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The Effect Of Increasing Concentrations Of Sodium Saccharin As Sweetener On Physical Properties Of Salbutamol Dispersible Tablet With Mannitol As Filler

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ABSTRACT

Salbutamol one of asthma medicine which can be made in to dispersible tablet with the addition of sodium saccharin as sweetener. This study aimed to determine effect of increasing concentration of sodium saccharin as sweetener on physical properties and patient acceptabelity of the tablet. The tablet was made into 5 formulas with the 0% of sodium saccharin concentration as Formula 1, 0.2% as Formula 2, 0.4% as Formula 3, 0.6% as Formula 4, and 0.8% as Formula 5. The tablet made by direct compression method. The evaluation of granule including flow time test, angle of repose, and compressibility test. The tablet evaluation including organoleptic, weight uniformity, size uniformity, friability, hardness, wetting time, disintegration time, content uniformity, and hedonic test. The results of the physial properties were the hardness F1 until F5 subsequently 1.70, 1.54, 2.48, 2.67, and 2.73 Kp; the disintegration time F1 until F5 subsquently 55.67, 56.67, 56.67, 57.00, and 58.00 seconds; the friability test 1.09, 1.98, 0.77, 0.65, and 0.63%. The results showed that there were significant differences among all the formulas. It could be concluded that increasing concentration of sodium saccharin as sweetener in salbutamol dispersible tablet increase physical properties and could be made as preferable and acceptable tablet.

Keywords : Salbutamol Dispersibel Tablet, Sweetener, Sodium Saccharin, Mannitol

INTRODUCTION

Asthma is a chronic respiratory tract inflammatory disorder which involves different inflammatory cells (Priyanto, 2019). One pharmacological therapy for remedy asthma known as bronchodilators, refers to medications action to dilate bronchi work as β2 agonists such as salbutamol (Priyanto, 2019).

There are different dosage forms of salbutamol as medicine such as tablets, syrups, inhalers, and nebulizers. The tablet dosageform is commonly used (Aulton, 2022) However, certain patients have difficulty swallowing tablets that commonly occur in elderly / geratri and children / pediatrics. Also, some difficulties occurred on patients swallow tablets for where no air enough whereas asthma. The asthma treatment requires action and handling rapidly, so dispersibel salbutamol tablet dosage suitable for asthma management remedy.

Dispersibel tablets are intended for oral consumption with drug released relatively short time due to materials disintegrant. Dispersibel tablets containing some of which is supplementary material fillers, disintegrant, binders, glidan, ointments (Aulton, 2022). Dispersibel tablets have to crush and dissolve in the mouth saliva, it will make bitter taste so it need a matter to change of taste. Closing the bitter taste of drugs is adding sweetener in formula with sweetener. There are 2 kinds of sweetener, natural and synthetic. Synthetic sweeteners more than used natural sweeteners. Widely used due to the sweetness intensity high and cheap. The sweetener used in salbutamol dispersibel tablets soluble in water as mannitol, aspartame and saccharin. Saccharin is usually used in forms other than saccharin sodium. Selection of sodium saccharin as a sweetener in salbutamol dispersible tablets because sodium saccharin is stable, and intensity of the sweet taste of saccharin sodium more than sucrose (Anonim, 2021). In this research, 5 formulas of dispersibel salbutamol tablet were created. Each formula using mannitol as filler and sodium saccharin as a sweetener with different concentrations. This research aimed to determine the effect on the Physical Properties of tablets and patient acceptability.

METHOD

Material

Salbutamol (Andenex Chemie – Germany), Sodium Starch Glycolate (Achemco b.v.b.a - BELGIUM), Manitol (SPI Pharma – USA), Avicel ph 102 (Mingtai Chem), sodium Saccarin (China), Aerosil (Cabot) dan Magnesium Stearat (Faci).

Tablet Processing

Table 1. Formula of Salbutamol Dispersibel Tablet

ingredient	F1 (gram)	F2 (gram)	F3 (gram)	F4 (gram)	F5 (gram)
Salbutamol	2	2	2	2	2
Sodium Stach Glycolate	12,5	12,5	12,5	12,5	12,5
Avicel PH 102	25	25	25	25	25
Natrium Sakarin	0	0,2	0,4	0,6	0,8
Aerosil	0,5	0,5	0,5	0,5	0,5
Magnesium Stearat	2	2	2	2	2
Manitol	58	57,8	57,6	57,4	57,2

Salbutamol dispersibel tablets made by direct compression with formula shown on Table 1. Salbutamol, Sodium Starch glycolate, Avicel PH 102, Saccharin Sodium, Magnesium Stearate, Aerosil and Mannitol homogenized in a container. The materials mixed to obtain the homogenous mass. It was evaluated for flowability and compressibility. The mass was then directly compressed using a tableting machine to obtain 200 mg tablets, with a preliminary test for weight uniformity and hardness test. After the tablet was obtaied, then evaluated for organoleptic, weight uniformity, uniformity of size, friability, hardness, wetting time, disintegration time, content uniformity, and patient acceptable.

RESULT & DISCUSSION

The results of the mass evaluation could be seen in Table 2 and the results of tablets evaluation were shown in Table 3.

Flow test of granule rate is needed to find out whether the tablet mass can pass through the funnel granule flow tester. The mass of the tablet is good flow if it has flow rate of powder ≤ 10 g / sec (Siregar, 2010). The test flow time was done of 50 g, so the time obtained in this formula should ≥ 10 g/sec. A mass of tablet showed good flow properties if the value angle of repose between 25o and 40o with some types of streams are angle of repose < 25o types of excellent flow, good flow type 25-30o, 30-40o type of flow was good enough, and > 400 bad flow type (Wells, 2017). Angle of repose is the angle the free surface of the powder piles with the horizontal plane (Siregar, 2010). Angle of repose obtained from measurements of the mass of the cone mass tablet at the time of testing. As in the table data it can be seen that the angle of repose of Formula 1 until 5 got range between 30^o-40^o, so the all formulas can be concluded were good enough in this test.

Table 2. The Results of the Mass Evaluation Salbutamol Dispersible Tablet

Evaluation	F1	F2	F3	F4	F5
Flow rate (g/sec)	4,28	4,84	5	5,36	4,84
Angel of respose (^{o})	35,65	32,59	31,84	32,11	31,91
compressibility properties (%)	12,67	15	14,67	14	14,67

Compressibility test is used to predict the flow characteristics of the powder by looking at the compressibility indexes (Agoes, 2017). The compressibility test is performed to determine the ability of the tablet mass to fill the space between the particles and in conditions most compressible, without change in particle shape. In the Table 2, it can be seen that the value of the compressibility of formula 1 until 5 showed range value between 13% - 15%. The compressibility index of all categories of all formulas was special, because it was in the range of 5-15% (Aulton, 2022). Organoleptic test results indicate that the salbutamol dispersibel tablet has white color, rounded shape, and sweetness.

Salbutamol dispersibel tablets weigh about 200 mg. The average weight about 151-300 mg have requirements weighted average deviation was not more than two tablets deviates by more than 7.5% and no one tablet that deviate more than 15% (Agoes, 2017). The results of weight uniformity of formula 1 until 5 were carried out on 20% deviation tablet has averaged between 1.52 to 2.12%. It showed that each formula fullfil the requirements of the weighted average deviation.

The tablet size uniformity can be seen from the thickness and diameter of the tablet. Terms uniformity of size tablet is tablet diameter should not be more than 3 times and not less than 1 1/3 of tablet thickness (Agoes, 2017). The performed data of the size uniformity formula 1 until 5, tablet diameter of 0.91 cm and 0.25 cm thick tablet. From the results obtained, the entire formula did not meet the requirements. The results obtained diameter exceeding 3 times the size of thick. This was obtained because the size of the punch and die were unsuitable for tablets with weight of 200 mg.

Table 3. Results of Properties Salbutamol Dispesible Tablets

Evaluation	F1	F2	F3	F4	F5
Colour	White	White	White	White	White
Shape	round	round	round	round	round
weight uniformity (%)	1,6	2,12	1,68	1,98	1,52
hardness (kp)	1,7	1,54	2,48	2,67	2,73
friability (%)	1,09	1,98	0,77	0,65	0,63
thickness (cm)	0,25	0,25	0,25	0,25	0,25
Diameter (cm)	0,91	0,91	0,91	0,91	0,91
wetting time (second)	35,33	36,33	37,67	38,33	39,67
disintegration time (second)	55,67	56,67	56,67	57	58
content uniformity (%)	92,37	99,79	108,18	98,56	103,22
relative standard deviation (%)	0,89	0,85	0,96	0,86	0,99

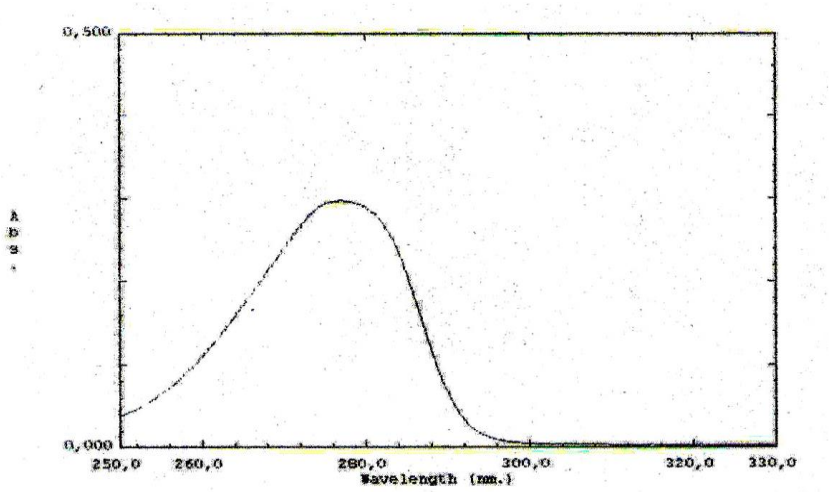
Friability expressed as mass is released from the tablet due to the mechanical load testing. A good tablet has friability between 0.5-1% (Lachman and Lieberman, 2020). The results of friability of formula 3 to 5 are eligible. Shown in the table increasing sodium saccharin, the increasing tablet hardness. Hardness associated with friability tablet tablet (Siregar, 2010). The increasing hardness tablet, the smaller the resulting friability.

A good dispersibel tablet has hardness of 1-3 kp (Abu-izza, et al., 2019). The data in the table can be seen got difference in the resulting hardness each formula. All formulas have a tablet hardness was good and meets the requirements of between 1.73 to 2.55 kp.

A wetting time test is performed to determine the time required to absorb saliva to all parts of the tablet (Debjit, et al., 2019). This test is performed using petri dish and filter paper with diameter of 9 cm. The data in the table could be seen that increasing wetting time of formula 1 to formula 5. This was due to the higher concentration of sodium saccharin, the lower the hardness and friability were obtained. Hardness related to the tablet density and porosity of the tablets formed (Hadisoewignyo and Fudholi, 2018). Which leads to high tablet hardness resulting in a gap between the particles that are small and difficult fluids to permeate into the tablet so that the time required increasing the wetting of formula 1 to formula 5.

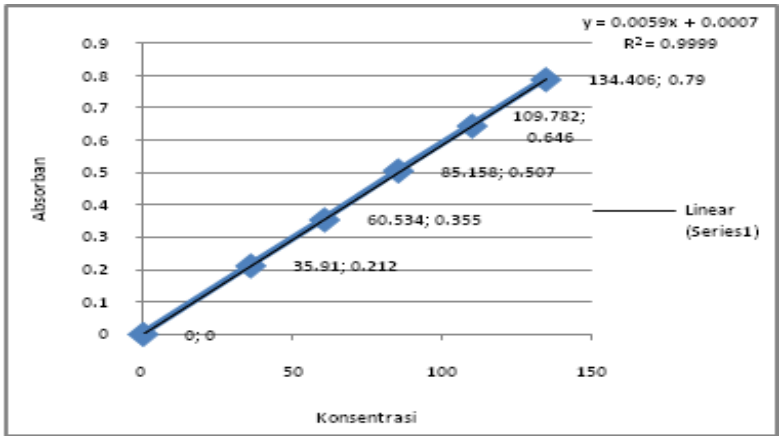
A good dispesible tablet has disintegration time less than one minute, but it would be like if disintegration occurs as soon as possible in the oral cavity (Hadisoewignyo and Fudholi, 2018). Disintegration time scale of few seconds is the target of a tablet dosage dispersibel Agoes, 2017) Dispersibel tablet disintegration time is determined when the tablet turns soft or become gel-like. The data obtained that the reduction in the concentration of the use of sodium saccharin, the increasing friability of the tablet, the more increases the time required for the tablet can be crushed. Formula 1 has destroyed the fastest time and formula 5 has slowest disintegration time. Fifth formulas have crushed in good time or meet the requirements for tablet disintegration time dispersibel, less than 1 minute.

The essay of Salbutamol tablets did not do because it considers the tablet dosage level is 100%, 4 mg each tablet.



Pigure 1. Salbutamol Spectrum

The results produce a spectrum of wavelength 277 nm in absorbance 0.298. Absorbance been at the maximum wavelength is formed.



Pigure 2. Calibration Curve Graph Salbutamol

Uniformity preparations done at all preparations containing the active substance of less than 50 mg or 50% of the weight of the tablet. For the 10-unit dosage requirements of content lies between 85.0 to 115.0% of that indicated on the label and the relative standard deviation of less than or equal to 6.0% (Anonim 2021). Calculations carried out with regard levels tablet dosage level is 100%, 4 mg each tablet, this was not done in the research. Supposedly level calculation was done by using the assay results and see the results of the correction factor was obtained. The correction factor was valid can be used only if the F value was not less than 1.03 and not more than 1.10 or less than 0,900 nor more than 0.970 or if F between 0.970 and 1.030 was not required corrections. If the value of F is between 1.03 and 1.10 or between 0.900 and 0.970, calculate the weight of active ingredient in each dosage unit by multiplying each weight obtained by F (Anonim, 2021). The data showed that the five formulas have% level of 92.37 to 103.22%. These five tablets have uniform concentration which meets the requirements that containing of 85.0 to 115.0% with relative standard deviation of less than 6%.

Analysis of the data on the hardness, friability, and disintegration time dispersibel tablet. Statistical analysis for hardness and disintegration time using one-way ANOVA and Tukey HSD test. Friability test and analyzed with the Kruskal Wallis test. Normality test results on hardness, disintegration time and friability generate sig> 0.05 it indicates that the data are normally distributed. The results of the homogeneity test data on hardness and disintegration time that was generating sig> 0.05 it indicates that H_0 was accepted, it means that data on hardness and disintegration have the same variance (homogeneous) followed by ANOVA and Tukey test. Meanwhile, the friability generates significant value <0.05 it indicates that H_0 is rejected, meaning the data friability hasdifferent variant (not homogeneous), then the friability of the data analysis followed by Kruskal Wallis test. The results of analysis of variance test on hardness and disintegration time the data has significant value <0.05 then H_0 is rejected. This showed that there was significant difference between the formula to the data of hardness and disintegration time. The Tukey HSD test and the results showed that there were significant differences (<0.05).

The results of Kruskal Wallis test of friability, the data got significant value <0.05 mean Ho was rejected. This showed that there was significant difference among all formulas in the friability data.

Furthermore, hedonic test for appearance, sweet, and desire to salbutamol dispersibel tablets using non-parametric statistical test Chi-square analysis, got differences in increasing concentration of sodium saccharin as sweetener due to the appearance and sweet taste in the formula 1,2,3,4, and 5.

CONCLUSION

The results showed that the increasing concentration of sodium saccharin as sweetener in salbutamol dispersibel tablet increased tablets physical properties and reached preferable and acceptable tablet.

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