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Formulation of Orally Disintegrating Tablets of Captopril as Superdisintegrant using Corncob (*Zea mays* L.)

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Abstract

AIM: This study aimed to make corncobs the basic material for the manufacture of microcrystalline cellulose.

METHODS: Manufacture of corncob cellulose microcrystals (CCMs) by isolating alpha-cellulose from corncobs, then hydrolyzed with HCl 2.5 N. The yield of CCMs of 14.51% can be used as orally disintegrating tablet (ODT) and has similarities with Avicel as standard comparison.

RESULTS: Both organoleptic results were pH 5.6 and 6.54; drying shrinkage 3.33% and 4.39%; total ash content 0.17% and 0.02%; and water solubility 0.9% and 0.12%. Furthermore, the real specific gravity is 0.317 and 0.306 g/cm^3, incompressible density is 0.379 and 0.375 g/cm^3, the true density is 1.291 and 1.206 g/cm^3, Hausner index is 1.195 and 1.225, compressibility index is 19.55 and 22.55%, and porosity is 75.5 and 74.6%.

CONCLUSION: Captopril ODT tablet preparations with CCM as filler have almost the exact tablet evaluation results compared to Avicel and to meet the requirements.

Introduction

Corn is one of the world's largest agricultural productions whose seeds are processed into various main food preparations such as canned corn seeds, and corn silk by-products, husks, and cobs. For every 100 kg of corn kernels produced, the cob content is 18 kg and most of it is used as feed, into organic fertilizer and into waste [1]. The content contained in corncobs includes cellulose 39.1%, hemicellulose 42.1%, lignin 9.1%, protein 1.7%, and ash 1.2% [2]. In addition, corncobs are also reported to have potential utilization as natural antioxidants and absorbents [3], [4]. The high content of corncobs can be applied in the cosmetic field food and pharmaceutical industry [5]. The cellulose content can be converted into corncobs microcrystalline by mineral acid degradation [6], [7].

The microcrystalline content obtained is widely used in the food, cosmetic and pharmaceutical industries, suspension stabilizers, fat substitutes, texture regulators, and other fillers [7], [8], [9]. The microcrystalline content produced from various isolated raw materials varies. Oral drug delivery systems are of great interest in drug development. One of the factors in oral drug delivery is the rate of absorption and duration of absorption. Modifications in the development of drug preparations require sustained-release absorption to maintain the drug in its absorption site at the absorption site to achieve maximum absorption and also not to saturate the transport traversed in the mechanism [9].

Captopril is one of the drugs commonly used in the treatment of hypertension. This drug is taken orally and works by inhibitory the action of the angiotensin converting enzyme to treat high blood pressure, blood pressure, heart failure, and prevention of kidney failure due to hypertension and diabetes. Disadvantages of the available drug captropil in the formulation do not apply the principle of slow release drug and fast disintegration time [9], [10]. Therefore, the purpose of this study was to formulate captopril drug preparations

with fillers using microcrystalline corncobs compared to Avicel PH 102.

Experimental

Materials

The materials used were 20 mesh sieves, oven, blender (National), pH meter, weighing bottle, desiccator, porcelain crucible, pycnometer (Merk Iwaki), funnel, hardness tester *(Vanguard type YD-2*), friabilator tester (Erweka), disintegrating tester (Hanson research), Petri dishes, analytical balance (Sartorius), spectrophotometry (Shimadzu), dissolution test equipment (Hanson Research), and other glassware and the chemicals used were Captopril®, Avicel PH102®, sodium hydroxide (Merck), distilled water, sodium hypochlorite (Merck), hydrochloric acid (Merck), starch (pro analysis), lactose anhydrous (Merck), sodium starch glycolate (Pharmaceutical Grade), mannitol DC (Merck), aspartame (Merck), Mg stearate (Merck), talc powder (Merck), and mint flavor.

Sample preparation

Corncobs cleaned of impurities, washed, drained, and aerated, then dried in a drying cabinet at a temperature of 60°C until brittle. Corncobs were ground using a blender and sieved using a size of 20 mesh. The sieved corncob powder was stored in a tightly closed plastic container and stored in a pharmaceutical biotechnology laboratory before use.

α-cellulose isolation process

A 100 g corncobs powder added 1.5 L of NaOH 4% and heated for 2 h at 100°C. After that, it was filtered and the residue was washed with distilled water until the pH was neutral. The residue was bleached with 1 L of sodium hypochlorite 2.5% for 24 h at room temperature, then filtered and the residue was washed with distilled water until the pH was neutral followed by the addition of 650 mL of NaOH 17.5% and heated at 80°C for 1 h. Subsequently, it was bleached again with 500 mL sodium hypochlorite of 2.5% and heated at 100°C for 5 min. It was filtered and the residue was washed with distilled water until the pH was neutral and then dried in an oven at 60°C [6], [11].

Manufacturing of corncob cellulose microcrystalline

A 50 g of alpha-cellulose was hydrolyzed with 1.2 L of HCl 2.5 N by boiling for 15 min in a glass beaker. Then, it was poured into cold water while vigorously stirring with a magnetic stirrer at a speed of 300 rpm for 10 min and then allowed to stand overnight and filtered. Corncob cellulose microcrystals (CCMs) were washed with distilled water until neutral, then dried in an oven at a temperature of 57–60°C for 60 min and then ground [12], [13], [14].

Captopril orally disintegrating tablet (ODT) tablet manufacturing

The modified ODT was made using FI (microcrystalline) cellulose from corncob, filler F II (Avicel PH-102) captopril, DC mannitol, aspartame, sodium starch glycolate, Mg stearate, talc, and mint flavor (Table 1). The two components are put into the mortar and then stirred until homogeneous. Pre-formulation testing was continued by evaluating the results of captopril ODT tablets [15].

Table 1: Captopril ODT tablet formula

Material name (mg)	F I	F II
Captopril	12.5	12.5
CCM	78	-
Avicel PH 102	-	78
Sodium starch glycolate	13	13
Mannitol	19.5	19.5
Aspartame	3.9	3.9
Stearate Mg	1.7	1.7
Talc	1.3	1.3
Pepper mint	q.s	q,.s
Total	130	130

ODT: Orally disintegrating tablet, CCM: Corncob cellulose microcrystal

ODT tablet evaluation

Evaluations carried out on ODT included weight uniformity test, tablet hardness test, friability test, disintegration time test, and wetting test [10], [16], [17]. Uniformity was determined by taking 20 tablets and cleaned and then weighed each tablet. Hardness test using a hardness tester by taking six samples of tablets and referring to the tablet hardness requirements of 0.1–0.3 kP (1 kg = 1 kP). Friability test aims to measure the friability of tablets by taking 10 tablets of ODT samples, cleaned and put into the friabilator tester, and rotated at a speed of 25 revolutions/minute for 4 min, then weighed. The value of tablet friability is quite good 0.1–0.9%. Disintegration time testing was carried out on six tablet samples, used 800 ml of water with a temperature of 37°C ± 2°C as the medium, and put one tablet in each tube from the basket. Then, the tool is run with a frequency of up and down from the basket 30 times/min. At the end of the time limit as indicated in the monograph, lift the basket and examine the six tablets. All tablets must be completely crushed. Requirements: The time required to crush the tablet is <1 min.

Results and Discussion

Manufacture of CCM

Corncob powder 100 g obtained 18.5 g of alpha cellulose, then continued in the hydrolysis

stage and obtained 14.51 g of microcrystalline cellulose (14.51%) (Figure 1). This shrinkage occurs due to the loss of lignin, hemicellulose, and other compounds when alpha-cellulose undergoes a hydrolysis reaction.

The organoleptic results of CCM compared with Avicel had similarities including odor, white color, and tasteless and had a pH of 5.6 while Avicel had 6.54 and met the standard for medicinal raw materials. The physicochemical properties of CCM and Avicel are presented in Table 2.

Table 2: Physicochemical properties of CCM and Avicel

Parameter	CCM	Avicel
Organoleptic	Odorless, white, and tasteless	Odorless, white, and tasteless
pH	5.6	6.54
Drying shrink	3.33%	4.39%
Solubility of substances in water	0.9%	0.12%
Total ash content	0.17%	0.02%
Specific weight		
Real specific gravity (g/cm^3)	0.317	0.306
Compressed specific gravity (g/cm^3)	0.379	0.375
Correct specific gravity (g/cm^3)	1.291	1.206
Hausner index (%)	1.195	1.225
Compressibility index (%)	19.55	22.55
Porosity (%)	75.5	74.6

CCM: Corncob cellulose microcrystal

ODT Pre-formulation

The results of the pre-formulation tests carried out showed that CCM and Avicel met the requirements, had almost the same flow time, and had uniformity of granules. The time required for the granules to flow must be <10 s. The results of the pre-formulation test of captopril ODT tablets from CCM with Avicel are presented in Table 3. The results of the evaluation of the ODT granules from the angle of repose and the index for CCM and Avicel showed that they met the specified requirements.

Table 3: Captopril ODT tablet pre-formulation test results

Formula	Flowability time (second)	Angle of friction (°)	Tab index (%)
CCM	1.65	21.02	16.23
Avicel	1.48	20.58	18.64

ODT: Orally disintegrating tablet, CCM: Corncob cellulose microcrystal

Formulation and ODTs of captopril drugs

The results of the captopril tablet formulations of CCM and Avicel are shown in Figure 2. The results of the evaluation showed uniformity of weights for CCM and Avicel (Table 4) and meet the requirements in accordance with the drug standards that have been determined. The formulation of captopril drug produced was in accordance with the dosage for use as a therapeutic drug.

Table 4: The results of the uniformity of the weight of the captopril drug

Observation parameters	Captopril tablets	
	CCM	Avicel
Average weight (mg)	130.15	132
The highest weight of 1 tablet (%)	1.51	2.05
Lowest weight of 1 tablet (%)	1.15	1.41
Lowest weight of 1 tablet (%)	1.51	1.31

CCM: Corncob cellulose microcrystal

The hardness and friability tests of the captopril CCM and Avicel tablets formulation results are shown in Table 5. The purpose of the hardness test was to provide an overview of resistance to mechanical shock during the distribution process. In addition, the tablet hardness test also provides an overview of the speed of disintegration and dissolution of the tablet adsorption. Friability testing aimed to ensure the consistency of the weight during the production process until it reaches the consumer within the specified time, the results show compliance with Indonesian drug formulation standards.

Table 5: Evaluation of the formulated captopril CCM and Avicel tablets

Tablet	Hardness	Friability (%)
CCM	4.92	0.76
Avicel	3.5	0.68

CCM: Corncob cellulose microcrystal

In vitro disintegrating test data with the use of disintegration tester, *in vitro* model consists of two tests; Model I (disintegration testes had a mimicking up and down peristaltic movement) whereas Model II without, and *in vivo* model (in the oral cavity) is shown in Table 6. *In vitro* disintegration time test of tablets used as ODT medium was water. This was because ODT is designed to disintegrate in the oral cavity [14]. Table 6 data showed that the *in vivo* disintegration time in the mouth for all ODT formulas is the fastest disintegration time compared to the other two types of disintegration time. This was thought to be due to the movement of the tongue, the alkaline pH of the saliva, and the presence of the enzyme ptyalin which

Figure 1: CCM manufacturing process; (a) corncob, (b) corncob powder, (c) corncob alpha-cellulose, and (d) CCM. CCM: Corncob cellulose microcrystal

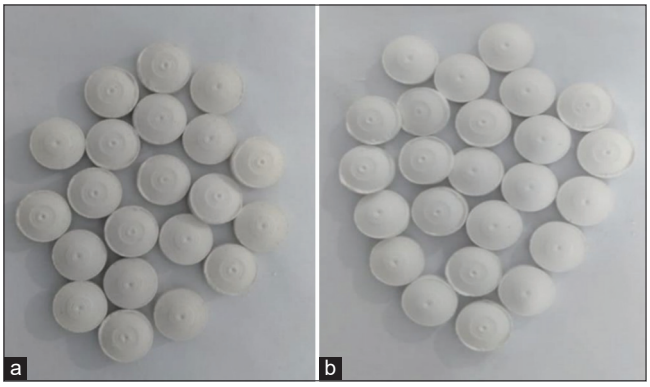

Figure 2: Captopril tablet formulation results from CCM and Avicel; (a) CCM and (b) Avicel. CCM: Corncob cellulose microcrystal

helps speed up the disintegration of the tablet in the mouth.

Table 6: Evaluation of the ODT time formulated CCM and Avicel captopril tablets

Formulated captopril CCM	Test	Disintegrate time (second)
CCM	Model I	18.46
	Model II	37.15
	In vivo	12.26
Avicel	Model I	12.22
	Model II	31.12
	In vivo	9.27

ODT: Orally disintegrating tablet, CCM: Corncob cellulose microcrystal

Conclusion

The results of the evaluation of the captopril ODT tablet formulation with CCM as a filler have similarities with Avicel as a standard filler in tablets and all the parameters of the tablet requirements are met. The results of this study indicate that CCM can be used as a substitute for Avicel as a filler in the formulation of ODT tablets and further research is needed to maximize the function of CCM in tablet formulations.

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