

The Effects of Binder on the Physical Characteristic of Squeezed Rhizome of *Kaempferia galanga L* Lozenges

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ABSTRACT

Background: The lozenge is one of the drugs to overcome a sore throat. This contained an active ingredient can be either a synthetic or herbal materials. *Kaempferia galanga L* is a medicinal plant that able to relieve cough and sore throat. So, its potential made be lozenges. Lozenges are compressed tablets which it must be using the binders on formulation. **Objectives:** This study was to investigate the effect of the binder on physical characteristic of squeezing rhizome of *Kaempferia galanga* lozenges using mannitol base. Evaluation was conducted using different kinds of binders (i.e., gelatin, hydroxypropylmethylcellulose (HPMC) 1290 cps and polyvinylpyrrolidone (PVP) K30 at 1%, 2%, and 3% concentrations. **Methods:** The squeezed rhizome of *Kaempferia galanga L* was dried using mannitol. The lozenges were prepared by a wet granulation method and compressed by a hydraulic press at 2-ton pressures. Lozenges had been evaluated, including hardness, fragility, and dissolves time of lozenges. **Conclusion:** Lozenges that contained Gelatine and PVP K30 in the concentration of 2% and 3%, both of them were as well at the range. While the lozenges that contained HPMC 1290 cps provides good results at the concentration of 3%. All parameters are dependent on the type, quality and concentration of a binder.

Keywords: *Kaempferia galanga*; Gelatin; HPMC 1290 3 cps; PVP K-30; wet granulation; lozenges.

INTRODUCTION

Lozenge is one of the drug used to overcome the sore throat. The active ingredients of lozenge formulation can be either synthetic or herbal materials (Mendes & Bhargava 2006). One of the herbal ingredients that can be used as an active ingredient of lozenges is *Kaempferia galanga L* because it contained essential oil especially ethyl trans-p-methoxycinnamate that has antibacterial activity (Wong, Ong, & Lim 1992; Supinya et al. 2005).

Lozenges are compressed tablets formulated, without a disintegrate that contain one or more medicaments, usually in a flavored, sweetened base, and intended to dissolve or disintegrate slowly in the mouth to provide drug delivery locally to the mouth, tongue and throat. They can be prepared by molding (gelatin and/or fused sucrose and sorbitol base) or by compression of sugar-based tablets. Lozenge tablets are generally formulated as relatively large-diameter (> 12.5mm), flat-faced (beveled edge), heavy (> 700 mg) tablets more hardness (> 15 kg) (Mendes & Bhargava 2006).

Wet granulation is most commonly used method for the manufacturing of tablets. The advantages of wet granulation method is reduced segregation of formulation components during storage and processing. Leading to reduced intra and inter batch variability. In wet granulation process, binders promote size enlargement to produce granules and thus improve flow ability of the blend during the manufacturing process. The classification of binders are sugar (i.e., sukrosa, mannitol, liquid glucose), natural binders (i.e., acasia, tragacanth, gelatin, starch paste, pregelatinized starch, alginic acid, cellulose), and synthetic/semi-synthetic polymers (i.e., Methyl Cellulose, Ethyl Cellulose, Hydroxy Propyl Methyl Cellulose (HPMC), Sodium Carboxy Methyl Cellulose, Polyvinyl Pyrrolidone (PVP), Polyethylene Glycol (PEG), Polyvinyl Alcohols, Polymethacrylates) (Fred J. Bandelin 1989, Karthik Varma 2016)

Therefore, this study has been done to investigate the effects of different binders on the physical characteristic of squeezed *Kaempferia galanga* rhizome lozenges prepared by the wet granulation method. To achieve this research, studies were conducted using three different binders with different concentration, namely Gelatin, HPMC 2910 3cps, PVP K30 at 1%, 2% and 3%. Effects of binders were assessed by testing hardness, friability and dissolve time.

METHOD

Materials

Kaempferia galanga L rhizome as a drug. Mannitol as the filler. Polyvinylpyrrolidone (PVP) K 30, hydroxypropyl methylcellulose (HP MC) 2910 3cPs and gelatine were used as binders. Magnesium stearate was used as a lubricant. Aspartame was a sweating agent.

Preparation of drying squeezed of Kaempferia galanga in mannitol

The freshness of *Kaempferia galanga* Rhizoma was blended, then squeezed. The squeezed were evaporated in water bath until the volume reduced about a half and then added the mannitol. It was dried at 40-50°C for 24 hours.

Preparation of granules

Batch of *Kaempferia galanga* lozenges formulations containing drying squeezed of *Kaempferia galanga* in mannitol + Gelatine or HPMC 2910 3cPs or PVP K30 + aspartame + magnesium stearate (Table 1).

Table 1 The Formulation of *Kaempferia galanga* L rhizome lozenges with 1%, 2% and 3% of the binders (w/w)

Materials	Gelatine				HPMC 1920 3 cps			PVP K30		
	0%	1%	2%	3%	1%	2%	3%	1%	2%	3%
Drying squeezed rhizome of <i>Kaempferia galanga</i> in mannitol (mg)	1980	1960	1940	1920	1960	1940	1960	1960	1940	1920
Gelatine (mg)	-	20	40	60	-	-	-	-	-	-
HP MC 2910 (mg)	-	-	-	-	20	40	60	-	-	-
PVP K30 (mg)	-	-	-	-	-	-	-	20	40	60
Aspartame (mg)	10	10	10	10	10	10	10	10	10	10
Magnesium stearate (mg)	10	10	10	10	10	10	10	10	10	10
Weight of tablet (mg)	2000	2000	2000	2000	2000	2000	2000	2000	2000	2000

The drying of the squeeze of *Kaempferia galanga* rhizome in mannitol was mixing with binder solution and aspartame to get consistency of wetness and then kneaded well. The wet mass was screened through sieve #12 (710µm) to making small granules. The granules were dried at 50°C overnight in an oven and screened through a sieve #16 (100µm). The granules were stored in airtight containers.

Evaluation of the granules

Determination of moisture content

The moisture content of each batch of the granules was determined on a wet-weight basis on an Ohaus moisture balance (Ohaus Scale Corporation, New Jersey, USA). Quantities (2g) of each sample was uniformly spread on the sample pan and then the heating cycle was started. The percentage moisture content which is the percent weight loss from the sample by heating was displayed on the equipment. The instrument was allowed to cool between tests.

Angle of repose

The static angle of repose was determined using the fixed base cone method. A 100 g quantity of the sample was transferred into an open-ended cylinder placed on a static base cone on a horizontal surface. The cylinder was gradually withdrawn vertically and the sample formed a cone-shaped heap. The height of the sample (h) was determined using a cathetometer; the radius (r) was gotten by dividing the fixed diameter by two. Angle of repose (Θ) for each sample was gotten using the equation;

$$\Theta = \tan^{-1} h/r \dots\dots\dots(1)$$

Granule size distribution

The size distribution of each granule formulation was determined by sieve analysis (British Standard 1460). A stack of sieves of the following sizes: 40 mesh (425 µm) 60 mesh (250 µm), 80 mesh (180 µm), 120 mesh (125 µm) and the receiver, was arranged in descending order of aperture size with the receiver at the bottom. One hundred gram of granules was put on the uppermost sieve, firmly covered and the stack of sieves was shaken for 10minutes on a sieve shaker (Pascal Engineering, Essex, England). The quantity of granules retained on each sieve was weighed and the percentage of fine, was calculated.

Preparation of lozenges

Quantities (2000mg) of the powder and granule formulations of lozenges were compressed for 1 min into tablets with pre-determined loads, using hydraulic hand , using 20mm die and flat faced punches. After compression, lozenges was stored in airtight containers for 24 hours to allow for elastic recovery and hardening and to prevent falsely low yield value.

Evaluation of Lozenges

Hardness test

Tablet hardness tester was used to measure the hardness. Five lozenges tablets were selected randomly from each formulation for tested. Lozenge was placed between the spindle and anvil of the tester and the calibrated length adjusted to zero. The knob was then screwed to apply a diametric compression force on the tablet and the position on the calibrated length at which the tablet broke was recorded in kg units. A mean hardness was calculated for each batch and thus their standard deviations and coefficient of variations were calculated. Term of hardness lozenge is 10kg to 20kg (Parrot 1970).

Friability test

The friability testing of lozenges made using friabilator tester. Performed with 10 lozenges selected randomly. The lozenges Dusted carefully from the prior testing Lozenges weighed accurately, and place in the drum. The drum is rotated at 25 rpm for 100 rotations and remove the lozenges. Then lozenges are dusted with a brush, and then accurately weighed. The friability expressed as a weight loss percentage (USP 29 2006).

Dissolve time

Testing time dissolving tablet using a Disintegration Tester. This device consists of a basket containing six plastic cylinder that opened on top and base covered with a sieve size of 10 mesh. The number of tablets used to test amounted to 6. The basket put in a beaker containing water with a temperature of $37^{\circ} \text{C} \pm 0,5^{\circ} \text{C}$, as the media. Each tablet is inserted into each cylinder, then raised and lower the basket with a fixed frequency between 28-32 times per minute until the tablets disintegrate. Time-dissolving tablet is calculated when the tablets on the basket starts lowered into the media tablet runs until dissolved. The test was repeated 3 times and the average was determined (USP 29 2006).

RESULT AND DISCUSSION

The squeeze was obtained from 1 kg of fresh *Kaempferia galanga* L rhizome is 300 ml, the juice is subsequently dried with 265g of mannitol. The obtained of the squeeze rhizome of *Kaempferia galanga* in mannitol powder was 280g.

The result of evaluating the granules of Squeezed Rhizome of *Kaempferia galanga* L, namely the values of percentage moisture content, angle of repose, and percentage of fine are presented in Table 2.

Moisture content. The moisture content of all batch granules with different types and quantities of binders are within the specified range (1-2%). The moisture content in granules is an important factor in granule quality, chemical stability of the material, and the possibility of microbial contamination. The dried granules still contain certain moisture. The moisture content that is too low increases the likelihood of capping while the moisture content is too high increases the likelihood of picking on the preparation (Aulton, M.E. 2002).

Table 2 Properties of formulations containing different types and quantities of binders

Parameters	Binder Conc.	Type of Binder		
		Gelatin	HPMC 1920	PVP K330
Moisture content (%)	0%	1,47 ± 0,13	1,31 ± 0,35	1,47 ± 0,13
	1%	1,35 ± 0,10	1,19 ± 0,03	1,35 ± 0,10
	2%	1,14 ± 0,04	1,26 ± 0,11	1,14 ± 0,04
	3%	1,47 ± 0,23	1,37 ± 0,23	1,47 ± 0,23
Angle of repose (°)	0%	35,57 ± 1,97	36,23 ± 0,08	35,57 ± 1,97
	1%	31,61 ± 0,42	36,27 ± 1,05	31,61 ± 0,42
	2%	33,85 ± 0,29	35,76 ± 0,99	33,85 ± 0,29
	3%	34,78 ± 0,82	28,89 ± 0,35	34,78 ± 0,82
Fines (%)	0%	1,30 ± 0,20	1,30 ± 0,20	1,30 ± 0,20
	1%	0,85 ± 0,17	0,59 ± 0,10	0,85 ± 0,17
	2%	0,43 ± 0,04	0,42 ± 0,04	0,43 ± 0,04
	3%	0,66 ± 0,02	0,30 ± 0,01	0,66 ± 0,02

Angle of repose

For result of angle of repose measurement, all batch formulation are within the range of 30° -40°, this means that the flow rate of the granules are good (Carl RL 1965, USP 29) The magnitude of the angle of repose is influenced by the shape, size and moisture of granules The angle of repose test describes the flow properties of the powder during the process of making the tablet. The magnitude of the angle of repose is influenced by the tensile force and friction between the particles, if the tensile force and friction force are weak, the granules will be faster and easier to flow (Fonner, et al, 1981, USP 29). The more conical the resulting, the smaller the angle the slope and the better the flow properties of the powder.

Percentage of fine

Particle size can affect the average weight, weight variation, crushed time of the tablet, flow rate and kinetics of drying speed in wet granulation. A good granules have a number of fines <20%. If the number of fines a bit then it will reduce the angle of repose, otherwise if the number of fines a large, it will increase the angle of repose. In addition, fines affect the flow properties and uniformity of tablet weight. Resulting measurement of fines in all formulation showed that 2 all batch formulation have fine less than 20%, thus distribution of particle size for all batch are good.

Effects of the binder on the tablet hardness

Tablet hardness of all batch was shown in Table 3. It appears that with the increasing concentration of the binder, the hardness of the tablet is also increasing. Increasing the amount of binder added to a compound resulted in a gradual decrease in tablet porosity as more of the interparticulate voids were filled with binder. That tablets hardness for all formulations used binder at 2% and 3% concentrations were more than 10kg and less than 15kg, except which used HPMC 1920 3cps at 2% concentration. This indicated that hardness varied with the binder type. Polymeric binder, PVP, and natural binder, gelatine showed high values and starch binder, otherwise HP MC 1920 3cps gave the lowest value for hardness.

Table 3 The Quality Physical of Squeezed Rhizome of Kaempferia galanga Lozenges

Parameters	Binder Conc.	Type of Binder		
		Gelatin	HPMC 1920	PVP K330
The Hardness	0%	6.20±0.16	6.20±0.16	6.20±0.16
	1%	8.25±0.26	7.58±0.57	8.33±0.21
	2%	10.25±0.20	9.33±0.35	10.40±0.32
	3%	12.20±0.16	11.18±0.33	12.20±0.20
The Friabilitas	0%	1.11 ±0.12	1.11±0.12	1.11±0.12
	1%	0.28±0.05	0.97±0.02	0.33±0.11
	2%	0.28±0.03	0.79±0.05	0.26±0.05
	3%	0.26±0,20	0.33±0.06	0.20±0.05
The Dissolve Time	0%	6.17±0.29	6.17±0.29	6.17±0.29
	1%	7.00±0.00	8.17±0.29	6.67±0.29
	2%	7.67±0.29	8.83±0.29	7.17±0.29
	3%	8.50±0.50	9.83±0.29	8.67±0.29

Hardness of tablets depends on the degree of binding which relies on the amount of the binder and the compression force. The higher hardness of the tablet with the binder can be related to its film formation ability and its cohesive strength to make solid bonds between particles. As a result, the binder is forced into the inter particulate spaces resulting more solid bond between granules (Rowe 1990)

Effects of the binder on the friability

Friability corresponding to each binder (table 2), it was observed that tablets friability for all formulation was less than 1%, indicating the intergranular forces between the granules is higher (USP 29 2006), it means that all lozenges pass the friability test. The lozenges used gelatin showed the low percentage weight loss at 1%, 2% and 3%, as same as showed the lozenges used PVP, which have percentage weight slightly different with lozenges used gelatine. Otherwise, lozenges used HP MC 1290 3cps have percentage weight less more than the others. This proves that tablets that have high hardness will have low fragility.

Effects of the binder on the dissolve time

The dissolve times obtained for all formulations were shown at Table 2. The dissolve time for all formulation were more than 5 minutes and less than 10 minutes, as shown in Fig.1, this indicates the all lozenges pass to dissolve time test (USP 29 2006). Gelatin softens and dissolves in water, HP MC 1290 3cps swelling and dissolve in water, and PVP K30 dissolves in water, too (Rowe, Sheskey, & Quinn 2009). Lack of hydrophobic material on formulation of lozenges makes it easy to dissolve.

CONCLUSION

In conclusion, I would like to mention that the investigated on the effects of the binder to the physicochemical properties of the lozenges has established the fact that the physicochemical properties, type, quality and concentration of binder itself are the main factors that affect the ultimate quality of the tablet. Results proved that the binders, PVP and gelatine solution, are good binders for preparation of the squeeze of Kaempferia galanga rhizome lozenges at 2% and 3% concentration. While HP MC 1290 3cps at concentration of 3%.

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