13071022.

[10] BPOM RI, "Peraturan Badan Pengawas Obat Dan Makanan Nomor 29 Tahun 2023 Tentang Persyaratan Keamanan Dan Mutu Obat Bahan Alam," *Badan Pengawas Obat dan Makanan*, vol. 11, pp. 1–16, 2023, [Online]. Available: https://standar-otskk.pom.go.id/storage/uploads/6dab78f8-9598-454f-a62f-7b5348ae7206/PerBPOM-No.-29-tahun-2023.pdf.

[11] Rudolf Voigt, *Buku pelajaran teknologi farmasi*. Gadjah Mada University Press, 1995.

[12] R. Sri Wahjuni, E. Koestanti Sabdoningrum, and S. Hidanah, "Immunomodulation Effect of Meniran (Phyllanthus niruri linn) on Blood Profile of Broiler Chickens Infected with Enterotoxin of Antibiotic- Resistant Escherichia coli," vol. 98, no. Icpsuas 2017, pp. 311–313, 2018, doi: 10.2991/icpsuas-17.2018.66.

[13] U. Harahap, M. Marianne, Y. Yuandani, and L. Laila, "Preformulation study of Pugun Tano (Curanga fel-terrae [lour.] merr) ethanolic extract granule mass in capsule as hepatoprotective drug," *Open Access Maced. J. Med. Sci.*, vol. 7, no. 22, pp. 3729–3732, 2019, doi: 10.3889/oamjms.2019.491.

[14] Marian e. quinn rowe, r. c., paul j. sheskey, "Pharmaceutical excipients," *Remingt. Sci. Pract. Pharm.*, pp. 633–643, 2020, doi: 10.1016/B978-0-12-820007-0.00032-5.

[15] A. Suparman, Y. Susilawati, and A. Y. Chaerunisaa, "Formulasi Tablet dengan Bahan Aktif Ekstrak Tumbuhan Obat Indonesia: Review," *Maj. Farmasetika*, vol. 6, no. 3, p. 234, 2021, doi: 10.24198/mfarmasetika.v6i3.32259.

[16] A. N. Aisyah *et al.*, "Formulation and Test of Physical Characteristics of Ethanol Extract Capsules of Red Atai Tuber (Angiopteris ferox Copel)," *Indones. J. Pharm. Sci. Technol.*, vol. 1, no. 1, pp. 72–79, 2023, doi: 10.24198/ijpst.v0i0.46179.

[17] I. Pertiwi, S. Sriwidodo, and B. Nurhadi, "Formulasi dan Evaluasi Tablet Hisap Mengandung Zat Aktif Bersifat

Higroskopis," *Maj. Farmasetika*, vol. 6, no. 1, pp. 70–84, 2020, doi: 10.24198/mfarmasetika.v6i1.27419.
[18] M. Rahmayanti, "Pengaruh Variasi Kadar Pengisi Laktosa dan Manitol terhadap Sifat Fisik Granul sebagai Produk Antara Tablet Effervescent Ekstrak Daun Senna (Cassia acutifolia)," *J. Islam. Pharm.*, vol. 6, no. 2, pp. 58–62, 2022, doi: 10.18860/jip.v6i2.14087.
[19] Kementerian Kesehatan RI, *Farmakope Herbal Jilid II*. 2017.
[20] Y. Syukri, J. T. Wibowo, and A. Herlin, "Pemilihan Bahan Pengisi untuk Formulasi Tablet Ekstrak Buah Mahkota Dewa (Phaleria macrocarpa Boerl)," *J. Sains Farm. Klin.*, vol. 5, no. 1, pp. 66–71, 2018.
[21] R. Mustarichie and D. Priambodo, "Tablet formulation from meniran (phyllanthus niruri l.) extract with direct compression method," *Int. J. Appl. Pharm.*, vol. 10, no. 4, pp. 98–102, 2018, doi: 10.22159/ijap.2018v10i4.26795.
[22] F. W. A. Owusu *et al.*, "Formulation and in Vitro Evaluation of Oral Capsules and Suspension from the Ethanolic Extract of Cola nitida Seeds for the Treatment of Diarrhea," *Biomed Res. Int.*, vol. 2021, 2021, doi: 10.1155/2021/6630449.