

CHARACTERIZATION AND CONCENTRATION OPTIMIZATION OF *HIBISCUS ROSA-SINENSIS* L. MUCILAGE POWDER AS SUPERDISINTEGRANT

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ABSTRACT

Objective: The main purpose of this study is to characterize *Hibiscus rosa-sinensis* L. mucilage (MHR) powder as superdisintegrant and to decide the optimum concentration of *Hibiscus rosa-sinensis* L.

Methods: Characterization was conducted in many tests such as organoleptic, swelling ratio, solubility, polysaccharide, viscosity, particle size distribution, flowability and compressibility index. Next, MHR powder was included in fast disintegrating tablet (FDT) domperidone formulation in several concentrations and compared with FDT domperidone formulation that using sodium starch glycolate as superdisintegrant.

Results: The result of characterization of MHR powder were brownish powder, specific smell like traditional medicines, swelling ratio of 24, solubility of 0.426 ± 0.034 mg/ml, positive polysaccharide, the viscosity of 491.33 ± 119.44 cps (2% w/v), 4520.00 ± 1224.42 cps (4% w/v), $D_v(10)$ of 26.2 μ m, $D_v(50)$ of 157 μ m, $D_v(90)$ of 260 μ m, $D_v(100)$ of 380 μ m, flowless, and average compressibility index of $26.75 \pm 1.79\%$. The optimum MHR powder concentration was 1% because the average disintegration time was 39.67 ± 4.73 seconds and the average wetting time was 66.33 ± 14.29 seconds. Those times were faster than domperidone FDT that used this superdisintegrant in other concentrations or sodium starch glycolate in the same concentration.

Conclusion: *Hibiscus rosa-sinensis* L. mucilage powder can be used as superdisintegrant in FDT formulation with an optimum concentration of 1%.

Keywords: *Hibiscus rosa-sinensis* L., Superdisintegrant, Fast disintegrating tablet

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INTRODUCTION

Hibiscus rosa-sinensis L. is a well-known plant in Indonesia that also grows widely in other countries to such as India, Thailand, and China. The leaves of this plant contain many essential substances such as carotene, mucilages, and many trace elements such as alkaloids and terpenes. Mucilages are glutinous substances which mostly consist of polysaccharides. In modern era, mucilages are widely used in pharmaceutical industries as thickener agent, suspending agent and binder. Mucilages of *Hibiscus rosa-sinensis* L.'s consist of L-rhamnose, D-galactose, D-galacturonic acid and D-glucuronic acid [1]. In a previous study by Ameena, *et al.* (2010), *Hibiscus rosa-sinensis* L. mucilage powder as tablet binder meanwhile Shah and Patel used it as tablet disintegrant [1, 2]. Fast disintegrating tablet (FDT) is an advanced pharmaceutical dosage form which is different from conventional tablet because disintegration time in FDT should be conducted under 1 minute [3]. Domperidone is one of the antiemetic drugs that is usually consumed by patient to prevent vomit. The objective of this study is to propose a method to optimize the yield of *Hibiscus rosa-sinensis* L. mucilage powder, characterize *Hibiscus rosa-sinensis* L. mucilage powder, obtain its optimum concentration for FDT domperidone formulation as superdisintegrant and compare it with sodium starch glycolate.

MATERIALS AND METHODS

Materials

The leaves of *Hibiscus rosa-sinensis* L. Were collected from the Kalimulya, Depok, West Java, Indonesia and were authenticated at LIPI (Indonesian Institute of Sciences) Bogor, West Java, Indonesia with certification number of 35/IPH.3./KS/1/2016. Other materials are: domperidone base (Vasudha Pharma, India); sodium starch glycolate (Yung Zip Chemical, China); Avicel PH 102 (Asahi Kasei, Japan); anhydrous lactose (Meggle, USA); mannitol (Roquette, France); talcum (Haichin, China); stearic magnesium (Haichin, China); HCl_(p) (Merck, Germany); purified water; technical acetone; H₂SO₄(p); Alpha naphthol (Merck, Germany); potassium phosphate

(Merck, Germany); sodium hydroxide (Merck, Germany); ethanol 96% (Merck, Germany); red colouring agent.

Extraction of mucilage

This method was a modification from the extraction of mucilage method demonstrated by Shah, Patel and Ameena, Dilip, Saraswathi, Krishnan, Sanker, Simi [1, 2]. The fresh leaves of *Hibiscus rosa-sinensis* L. were collected, washed to remove dirt and debris, and dried. The powdered leaves were soaked for 1 h, boiled for 6 h in 80 °C, kept aside for 1 hour for complete release of the mucilage into water. The material was squeezed from four-fold muslin cloth bag to remove the residual from the filtrate. Acetone was added to the filtrate to precipitate the mucilages in a quantity of three times the volume of total filtrate then mucilages were separated and dried in an oven at 40 °C. The dried mucilages were collected and powdered using powder machine. The powdered dried mucilages were passed through 80 mesh sieve, then the mucilages powder was dried again in an oven at 80 °C for 4 h The *Hibiscus rosa-sinensis* L. mucilage powder was ready to use in FDT domperidone formulation.

Characterization of *Hibiscus rosa-sinensis* L. mucilage powder

First, physical observation was performed for *Hibiscus rosa-sinensis* L. mucilage powder consisting of its shape, colour, smell and taste [1]. Second characterization was conducted by measuring the particle size distribution of *Hibiscus rosa-sinensis* L. mucilage powder using Particle Size Analyzer (Mastersizer 3000, Malvern, UK) in dry mode [4]. The third step of characterization was performed by measuring loss on drying. Sample was put into moisture analyzer (Adam, Singapore) then the temperature in chamber of moisture analyzer was raised up to 105 °C. Moisture analyzer stopped after the weight of *Hibiscus rosa-sinensis* L. mucilage powder was constant at 105 °C. Data was recorded [5], and solubility test of *Hibiscus rosa-sinensis* L. mucilage powder was performed. Sample was weighted ± 50 mg, dispersed in 250.0 ml of Purified water, then agitated using magnetic stirrer for 15 min and sonicated for 2 h. Sample was taken using syringe that was equipped with 0.45 μ m

filter and then put in a small container then dried in an oven at 105 °C for 1 hour. The dried mass was weighted and the solubility was calculated with the formula: dried mass (mg)/sample volume in syringe (ml) [6, 7]. Polysaccharide identification of *Hibiscus rosa-sinensis* L. mucilage powder was then conducted. Mucilages were dispersed in molisch reagent (α -naphthol in ethanol) and added with concentrated sulphuric acid, then the change of colour in mucilage solution was observed [5]. Swelling ratio of *Hibiscus rosa-sinensis* L. mucilage powder was subsequently added in the volumetric glass then the volume (V_0) in volumetric glass was recorded. Purified water was added in volumetric glass until its limit. Data was recorded based on volume observation at 1, 2, 5, 10, 15, 30, 60, 75 and 90 min. Swelling ratio was calculated with formula: Ratio swelling = Volume in 90 min/ V_0 [5]. Afterward, the viscosity of *Hibiscus rosa-sinensis* L. mucilage powder was examined. *Hibiscus rosa-sinensis* L. mucilage powder was dispersed in purified water at

a concentration of 1, 2, and 4% w/v, then its viscosity was measured with Brookfield Viscometer (Brookfield, USA). Data was collected [5]. Finally, compressibility of *Hibiscus rosa-sinensis* L. mucilage powder was measured with bulk density tester (Erweka, Germany) and its flowability was measured with Flowmeter (GDT type, Erweka, Germany) [5].

FDT domperidone formulation

FDT domperidone was prepared by the conventional direct compression technique using *Hibiscus rosa-sinensis* L. mucilage powder and sodium starch glycolate at a concentration of 1, 2, 4, 6 and 8%. All the required ingredients as per the formulation tablet were weighted and mixed with mixer, evaluated based on compressibility and flowability evaluation then compressed on Korsch single punch compressing tablet machine (Korsch, Germany). The composition of each formulation is given in table 1.

Table 1: FDT domperidone formulation

Ingredients	F0	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
Domperidone	5	5	5	5	5	5	5	5	5	5	5
Avicel PH102	40	40	40	40	40	40	-	-	-	-	-
MHR	-	2.5	5	10	15	20	-	-	-	-	-
SSG	-	-	-	-	-	-	2.5	5	10	15	20
Mannitol	70	70	70	70	70	70	70	70	70	70	70
Anhydrous lactose	125	122.5	120	115	110	105	122.5	120	115	110	105
Talc	5	5	5	5	5	5	5	5	5	5	5
Mg-Stearate	5	5	5	5	5	5	5	5	5	5	5
Total	250	250	250	250	250	250	250	250	250	250	250

Notes: All ingredients and total tablet weight are in mg; MHR: *Hibiscus rosa-sinensis* L. mucilages powder; SSG: Sodium starch glycolate

FDT domperidone evaluation

Tablets for each formulation were evaluated for appearance, weight variation, thickness, hardness, friability, disintegration time, wetting time, and uniformity of active pharmaceutical ingredients. In weight variation test, ten tablets were selected randomly and average weight was determined using an analytical electronic balance (Mettler Toledo, USA) [8]. Tablets were weighted individually and compared with average weight. Hardness tester (Erweka, Germany) and friability tester (Erweka, Germany) were used to test hardness and friability of the tablet in each formulation, respectively [8]. Thickness of tablet was determined by using manual calliper (Butterfly, Japan) [8]. Disintegration test was performed by 10 ml of phosphate buffer 6.8 was added into petridish and then tablet was put into the petri dish. Disintegration time was calculated start from tablet was put into the petri dish until the core tablet could not be seen clearly [3]. Wetting time of the tablet was performed by using

fivefold filter paper that was placed into the Petri dish containing 10 ml of red coloured phosphate buffer 6.8. A tablet was kept on the paper and the time for complete wetting of tablet was measured [9]. In uniformity of active pharmaceutical ingredients, ten tablets were selected randomly and an average percentage of domperidone was measured using spectrophotometer UV-Vis (Shimadzu, Japan) [8].

RESULTS

Extraction of *Hibiscus rosa-sinensis* L. mucilage powder

Hibiscus rosa-sinensis L. mucilage powder was brownish, tasteless, and has specific odor like traditional medicine. The average yield of *Hibiscus rosa-sinensis* L. mucilage powder was 11.50±1.40% (n=3).

Hibiscus rosa-sinensis L. mucilage powder's characterization

All characterization of *Hibiscus rosa-sinensis* L. mucilage powder was described in table 2.

Table 2: *Hibiscus rosa-sinensis* L. mucilage powder's characterization

Characterization parameter	Results
Particle size distribution	Dv(10) = 26.2 μ m Dv(50) = 157 μ m Dv(90) = 380 μ m Dv mean = 155 μ m
Loss on drying	1.69±0.18%
Solubility	0.426±0.034 mg/ml
Polysaccharide identification	Molisch reaction (+) (violet precipitate was formed)
Swelling ratio	24 times from before
Viscosity	1%=can't be measured 2% = 491.33±119.44 cps 4%=4520.00±1224.42 cps
Compressibility index	26.75±1.79%
Flowability	Cannot flow

Note: Solubility, loss on drying, viscosity and compressibility index results are in mean±SD; n = 3

FDT domperidone formulation

The mass evaluation of FDT domperidone was described in table 3

FDT domperidone evaluation

FDT domperidone evaluation was described in table 4 and table 5

Table 3: Mass evaluation of FDT domperidone

Formulation	Compressibility index (%)	Haussner ratio	Flowability (gram/second)	Angle of repose (°)
F0	9.50±0.52	1.100±0.010	1.26±0.05	24.33±0.48
F1	12.10±0.61	1.140±0.010	2.38±0.23	31.36±0.38
F2	13.18±0.97	1.150±0.010	3.51±0.09	32.62±0.39
F3	14.52±0.81	1.170±0.010	3.78±0.12	32.81±0.36
F4	15.62±0.62	1.190±0.010	4.03±0.15	31.81±0.46
F5	15.97±0.97	1.190±0.010	5.64±0.17	31.57±0.57
F6	13.62±0.25	1.158±0.003	5.26±0.27	31.52±0.39
F7	14.83±0.28	1.174±0.004	5.20±0.31	29.12±0.27
F8	15.46±0.77	1.183±0.011	4.07±0.15	29.70±0.51
F9	15.66±0.87	1.186±0.012	3.53±0.07	31.24±0.27
F10	16.66±0.34	1.200±0.005	3.05±0.05	31.47±0.27

Notes: F = Formulation FDT domperidone; all results are in mean±SD; n = 3

Table 4: FDT domperidone evaluation (weight, thickness, hardness, friability)

Formulation	Average weight (mg)	Thickness (cm)	Hardness (kPa)	Friability (%)
F0	251.11±0.70	0.447±0.005	0.88±0.18	2.43±0.10
F1	252.60±1.04	0.443±0.006	0.96±0.06	2.60±0.01
F2	252.39±0.88	0.446±0.008	0.67±0.17	2.59±0.02
F3	252.68±0.91	0.450±0.000	0.90±0.28	2.47±0.02
F4	252.40±1.08	0.466±0.009	0.57±0.21	2.40±0.01
F5	252.65±0.95	0.466±0.005	0.61±0.16	2.40±0.03
F6	252.21±1.25	0.434±0.005	0.76±0.33	2.52±0.08
F7	252.29±1.07	0.432±0.008	0.62±0.29	2.58±0.03
F8	252.39±0.96	0.453±0.007	0.67±0.24	2.67±0.04
F9	252.39±0.88	0.440±0.009	0.67±0.28	2.72±0.04
F10	252.41±0.93	0.446±0.005	0.61±0.13	2.73±0.02

Table 5: FDT domperidone evaluation (disintegration time, wetting time, API uniformity)

Formulation	Disintegration time (s)	Wetting time (s)	API uniformity (%)
F0	3419±100.73	5182.00±292.65	99.01±1.96
F1	39.67±4.73	66.33±14.29	98.50±2.00
F2	276.33±74.90	508.67±142	100.00±2.66
F3	329±22.87	868.33±259.05	101.84±1.67
F4	3209±136.72	3209.00±136.72	103.03±2.22
F5	6011±97.53	8150.67±312.55	100.82±1.64
F6	109.33±18.88	120.00±3.00	100.20±2.17
F7	72±3.46	98.33±9.61	100.03±2.79
F8	39.33±2.52	75.33±3.79	99.63±2.13
F9	38.33±2.52	68.00±2.00	97.18±1.63
F10	41±3.46	70.33±2.52	99.12±2.13

Note: F0 = negative control; *Hibiscus rosa-sinensis* L. mucilage powder: F1 = 1%; F2 = 2%; F3 = 4%; F4 = 6%; F5 = 8%; Sodium starch glycolate: F6 = 1%; F7 = 2%; F8 = 4%; F9 = 6%; F10 = 8%; all results are in mean±SD, n = 3

DISCUSSION

Extraction of *Hibiscus rosa-sinensis* L. mucilage powder

In the preliminary study, we tried to reproduce the method by Shah and Patel in 2012 [1]. That method produced 8% yield of MHR powder. Hence, in this study, we modified that method by changing the soaking time and heating time. Yield of *Hibiscus rosa-sinensis* L. mucilage powder was optimum in 1 hour soaking time and 6 h heating time that produce 11,5% w/w; therefore, we used this method for further analysis. Extending heating time can increase the extraction on the substance in its solvent [10]. *Hibiscus rosa-sinensis* L. mucilage powder consists of L-rhamnose, D-galactose, D-acid glucuronic and D-acid galacturonic [1].

Hibiscus rosa-sinensis L. mucilage powder's characterization

Superdisintegrants are the urgent materials for any formulation of fast disintegrating tablet. Superdisintegrants are another type of super absorbing materials with tailor-made swelling properties [11]. Based on the results of characterization *Hibiscus rosa-sinensis* L. mucilage powder, we can observe that *Hibiscus rosa-sinensis* L. mucilage powder is a promising superdisintegrant because its swelling ratio was 24 times from before. This material is not assumed to absorb a significant amount of water or aqueous fluid but to swell very fast [11]. The

solubility of *Hibiscus rosa-sinensis* L. mucilage powder was 0.426±0.034 mg/ml. Superdisintegrants should have low solubility in water. Water-soluble materials tend to dissolve rather than disintegrate, while insoluble materials generally produce rapidly disintegrating tablets [12]. Particle size is an important property for superdisintegrant. Larger particles usually promote faster disintegration [13]. Larger particles (>150 µm) can made pores in tablet; therefore, water can enter and wet the superdisintegrant, then superdisintegrant can swell well and break up the tablet to disintegrate the tablet to become granules and fines [14]. *Hibiscus rosa-sinensis* L. mucilage powder can become an effective superdisintegrant candidate. Loss on drying of *Hibiscus rosa-sinensis* L. mucilage powder should be kept under 2% because *Hibiscus rosa-sinensis* L. mucilage powder is a hygroscopic superdisintegrant and when it has more moisture content, the disintegration time became slower. This will be happen because high moisture content in this polymer make cohesive bonding and produce gel layer that can promote slower disintegration of FDT.

FDT domperidone formulation

Based on the results in table 3, we can observe that all formulations have acceptable compressibility index, haussner ratio and angle of repose. *Hibiscus rosa-sinensis* L. mucilage powder poor compressibility index did not affect the compressibility index of FDT

domperidone mass because this polymer only gave small proportion in the FDT domperidone formulation. Hence, all formulations can be processed using the direct compress technique.

FDT domperidone evaluation

Hibiscus rosa-sinensis L. mucilage powder is a promising natural superdisintegrant because the disintegration time at 1% concentration was faster than sodium starch glycolate in same concentration or other concentration of *Hibiscus rosa-sinensis* L. mucilage powder. This can be explained because its rapid swelling made it viscous and formed gel layer at a concentration above 1%, which can delay tablet disintegration. This case happened with other superdisintegrants that have rapid swelling ability [15]. Its rapid swelling was caused by large number of hydrophilic groups in this polymer that can make hydrogen bonding with water and its bulky structure make this polymer did not dissolved in water medium. Meanwhile, sodium starch glycolate do not make gel layer when its concentration is increased because its crosslink reduced both the water-soluble fraction of polymer and the viscosity of dispersion in water [11].

CONCLUSION

Hibiscus rosa-sinensis L. mucilage powder is the effective natural superdisintegrant at specific concentration. Its optimum concentration is 1%. The disintegration time and wetting time of FDT domperidone that contain 1% concentration of *Hibiscus rosa-sinensis* L. mucilage powder was better than formulation that contain other concentration of *Hibiscus rosa-sinensis* L. mucilage powder or sodium starch glycolate in the same concentration.

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AUTHORS CONTRIBUTIONS

All the authors have contributed equally.

CONFLICT OF INTERESTS

The authors have no conflict of interests to declare.

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