International Journal of Applied Pharmaceutics

ISSN- 0975-7058 Vol 10, Issue 3, 2018

Reveiw Article

COMBINATION OF HPMC AND PEG 400 AS A TASTE MASKING AGENT OF FILM-COATED TABLETS CONTAINING *MOMORDICA CHARANTIA* LINN. EXTRACT

RADITYA ISWANDANA, DESI ARYANI TRI LESTARI, SUTRIYO*

Laboratory of Pharmaceutics and Pharmaceutical Technology Development, Faculty of Pharmacy, Universitas Indonesia, Depok 16424, Indonesia
Email: sutriyo@farmasi.ui.ac.id

Received: 29 Nov 2017, Revised and Accepted: 10 Mar 2018

ABSTRACT

Objective: The objective of this study was to formulate and prepare film-coated tablets containing *Momordica charantia* Linn. to mask its bitter taste.

Methods: The core tablets of *Momordica charantia* Linn. were prepared by wet granulation method using sodium carboxymethyl cellulose (CMC-Na) as a binder, and then coated with hydroxypropyl methyl cellulose (HPMC) 5%. Film coating formulation was made in 3 formulae using the additional amount of polyethylene glycol (PEG) 400 as the plasticizer at 16%, 20%, and 24% concentration of HPMC weight. The obtained film-coated tablet was evaluated including organoleptic, the percentage of weight increase, surface morphology, coating thickness, disintegration time, and taste masking evaluation. Taste masking evaluation was performed on 30 respondents by giving the bitter taste level questionnaire of the three formulae film-coated tablets, core, and extract powders.

Results: Film-coated tablets that coated by using 20% PEG 400 as plasticizer had 4.78% of weight increase. The surface morphology was smooth and showed±34.67 µm of coating thickness. Furthermore, it also disintegrated within 5.34±1.1 min and successfully masked the bitter taste.

Conclusion: Combination of HPMC and PEG 400 20% as a plasticizer can give a good appearance and masked the bitter taste of *Momordica charantia* Linn.

Keywords: *Momordica charantia* Linn. Extract, Bitter taste masking, Film-coated tablet, HPMC, PEG 400

DOI: http://dx.doi.org/10.22159/ijap.2018v10i3.24025

INTRODUCTION

Studies on traditional medicinal plants (herbs) continue to this day as an effort of promotion, palliation, prevention, and rehabilitation. Bitter melon (*Momordica charantia* Linn.) is one of the most studied plants which has many therapeutic effects such as antidiabetic, antioxidants, antiviral, anticancer, immunomodulator, and anthelmintic effects [1-3]. The bioactive composition that contained in the bitter melon extract includes charantine, a sesquiterpene, linalool, catechin, palmitoic acid, curcubitane, diosgenine, momordicine, momordenol, and momordicilin [4-6]. Momordicine content in bitter melon causes the bitter taste which makes bitter melon less consumed by people [7].

Oral administration of pharmaceuticals is one of the most popular methods of drug delivery [8]. Oral administration of bitter drugs with an acceptable degree of palatability is a key issue for health care providers, especially for pediatric patients. Taste masking in the present day pharmaceutical industry has become a potential tool to improve patient compliance and commercial success of the product [9].

For the reasons above, a dosage form to mask the bitter taste of bitter melon extract was developed, *i.e.,* film-coated tablets. The bioactive compounds in bitter melon are thermodynamically stable and stay stable in the presence of water. Based on these properties, wet granulation method can be used to produce core tablets [10]. Wet granulation method can improve the flow properties and compatibility of powder extract, thus easier in compressing process [11]. The film-coated tablet is a tablet that coated with thin layer polymer that is soluble or insoluble in water [12]. The purpose of the coating was to improve its physical appearance, mask an unpleasant taste, odor and color, provide chemical and physical protection for unstable drugs in an acidic environment, protects the stomach from drugs that cause irritation, and provides a delayed drug release from the tablet [13].

The objectives of this research work were to develop a film-coated tablet which can mask a bitter taste from the bitter melon and to evaluate the effect of hydroxypropyl methylcellulose (HPMC) and polyethylene glycol (PEG) 400 on the fabrication of the film-coated tablet.

MATERIALS AND METHODS

Materials

Momordica charantia Linn. extracts (Deltomed Laboratories, Indonesia), aerosil (Nippon Aerosil, Japan), avicel PH 101 (Alcma, USA), sodium carboxymethyl cellulose (CMC-Na) (Ashland, USA), explotab (Evonik Industries, Germany), glycerin (Sinarmas Oleochemical, Indonesia), hydroxypropyl methyl cellulose (DOW Chemical Pacific, Singapore), magnesium stearate (FACI Asia Pte. Ltd., Singapore), polyethylene glycol 400 (Duchefa Biochemical, The Netherlands), sunset yellow (Sensient, Indonesia), aquadest (Brataco, Indonesia).

Preparation of bitter melon extract core tablet

Core tablets were made by using wet granulation method. Bitter melon powder extract, Avicel PH 101, and explotab were mixed until homogeneous and CMC-Na solution was added to create a wet granular mass. Wet granular mass was sieved with mesh 16 and dried in the oven at 60 °C. Dry granules obtained were sieved with mesh 18. Then, aerosil and Mg stearate were added. The flow rate, the angle of repose, and compressibility index of the mass were evaluated. After that, tablet mass was compressed into biconcave tablets using a tablet press (Erweka, Germany).

Table 1: Composition of bitter melon core or uncoated tablet formulations prepared by wet granulation method

Components	F1 (mg)	F2 (mg)	F3 (mg)	F4 (mg)
Bitter melon powder extract	200	200	200	200
CMC-Na	6	9	12	15
Explotab	12	12	12	12
Aerosil	1.5	1.5	1.5	1.5
Mg stearate	1.5	1.5	1.5	1.5
Avicel PH 101	79	76	73	70

Flow properties of granule

Flow rate and angle of repose

The measurement was done using a flow meter (Erweka GDT, Germany), ±25 g of the sample was placed in flow meter funnel and the surface was evenly levelled without any pressure. The flow meter was run and the time for all sample to flow through the funnel was recorded. The flow rate was expressed in g/sec. The angle of repose (α) was obtained by measuring the height (h) and radius (r) of the pile of the sample that flowed through the funnel [13].

Compressibility index

Compressibility index and Hausner ratio are a measure of the tendency of the powder to be compressed. The tablet mass was added to a measuring glass (50.0 ml) and evaluated using the standard procedure by measuring the original volume (V_0) and final tapped volume (V_f) [14].

Evaluation of the core tablet

Weight uniformity

Twenty tablets were weighed individually, and the average weight was calculated. The individual tablet weight was then compared to the average weight [14].

Hardness

The analysis was done using hardness tester (Erweka TBH 28, Germany). In this study, six tablets were used. Tablet was placed horizontally in the machine, and the start button was pressed to commence the test.

Friability

The analysis was done using friability tester (Erweka TAR, Germany). Twenty tablets were cleaned from dust, weighed, placed in the machine which was run at 25 rpm for 4 min. The tablets were taken out, dusted and weighed. The loss due to abrasion is a measure of tablet friability.

Disintegration time

The disintegration test was carried out using the disintegration tester (Electrolab ED-2-SAPO, India). Each of the tablets was placed in each basket. Water with a temperature of 37±2 °C was used as a medium. At the time limit, the basket was taken out, and the tablet was observed [14].

Preparation of film coated tablet

All components were weighed according to the formulations. HPMC was added to a beaker glass, and aquadest was added gradually while being stirred until homogeneous. PEG 400, glycerin and sunset yellow were added, the volume was adjusted using aquadest to 100 ml. Tablet coating was done by spraying the coating solution gradually and evenly on the tablet surfaces using a rotating coating pan. Tablets were then left rotated in the pan until it reached the room temperature. Film-coated tablets were weighed and stored in a clean and dry container.

Table 2: Formulations of coating solution

Components	FA (%)	FB (%)	FC (%)
HPMC	5	5	5
PEG 400	0.8	1	1.2
Glycerin	1.5	1.5	1.5
Sunset yellow	0.05	0.05	0.05
Aquadest ad.	100	100	100

Bitter taste evaluation

Bitter taste evaluation was performed on 30 respondents by giving the bitter taste level questionnaire of the three formulae of film-coated tablets, core, and extract powders. The questionnaire results were analyzed using statistical package for the social sciences (SPSS) program with Kruskal Wallis method. The bitterness level is from 1 (not bitter) until 5 (very bitter) [15, 16].

RESULTS AND DISCUSSION

The core tablet mass evaluation was done to measure the flow rate, the angle of repose and the ability of the mass to be compressed into a tablet.

The core tablet physical appearance test was done by observing the shape and color of the tablet [17]. Physical appearance is the first thing that affects patient acceptance of a pharmaceutical dosage form. All tablet formulations had the same physical appearance with a smooth surface due to magnesium stearate that acts as a glidant.

Core tablets F1-F4 qualify the weight variation requirements within a range of 85.0-115.0% from what was written on the label with relative standard deviation ≤6. This has proven that powder mass of bitter melon core tablet had a good flowability and could produce tablets with a good weight and content uniformity [18].

Table 3: Core tablet mass evaluation results

Evaluations	F1*	F2*	F3*	F4*
Flow rate (g/sec)	5.26±0.09	5.13±0.14	5.04±0.14	4.73±0.17
Angle of repose (°)	19.96±0.57	21.14±0.39	22.05±0.59	22.32±0.90
Compressibility index	17.31±0.29	18.26±1.52	19.21±1.96	21.43±0.33
Hausner ratio	1.21±0.01	1.22±0.02	1.24±0.03	1.27±0.01

*n=3; Data are expressed as mean+/-SD.

Table 4: Core tablet evaluation results

Parameters	F1	F2	F3	F4
Physical appearance	Round, biconvex, light brown	Round, biconvex, light brown	Round, biconvex, light brown	Round, biconvex, light brown
Average weight (mg)*	311.12±1.43	312.66±2.26	312.14±2.44	308.74±3.40
Tablet diameter (mm)*	9.21±0.01	9.21±0.01	9.21±0.01	9.21±0.01
Tablet thickness*	5.29±0.02	5.31±0.02	5.30±0.02	5.31±0.02
Friability (%)	0.13	0.20	0.22	0.24
Hardness (kP)†	8.91±0.39	8.92±0.68	7.28±0.81	9.48±1.31
Disintegration time (min)†	2.64±0.96	3.30±0.58	3.53±0.26	3.94±0.33

*n=20; Data are expressed as mean+/-SD., †n=6; Data are expressed as mean+/-SD.

In this study, friability evaluation was crucial since the core tablet will be coated. Core tablets must have a low friability during the spraying process. The result showed that all formulae did not meet the criteria. F1 had a low friability value at 0.13%. Theoretically, the use of a binder in higher concentration causes lower friability value, but in this case, the increase of CMC-Na increased the friability [19, 20]. This might be because CMC-Na will produce a frailer and harder tablet. F1 with the lowest CMC-Na concentration was chosen since it had the lowest friability and enough hardness to be processed as film-coated tablets.

HPMC was used to mask the bitter and unpleasant taste also the stability of the formulation. Five percent was chosen because it was the optimum concentration of a polymer in the coating solution [13]. Each formula had different concentration of PEG 400 as a plasticizer. Variation was needed to understand the elasticity, flexibility and any defect in the coating layer that was formed.

Morphological evaluation of film-coated tablet was done to observe the tablet surfaces condition microscopically using scanning electron microscopy (SEM). Films were expected to keep forming during the spraying process until all coating solution was used. Overall, the tablet was coated with the coating solution. Based on SEM images with 3000x magnification, FA surface was not as smooth as expected due to the low concentration of PEG 400 and the excessive heating process, while FB and FC surfaces were smooth.

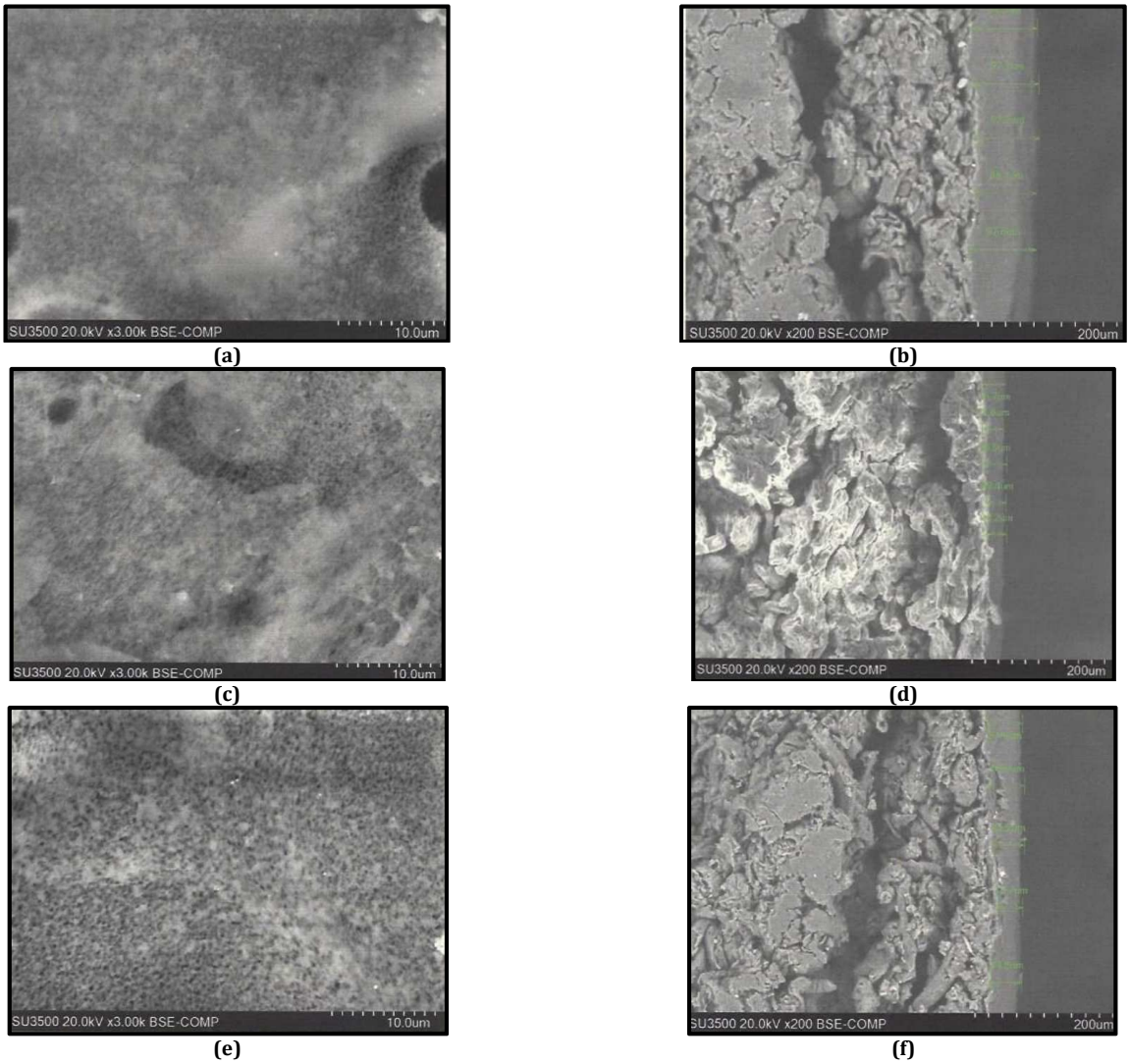

Fig. 1: Scanning electron microscope result for film coated surface with 3000x magnification (left) and thickness of coating layer with 200x magnification (right): FA (a,d), FB (b,e), and FC (c,f)

The thickness of coating layer of a tablet is usually about 10-100 µm. CTFA (coated tablet formula A) had a thickness of 91.03 µm, CTFB (coated tablet formula B) was 34.67 µm, and CTFC (coated tablet formula C) was 48.93 µm. The thickness of coating layer was proportional to the increase of film-coated tablets weight. Coating layer thickness is also affected by the viscosity of coating solution, the increase in viscosity will increase the thickness of coating layer.

Tabel 5: Disintegration time of the film-coated tablet

Formula	Disintegration time (min)*
A	7.95±0.6
B	5.34±1.1
C	4.59±0.6

*n=6; Data are expressed as mean+/-SD.

Disintegration time evaluation results of film-coated tablets are shown in table 5. Based on the data, film-coated tablets had a considerably fast disintegration time but still slower than core tablet. This was due to the pores of core tablet that was shielded and protected by film coatings, in consequence, it made the medium difficult to penetrate the tablet. Also, more time was needed as the coating layer must be disintegrated first.

The bitter taste evaluation showed 43.33% respondents stated that there was a slightly bitter taste in core tablet. Most of the respondents (70%) stated that CTFA did not have any bitter taste and almost all respondents (93.3%) stated CTFB did not have any bitter taste. 73% of the respondents also stated that CTFC did not have any bitter taste while 63.3% stated that F1 had a bitter taste.

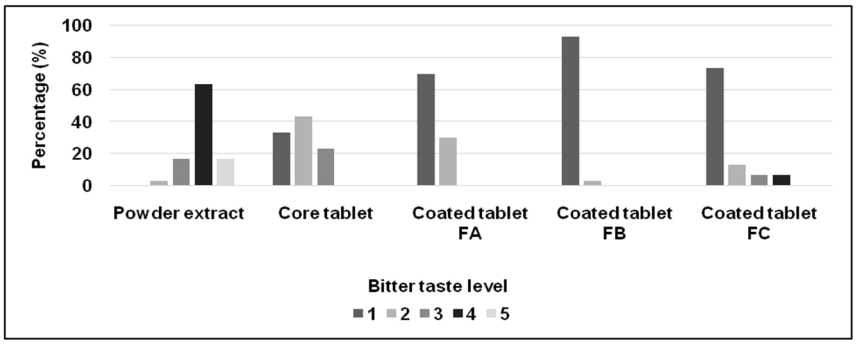

Fig. 2: Bitter taste evaluation result. Not bitter (1), slightly bitter (2), sparingly bitter (3), bitter (4), very bitter (5)

Wilcoxon test was used as a nonparametric statistical method. Hypothesis (H_a) was made for an easier conclusion withdrawal, which there was a significant difference in bitterness level between bitter melon powder extract and tablet extract dosage form. The hypothesis is approved if $p<0.05$. If $p>0.05$, the hypothesis was rejected. From the Wilcoxon test results, the value of p of core tablet and the coated tablet was<0.001. Wilcoxon test was done to know if there is any difference in bitterness level of each coated-tablet formulations. There was no difference in the level of bitterness between CTFA and CTFB ($p>0.05$). However, there was a difference between CTFB and CTFC ($p<0.05$).

Kruskal Wallis method was used for further analysis to see the bitterness level of each formulation. The lowest Kruskal Wallis test value showed that the bitterness was well masked. Based on average value, CTFB had the lowest score of bitterness. CTFA had the thickest coating layer, but it was reneging easily due to the low concentration of PEG 400. CTFB with a higher concentration than CTFA had a stronger coating layer that was not prone to flaking and hence it could mask the bitterness. Based on Kruskal Wallis analysis, all coated tablet formulations had a p-value of 0.07. Statistically, there was no significant difference in the level of bitterness in the variation of PEG 400 concentration of the formulations.

CONCLUSION

Film-coated tablets evaluation of CTFA, CTFB, and CTFC complied the criteria of a good physical appearance of coated tablet. From the formulations, PEG 400 with the concentration of 20% was the best formulation in producing a film-coated tablet with smooth surfaces, lowest bitterness level with an average value of 1.10±0.40. Based on the statistical analysis, there was a significant difference in bitterness level with $p<0.05$ from core tablet, CTFA, CTFB, and CTFC compared to bitter melon powder extract. CTFB had the lowest bitterness score which was 1.10 (not bitter). Moreover, the statistical analysis of coated tablet formulations showed a p-value of 0.07 and hence there was no significant difference in bitterness level from the concentration variations of PEG 400 which were used in the formulations.

AUTHORS CONTRIBUTIONS

The authors also gratefully acknowledge the financial support for this study by PITTA Research Grants 2017

CONFLICT OF INTERESTS

The authors have no conflict of interest to declare

REFERENCES

1. Tan HF, Gan CY. Polysaccharide with antioxidant, α-amylase inhibitory and ACE inhibitory activities from *Momordica charantia*. Int J Biol Macromol 2016;85:487–96.
2. Amira K, Aminah A, Zuhair A. Evaluation of bitter melon (*Momordica charantia*) extract administration in the antioxidant and free radical scavenging activities of plasma and liver in the male rat. Int Food Res J 2013:319-23.
3. Drewnoswski A, Carneros C. Bitter taste, phytonutrients, and the consumer: a review. Am J Clin Nutr 2000;72:1424-35.
4. Sharma S, Tandon S, Semwal B, Singh K. *Momordica charantia* linn.: a comprehensive review on the bitter remedy. J Pharm Res Opin 2011;1:42-7.
5. Nagarani G, Abirami A, Siddhuraju P. Food prospects and nutraceutical attributes of momordica species: potential tropical bioresources–a review. Food Sci Human Wellness 2015;3:117-26.
6. Semiz A, Sen A. Antioxidant and chemoprotective properties of *Momordica charantia* L. (bitter melon) fruit extract. Afr J Biotech 2007;6:273–7.
7. Gupta M, Sharma S, Gautam AK, Bhadauria R. Review article: *Momordica charantia* Linn. Int J Pharm Sci Rev Res 2011;11:32-7.
8. Sharma S, Lewis S. Taste masking technologies: a review. Int J Pharm Pharm Sci 2010;2:6-13.
9. Sonar YA, Bele MH, Sonar NH, Bagul VS, Shimpi PS. Taste abatement and characterization of dispersible tablets of artemether prepared by hot melt extrusion. Int J Appl Pharm 2017;9:28-33.
10. Navveen RM, Priya B. Optimization of drying methods for bitter gourd (*Momordica charantia* L.) extract. Indian J Sci 2016; 22:574-82.
11. Banker GS, Anderson NR. Tablet in the theory and practice of industrial pharmacy. In: Lachman L, Lieberman HA, Kanig JL, Jakarta: UI Press; 1990.
12. Ansel H, Popovich N, Allen J. Pharmaceutical dosage form and drug delivery systems (6th ed.). USA: Williams and Wilkins; 1995.
13. Lachman L, Lieberman H, Schwartz J. Pharmaceutical dosage form: tablets. Vol. 3. (2nd ed.). USA: Marcel Dekker; 1990.
14. United States Pharmacopoeia Convention. The United States Pharmacopoeia, 38th and the National Formulary, 33rd. Rockville: United States Pharmacopoeia Convention, Inc; 2014.
15. Datrange P, Kulkarni S, Padalkar RR. Development of taste masked formulation for bitter drug. Res J Pharm Biol Chem Sci 2012;3:727–53.
16. Alghabban FM, Alani IH, Hassan SF. Taste masking of prifinium bromide in orodispersible tablets. Int J Pharm Pharm Sci 2014;S1:315-9.
17. United States Pharmacopoeia Convention. The United States Pharmacopoeia, 32nd and The National Formulary. 27th (1st ed.). Rockville: United States Pharmacopoeia Convention, Inc; 2009.
18. British Pharmacopoeia Commission. British Pharmacopoeia. London: Crown; 2007.

19. Rowe R, Sheskey P, Quinn M. Handbook of Pharmaceutical Excipients (6th ed.). London: Pharmaceutical Press; 2009.

20. Felton AL. Remington Essentials of Pharmaceutics. Pharmaceutical Press: 1st; 2013. p. 46, 169.