International Journal of Medical Science in Clinical Research and Review
Online ISSN: 2581-8945
Available Online at http://www.ijmscrr.in Volume 3|Issue 04 (July-August) |2020 Page: 127-133
Original Research Paper

FORMULATION AND EVALUATION NON-EFFERVESCENT FLOATING TABLET OF CAPTOPRIL USING COMBINATIONS OF POLYMER HPMC AND NA-CMC

Authors:
Anggun Hari Kusumawati M.Si., Anggun Hari Kusumawati[1],
Apt, Faculty of Pharmacy, Buana Perjuangan Karawang University, West Java 41361, INA.
Iin Lidia Putama Mursal[1], Neni Sri Gunarti[1],Karina Risnawati[1]
[1]Faculty of Pharmacy, Buana Perjuangan Karawang University, Karawang, West Java, Indonesia 41361.
Corresponding Author: Anggun Hari Kusumawati M.Si.,

Article Received 08-06-2020 , Accepted 05-07-2020 , Published 08-07-2020

ABSTRACT:
Captopril has a rapid elimination half-lifefor about 2-3 hours and degrades in the intestine. The pH increasing causes captopril to become unstable and degrades, so captopril suitablefor floating tablet preparations. The preparation a floating tablet in this study used a combination of HPMC and CMC-Na polymers, where HPMC can control drug release and inhibit excessive erosion of tablets. While CMC-Na can be used to increase the viscosity of preparation so that it will take more time the drug to floats in the gastric. This study aims to determine theinfluence of the combination of HPMC and CMC-Na polymers against the physical properties and dissolution profiles of floating captopril tablets. The tablet was made bya wet granulation methods with a combination of HPMC and CMC-Na F1 (55%: 13%), F2 (50%: 18%), and F3 (45%: 23%). Test parameters that are used were hardness, friability, floatingassay,and% dissolution. The result of the study was processed statistically with SPSS version 20. The results showed that the differences in the concentrations of HPMC and CMC-Na did not affect the friability, floating test, and % dissolution of the preparation. The results showed that the differences in the concentration of HPMC and CMC-Na affected the results of tablet hardness, the more concentrations of HPMC were used it would increase tablet hardness, and the more concentration of CMC-Na used would reduce tablet hardness. Comparison of 55% HPMC and 13% CMC-Na is the formulation with optimum % dissolution is 92.6543 % for 12 hours.

Keywords: Captopril, HPMC, Na-CMC, Floating tablet

INTRODUCTION:

Types of Floating Drug Delivery Systems Based on the mechanism of buoyancy, two distinctly different technologies have been utilized in development of Floating Drug Delivery Systems which are: Effervescent System, and Effervescent systems include use of gas generating agents, carbonates (e.g. Sodium bicarbonate) and other organic acid(e.g. citric acid and tartaric acid) present in the formulation to produce carbon dioxide(CO_2)gas, thus reducing the density of system and making it float on the gastric fluid. An alternative is the incorporation of matrix containing portion of liquid, which produce gas that evaporate at body temperature.

Non-Effervescent System:

The non effervescent FDDS based on mechanism of swelling of polymer or bioadhesion to mucosal layer in GI tract. The most commonly used excipients in non effervescent FDDS are gel forming or highly swellable cellulose type hydrocolloids, polysaccharides and matrix forming material such as polycarbonate, polyacrylate, polymethacrylate, polystyrene as well as bioadhesive polymer such as chitosan and carbopol.

Captopril is medicine the companions of the an Angiotensin Converting Enzyme (ACE) Inhibitor that is used in the management of hypertension, heart failure and diabetic nephropathy. The elimination half-life of unchanged captopril was approximately 2 - 3 hours (14). Bioavailability captopril is about 60-75 % and stable at pH the action of dilute acids 1,2(11).An increase in ph causing a drug unstable and Based on the background here on wednesday and thursday, they are also required to the development of formulation of a preparations a captopril tablet with a Floating drug delivery systems. Floating drug delivery systemare low

density systems that have sufficient buoyancy to float over the gastric contents and remain in the stomach for a prolonged period.The system is filled with seasons of a kind of value is smaller than the gastric juices so that it stays float on a prolonged period of time (8).The size of the system is an important factor affecting gastric retention.

Floating systems remain buoyant on gastric fluids and are less likely to be expelled from the stomach, compared with the non-floating systems, which lie in the antrum region and are propelled by peristaltic waves (16). Hydroxypropyl methylcellulose (HPMC) is one of the polymers that is used to control release floating tablet non-effervescent. Drug release from HPMC matrices follows the classical Higuchi dissolution equation, related drug release with square root of time. Swell able systems consisting of hydrophilic polymers in the presence of water absorb a significant amount of water to form a gel. As dissolution medium penetrate the matrix, polymer material swelling starts and drug molecules begin to move out of the system by diffusion (3). CMC-Na is polymer which can used to increase viscosity preparation so that a prolong time floats the drug in the stomach and the release of the drug can be controlled (1). A modification of the Floating drug delivery system can be used to improve captopril remaining in the stomach. One of them is to polymers in the form of hydrocolloid as HPMC and CMC-Na. It is expected that HPMC combination with CMC-Na can control the release of drugs on floating tablet non-effervescent preparation.

METHODS:

Table 1. Composition of Non-Effervescent Floating Tablet Of Captopril

Materials	Percentage (%)		
	F1	F2	F3
Captopril	50 mg		
HPMC	55	50	45
Na-CMC	13	18	23
PVP K-30	5	5	5
Primojel	1.5	1.5	1.5
Talk	3	3	3
Mg Stearat	2	2	2
Primojel	0.5	0.5	0.5

Sample Preparation:

Preparation tablets are processed by wet granulation, and yet it is the most complex means of tablet processing. During wet granulation PVP K-30 is mixed with water then mixed with gradually Captopril, HPMC and Na-CMC with primojel intragranular mix its until homogen. Wet granule that forms in the sieve of granule size 20 mesh. Oven at a temperature 60°C went the moisture is qualified. Then blend the available dried granules by using primojel, talc, magnesium Stearate. Then compressed the available granules.

Evaluation of granules:

Flow Characteristics of Granular Bulk Materials

Some granule entered into flow tester. Note the time it takes to flow granule. The speed requirement of the flow of granule is 10 g per second (13).

Density:

The Specific Gravity measures the weight of individual granules and compares this with water, which is ascribed a Specific Gravity of 1. As such, it is a ratio and has no units. The Bulk Density is the weight of the product in a given volume, e.g. kg per cubic meter (m^3) or kilolitre (kL). It takes into account the space/air between the granules and is typically about 50 – 60% of the Specific Gravity, when expressed on a volumetric basis.Tapped density is determined by placing a graduated cylinder containing a known mass of granules and mechanical tapper apparatus, which is operated for a fixed number of taps until the powder bed volume has reached a minimum volume.

Hausner ratio:

The Hausner ratio is a number that is correlated to the flowability of a powder or granular material. Hausner's Ratio It indicates the flow properties of the powder and ratio of Tapped density to the Bulk density of the powder or granules. Hausner's Ratio = Tapped density/Bulk density

Carr's Index:

Carr's Index is measured using the values of bulk density and tapped density. The following equation is used to find the Carr's Index,

$$CI = \frac{(TD-BD)}{==========} \times 100$$

TD

Where, TD = Tapped density BD = Bulk density

Evaluation of Non-Effervescent Floating Tablet Of Captopril

Hardness

It is important to know that parameter tablet have the necessary strength to withstand earth in the handling of the manufacture of mechanical (Tekade *et al.*, 2014) , of packaging and mailing. A tablet to be wrecked with a load 4 to 8 kg per cm^2 (12).

Friability

As many as 10 tablet known weighs placed in friabilator played on 25 rpm for four minutes and a round 100. Tablets are cleaned and weighed and tablet. The weight tablet expressed as a percentage and better <1.0% (7).

Dissolution Studies:

In-vitro release studies were carried outusing paddle dissolution testapparatus (900ml of0.1N HCl (pH 1.2) was taken indissolution vessel and the temperature of the medium were maintained at 37°C±0.1°C. The speed was 50 rpm and1ml of sample was withdrawn atpredetermined time intervals for 12hours and same volume of fresh mediumwas replaced (17).

Evaluation	Requirement	F1	F2	F3
Flow Characteristics of Granular	≤ 10 g/second	4.559	4.285	4.273
Bulk Density (g/ml)	< 1 g/mL	0.250	0.244	0.244
Tapped Density (g/ml)	< 1 g/mL	0.303	0.303	0.303
Carr'sindex(%)	< 20 %	17.49	19.47	19.47
Rasiohausner	< 1.25	1.21	1.24	1.24

Buoyancy/Floating Test:

The time between introduction of dosage form and its buoyancy on the simulated gastric fluid and the time during which the dosage form remain buoyant weremeasured (4). The time taken for dosage form to emerge on surface of medium called Floating Lag Time (FLT) or BuoyancyLag Time (BLT) and total duration of time by which dosage form remain buoyant is called Total Floating Time.

Statistical Data Analysis:

Testing data processed in statistics with SPP test version 20 use ANOVA one direction for data that meet the requirements ANOVA test. The nonparametric tests for multiple independent samples are useful for determining whether or not the values of a particular variable differ between two or more groups. This is especially true when the assumptions of ANOVA are not met.

RESULTS

Evaluation of granules

Table 1. The evaluation results granuleNon-Effervescent Floating Tablet Of Captopril

Evaluation of Non-Effervescent Floating Tablet Of Captopril

Table 3. Evaluation of Non-Effervescent Floating Tablet Of Captopril

Hardness

Evaluasi	Syarat	F1	F2	F3
Hardness (kg/cm^2)	4-8 kg/cm^2	5.875	4.75	4.25
Friability (%)	< 1 %	0.161	0.260	0.281
lag floating time (second)	< 60 second	0	0	0
total floating time (hour)	>12 hour	>12	>12	>12

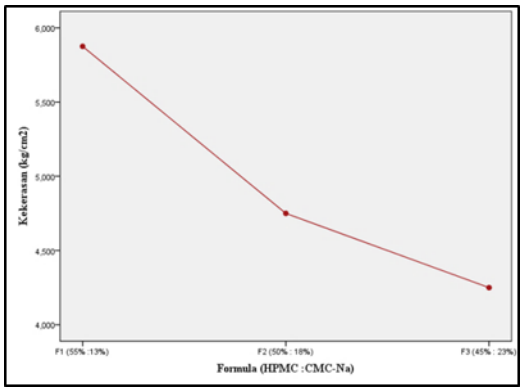

Image 1.The influence of concentration Na-CMC and HPMC combination of the results of the violence tablet

Friability Test

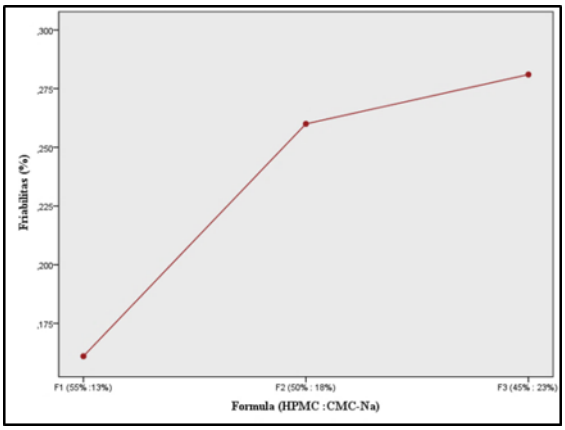

Image 2. The influence of the concentration of combination Na-CMC and HPMC the results percentage of friability tablet

Buoyancy/Floating Test

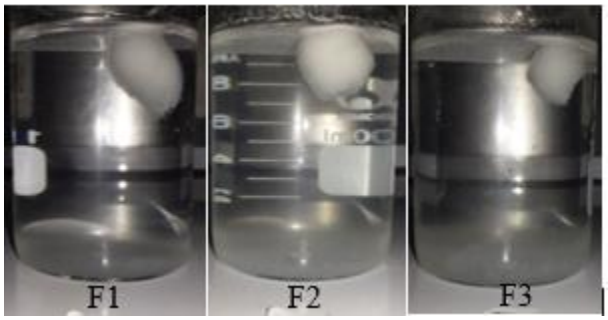

Image 3.Buoyancy/Floating Test

Dissolution Testing:

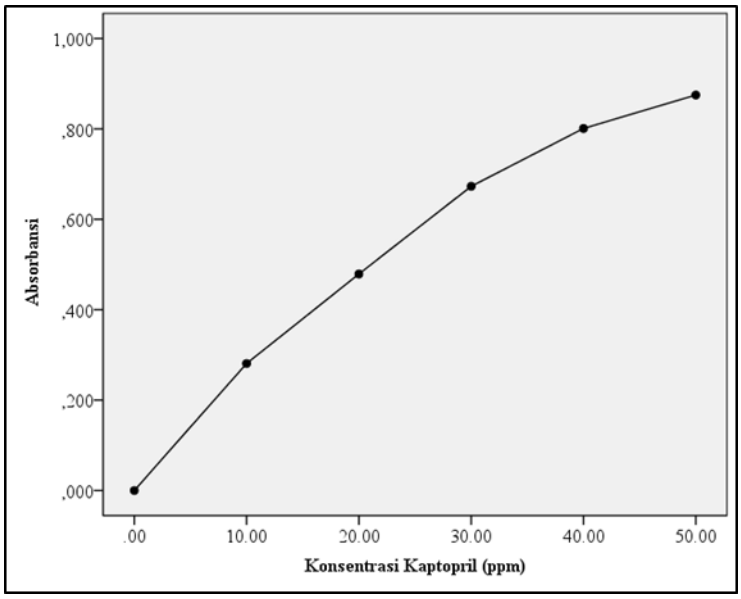

Image 4.A curve calibration Non-Effervescent Floating Tablet Of Captopril

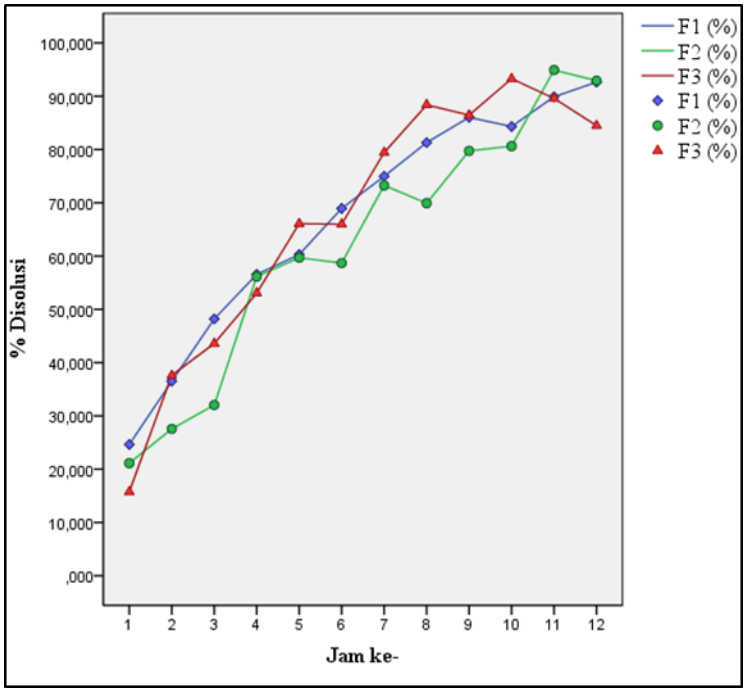

Image 5.The preparations % dissolution Non-Effervescent Floating Tablet Of Captopril

DISCUSSION:

In all three formulas granules flow as much as 4,273 - 4,559 g / second which shows that the granules can flow well. Real density and incompressible density are used to calculate the carr's index and hausner granule ratio. The carr's index value and acceptable ratio are <20% and <1.25 respectively (2). All of the three formulas fulfilled the requirements of the results, namely 17.49 - 19.47% and 1.21 - 1.24 for the carr's index and hausner ratio respectively. These results indicate that the nature of the flow of granules into the category is quite good. According to statistical tests, there was no significant difference in the results of each granule evaluation of the three formulas, where the combination of HPMC and Na-CMCconcentrations did not affect the results of each granule evaluation of the three formulas. If the tablet is made very hard then the water penetration into the tablet will be difficult, so it takes a long time to release the active substance (9). The results of the three formulas have a hardness value ranging from 4.25 ± 0.645 - 5.875 ± 0.844 kg / cm2. This value is within the range of tablet hardness requirements. According to statistical results, different concentrations of the combination of HPMC and Na-CMC affect tablet hardness. The more

concentration of Na-CMC that is used, then the hardness of the tablet decreases, while the more concentration of HPMC used, the hardness of the tablet will increase.

The friability test results obtained from these three formulas are in the range 0.161 - 0.281%. These results are in accordance with the friability test requirements. According to the graph in figure 2, it can be seen that the friability of tablets decreases with increasing HPMC concentration. In the statistical results, the friability of tablets from the three formulas did not have a significant difference, where the difference in concentration of the combination of HPMC and Na-CMC did not affect the friability of tablets. Based on the results obtained from the three formulas, the release of active substances in the first hour has a high percentage, this is due to the burst effect, wherein the active substances in the membrane are released at a high initial speed.At concentrations of 10–80%, HPMC can be used as a regulator of drug release because of its high viscosity. Liquid hydrated HPMC has a mechanism of drug release with diffused hydration and the layer that has become a gel will experience erosion and drug release (5). HPMC is a matrix material that has a high viscosity so that the gel layer formed is relatively difficult to be eroded by solvents and the matrix is difficult to erode (6). Based on this background, drug release can occur for 12 hours. The results of% dissolution compared to the time (hours) of the three formulas can be seen in Figure 5, where% dissolution has increased and decreased. The viscosity of dissolution media is a factor that affects the dissolution rate. When the viscosity of dissolution media increases, the dissolution rate will decrease. HPMC and CMC-Na have gel properties when in contact with liquids, causing the dissolution media viscosity to increase, this is what causes the% dissolution yield to increase and decrease with increasing dissolution time (13).

REFERENCES:

1. Agatha, A. G. Optimization of Ranitidine HCl Tablet Floating Formula with the Combination of HPMC Matrix and Na-CMC Using the Simplex Lattice Design Method. Muhammadiyah University of Surakarta, Surakarta, Indonesia, 2017.

2. Agoes, G. Solid Pharmaceuticals (SFI-6). ITB Press, Bandung, Indonesia, 2012.

3. Callewaert, M., Millot, J., Lesage, J., Laurent-Maquin, D., and Edwards-Levy, F. "Serum Albumin-Alginate Coated Microspheres: Role of the Inner Gel in Binding and Release of the KRFK Peptide. " Intl. J. Pharm, 2009; 366 (1-2): 103-10.

4. Edith Madithowitz. Encyclopedia of Controlled Drug Delivery. 1st ed. Jhon Wiley and Sons, New York, 1999.

5. Huichao, W., Shouying, D., Yang, L., Ying, L., & Di, W. The Application of Biomedical Polymer Hydroxypropyl Methyl Cellulose (HPMC) Materials in Pharmaceutical Preparations. Journal of Chemical and Pharmaceutical Research, 2014; 155-160.

6. Iriawan, B. A. Optimization of the Combination of Hydroxypropyl Methylcellulose and Xanthan Gum for the Slow Release Captopril Tablet Formula with the Floating System. Muhammadiyah University Surakarta Press, Surakarta, Indonesia, 2013.

7. Kodre, A., Bhosale, A., & Ravindra Patil, S. K. Formulation and Evaluation of Ranitidine Hydrochloride Floating Tablets by Using Co-Processed Excipients. International Journal of Pharmacy & Pharmaceutical Research, 2017; 9 (4): 100-124.

8. Kshirsagar, K. Y. Floating Drug Delivery System: An Overview. World Journal of Pharmaceutical Research, 2015; 4 (4): 1439-1460.

9. Kurniawati, F. Effect of the Use of Na-Montmorillonite Matrix Pillar Chitosan Weighted Molecules Low on Physical Properties and Profiles of Slow Release Tablets of Theophylline. Thesis University Eleven March, 2011.

10. Pradana, A. T., Parfati, N., & Shira, S. A. Floating Tablet Formulations Using Variations in HPMCK100M Concentration on the Ability of Floating and Dissolution Profile of Ranitidine HCl Tablets. Scientific Journal of Science & Technology, 2015; 9 (1); 11-21.

11. Rajput, H. S., Bhowmick, M., Rathi, V., & Rathi, J. Design and Evaluation of a Sustained Release Gastroretentive Dosage form of Captopril. International Journal of Research and Development in Pharmacy & Life Science, 2017; 6 (2); 2535-2547.

12. Prakash Rajak, A Bhattacharya, Neha Sharma, Manjir Sarma Kataki, Ananya Rajkumari. Gastro-Retentive Floating Drug Delivery System - An Approach In Gastroretentive Drug Delivery. International Journal of Pharmacy and Pharmaceutical Sciences, 2011; 3 (4).

13. Shiregar, C. Pharmaceutical Technology for Tablet Practical Basics. ECG, Jakarta, 2008.

14. Sweetman, S. C. Martindale The Complete Drug Reference (30th ed.). Pharmaceutical Press, London, 2009.

15. Tekade, B. W., Thakare, V. M., Jadhao, U. T., & Khatale, S. B. Formulation and Evaluation of

Metaprolol Tartarate Non-Effervescent Gastric Floating Tablets. Hygeia Journal for Drugs and Medicines, 2014; 6 (12): 63-73.
16. Timmermans J, Moes AJ. Factors controlling the buoyancy and gastric retention capabilities of floating matrix capsules: New data for reconsidering the controversy. J Pharm Sci, 1994; 83: 18-24.
17. USP Convention. US Pharmacopeial 37. United States Book Press, Inc. USA, 2014.