Strada Journal of Pharmacy
ISSN: 2776-34544 (print); 2797-9180
Vol. 3, No 2 Oktober 2021, 49-52

Physical Evaluation of Chlorpheniramine Maleate Wet Granulation

Adjie Wahyu Pradana[1], Putri Liana Dewi[1], Riska Septia Indriana[1]
[1]Pharmaceutical Study Program, Faculty of FAKAR, Institut Ilmu Kesehatan Strada Indonesia Kediri, Indonesia
***Corresponding author:** adjie.wahyu03@gmail.com

ABSTRACT

Allergy is commonly happened in society, anti-histamine such as Chlorpheniramine Maleate (CTM) are fairly used to treat allergy. Granulation on CTM formulation plays major impact of mass produced of CTM tablets. Evaluation of granule formulation is conducted by observing flowability, moisture contents (MC), and angle of repose of granule. Flowability of granule is essential when compression phase of tablet. The result is moisture content is highly related with flowability, higher moisture content will reduce the flowability of granule. Hygroscopic material will more likely increased the MC and reduced the flowability. Leaner Angle of repose indicated rough surface of granule nucleation, which also related with flowability of granule.

Keywords : chlorpheniramine maleate, evaluation, formulation, granule, wet granulation

INTRODUCTION

Allergies now affect up to 30% to 40% of the population worldwide with the children and young adults bear the greatest burden of these diseases as the escalation of the prevalence of the diseases is mostly seen in these populations (Pawankar, 2011). Allergic rhinitis (AR) is an atopic disease characterized by symptoms of nasal congestion, clear rhinorrhea, sneezing, postnasal drip, and nasal pruritis (Kakli, 2016). Most patients are experiences uncomfortable feeling, reducing productivity. Chlorpeniramine Maleate or known such as "CTM" are commonly used to treat allergic disease, such as allergic rhinitis, urticaria, and angioedema.

Allergy can occur because cascade of immune respond. Histamine released from mast cells and basophils plays an important role in the pathophysiology of allergic diseases, such as asthma, allergic rhinitis, urticaria, and anaphylaxis. Histamine exerts various effects through four histamine receptors. Allergic symptoms, such as itching, pain, vasodilation, hypotension, flushing, bronchoconstriction, and the stimulation of cough receptors, develop mainly through histamine receptor 1 (H1R), making this receptor a major target of allergic medications (Holgate et al, 2009). CTM are targeting histamine receptor 1 to avoid these allergy respond to occurs. CTM is commonly used orally by form of tablet.

Granulation is one of technique used to make tablets. Granulation is the process of particle enlargement by agglomeration technique which transform fine powder into free-flowing, dust-free granules that easy to compress (Shanmugam, 2015). Granules also a lot easier to handle than fine powder to making tablets in larger scale. Flow-free, low moisture contents, and angle of repose of granule are essential parameter to evaluation of granule.

From the above background, this study aims to determine the formulation and its evaluations.

METHODS

1. Materials

Chlorpheniramine maleate powder, amylum manihot, calcium lactate, magnesium stearate, avicel, aquadest, aerosil are taken from STRADA Pharmaceutical and Technology of Pharmacy Laboratorium.

2. Tools

Flow-tester, mortar and stamper, Ohauss Moisture Analyzer, 14 mesh sieve, vernier callipers, analytical balance, stopwatch is rented from STRADA Pharmaceutical and Technology of Pharmacy Laboratorium.

3. Granule Preparation

CTM powder, amylum manihot, calcium lactate, avicel, and magnesium stearate are mixed together in mortar with stamper, once reached homogeneity then add aquadest sparingly, then mixed again until reached homogeneity.

Prepared mixture then sieved with 14 mesh, until formed granules, then sprinkled with aerosil, then use oven to drying the granules with 50^{o}C temperature for 30 minutes. Dried granules then sieved again using 14 mesh.

4. Formulation

Table 1. Granule Formula

Materials Name	Quantity of ingredients (%)
Chlorpheniramine maleate	0,66
Amylum manihot	56,1
Calcium lactate	15
Magnesium stearate	1,5
Avicel	25
Aerosil	1,74

5. Granule Evaluations
   1. Flow test

      Prepared granules are measured 50 grams, then pour the granules into Flow-tester. Timed when all granules falling off from the cone using stopwatch.
   2. Moisture contents test

      Prepared granules are measured 500 miligram, then heated wih 105^{o}C temperature for 10 minutes in Ohauss Moisture Analyzer.
   3. Angle of repose of granule test

      After flow test, measure the length of diameter and height of the heap of granules using vernier callipers.

RESULTS AND DISCUSSION

The result of granule formulation of flow test evaluations is announced failed, the measured granules are unable to falling off from the cone. Ideal time for flow test is under 10 second. This indicated there are also other aspect that must be observed. Moisture contents of the granule is 15,01%. According to conducted research by William et al in 2007, recommended moisture contents of granule is around 2% - 5%. Moisture contents also responsible to flow-test of granule, since majority of formula are using hygroscopic material, each of its particles will attract to each other if there any water content existed. Angle of repose of granule are calculated with this formula:

$$\text{Tan}^{-1}\left(\frac{h}{r}\right)$$

h = height of heap

r = radius of heap

$$\text{Tan}^{-1}\left(\frac{5}{4{,}95}\right) = 45{,}28^{o}$$

According to Pharmacopeia Forth Edition, desired angle of repose is between 25^{o} - 30^{o}. Conducted research by Beakawi Al-Hashemi et al in 2018, there is relevancy of granular shape with angle of repose. More circular shape of granules has flatter angle while more abstract shape of granules will have leaner angle. This also have connection with flowability of the granule. While better angle will have better flowability. Flowability of the granules is essential to mass produced tablets, powdered will create dust during compression. Not only the dust particle while compression is going to waste, but also it impacted of the dosage and weight equality of the tablets.

CONCLUSION

Based on the research above, it can be concluded that:

1. Moisture contents have a major impact of flowability of granule.
2. Hygroscopic materials are more prone to increased moisture contents, therefore reduced the flowability of granule.
3. The nucleation shape of granule are not perfectly rounded.

REFERENCE

Beakawi Al-Hashemi, H. M., & Baghabra Al-Amoudi, O. S. (2018). A review on the angle of repose of granular materials. Powder Technology, 330, 397–417. doi:10.1016/j.powtec.2018.02.003

Departemen Kesehatan Republik Indonesia.1995. Farmakope Indonesia. Edisi IV. Jakarta

Kakli HA, Riley TD. Allergic Rhinitis. Prim Care. 2016 Sep;43(3):465-75. [PubMed]

[Reference list]

Kim MH, Lee SM, Lee SH, Kwon HS, Kim SH, Cho SH, Min KU, Kim YY, Chang YS. A case of chlorpheniramine maleate-induced hypersensitivity with aspirin intolerance. Allergy Asthma Immunol Res. 2011 Jan;3(1):62-4. doi: 10.4168/aair.2011.3.1.62. Epub 2010 Jul 29. PMID: 21217928; PMCID: PMC3005322.

Holgate ST, Church MK, Lichtenstein LM. Allergy. 3rd ed. Philadelphia: Mosby Elsevier; 2006.

Pawankar R, Canonica GW, Holgate ST, Lockey RF, editors. WAO white book on allergy. Milwaukee (WI): World Allergy Organization; 2011.

Shanmugam S. Granulation techniques and technologies: recent progresses. Bioimpacts. 2015;5(1):55-63. doi: 10.15171/bi.2015.04. Epub 2015 Feb 18. PMID: 25901297; PMCID: PMC4401168.

Williams, J. C. and T. Allen. 2007. Handbook of Powder Technology Granulation. Vol 11.