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by Isnaeni Isnaeni

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Influence of Emcompress Concentration on the Physical Properties of Tablet containing Lactobacillus spp. and Guava Leaves Extract

Sugiyartono*, Tutiek Purwanti, Isnaeni, Dhenok Reso Fenda Asega

Pharmaceutical Department, Faculty of Pharmacy, Airlangga University, Indonesia
*Corresponding Author E-mail: **sgytnff@yahoo.com**

ABSTRACT:

Emcompress are widely used in tablet formulation because it has good compressibility. The objective of this research is to investigate the influence of emcompress concentration on the physical properties of tablet containing Lactobacillus spp. and guava leaves extract.

Tablets containing Lactobacillus spp. and guava leaves extract prepared into four series and compressed by direct compression method using emcompress as a filler. Each formula using emcompress with different concentration i.e.: 0% (F1), 0,1% (F2), 0,19% (F3) and 0, 5% (F4). All tablet met the pharmacopoeia requirements during following test: hardness and friability. The disintegration time and moisture contents did not meet the pharmacopoeia requirements.

Conclusion of this research is: increasing the concentration of emcompress will increase the tablet's hardness and decrease the tablet's friability but did not influence other physical properties of tablet containing Lactobacillus spp. and guava leaves extract.

KEY WORDS: Emcompress, physical properties, tablet.

INTRODUCTION:

Benefits of probiotic bacteria in support of human health when used in sufficient amounts already widely attested (Michail et al., 2006). Probiotic strains are the most widely used is a species of Bifidobacterium or Lactobacillus (WHO, 2002). *Lactobacillus acidophilus*, *Lactobacillus casei* and *Lactobacillus bulgaricus*, have been proven to prevent invasion and adhesion *Escherichia coli* in the intestinal mucosa as well as being able to modulate the immune system naturally and produce specific antibacterial compounds (Servin, 2004). The use of a combination of several probiotic has been reported can increase the effects of addition on the wall of the bowel Mucosa (Collado, et al., 2007) and can increase the drag power activity against pathogenic bacteria growth when compared to its use in singles (Chapman, et al., 2012)

Probiotic bacteria activity can occur when consumed in a minimal amount of 10^6-10^7cfu gram a day (Krasaekoopt et al., 2003). Some conditions that can lower the viability of probiotic bacteria which are: high temperature during the process of preparation and during storage, the low pH at the gastric fluid and bile salt in the digestive tract (Teanpaisan et al., 2012).

Generally probiotic products are mainly in the form of fermented milk have a weakness in maintaining the viability of the microorganism (Mortazavian et al., 2007), in addition to its distribution and storage processes also require certain conditions with larger volume that causes the storage costs, becomes high (Johnson and Etzel, 1995).

Microencapsulation is one of the most efficient methods in the development of probiotic formulations (Mortazavian et al., 2007). This method can protect probiotic bacteria from environmental influences that do not fit as well as it's amazing being able to control to the target site as colon therapy by using the appropriate matrices (Gbassi and Vandamme, 2012). Microecapsulation can improve the viability of the bacteria during the process of production, storage and as long as the probiotic in the digestive tract, so that the effectiveness of probiotic therapy can be improved (Mortazavian et al., 2007). One of the widely used microencapsulation techniques are techniques of spray drying, which is capable to produce milk probiotic into dry substance with the size of microns (Teanpaisan et al., 2012).

Microparticle is not a final product, which can be developed into tablet form, which is more stable and more accurately determine dosages (Niazi, 2004; Klayraung, et al., 2009; Silva, et al., 2012). Method of making a tablet is the most suitable formula for direct compression because it do not need a lot of heat and humidity (Yuan et al., 2013). This will affect the viability and activity of the probiotic (Teanpaisan, et al., 2012; Mortazavian, et al., 2012). The compression force that does not cause the death of a significant number of probiotic bacteria is 9.8 – 39.8 kN (Silva, et al., 2012). HPMC K100LV matrix and skim milk cannot produce a good physical quality if compressed without the charger because of the nature of the microparticles that still has the ability to absorb moisture in the air (Rowe, et al., 2009; Sweetman, 2009). Therefore, it takes the appropriate filler for direct compression methods. There are fillers for the direct compression such as avicel, was spray-dried lactose (SDL), and emcompres (Lachman, 1990). The advantages of emcompress i.e. perfect compatibility and minimal water content (0.1 – 0.2) (Rowe, et al., 2009) that is expected to keep the moisture which will then be able to maintain tablets quality.

Physical quality levels of tablet is influenced by emcompres used. The disintegration time of tablet will be too long (Lachman, 1990; Rowe, et al., 2009) and reduced the release of the active substance. The addition of disintegrants such Primogel necessary to improve hardness, fragility, disintegration time and release of active substance (Lachman, 1990). In this formula also added Cab-O-Sil who serves as glidant and Stearic Magnesium that has a role as a lubricant to address moisture microparticles are quite high and the difficulty in tablet ejection in the manufacturing process.

From the explanation above, the research on the effects of Emcompres levels on tablet combination probiotic milk microparticles of Lactobacillus spp. On physical quality tablets has been done. The Data obtained will be analysed by the method of one-way ANOVA and tested Honesty Significant Difference (HSD) 0.95 confidence level with Tukey.

MATERIAL AND METHODS:

Materials:

(i) Aconsortium of probiotics (*Lactobacillus acidophillus* and *Lactobacillus. casei* obtained from Gadjah Mada University. *Lactobacillus bulgaricus* obtained from the Faculty of Science and Technology, Airlangga University); (ii) Water extract of Guava leaf (Guava leaf Simplisia obtained from Materia Medika Store); (iii) HPMC K100LV; (iv) skim milk powder; (v) Emcompres; (vi) Cab-O-Sil; (vii) Mg Stearic (obtained from PT Brataco); and (viii) Primogel.

Research Tools:

Analytical scales, pH meter, Otoklaf, Mikropipet, Incubator, Tumbling mixers, Scanning Electron Microscopy (SEM)

Brand FEI Type: Inspect-S-50, microscope, Tabletasi Tool (machine Hidraulic Press GrasebySpecac), Infrared Spectrophotometer, Laminar Air Flow (LAF), tablet hardness test equipment (Erweka TBH type 220), the fragility of the test equipment (Erweka Friabilator Type TAP) test tool, content of lengas (Moisture Analyzer HB43-S Type), time-tested tools were destroyed (Erweka ZT disintegrator type 501 Series No. 114021d4c), the, test tubes, petri dish, glass tools and more.

RESEARCH WORK PROCEDURES:

1. Identification of the material Research:

1.1. Microparticles:

The active ingredient in the tablets are combination of probiotic milk microparticles of Lactobacillus spp. and water extract of leaves of the microparticles of guava.

The morphology of the surface characteristics of microparticles is observed using Scanning Electron Microscopy help (SEM). Microparticles is placed on the grip there is a binder containing a grain of metal, e.g. Pt Then gold at chamber evaporated so that the steam can Gold coat entire surface of microparticles. The surface of gold microparticles coated. Then observed by SEM (Hoediasmoro, 1985).

Moisture Content of Microparticle:

Use Moisture Analyzer HB43-S Type. Weighed granule 0.5– 1.0 g is inserted into the Cup, then the tool is turned on and waits for 10 minutes. Moisture content will appear in the tool. The criteria of MC probiotics is 2 – 4 (Teanpaisan, et al., 2012; Yonekura, et al., 2013).

Particle Size of Microparticles:

Examination of particle size using the microscope begins with ocular scale calibration with how to install ocular and objective micrometers in place, observing scale until both clearly visible under a microscope, the initial line by comparing with ocular scale with objective scale. Start the measurement of particle diameter $\geq$ 300 as many particles.

1.2. Excipient:

Excipient materials that are used in these tablets were Emcompres, Primogel, Cab-o-sil, Mg Stearic.

Organoleptic:

Observed color, odor, flavor, and shape of the SDL is obtained, then compared with the literature (Florey., 1986 in Rahardjo 2011).

The Infrared Spectrum:

Examination of the Infrared Spectra with using the technique of pellets KBr. as much as 1 mg of the substance with 100 mg of KBr crushed until it is homogeneous. Then put in a vacuum dryer, then printed with hydraulic presses up to gained a thin opaque plates. Inspection results compared to the infrared spectrum of materials in the library (Silverstein, et al., 2005).

2. Tablets Preparation:

The Formula of Tablet Probiotic Microparticles and Microparticles of Guava Laves Water Extract:

Table 1 The Formula of Tablet probiotic Microparticles and Microparticles of Guava Leaves Water Extract:

No.	Material	Function	F1	F2	F3	F4
1	Granul*	Active Substance	350 mg	350 mg	350 mg	350 mg
2	*Emcompres*	Filler	-	45 mg	95 mg	145
3	Mg Stearat	Lubricant	10 mg	10 mg	10 mg	10 mg
4	Cab-o-sil	Glidant	5 mg	5 mg	5 mg	5 mg
5	Primogel	Disintegrant	40 mg	40 mg	40 mg	40 mg
Tablet Weight			405 mg	450 mg	500 mg	550 mg

Description:

Granule is a combination of probiotic milk microparticles of Lactobacillus spp. and water extract of leaves of the microparticles of guava with a 7: 3

Procedure:

1. Materials and tools prepared and weighed according to the needs that exist in the draft formula;

2. Mg stearic and Cab-o-sil is mixed ad homogeneous for 5 minutes;

3. Compression the mixture (2) using the printer using the hydraulic punch tablet diameter 12 mm (according to the table size of punch with a mass of tablets to be compressed). The condition of compression was: 2 tons compression force for 10 seconds

4. Physical Quality Test of Tablets include:

Tablet Hardness Test:

Inspection conducted using the Erweka TBH 220 tool. Taken 10 tablets in each batch formula, measure the violence by giving the weight load on the tablet. When the tablet is broken, will read the maximum load that can be held by tablets (Lachman, et al., 1990). Criterion harshness for tablets in general are 4 – 8 kP (Parrot, et al., 1970)

Tablet Friability Test:

Taken a number of tablet equivalent to 6,5 g, tablets and cleaned with a brush carefully, then weighed and measured with the ERWEKA Friabilator tools Kerapuhannya Type TAP for 4 minutes at speed 25 rpm. After it was weighed and calculated the percentage of tablet weight reduction in severity. The criteria of the fragility of the tablet is 0.8 (Lachman, et al., 1990).

Tablet Disintegration Time:

Checked the disintegration time of tablets using Disintegrator Type Erweka ZT 501. Put 5 tablet into the basket on the tools, then ride the lower basket 30 times each minute on a regular basis in water 1000 ml, temperature (36 – 38) 0 c. Tablet revealed disintegrated if no part of the tablet is left above the gauze, and time needed to destroy the fifth tablet of no more than 15 minutes (anonymous, 1979).

Moisture Content of Tablet:

To analyze the moisture content of tablets can be used tools Karl Fischer Titrator. However due to the limited availability of tools, used Moisture Analyzer HB43-S Type. The Tablet is destroyed slowly, weighted 0.5 g granule put into vials, then the tool is turned on and wait for 10 minutes. Moisture content will appear in the tool. The criteria of MC powder tablet to tablet probiotics is 2 – 4% (Teanpaisan, et al., 2012; Yonekura, et al., 2013).

RESULTS AND DISCUSSION:

Determination of Particle Size Distribution

Table 2: The average particle size of each formula microparticles

Microparticle Formula	The average of particle size (µm)
Formula I	60,68 µm
Formula II	64,51 µm
Formula III	83,60 µm
Formula IV	87,27 µm

Determination of moisture content (MC):

Results of inspection of moisture content (MC) of each formula in the table presented below

Table 3 Moisture Content (MC) of each formula of microparticle

Microparticle Formulation	Moisture Content (%)
Formula I	8,47 ± 0,57
Formula II	8,91 ± 0,62
Formula III	10,47 ± 0,85
Formula IV	10,97 ± 0,44

Description:

Data inspection results moisture content (MC) is the average observations 3 x ± SD.

Replication. From these data it can be seen that an increase in the levels of HPMC K100LV of 0, 0.1, 0.2 and 0.3 can increase the content of moisture (MC) microparticles milk probiotic Lactobacillus spp.

Results of the Characterization of Materials:

Qualitative material inspection results of HPMC K100LV, Emcompress, Mg, Stearic Primogel, Cab-O-Sil, and microparticle scan are seen in table 4, 5 and 6.

HPMC K100LV:

Results of the characterization of the HPMC K100LV examination generally include qualitative organoleptic FTIR spectra, inspections, examination of viscosity checking pH and presented in table 4 (Rowe et al., 2009, Silverstein et al., 2005, The Dow Chemical Company). From the results of the qualitative examination noted that the K100LV meet the requirements of HPMC.

Table 4. The Result of characterization of HPMC K100LV

No.	Inspection	Result	References
1.	Organoleptic	Fine powder. White, odorless and tasteless.	Powder (granule or fiber), white or cream white, odorless and tasteless *
2.	FTIR Spectra:	Wave numbers:	Wave numbers **:
	OH (Hydroxyl)	3466cm^{-1}	3650 - 3584 cm^{-1}
	C-H (Alkyl)	2918cm^{-1}	2800 - 3000 cm^{-1}
	C-O (Ether)	1065cm^{-1}	1260 - 1000 cm^{-1}

Table 5. The Result of Characterization of Emcompress

No	Method	Result	References
1.	Organoleptic	White powder, tasteless and odorless.	Powder or crystal, white, *
2.	FTIR spectra : OH (Hydroxyl)	Wave numbers : 3435cm^{-1}	Wave numbers **: 3650 - 3400 cm^{-1}

Data examination results are the average of the observations 3 x ± SD replication

Emcompress:

Inspection results qualitative emcompress include organoleptis, MC, checks and FTIR spectra can be seen in table 5.

Description:

Data examination results are the average of the observations 3 x ± SD replication) Rowe et al., 2009; Silverstein et al.), 2005.

From the results of the qualitative examination revealed that the Emcompress meet the requirements.

Primogel:

Inspection results qualitative Primogel include examination of organoleptic and FTIR spectra can be seen in table 6.

Description:

Data examination results are the average of the observations 3 x ± SD replication) Rowe et al., 2009 Silverstein et al.), 2005.

From the results of the qualitative examination noted that the Primogel the requirements

Results of the Characterization of Microparticles:

Microparticles are used in these research is a probiotic bacteria microparticles and microparticles extract guava leaves water with formula as follows:

Before microparticles made tablets, screening performed physical examination microparticles quality morphology, particle size distribution, content of examination and lengas. Further examination of the viability of probiotic bacteria do in microparticles.

Table 6. The Result of Characterization of Primogel

No	Methods	Results	References
1.	Organoleptic	White powders, tasteless, odorless.	White powder, odorless, tasteless. *
2.	Spectra FTIR :	Wave numbers :	Wave numbers **:
	Gugus Aromatic ring	1634 cm^{-1}	1660-2000 cm^{-1}
		1427 cm^{-1}	1450-1600cm^{-1}
	C-H (Alkyl)	2927 cm^{-1}	2800 - 3000 cm^{-1}
	C-O (Ether)	1162 cm^{-1}	1260 - 1000 cm^{-1}
	OH (Hydroxyl)	3655 cm^{-1}	3650 - 3584 cm^{-1}
	O-H (Carboxylic acid)	2927 cm^{-1}	2500-3100 cm^{-1}
	O-H (Alcohol)	3573 cm^{-1}	3400-3650 cm^{-1}
	C-O (Alcohol)	1084 cm^{-1}	1050-1150 cm^{-1}

Table 7. Tablet hardness testing results

Formula	No	Hardness (Kp)	Average ± SD
1	1	20.45	21.06±0.55
	2	21.20	
	3	21.52	
2	1	23.20	24.62±1.23
	2	25.20	
	3	25.46	
3	1	26.14	26.75±1.15
	2	28.08	
	3	26.02	
4	1	32.52	32.73±0.22
	2	32.96	
	3	32.71	

Fig.1. Microparticles of Probiotic Milk-Water extract of Guava Leaf (magnification 10,000 x)

Results of the Examination of the Morphology of Microparticles

The results of the examination of the microparticles of milk probiotic Lactobacillus spp. and leaf water extracts microparticles guava is carried out using scanning electron microscope (SEM) which can be seen from figure 1.

5.2 Examination for physical quality of Tablet

The quality of the physical examination results of tablets that include hardness, friability, time for disintegration, and the content of moisture can be seen on 7, 8, 9 and 10.

On examination the hardness formula I to IV in a row is, 21.06 ± 0.55, 24.62±1.23, 26.75±1.15, 32.73±0.22 (table 7). When compared with the requirements of Wagner, then all formulas meet the requirements of the Kp 7. results of the statistical analysis used one-way ANOVA is known to all different meaningful formula except formula 2 formula 3 was no different to be meaningful.

On examination of the friability of the successive results obtained from the formula I to IV (table 8) of the fourth such formula has met the requirements of the friability of a tablet that is less than 1 (Lachman et al, 1986).

Table 8. Results of Examination of the Friability of the Tablet

No.	Formula	Observation at (min.)			
		1	2	3	Mean± SD
1	I	28	24	28	26.67±2.31
2	II	26	24	27	25.67±1.53
3	III	25	25	28	26.00±1.73
4	IV	25	23	24	24.00±1.00

Table 9. Disintegration Time of Tablet

No.	Formula	Observation at (min.)			
		1	2	3	Mean± SD
1	I	28	24	28	26.67±2,31
2	II	26	24	27	25.67±1,53
3	III	25	25	28	26.00±1.73
4	IV	25	23	24	24.00±1.00

On examination results obtained by successively disintegration time. Based on the results of the statistical analysis used one-way ANOVA revealed that there is no significant differences between each formula. This is due to the amount of primogel (disintegrant) used different weights period though remains, while the greater content of Moisture (MC) on increasing the weights so that time destroyed does not differ significantly.

Table 10. Moisture Content of Tablet

NO.	F I	F II	F III	F IV
1	6.05%	5.58%	6.31%	6,97%
2	6.06%	6.30%	6.20%	6.94%
3	6.02%	6.83%	6.31%	6.65%
Averages ± SD	6.04±0.02	6.24±0.62	6.27±0.63	6.85±0.17

On examination of the content of successive results obtained from formula I to IV (table 9), gets the content of a relative of moisture due to microparticles which used to have a large content of moisture. Based on the results of the statistical analysis used one-way ANOVA revealed that there is no meaningful difference between a formula for each formula.

Table 11. : Average Physical Quality Inspection Results Tablet

Quality Inspection	F1	F2	F3	F4
Hardness (Kp)	21.06±	24.62±	26.75±	32.73±
	0.55	1.23	1.15	0.22
Friability (%)	0.08	0.79	0.92	0.53
Disintegration Time (Min.)	24.19±	23.92±	24±	22.69±
	1.31	1.31	0.17	0.47
Moisture Content (%)	6.04±	6.24±	6.27±	6.85±
	0.02	0.62	0.63	0.17

CONCLUSION:

Conclusion of this research is increasing the concentration of emcompress will increase the tablet's hardness and decrease the tablet's friability but did not influence other physical properties of tablet containing *Lactobacillus* spp. and guava leaves extract.

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