



**DETERMINATION OF METRONIDAZOLE MICROPARTICLE
CONTENTS IN THE HEMISELLULOSE MATRIX OF CORN COB USING
ULTRAVIOLET SPECTROPHOTOMETRY**

Authors:

**Gabena Indrayani Dalimunthe¹, Zulmai Rani¹, Ainil Fithri Pulungan¹, Robiatun Rambe²,
Haryani Sismona¹**

¹Faculty of Pharmacy, Universitas Muslim Nusantara Al Washliyah, Medan, North Sumatra,
Indonesia

²Faculty of Pharmacy, Universitas Haji Sumatera Utara, Medan, Indonesia, 20226
Corresponding Email: *gabenaindrayani03@gmail.com

About the Author

1. 1st Author : Dr. apt. Gabena Indrayani Dalimunthe, M.Si
Affiliation : Faculty of Pharmacy, Universitas Muslim Nusantara Al Washliyah, Medan, North Sumatra, Indonesia
Mailing address : Jalan Garu II Medan, Sisingamaraja, Medan, Indonesia
Email of author : gabenaindrayani03@gmail.com
Orcid ID : <https://orcid.org/0000-0002-5198-1887>
Google Scholar URL: https://scholar.google.com/citations?view_op=list_works&hl=id&user=h6wgPCMAAAAJ
Phone number : 085262615909

2nd Author : apt. Zulmai Rani, S.Farm., M.Farm
Affiliation : Faculty of Pharmacy, Universitas Muslim Nusantara Al Washliyah, Medan, North Sumatra, Indonesia
Mailing address : Jalan Garu II Medan, Sisingamaraja, Medan, Indonesia
Email of author : zulmairani22@gmail.com
Orcid ID : <https://orcid.org/0000-0003-4547-9054>
Google Scholar URL: <https://scholar.google.com/citations?user=xg4oS8sAAAAJ&hl=id>
Phone number : 08358950338

3th Author : apt. Ainil Fithri Pulungan, S.Farm., M.Si
Affiliation : Faculty of Pharmacy, Universitas Muslim Nusantara Al Washliyah, Medan, North Sumatra, Indonesia
Mailing address : Jalan Tanjung Morawa, Medan, Indonesia
Email of author : ainilfithri240@gmail.com
Orcid ID : <https://orcid.org/0000-0003-0665-3558>
Google Scholar URL: <https://scholar.google.com/citations?user=DisccyIAAAAJ&hl=id>
Phone number : 085296611897

4th Author : apt. Robiatun Rambe, S.Farm., M.Si
Affiliation : Faculty of Pharmacy, Universitas Haji Sumatera Utara, Medan, Indonesia, 20226
Mailing address : Jalan Namorambe Medan, Indonesia
Email of author : robiatunrambe1990@gmail.com
Orcid ID : <https://orcid.org/0000-0002-7109-3836>
Google Scholar URL: <https://scholar.google.com/citations?user=Yva8oK0AAAAJ&hl=id>
Phone number : 081260281130

5th Author : Haryani Sismona, S.Farm
Affiliation : Faculty of Pharmacy, Universitas Muslim Nusantara Al Washliyah, Medan, North Sumatra, Indonesia
Mailing address : Jalan Garu I, Sisingamaraja, Medan, Indonesia
Email of author : sismona64@gmail.com
Orcid ID : -
Google Scholar URL: -
Phone number : 085359902596

ABSTRACT

Microparticles can be an accurate drug delivery agent, reducing drug concentration in the target and providing an effective delivery system for substances that are slightly soluble in water. Corn cobs contain the most hemicellulose, and this hemicellulose can be employed as a matrix to restrict medication release if administered orally. The purpose of this study is to use UV spectrophotometry to evaluate the concentration of metronidazole microparticles in the hemicellulose matrix of corn cobs. This research is divided into two stages: separating hemicellulose from corn cobs and characterization of hemicellulose, which includes visual organoleptics, taste, smell, and form. Solubility test in alkaline conditions (NaOH), followed by FTIR test using the KBr pellet method with typical peaks seen in the FTIR spectrum, SEM test to get structural morphology, and PSA test to determine particle size and distribution of representative samples. After the microparticles are formed, further characterization is carried out, including an organoleptic test, solubility test, PSA test, FTIR test, and SEM test. Next, the levels of metronidazole microparticles in the corncob hemicellulose matrix were determined using ultraviolet spectrophotometry by comparing metronidazole tablets on the market. The concentration of metronidazole microparticle sample in the corncob hemicellulose matrix was determined to be 80.12 ± 0.5290%, and the concentration of metronidazole tablets on the market was 100.51 ± 0.7576%, which meets the requirements for metronidazole tablet concentration, namely not less than 90.0% and not more than 110% of the amount stated on the label.

Keywords: Hemicellulose, Microparticles, spectrophotometry, Metronidazole tablets

ABSTRAK

Mikropartikel adalah partikel dengan diameter 1 sampai 1000 µm. Mikropartikel dapat menjadi penghantaran obat yang akurat, mengurangi konsentrasi obat pada target dan memberikan sistem penghantaran yang efektif untuk zat yang sedikit larut dalam air. Tongkol jagung mengandung hemiselulosa tertinggi dan pada hemiselulosa ini dapat digunakan sebagai matriks yang dapat mengontrol pelepasan obat jika diberikan melalui rute oral. Tujuan penelitian ini yaitu untuk mengetahui penetapan kadar mikropartikel metronidazol dalam matriks hemiselulosa tongkol jagung dengan spektrofotometri ultraviolet. Tahap penelitian ini yaitu isolasi hemiselulosa dari tongkol jagung, karakterisasi, hemiselulosa meliputi organoleptis visual, rasa, bau dan bentuk, uji kelarutan hemiselulosa, uji FTIR menggunakan metode pelet KBr, uji SEM dan uji Particle Size Analyzer. Setelah terbentuk mikropartikel selanjutnya dilakukan karakterisasi kembali meliputi :uji organoleptis, uji kelarutan, uji PSA, uji FTIR dan uji SEM. Selanjutnya dilakukan penentuan kadar mikropartikel metronidazol dalam matriks hemiselulosa tongkol jagung secara spektrofotometri ultraviolet dengan perbandingan tablet metronidazol yang beredar dipasaran. Hasil penetapan kadar dari sampel mikropartikel metronidazol dalam matriks hemiselulosa tongkol jagung 80,12 ± 0,5290 % dan kadar tablet metronidazol yang beredar dipasaran yaitu 100,51 ± 0,7576 % yang memenuhi persyaratan kadar tablet metronidazol yaitu tidak kurang dari 90,0 % dan tidak lebih dari 110 % dari jumlah yang tertera pada etiket.

Kata kunci: Hemiselulosa, Mikropartikel, spektrofotometri, Tablet metronidazol

INTRODUCTION

Corn cobs contain the highest hemicellulose compared to other agricultural waste such as sugar cane bagasse, oat hulls, husks, peanut shells and cotton seed shells, so the hemicellulose component of corn cobs has the potential to be developed in pharmaceutical preparations, one of which is to become a matrix for medicines (Harini & Mohan, 2020; Liu et al., 2020). Hemicellulose can be used as a (matrix) that can control drug release if administered via the oral route (Dalimunthe et al., 2019).

Hemicellulose is a natural polymer that is non-toxic, mucoadhesive, biodegradable, biocompatible, and has a low level of immunogenicity, hemicellulose does not dissolve in gastric juices or small intestine fluids, is very good as a matrix so that efficacy in treatment is better and side effects are reduced or even eliminated (Doppalapudi et al., 2015; McClements et al., 2015). Sources of corn cobs are widely available, easy to find, and cheap (Iram et al., 2022). Meanwhile, other natural polymers such as chitosan and pectin which have been used in previous research are still more expensive than polymers from corn cobs (Jiang et al., 2017; Safitri, 2018).

Microparticles can be an accurate drug delivery agent, reducing the drug concentration on the target and providing an effective delivery system for substances that are slightly soluble in water (Lengyel et al., 2019). In addition, microparticle preparations can release more than 80% of the active substance within 10 minutes. Microparticles can be used to produce amorphous drugs with desired physical characteristics and can reduce local side effects such as gastrointestinal tract irritation upon oral administration (Parida et al., 2013).

Metronidazole was used as a model because it is an antibiotic that has a broad antiprotozoal and antibacterial spectrum (Leitsch, 2019). Strongly efficacious against all forms of Entamoeba, as well as against other anaerobic protozoan pathogens, such as Trichomonas and Giardia. This drug is also active against anaerobic bacteria (García et al., 2017). Diseases caused by protozoal and bacterial infections make this antibiotic one of the choices commonly consumed by the public and widely used (Sreeja et al., 2017).

The drugs consumed need to be tested to ensure the drugs are quality and safe for the public. Where so far there has not been much information regarding drug levels provided by drug manufacturers. Based on the above research, the research was carried out to test drug levels and compare them with the microform of metronidazole.

METHOD

The research method used was experimental research. The research was carried out at the Integrated Laboratory of the Al - Washliyah Muslim Nusantara University, Medan, at the Institute for Food, Medicine and Cosmetics Studies of the Indonesian Ulema Council (LPPOM - MUI) Medan City.

Sample Collection

Corn cobs were collected on Jalan Pintu Air IV Simalingkar B, Medan Tuntungan District, North Sumatra Province, and metronidazole tablets

Isolation of hemicellulose from corn cobs

Extracting the starch content from banana peels is done by peeling the bananas and separating them. Corn cobs collected from the research location were washed thoroughly with water, and then dried in the sun, then the samples were cut into small pieces and ground using a blender, then sieved using 80 mesh, then weighed at 500 mg and the sample was then put into a 500 ml glass beaker. and the corn cob powder was dissolved by adding 0.1 N sodium hydroxide solvent, left for 6 hours, and

filtered, to precipitate the cellulose, 70% alcohol was added, with occasional stirring, then left for 3 hours. The process of pouring is carried out. Next, it was filtered, and the precipitate was washed with distilled water, poured again, then air dried, crushed, and weighed for hemicellulose (Muchlisyam & Harahap, 2016).

Hemicellulose Characterization

Hemicellulose organoleptics

Organoleptic testing consists of visual observation, taste testing, odor testing, and shape. Visual observations were made on the color texture of the hemicellulose produced (Rani et al., 2023).

Hemicellulose solubility test

The solubility of hemicellulose was tested by dissolving hemicellulose in an alkaline solvent (NaOH 0.1%), HCl 0.1N, hot water, and cold water. The solubility of a compound shows how far the compound can dissolve in a solvent (Dalimunthe et al., 2018).

FTIR (Fourier Transform Infrared) test of hemicellulose

FTIR (Fourier Transform Infrared) hemicellulose test. FTIR analysis was carried out using the KBr pellet method. Characteristic peaks appear in the interpreted FTIR spectrum of hemicellulose (Kostyukov et al., 2023).

SEM (Scan Electro Magnetic) hemicellulose test

SEM (Scan Electro Magnetic) hemicellulose test. Based on analysis using SEM, the structure of corncob hemicellulose, morphology, and topology of the structure were obtained (Qi et al., 2019).

Making Corn Cob Hemicellulose Microparticles Using Metronidazole

Corn cob hemicellulose (50 mg dissolved in 100 ml of NaOH. Next, add tripolyphosphate (STPP), stir continuously until homogeneous, add propylene glycol, stir until homogeneous, add BPI standard metronidazole, stir homogeneously, stir for 2 hours, centrifuged at 1000 rpm for 3 hours, will 2 layers are formed, namely solution and precipitate and separated and dried (forming microparticles) which are then tested on the microparticles including microparticle organoleptic tests, solubility tests, FTIR and SEM.

Determination of Metronidazole Tablet Concentrations

Weighed and powdered 10 metronidazole tablets. Then carefully weigh an amount of powder equivalent to 50 mg of metronidazole (the powder is weighed 6 times), put into a 50 ml volumetric flask. Dissolve with 10 ml of 0.1 N NaOH, shake then add 0.1 N NaOH to the mark line, filter and discard 5 ml of the filtrate and then collect the filtrate ($C = 500 \mu\text{g/ml}$). Pipetted 5 ml into a 50 ml volumetric flask and diluted with 0.1N NaOH to the mark line ($C = 50 \mu\text{g/ml}$). Pipetted 2 ml into a 25 ml volumetric flask and diluted with 0.1N NaOH to the mark line ($C = 10 \mu\text{g/ml}$). The absorption at the maximum wavelength obtained was measured.

Determination of Metronidazole Microparticle Content in Corn Cob Hemicellulose Matrix

Weighed 0.0130 g of hemicellulose microparticle powder and put it into a 25 ml volumetric flask. Dissolve in 10 ml of 0.1 N NaOH, shake then add 0.1 N NaOH to the mark line. Pipette 2 ml into a 50 ml volumetric flask and dilute with 0.1 N NaOH to the mark line. Pipetted 2 ml into a 50 ml volumetric flask and diluted with 0.1 N NaOH to the mark line. Then the absorption at a wavelength of 319 nm was measure (Dalimunthe et al., 2019).

RESULTS AND DISCUSSION

Isolation of corn cob hemicellulose from 500 mg of isolated corn cob powder resulted in a hemicellulose yield of 10%. Isolation of Corn Cob Hemicellulose The amount of hemicellulose obtained was 12.95%.

Characterization of Corn Cob Hemicellulose

Organoleptic Test

Visual observations were made on the color texture of the hemicellulose produced. The test results can be seen in Table 1.

Table 1.

Organoleptic Test Results for Corn Cob Hemicellulose (*Zea mays L.*)

Organoleptic Testing	Test results
Form	Granule
Color	Light brown
Flavor	Tasteless
Smell	No smell

Visual observations were made on the color texture of the hemicellulose produced. From the test results, the results were obtained according to the description in the hemicellulose literature.

Hemicellulose Solubility Test

The solubility of a polymer, including carbohydrates, will decrease with the higher the molecular weight. Hemicellulose is also difficult to dissolve in cold water. Hemicellulose solubility test results can be seen in Table 2.

Table 2.

Solubility Test Results for Corncob Hemicellulose (*Zea mays L.*)

Solvent	Solubility
NaOH 0.1N	soluble
Hot water 100°C	Late
Cold water	difficult to dissolve
HCl 0.1N	practically insoluble

In this case, it is shown that the solubility of hemicellulose is the same as the solubility of microparticles.

Hemicellulose FTIR (Fourier Transform Infrared) Test

The results of the corncob isolation were then analyzed using an infrared spectrophotometer (Fourier transform infrared, FTIR). FTIR analysis was carried out using the KBr pellet method. Corncob hemicellulose FTIR interpretation data can be seen in Figure 1 and Table 3.

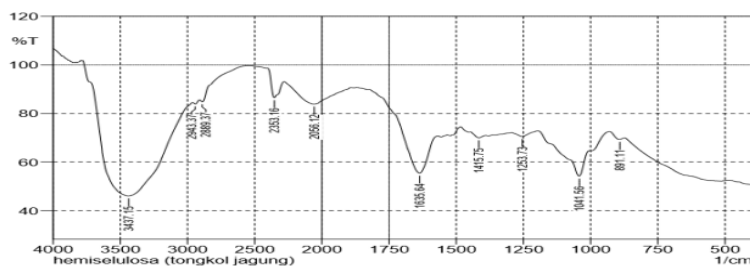


Figure 1.

FTIR Absorption Graph of Corncob Hemicellulose (Isolation Results)

Table 3.
FTIR results of corn cob hemicellulose

No.	FTIR research results	
	Wavelength	Function group
1	3437,15 cm ⁻¹	OH
2	2943,37 cm ⁻¹	CH
3	1635,64 cm ⁻¹	C=O
4	1041,56 cm ⁻¹	C-OH
5	891,11 cm ⁻¹	C-C

Obtained absorption band at wave peak 3437.15 cm⁻¹ range of OH groups. The absorption band at wave number 2943.37 cm⁻¹ shows the CH range vibration of the alkane. The absorption band at the wave peak 1635.64cm⁻¹ ranges from the C=O group of the secondary amide. The absorption band from the C-OH range in aldehydes at a wave number of 1041.56 cm⁻¹, and the CC absorption band at a wave peak of 891.11 cm⁻¹ indicate that the functional groups contained in isolated corncob hemicellulose are almost the same as the functional groups contained in on the chemical structure of hemicellulose in previous research (Afriyanti et al., 2020).

The FTIR test on hemicellulose shows that the groups contained are OH, CH, secondary amides, and aldehydes, as well as the functional groups contained in hemicellulose microparticles, it is stated that there are still the same groups.

Hemicellulose SEM (Electro Magnetic Scan) Test

Hemicellulose Scan Electro Magnetic (SEM) test results can be seen in Figure 2.

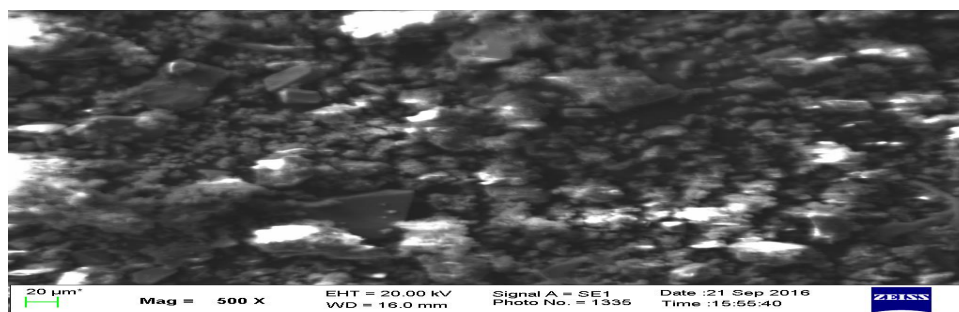


Figure 2.
SEM of corn cob hemicellulose with 500 x magnification

Based on analysis using SEM, the structure of corncob hemicellulose was obtained at 500x magnification, showing that the hemicellulose structure still looks large, namely xylan powder consisting of a mixture of aggregate and non-aggregate particles with an irregular, round, rough morphology, in the form of an irregular structure in the form of cavities. This is due to the developer effect. As observed through a scanning electron microscope (SEM).

With an irregular morphology, round shape, rough surface, and irregular structure in the form of cavities, this is due to the expanding effect. As observed through a scanning electron microscope (SEM)

Microparticle Evaluation

Microparticle Organoleptics

Organoleptic testing of microparticles consists of visual observation, taste testing, odor testing, particle shape and size. Visual observations were made on the color texture of the resulting microparticles. Test results can be seen in Table 4.

Table 4.
Organoleptic Test Results for Microparticles

Organoleptic Testing	Test results
Form	Granule
Color	Light brown
Flavor	Tasteless
Smell	No smell

The results of organoleptic observations of hemicellulose and cellulose microparticles gave the same results in terms of color, shape, and odor, this shows that there is no influence from other materials.

Microparticle Solubility Test

The results of the microparticle solubility test can be seen in Table 5

Table 5.
Solubility of Hemicellulose microparticles

No	Solvent	Solubility results
1	Base (NaOH 0.1 N)	Soluble
2	Acid (HCL 0.1 N)	Practically insoluble
3	Hot water 1000C	Late
4	Cold water	Difficult to dissolve

The solubility of a compound shows how far the compound can dissolve in a solvent. The hemicellulose solubility test shows that hemicellulose easily dissolves in alkaline conditions (NaOH 0.1N), in this case, microcrystalline hemicellulose also shows that the solubility of hemicellulose is the same as the solubility of microparticles. From this solubility analysis, it can be concluded that no chemical reaction occurred between metronidazole and hemicellulose as a polymer after the formation of microcapsules because there was no difference in solubility in the solvents tested.

PSA (Particle Size Analyzer) Microparticle Test

The PSA test results of microparticles can be seen in Table 6.

Table 6.
PSA Results of Corn Cob Hemicellous Micropathicles

No	Formula (mg Hemicellulos)	Microparticle size (μm)	PDI (μm)
1	Formula1=100	0,45336	0,00105
2	Formula2=200	0,63593	0,0009
3	Formula3=300	0,71732	0,00108
4	Formula4=400	0,89322	0,00105
5	Formula5=500	0,91857	0,00112

SEM (Electro Magnetic Scan) Microparticle Test

Based on analysis using SEM, the structure of hemicellulose microparticles can be seen in Figure 3.

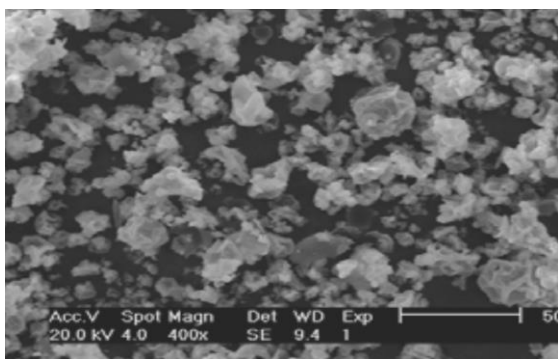


Figure 3.
SEM microparticles with 400x magnification

Hemicellulose microparticle structure produces microparticles with an average diameter of around $10.17 \pm 3.02 \mu\text{m}$, while the hemicellulose structure still looks large, namely xylan powder consisting of a mixture of aggregate and non-aggregate particles with an irregular morphology, round, rough surface, in the form of a structure. These irregular cavities are due to the developer effect (Baksi et al., 2018; Saha et al., 2013). According to SEM analysis, polymeric microparticles are proven to be very similar in shape, regardless of formulation, they appear to be mostly concave and asymmetrical and already appear smaller and united, possibly the particles have dissolved in the solvent.

The results of the particle size distribution examination carried out showed that the difference in particle size was influenced by the amount of hemicellulose used to form the microcapsule walls. The results obtained showed that the microcapsules produced for each formula produced different sizes. The greater the amount of polymer used, the thicker the coating that covers the metronidazole so that the size of the microcapsules produced is larger. The results show that the formula has an appropriate microparticle size and a very small polydispersity index (PDI) value. The polydispersity index is a data value of the cumulant analysis of two parameters (size and number) that is dimensionless and scaled, where a value smaller than 0.05 indicates the sample has a narrow and homogeneous size distribution (monodisperse), while a value greater than 0.7 shows that the sample has a very wide size distribution (polydisperse) (Khan & Irchhaiya, 2020).

Determination of Metronidazole Microparticle Content in Corn Cob Hemicellulose Matrix

Determination of Metronidazole Microparticle Content in Corn Cob Hemicellulose Matrix can be seen in Table 7.

Table 7.

Average levels and ranges of hemicellulose and microparticles Metronidazole tablets

Name Preparation	Rate average (%)	Rate Actually
Metronidazole	100,51	$100,51 \pm 0,7576 \%$
Microparticles metronidazole inside hemicellulose matrix corncob	80,12	$80,12 \pm 0,5290 \%$

The metronidazole concentration can be calculated by substituting the sample absorption into the equation $y = 0.0566 x + 0.00033$. The data shows that the level of metronidazole tablets on the market is 100.51% and the level of metronidazole microparticles in the corncob hemicellulose matrix is 80.12%.

CONCLUSIONS AND SUGGESTIONS

Based on the results of the research that has been carried out, it can be concluded that the results of the levels of metronidazole microparticles in the corncob hemicellulose matrix using ultraviolet

spectrophotometry are $80.12 \pm 0.5290\%$ and the results of the levels of metronidazole tablets on the market using ultraviolet spectrophotometry are 100.51 ± 0.7576 .

ETHICAL CONSIDERATIONS

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Conflict of Interest Statement

With regard to this article, we certify that there are no actual or possible conflicts of interest

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