FORMULATION OF MANNITOL BASED PEGAGAN (*Centella asiatica L.*) EXTRACT LOZENGES (THE IMPACT OF HPMC 2910 3CPS AS BINDING AGENT TO TABLET PHYSICAL CHARATERISTICS)

Dian Ermawati1, Achmad Inoni, Bambang Widajaja, Saschita
Universitas Muhammadiyah Malang (dianerma@yahoo.com)

Abstract

Pegagan (Centella asiatica L.) is a plant that contains medicinal compounds that are useful to capture free radicals and improve concentration.Therefore an innovation that can provide comfort, convenience, and able to maximize the efficacy of this plant is needed.Lozenges is one option that are able to facilitate and provide comfort, as well as maximize the usefulness.This research is conducted to compare the affect levels of binder HPMC 2910 3CPS towards physical quality of the lozenges pegagan extract (Centella asiatica L) by using with an experimental research methodology.The results obtained are then processed statistically using SPSS 17 with One Way ANOVA method.From the research that has been done, it is found out that the usage of HPMC 2910 3CPS 1% levels in Centella asiatica extracts lozenges is the optimal levels in order to meet the test requirements of hardness, brittleness and the tablet dissolves.

Keyword : *Centella asiatica L., Lozenges, HPMC 2910 3CPS*

ISBN : 978-979-18458-5-4

INTRODUCTION

Pegagan or in Latin language called *Centella asiatica* is a plant that contains a variety of medicinal compounds such as Asiatikosida (triterpenoids), karotenoids, and beneficial mineral salts such as potassium, sodium, magnesium, calcium and iron.

Extracts from plants Centella asiatica (*Centella asiatica* L.) in the form of lozenges made with the expectation would be preferred because it has several advantages over the conventional way of eating. Among other advantages are obtained in terms of taste, acceptabilitas, ease of storage, and ease of taking it. In addition, the appropriate dose of easily obtainable in the form of lozenges so that the maximum therapeutic effect.

Binder formulations are often used for lozenges are Hypromellose (HPMC), ethyl cellulose, PVP, gelatin, acacia, and others. Lozenges can be prepared by wet granulation method. Wet granulation method was chosen because it has several advantages, among others, can improve the flow of powder, increasing the compressibility of materials that are difficult to print, prevent separation of components during the process and can improve compactibility of materials.

Based on the description above in this study made lozenges pegagan extract (*Centella asiatica* L.) by the wet granulation method using HPMC 2910 3CPS binder with different levels that qualify for the manufacture of lozenges that can be pegagan extracts produced lozenges that have good physical properties.

METHODS

Method of the research was carried out by the Experimental Research.

Comparing the influence of binder content of HPMC 2910 3CPS against physical quality lozenges pegagan extract (*Centella asiatic*a L.).

Population lozenges extract of pegagan is made in a study of 100 tablets.

Samples were taken with a probability sampling techniques - Simple Randomized Sampling by the number of samples in accordance with the number of tablets to be tested.

Independent variables: levels of HPMC 2910 3CPS. Dependent variable: The physical quality of lozenges pegagan extract (*Centella asiatica* L.)

The materials used are extracts of pegagan (*Centella asiatica* L.), Mannitol (Pharmaceutical grade), HPMC 2910 3CPS (Pharmaceutical grade), Magnesium stearate (Pharmaceutical grade), Talcum (Pharmaceutical grade).

In this study made four lozenges formula with gotu pegagan extract different levels of binding as follow.

Table I . Formulation of Pegagan extract lozenges

Material	Function	Total amount (mg) in Formulation			
		Fl	F2	F3	F4
Pegagan extract		100	100	100	100
Mannitol	Diluent	1100	1100	1100	1100
HPMC 2910 3CPS	Binder	0	12,49	25.24	38.26
Mg stearat (1%)	Lubricant	12.37	12.37	12.37	12.37
Talk (2%)	Lubricant	24.72	24.72	24.72	24.72
colouring	Coouring	5 gtt	5 gtt	5 gtt	5 gtt
Total weigh		**1.24 g**	**1.25 g**	**1.26 g**	**1.27 g**

ISBN : 978-979-18458-5-4

Description
F l = Formulation with HPMC content of 0%
F2 = Formulation with levels of 1% HPMC
F3 = Formulation with higher levels of 2% HPMC
F4 = Formulation with higher levels of 3% HPMC

Preparation of tablets the process of making these lozenges using wet granulation methods

RESULT

Physical Examination Quality of granules show in table II. Before the granules are compressed into tablet, granule must be inspection by thee criteria : moisture content (MC), flow rate, dwell angle, and the granule size distribution.

Table II. The results of the physical quality of the granules Inspection

Inspection	Formulation 1	Formulation 2	Formulation 3	Formulation 4
MC (%)	0.46 ± 0.03	0.56 ± 0.15	0.59 ± 0.09	0.97 ± 0.13
Flowability(g/dt)	7.62 ± 0.06	9.58 ± 0.03	9.49 ± 0.04	9.05 ± 0.13

Examination of the physical quality of the granules :

1. Determining the moisture content
2 . The size distribution of granules

Physical Examination Quality of Tablets

1. Examination of Tablet Hardness

   Tablet hardness is required to break the tablet is measured in units of kilograms. Test equipment used is ERWEKA tbh TEST-220.

2. Examination of Friability

   Examination of the friability of lozenges with devices Friabilitor tester. Time dissolving tablet

3. Organoleptis test

   Response to taste test conducted by visual observation of the physical quality of the tablet which include shape, color, flavor, and physical disability in the fourth formula.

Analysis of Data

The results of the determination of the physical quality of tablets include hardness, brittleness, and the soluble extract of Centella asiatica lozenges are made with 2910 levels HMPC different 3CPS analyzed using ANOVA Completely Randomized Design (CRD ANOVA), at $\alpha = 0.05$ confidence limit.

Granule size distribution of the test performed to determine the amount of fines that are in the granules having a granule size <100 mesh. Fines obtained from F1 = 18:04%, F2 = 12.4%, F3 = 12:49%, and F4 = 7.03%.

From the results of statistical calculations between the treatment is known that F calculated for the solubility is greater than the F table. This shows a significant difference between the formulas are made, while the value of F calculated brittleness and hardness is less than F table which shows that there is no significant difference between the formula. To dissolve the tablet followed by Tukey HSD analysis because the value of F calculated is greater than the F table, with 95% confidence level indicates that there are significant differences

It can be seen that between F1 (0%) and F2 (1%), F1 (0%) with F3 (2%), F1 (0%) and F4 (3%), F2 (1%) with F3 (2%), and F2 (1%) and F4 (3%) had significant differences. Thus the presence of elevated levels of HPMC 2910 3CPS 1% and 2%, which significantly influence the dissolving tablet can increase the time that the tablet dissolves over time, while increasing levels of HPMC 2910 3CPS levels of 2% to 3% did not provide a meaningful influence on dissolve the tablet.

It has been studied that the influence of HPMC 2910 3CPS levels of physical quality lozenges extract of Centella asiatica on the basis

ISBN : 978-979-18458-5-4

of mannitol made by wet granulation method. When viewed from the properties of materials used has a good stability of the extract of Centella asiatica less unstable to air, so the storage should be in airtight containers.

Manufacture of lozenges made with extracts of Centella asiatica wet granulation method. It starts with the manufacture of binder solution, namely the creation 3CPS HPMC 2910 with the first didisperskan with ¼ times as much hot water from the total amount of water needed (± 15 ml), then add cold water ¾ times the total amount of water needed, after was stirred and then allowed to stand for a binder solution ± 24 hours in order to obtain a binder solution is clear and homogeneous. Then weighed mannitol and pegagan extract. Centella asiatica extract as much as 25 drops of the dye spilled and mixed until a homogeneous dimortir. After that mannitol is added and mixed again until homogeneous. When the mixture was homogenized and then add the binder solution little by little, then stir until smooth to form the granules. After the sieve with 12 mesh sieve, then oven dried with the temperature of ± 40 ° C for ± 4 hours.

Physical quality test includes examining granules that form a moisture content, granule size distribution, flow velocity, and angle of rest. The purpose of this investigation to determine the characteristics of the granules into tablets before printing and to find out whether the granules are formed to meet the requirements of good physical quality before printing granules into tablets.

After the granules are dried and cold, moisture content measurements were taken (MC) first, to determine the water content contained in the granules. From the results obtained by measuring% MC for 0:46 F1 ± 0.03%, F2 of 0.56 ± 0.15%, F3 for 0:59 ± 0.09%, and F4 of 0.97 ± 0.13%. A moisture content of the test results that have been done, it's still not meet the requirements of between 1-2% (Wells and Aulton, 1988). The moisture content is too low can lead to capping during tablet compression. But when the tablet printing process, an issue arises that is partially sticking of the tablet mass attached to the top of the punch. Therefore, in making these lozenges pegagan extract before we add talc to prevent sticking tabletation.

Granule size distribution examination conducted to determine the amount of fines contained in the granules. Fines are particles that pass through 100 mesh sieve. Fines and absorb the electrostatic properties of air. In the presence of electrostatic forces then small particles will be the attraction to each other and come together with similar particles, and will cause clogging dihopper that can disrupt the flow of the granules into the die. Fines the requirements contained in the granules should not be more than 20%. From the results of the amount of fines contained in each formula is F1 = 18:05%, F2 = 12.4%, F3 = 12:49%, and F4 = 7.03%.

Flow rate was measured before the addition of magnesium stearate as external phase. Values obtained from each formula was F1 7.62 ± 0:06 g / sec, 9:58 ± 0:03 g F2 / sec, F4 9:49 ± 0:04 g / sec and F4 9:05 ± 0:13 g / sec. Quiet corner of the test obtained 26.99 ± 0.75 ° F1, F2 31.64 ± 1.81 °, 30.47 ± 1.78 ° F3, and F4 00:37 ± 27.65 °. From the test results can be seen that the results obtained are included in the conditions of 20 ° -40 °. Dwell angle is too large can cause the granules difficult to flow, otherwise the smaller the angle the greater silence speed.

After all the physical quality test completed granules, the granules were weighed according to the weight that had been planned for each formula. Granules which have been weighed according to its weight and then compressed to a pressure of 1 ton. Tablets that have to be later used to test the physical quality of the included trials tablet tablet hardness, tablet fragility test, and test the tablet dissolves.

Hardness lozenges as listed in the bibliography (Parrot, 1970) is generally between 10-20 kP. Research has been done on the results obtained kP F1 13:11 ± 0:43, 13:13 ± 0.65 kP F2, F3 13:59 ± 0:35 kP, and kP F4 13.75 ± 0.74. The

results of this test meets the requirements of 10-20 kp. From the test results of statistical analysis using SPSS 17 is performed by One Way Anova method known that F count less than the F table with the degree of significance <0.05%. This shows that there is no significant difference from each formula to elevated levels of HPMC 2910 3CPS.

On test the friabilility of the tablet, the results obtained from each formula is 0.89 ± 0.16% F1, F2 0.88 ± 0.08%, 0.82 ± 0.05% F3, and F4 0.76 ± 0.04%. Fragility of the test results obtained, all formulas have to meet the requirements of < 1% (Banker & Andersen, 1986). And from the test using SPSS 17 analysis by One way ANOVA method known that F count is less than the F table with degrees of significance <0.05. This indicates that for each formula there is no significant difference of elevated levels of HPMC 2910 3CPS. Can be concluded that there was no significant difference with the addition of HPMC 2910 3CPS 1%, 2% and 3%.

Dissolving lozenges time required is ± 1800 seconds (30 minutes) (Banker & Andersen, 1986). From the results obtained from each F1 formula is 461.17 ± 30.29 seconds (7 minutes), F2 540.33 ± 34.16 seconds (9 minutes), F3 690.33 ± 67.50 seconds (11 minutes), and F4 743.67 ± 72.46 seconds (12 minutes). From the results obtained can be seen that the presence of elevated levels of HPMC as a binder 3CPS 2910 can slow down the tablet dissolves. This is because the higher levels of binder used will strengthen the bonds between the particles and forces the smaller the porosity as a result of penetration of fluid into the tablet is more difficult so that the tablet dissolves over time (Voight, 1917). Statistical analysis of test results of each formula using SPSS 17 with the method One way ANOVA with 95% confidence level, indicating that the calculated F is greater than the F table. This suggests that there are significant differences between the formula. The results of Tukey HSD test showed that the presence of elevated levels of F2 3CPS 2910 HPMC (1%) with F3 (2%), which significantly influence the dissolving tablet can increase the time that the tablet dissolves over time, while increasing levels of HPMC 2910 3CPS levels of F3 (2%) to F4 (3%) had no significant effect to dissolve the tablet. The longer the time of dissolving tablet is comparable to the elevated levels of HPMC binder 3CPS 2910.

Taste responses of the test was done, showing that the resulting lozenges have a spherical shape, light green color, sweet taste and produces no physical defects on the tablet.

From the results of a physical quality inspection lozenges, can be seen that F1, F2, F3 and F4 have met the requirements of tablet hardness. Fragility can be seen on examination of each tablet formula meets fragility due to the fragility that is obtained in compliance with the requirements of <1%. Similarly, the test of time dissolving lozenges, each formula that is compliant with 1800 seconds (± 30 min) (Banker & Andersen, 1986).

CONCLUSION

From the research results can be concluded that:

1. HPMC 2910 3CPS with concentration of 1%, 2% and 3% had no significant influence on hardness and brittleness lozenges.
2. Increased concentration of HPMC 2910 3CPS from 1% to 2% gives a significant influence on the tablet dissolves, but elevated levels of HPMC 2910 3CPS from 2% to 3% did not provide a meaningful influence on the tablet dissolves.
3. The use of HPMC 2910 3CPS with levels of 1% on a gotu kola extract lozenges optimal levels to meet the test requirements of hardness, brittleness, and the tablet dissolves.

REFERENCES

Ansel, Howard C. 1989. "Pengantar Bentuk Sediaan Farmasi", Edisi Keempat. Jakarta: Universitas Indonesia Press. p. 244; 300; 606-608.

Aulton, Michael. 2002." Pharmaceutics The Science of dosage Form Design", Second Edition. London: Churchill Livingstone. P. 381, 382.

Banker, G.S., and Anderson N. R. 2008. Tablet, dalam Lachman L, Lieberman H.A., dan Kanig J.L." Teori dan Praktek Farmasi Industri" Edisi Ketiga, volume 2., Jakarta: Universitas Indonesia Press. p. 684-714.

Cartensen, Jens T. 1977." Pharmaceutics of Solids and Solid Dosage Forms". New York: John Wiley & Sons.

Dalimartha, Setiawan. 2005." Atlas Tumbuhan Obat Indonesia". Jilid 2. Jakarta: Trubus Agriwidya. p. 149-155.

Rowe, R. C., Sheskey, P. J., Weller, P. J. 2009. *Handbook of Pharmaceutical Exipient, Sixth Edition*. London: The Pharmaceutical Press and The American Pharmaceutical Association.

Rowe, R. C., Sheskey, P. J., Weller, P. J. 2009. *Handbook of Pharmaceutical Exipient, Sixth Edition*. London: The Pharmaceutical Press and The American Pharmaceutical Association.