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Study of Coating Tablet Extract Noni Fruit (*Morinda citrifolia*, L.) with Maltodextrin as a Subcoating Material

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The present study was carried out to investigate the effect of maltodextrin DE 1-5 from cassava starch as a subcoating material of noni fruit dry extract sugar coating tablets. Maltodextrin were obtained by hydrolysis of cassava starch with Liquezyme EX[®] (α -amylase enzyme from NOVO) at 95 \pm 3 $^{\circ}$ C for 2.5-4 min. Noni fruit dry extract was used in core tablets. The core tablets were prepared by wet granulation, then all of the tablets were coated with materials that composed of sucrose, maltodextrin, PEG 6000, CaCO₃, TiO₂ and distilled water. Core tablets and coated tablets were evaluated in accordance with Indonesian Pharmacopoeia or other pharmaceutical references. Quantitative and qualitative analysis of scopoletine as chemical marker in core and coated tablet has been conducted. Maltodextrin DE 1-5 from cassava starch indicated as coated material compound at noni fruit dry extract sugar coated tablet. The yield of scopoletine in core and coated tablet was 82.91 and 79.61%, respectively. Maltodextrin were potential as coating material in noni fruit dry extract sugar coating tablet and scopoletine as marker compound.

Key words: Maltodextrin, sugar coated tablet, noni extract

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INTRODUCTION

Among the medicinal plant discovered by the ancestors of Polynesians, *Morinda citrifolia* L. (Noni) is one of the traditional folk medicinal plants that has been used for over 2000 years in Polynesia (Whistler, 1985). *M. citrifolia* is also grown in Indonesia. Noni is one of the popular plant used in herbal remedies to treat various common diseases and to maintain overall good health (Krauss, 1993). This plant is in high demand in alternative medicine for different kind of illnesses such as arthritis, diabetes, high blood pressure, muscle ache and pain, menstrual difficulties, headaches, heart disease, AIDS, cancers, gastric ulcer, asthma (Wang and Su, 2001; Solomon, 1999; Gurib-Fakim and Brendler, 2004; Wiart, 2002). The fruit juice has bad smell or possesses a rancid cheesy flavor and odor due to its content of carboxylic acids (Fugh-Berman, 2003; Duke *et al.*, 2002). Sugar coating tablet is one of the solution to overcome that problem and improve stability and palatability of the tablets in order to be acceptable. Furthermore, tablets are now the most popular dosage form, accounting for some 70% of all ethical pharmaceutical preparations produced (Rubinstein, 2000).

Many tablets today are coated after being pressed to protect tablets ingredient from moisture in the air and eliminate bad smell or an unpleasant taste. Modern tablets coatings material is polymer and polysaccharide based, plasticizers. Maltodextrin ($C_6H_{10}O_5$)_n. H_2O is a polymer of saccharides, that proper to use as coating material. It is consists of glucose units primarily linked by α -1, 4 glucosidic bounds with DE (dextrose equivalent) values lower than 20. Maltodextrin has several physical and functional properties, such as plasticizer, compressibility and viscosity vary according to the extent of starch hydrolysis, which is characterized by DE determination (Lloyd and Nelson, 1984; Alexander, 1992). The varying properties of maltodextrin are indicated by the DE and the Degree of Polymerization (DP), they are depend on the degree of hydrolysis and enzymatic treatment. The high viscosity of maltodextrin is an important property in many applications (Kennedy *et al.*, 1995) especially as sub-coating material. The viscosity of maltodextrin will increase with the degree of polymerization or low DE. Although tablet sub-coating formula need a film forming material like maltodextrin, however composition of formula sub-coating tablet using maltodextrin has not been reported. Maltodextrin, one of the polymer derivatives can be used as film coating material (Wade and Weller, 2000; Effionora, 2002).

Maltodextrin was made by hydrolysis of cassava starch using amyolytic enzymes such as α -amylase and yields a complex mixture of different saccharides. Moore *et al.* (2005) reported that the action of the α -

amylase on cassava starch is different from corn starch at the first fifteen minutes of hydrolysis. Cassava starch and corn starch are different on amylose-amylopectin content and viscoamylographic properties, so maltodextrin from difference source of starch have difference properties even though in the same DE. Maltodextrin from cassava starch is potential material for coating tablet, because it is inexpensive and can be used in the coating with simple equipment process. Coating material must be dissolved or disrupted before the gastrointestinal fluids can promote disintegration of the core tablet and dissolution of the drug.

Core tablets are made with active ingredient noni fruit dry extract. Making tablet for natural product is more difficult than for synthesis drug. Hygroscopic properties of the dry extract can bad flow ability of the tablet mass. The most frequently employed technique for preparing tablets involves the convention is free of flowing drug particles properties. The flow properties of powders are critical for an efficient tableting operation. A good flow of the powder or granulation to be compressed is necessary to assure efficient mixing and acceptable weight uniformity for the tablets (Wadke *et al.*, 1989). To overcome the limitation, the tablets are processed by wet granulation method. A binder is usually added to ensure granule formation, Avicel PH 102 as a binder material was used in the core tablets formulas.

To identify the marker of the active ingredient in the herbal medicine is important for knowing how much active component intake by patient for single dose, especially in the sugar coating tablet. In this research scopoletine was used as a standard of comparison marker, because it was one of the mayor components in noni fruits. The major components in noni plant have been identified such as scopoletine, octoanoic acid, alkaloids, sugar, tannin, steroid, terpenoids, flavonol glucosides and glycoside antraquinon, accumulated mainly in roots, leaves, stems and fruits) (Hirazumi and Furusawa, 1999; Wang and Su, 2001).

The aim of this investigation is to study the effect of maltodextrin DE 1-5 from cassava starch as a sub-coating material in the sugar coated tablets of noni fruit dry extract.

MATERIALS AND METHODS

Material: Material used in this study were as follow: cassava starch (PT. Sungai Budi Industry, Indonesia), ethanol, methanol, acetic acid, n-hexane, dichloromethane, Na OH, $CaCl_2$ and HCl (Merck Chemical Co., Germany), Mg Stearate, talc and stearic acid (Takehara, Kagaku Kogyo Co LTD, Japan), Primojel (Avebe), Avicel PH 102, Pharmacoat 606, Pharmacoat 904 (Shin-Etsu, Japan), Aerosil (Degussa), PEG 6000 (Hoechst/Clarien), sucrose

(KIFA, Indonesia) and scopoletine (LIPI, Indonesia), silica gels (Wonder), lactose Spray Dried (DMV International).

Extraction of noni fruits: The noni fruit dry extract was made by squeezing ripe noni fruits, the seed was separated from flesh of the fruits, mixed with water (1:2) and filtered. The filtrate was evaporated at 50°C for 24 h, subsequently in vacuum dryer at 40° for 12 h. The noni fruit dry extract was grounded and passed through a 30, 45, 60 and 80-mesh screen.

The extract evaluation: Determination of ash content, loss on drying and microbial content were conducted on every extracts according to Indonesia Pharmacopoeia IV (ed.).

Determination of scopoletine concentration in the extract: Determination of calibration curve of scopoletine standard solution was conducted using LCMS (Mariner Biospectrometry) with a reversed phase column phenomenox C18, methanol-ethanol-water (25:35:40) as mobile phase, flow rate of 0.5 mL min⁻¹ and column pressure 178.2 Bar. Scopoletine content in the extract was calculated by comparing peak area of the samples with peak area of the scopoletine standard. The dry extract (5 g) was suspended in 100 mL of series solvents; n-hexane, dichloromethane, ethyl acetate, methanol and distilled water, respectively. All of the sample were shaken for 24 h. The liquid was filtered and evaporated at 50°C for 24 h, followed by drying of the sample at 105°C until constant weight. Finally, scopoletine content of the dry extracts were calculated by sum of scopoletine content of each solvent the extract.

Preparation of maltodextrine DE 1-5 from cassava starch: The suspension of cassava starch was prepared with 50% w/w of starch to distilled water, calcium chloride was added (5 ppm), pH adjusted to 6.5 with sodium chloride 0.1N and 0.1% v/b Liquezyme EX[®] was added. The suspension was heated at temperature 93±3°C for 4 min, in order to produce maltodextrin (DE 5-10). Then, the suspension was dried by drum dryer at 80°C. The dried product was grounded and passed through 100 screen mesh. Finally, Dextrose Equivalent (DE) of the product was determined by Lane Eynon method (AOAC, 1970).

Physicochemical properties of Maltodextrin: Determination of particle shape, size, color, loss on drying, residue of ignition and pH of maltodextrin were conducted.

Preparation and characterization of core tablet: The composition of core tablet formulation was listed in Table 1. Each tablet contains 250 mg extract noni fruits. Ethanol 95% was added to the powder mixture in a

Table 1: Composition of core tablet extract noni fruit

Ingredients	Formulation (mg)			
	F I	F II	F III	FIV
Noni extract	250.0	250.0	250.0	250.0
Corn starch	35.0	35.0	35.0	35.0
Avicel PH 102	0.0	3.5	7.0	10.5
Stearic acid	1.0	1.0	1.0	-
Magnesium stearate	3.5	3.5	3.5	3.5
Talc	3.5	3.5	3.5	3.5
Aerosil	7.0	7.0	7.0	7.0
Lactose spray dried	51.0	47.5	44.0	40.5

mixer (Erweka). The wetted mass was granulated manually by passing it through a 12-mesh screen. The granules dried in a vacuum oven at 45°C for 2 h. The dried granules from the each formula were manually passed through a 30-mesh screen. Then, the granules from each formulas were evaluated. Evaluation conducted includes lost on drying, flow ability, angle of repose and compressibility. Later, magnesium stearate, talc, aerosil were added to the granules and mixed by mixing chamber (Erweka AR 400) for 2 min. Finally, 350 mg tablets mass compacted using single punch with 9 mm concave punch and die sets.

The physicochemical properties of the core tablets: Samples of tablets picked randomly in order to evaluate the weight variation. The friability measured by using friabilator (Erweka TAR) and the hardness of the tablets measured by hardness tester (Erweka TBH28). Disintegration time Electronic balance (Ohaus TS120S) was used for measuring weight variation of the tablet and the friability of the tablet was measured by Erweka-TAR and disintegration time determined by place each tablet in a disintegration chamber. The end point of the disintegration time is considered to be when all the tablet pieces have fallen through the screen. Subsequently, only the best tablet was prepared to make sugar coated tablet and determined scopoletine concentration which was dissolved in (hexane, chloroform, ethyl acetate, ethanol) by LCMS.

Sugar coating tablets: The sugar coating process was divided into three steps; each step was designed to achieve a particular function. Consequently, a variety of excipient may be incorporated in to each type of formulation (Porter and Bruno, 1990).

- Sealing/water proofing; provides a moisture barrier and harden the tablet surface. Composition of sealing formula: 10 g of Pharmacoat 606; 72 g of Ethanol 95% and 18 g of distilled water. Pharmacoat 606 was dissolved in methanol and distilled water, then agitated to increase viscosity. The viscosity of the mixture was determined by Rheometer Hakke. Sealing was carried out with concurrent use of heated air (40°C) to facilitate evaporation of solvent.

Table 2: Composition of the sub-coating formulas

Material (g)	F1	F2	F3	F4
Sucrose	60.0	60.0	60.0	60.0
Pharmacoat 904	1.5	-	-	-
Maltodextrin	-	1.5	3.0	4.5
PEG 6000	4.5	4.5	4.5	4.5
CaCO ₃	22.5	22.5	22.5	22.5
TiO ₂	1.5	1.5	1.5	1.5
Distilled water	150.0	150.0	150.0	150.0

Table 3: Viscosity of the sub-coating formula

Formula	Viscosity (cps)
Formula 1	40.0
Formula 2	38.4
Formula 3	44.8
Formula 4	50.0

- Sub-coating: cause a rapid built up to round off the tablet edges. Sub-coating has four formulas. Composition of the formulas is described in Table 2. Sucrose was dissolved in hot water, then others materials like maltodextrin, PEG 6000, CaCO₃, TiO₂ were added. The suspension was sprayed to the tablets with concurrent use of heated air (40°C), it caused a rapid built up to round off the tablets edges. The viscosity of the sub-coating suspension is described in Table 3.

Coating material must be water soluble polymer, or provides swelling powder like maltodextrin, to make it possibly for the water to penetrate the surface of core tablet that could cause the tablet to disintegrate rapidly in digestive fluids to ensure the drug good bioavailability.

- Polishing: To produce the gloss characteristics to achieve a final elegant product. Polishing was achieved by applying the mixture of polishing wax to tablets in polishing pan. The polishing pan was rotated for 1-2 h. Polishing is conducted to achieve the gloss that is a typical appearance of finished sugar coated tablets.

Evaluation of the sugar coated tablet: Evaluation of the sugar coating tablet is similar to core tablet, which include weight variation, friability, hardness of the tablets, disintegration time and physical appearance of the tablets. Finally, the tablets was stored at 30°C, at 70% Relative Humidity (RH) for one month to measure the moisture absorption.

RESULTS AND DISCUSSION

Non-specific characteristics of noni fruit dry extract has been determined and the result is shown in Table 4. The data shows, noni fruit dry extract fulfilled the requirement to be used as active ingredient in tablet,

Table 4: Some characterization of the noni fruit dry extract

Parameters of characterization	Character
Color	Dark brown
Smell	Specific
Taste	Sweet sour
Loss on drying (%)	5.08
Residue of ignition (%)	6.91
Moisture content (%)	5.08
Concentration of the extract compound solved in hexan (%)	0.13
Concentration of the extract Compound solved in dichloromethane (%)	0.16
Concentration of the extract compound solved in ethyl acetate (%)	0.05
Concentration of the extract compound solved in methanol (%)	0.02
Total concentration of scopoletine (%)	0.046
Total plate count (%)	2.9x10 ³ /g
Yeast and mold value (%)	8.5x10 ² /g
Pathogenic microbial content (%)	Negative

although hygroscopic; addition of wetting agent as a filler overcame the hygroscopic problem to make dry mixture.

The amount of components present in three solvents were different, this indicated that the extract could be contained chemical compound with has different polarity based on the mass spectrums (Fig. 1). The component that was extracted with various solvent not only scopoletine but also the other chemical compound which content in noni fruit.

Specific component or scopoletine was determined by LCMS. The LC chromatogram of the standard and samples showed two peaks with retention time (rt) at 4.9 min and 5.8 min (figures is not shown), the MS spectrum showed the component with molecule weigh of 192 except in the methanol fraction (Fig. 1). The peak of the samples is almost as same as the scopoletine standard peak (Fig. 2). Based on Mass Spectrum (MS), it is shown that the molecule weigh of scopoletine was 193 which indicate M+1. To identify the chemical marker compound from the extract is important, because it can be used for qualitative and quantitative analysis of the extract in the dosage form. Quantitative analysis of scopoletine in the extract was done by measuring peak width of sample compare to peak with of scopoletine standard. Scopoletine content in the noni fruit dry extract was 0.0455% w/w. The noni fruit dry extract was used as active compound in the core tablet formulas. Core tablets were processed by wet granulation procedure to enhance the flow properties of the blend powder.

Core tablet must be stable and strong enough to survive the tablet handling, the tablets must not stick together during the coating process. Coated tablet are useful to extend the shelf-life of components that are sensitive to moisture or oxidation and to cover up the bed smell of the active ingredient. Physical properties of noni fruits extract core tablet is described in Table 5.

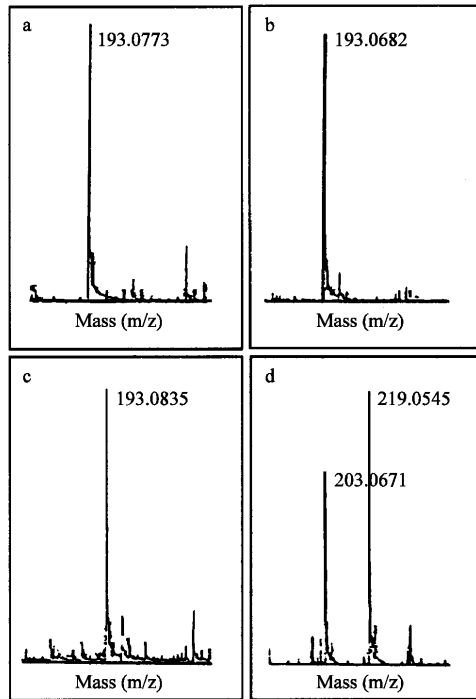


Fig. 1: Mass spectrum of fraction of (a) hexane, (b) dichlormethane, (c) ethylacetate and (d) methanol

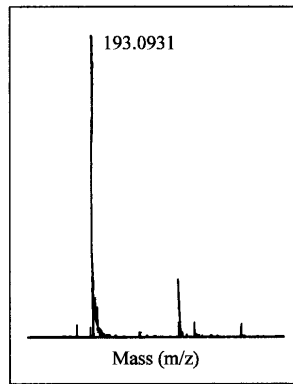


Fig. 2: Mass spectra of scopoletin standards shown m/z 193 for M+1

Table 5: Physical properties of noni fruits extract core tablet

Formula	Friability (%)	Hardness (kp)	Thickness (mm)	Diameter (mm)	Weight (mg)	Disintegration time (min)
1	0.28±0.08	6.00±0.48	5.40±0.05	9.0±0	352.64±2.16	19.5±0.05
2	0.06±0.01	4.92±0.74	5.43±0.06	9.0±0	362.06±5.89	22.3±0.83
3	0.10±0.01	5.75±0.92	5.40±0.08	9.0±0	352.94±3.23	24.5±0.59
4	0.12±0.01	5.86±0.80	5.48±0.08	9.0±0	363.48±2.36	25.0±0.01

Core tablet must be sufficiently robust to resist the stress to which they will be exposed during coating. The important properties of the core tablets such as hardness, friability must be particular attention for preventing tablets fragmentation during the coating process. (Porter and Bruno, 1990). Table 5 shows that only formula 1 complied with condition as core sugar coating tablets.

Table 6: Physical-chemical properties of maltodextrin

Particle shape	Powder
Color	White
Loss on drying (%)	4.60
Residue of ignition (%)	0.08
pH (20% w/v solution)	5.80
Dextrose equivalent	3.75
Particle size	0.40-0.60 μm

Table 7: Physical properties of noni fruit dry extract sugar coating tablet

Formula	Friability (%)	Hardness (Kp)	Thickness (mm)	Diameter (mm)	Weight (mg)	Disintegration time (min)
Formula 1	0.11±0.17	5.80±0.53	5.74±0.12	9.14±0.08	371.85±17.1	25.22±0.64
Formula 2	0.20±0.28	5.00±0.21	6.08±0.10	9.50±0.00	424.35±13.5	23.24±0.21
Formula 3	0.50±0.02	7.50±0.03	5.77±0.12	9.30±0.05	375.93±14.4	25.60±0.14
Formula 4	0.002±0.01	5.00±0.48	5.80±0.15	9.25±0.04	393.72±17.7	25.39±0.11

Consequently, only formula 1 core tablet was used to make sugar coating tablet. The purpose of sealing process was to offer this initial protection and to prevent some tablet core ingredients from migrating into the coating and ultimately spoiling the appearance of the final product. Sub-coating process was to build up the core weigh and also provides the foundation for the remainder process of the sugar-coating. Maltodextrin in the sub-coating formula had function as a film former to improve the structure integrity of coating. Therefore, the function of maltodextrin was important for preparing sugar coating tablet of noni fruit dry extract. Physical-chemical properties of maltodextrin is described in Table 6.

Table 7 shows physical properties of noni fruit dry extract sugar coating tablet. Among the four formulas, only formula 2 was the best of the appearance. Consequently, formula 2 (both core tablet and coated tablet) were determined scopoletine concentration by LCMS. The result shows that scopoletine content in the core tablet was 82.91% which higher than in the coated tablet, which was only 79.61%. According to the literature, dissolution of a small amount of drug from core tablet to the aqueous film may occur during the coating process (Dansereau *et al.*, 1993; Yang and Ghebre-Sellassie, 1990).

CONCLUSIONS

Maltodextrin could be used as one of sub-coating material for noni fruit dry extract sugar coated tablet. The core tablet was processed by wet granulation. As traditional medicine, scopoletine was used as a marker for the noni fruit dry extract, which was determined using LCMS. The chromatogram of sample extract was as same as scopoletine standard with retention times (rt) of 4.9 and 5.5 min and molecule weight of 192.

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