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FORMULATION OF ORALLY DISINTEGRATING TABLETS OF KAPTOPRIL AS SUPERDISINTEGRANE USING CORNCOB (*Zea mays* L.)

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ABSTRACT

This study aimed to make corn cobs the basic material for the manufacture of microcrystalline cellulose. Manufacture of microcrystalline cellulose from corn cobs by isolating alpha cellulose from corn cobs, then hydrolysis using HCl 2.5 N. The yield of microcrystalline cellulose from corn cobs of 14.51% can be used as Orally Disintegrating Tablet (ODT) and has similarities with avicel as standard comparison. Both organoleptic results were odorless, white, tasteless, pH 5.6 and 6.54, drying shrinkage 3.33% and 4.39%; total ash content 0.17% and 0.02%, water soluble substances 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, the Hausner index is 1.195 and 1.225, the compressibility index is 19.55 and 22.55%, the porosity is 75.5 and 74.6%. Captopril ODT tablet preparations with corncob microcrystalline cellulose as filler have the same tablet evaluation results compared to Avicel and meet the requirements.

Keywords: corncobs, microcrystalline cellulose, ODT, and Avicel

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 corn cobs include cellulose 39.1%, hemicellulose 42.1%, lignin 9 ,1%, protein 1.7%, and ash 1.2%.[2] In addition, corn cobs are also reported to have potential utilization as natural antioxidants and absorbents.[3,4] The high content of corn cobs can be applied in the cosmetic field food and pharmaceutical industry.[5] The cellulose content can be converted into corn cobs 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 in order to achieve maximum absorption and also not to saturate the transport traversed in the mechanism.[9]

Captropil is one of the drugs commonly used in the treatment of hypertension. The use of this drug orally with an inhibitory mechanism of action of *Angiotensin Converting Enzyme (ACE)* to treat high blood pressure, heart failure, and prevention of kidney failure due to hypertension and diabetes. Disadvantages of captropil in the formulation of drugs with a short release.[9] Therefore, the purpose of this study was to formulate captopril drug preparations with fillers using microcrystalline corn cobs compared to Avicel PH 102.

EXPERIMENITAL

Materials

The materials used were 20 mesh sieves, oven, blender (National), pH meter, weighing bottle, desiccator, porcelain crucible, pycnometer, funnel, hardness tester, 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 PH 102®, Sodium hydroxide (Merck), distilled water, sodium hypochlorite, hydrochloric acid (Merck), starch, lactose anhydrous, sodium starch glycolate, mannitol DC (Merck), aspartame (Merck), Mg stearate (Merck), talc, and mint flavour

Sample Preparation

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

α- Cellulose Isolation Process

100 g corncob powder added 1.5 L of NaOH 4% and heated for 2 hours 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 hours 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 hour. Then filtered and the residue was washed with distilled water until the pH was neutral. Subsequently, it was bleached again with 500 mL sodium hypochlorite of 2.5% and heated at 100°C for 5 minutes. 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 Microcrystalline Cellulose

50 g of alpha-cellulose was hydrolyzed with 1.2 L of HCl 2.5 N by boiling for 15 minutes 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 minutes and then allowed to stand overnight and filtered. Microcrystalline cellulose was washed with distilled water until neutral, then dried in an oven at a temperature of 57-60°C for 60 minutes and then ground.[11,12,13]

Captopril Orally Disintegrating Tablet (ODT) Tablet Manufacturing

The modified ODT was made using FI (microcrystalline) cellulose from corn cobs, 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. Preformulation testing was continued by evaluating the results of captopril ODT . tablets.[114]

Table-1: Captopril ODT tablet formula

Material Name (mg)	F I	F II
Captopril	12.5	12.5
MSTJ	78	-
Avicel pH102	-	78
Sodium starch glycolate	13	13
Mannitol	19.5	19.5
Aspartame	3.9	3.9
Stearate-Mg	1.7	1.7
Talk	1.3	1.3
Pepper mint	q.s	q,s
Total	130	130

Orally Disintegrating Tablet (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 6 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 frabiator tester and rotated at a speed of 25 revolutions/minute for 4 minutes, then weighed. The value of tablet friability is quite good 0.1-0.9%. Disintegration time testing was carried out on 6 tablet samples. Used 800 ml of water with a temperature of 37°C ± 2°C as the medium. Put 1 tablet in each tube from the basket. Then the tool is run with a frequency of up and down from the basket 30 times per minute. 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 less than 1 minute

RESULTS AND DISCUSSION

Manufacture of Corncob Cellulose Microcrystals (CCM)

Corn cob 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%) (Figures-1). This shrinkage occurs due to the loss of lignin, hemicellulose and other compounds when alpha cellulose undergoes a hydrolysis reaction.

(a) (b) (c) (d)

Fig.-1: Corncob Cellulose Microcrystals Manufacturing Process; (a) Corncob, (b) Corncob Powder, (c) Corncob alpha cellulose, and (d) Corncob Cellulose Microcrystals (CCM)

The organolective results of CMC compared with Avicel had similarities including odor, white color, and tasteless and had a pH of 5.6 while Focel had 6.5 and met the standard for medicinal raw materials. The physicochemical properties of corncob cellulose microcystaline 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

Orally Disintegrating Tablet Preformulation

The results of the preformulation tests carried out showed that CCM and frocel met the requirements, had almost the same flow time and had uniformity of granules. The time required for the granules to flow must be less than 10 seconds. The results of the preformulation test of Captopril ODT Tablets from CMM with frocel were presented in Table-3. The results of the evaluation of the ODT granules from the angle of repose and the index for CMM and Avicel showed that they met the specified requirements.

Table-3: Captopril ODT Tablet preformulation test results

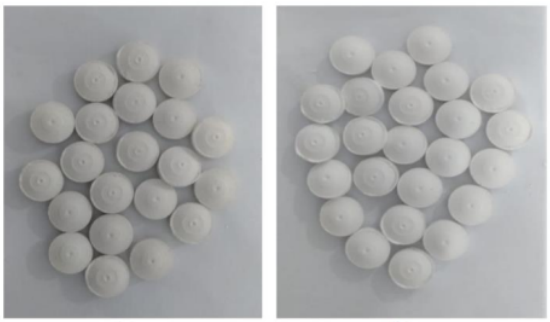
Formula	Waktu Alir (detik)	Sudut Diam (°)	Indeks tab (%)
CMM	1.65	21.02	16.23
Avicel	1.48	20.58	18.64

Formulation and Orally Disintegrating Tablets of Captopril Drugs

The results of the captopril tablet formulations of CMM and Avicel were shown in Figure-2. The results of the evaluation showed uniformity of weights for CMM 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**	
	CMM	**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



(a) (b)

Fig.-2: Captopril tablet formulation results from CMM and Avicel; (a) CMM and (b) Avicel

The hardness and friability test of the captropil CMM and Avicel tablets formulation results were 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 the standard.

Table-5: Evaluation of the formulated captropil CMM and Avicel tablets

Tablet	**Violence Result**	**Friability (%)**
CMM	4.92	0.76
Avicel	3.5	0.68

In vitro disintegration time test data using a disintegration tester, modified device and in vivo (in the oral cavity) are 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 pitalin which helps speed up the disintegration of the tablet in the mouth.

Table-6: Evaluation of the disintegration time formulated CMM and Avicel captopril tablets

Formulated captropil CMM	Testing	Time destroyed (second)
CMM	In vitro	18,46
	Modified tools	37,15
	In vivo	12,26
Avicel	In vitro	12.22
	Modified tools	31,12
	In vivo	9,27

CONCLUSION

The results of the evaluation of the ODT captopril tablet formulation with CMM 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 CMM can be used as a substitute for Avicel as a filler in the formulation of ODT tablets.

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