RESEARCH ARTICLE

Preparation of Microcrystalline Cellulose from Dissolving Cellulose Obtained from Jute Fibers and Its Application in the Formulation of Fexofenadine Hydrochloride Tablet Dosage Form

Md. Sohel Rana, Mohammad R. Haque, Mohammad S. Amran, Abu A. Chowdhury*

Abstract

Introduction: The most affordable tablet form is microcrystalline cellulose (MCC), a popular pharmaceutical excipient that is utilized as a filler or binder in immediately compressible tablets.

Methods: In the present study, we extracted dissolving cellulose from jute fibers by treatment with 0.1 N hydrochloric acid solution and 20% w/w sodium hydroxide solution at high temperature and pressure. The dissolving cellulose was subjected to acid hydrolysis at 100°C for 2 hours with 2 N hydrochloric acid. The identity of the MCC was confirmed by FTIR and by determining the degree of polymerization. To evaluate the flow property, we determined the bulk, density, tapped density, Hausner index, Carr's index and angle of repose. The tableting property of the prepared MCC was evaluated by making fexofenadine hydrochloride tablets.

Result and Discussion: The dissolving cellulose contains 94.67% α-cellulose The DP of the MCC was found 191. The powder properties such as bulk density, tapped density, Hausner index and Carr's index, angle of repose values are comparable with that of standard Avicel PH102. The hardness, friability, disintegration time and % dissolved in 30 minutes were dissolution value of the tablets 5.6 kg, 0.34%, 178.17 seconds and 83.89%, respectively. All these values are within the United State Pharmacopoeia range and are comparable with the tablets prepared from Avicel PH102 and marketed fexofenadine tablets.

Keywords: Jute fibers, Microcrystalline cellulose, Fexofenadine hydrochloride

Journal of Applied Pharmaceutical Sciences and Research, (2022); DOI: 10.31069/japsr.v5i4.04

Introduction

Microcrystalline cellulose (MCC) is a depolymerized α-cellulose and is widely used as directly compressible excipients in the formulation of different tablet dosage forms. Recently, the MCC has gotten high attention to the pharmaceutical industry because of its high compactness power, application of minimum compression pressure, and subsequent formation of hard tablets that can disintegrate easily. The degree of polymerization (DP) of MCC is lower than 350.[1] The MCC is prepared by acid hydrolysis of α-cellulose obtained from wood,[2] cereal straws,[3] corn cobs,[4] bagasse,[5] pineapple leaf,6 [5] soybean husk,[7] coconut husks,[8] flax straw,[9] cotton,[10] waste paper,[11] wheat straw[12] etc. Though it can be prepared from different sources, it must have sufficient bulk density, flow property, uniform particle size & size distribution to be an effective candidate for the formulation excipients. The value of these parameters depends upon the manufacturing process of MCC and also on the source.

Jute is a natural fiber grown widely in Bangladesh, India, China, etc. Chemically, the jute fibers contain 60–62 and cellulose, 2024% hemicellulose, 11-13% lignin and small amount of proteins, pectins, wax, minerals and tannins.[13] The synthesis of MCC from jute fibers has been reported earlier.[14] The authors have only characterized the prepared MCC by FTIR, SEM. XRD, TGA. No information regarding the bulk density, flow property and particle size that affect the property of MCC to be useable as tablet excipients has been reported. In the present study, we have extracted the dissolving cellulose from jute fibers with subsequent acid hydrolysis of the cellulose to prepare MCC. We also apply the prepared MCC in the formulation of fexofenadine hydrochloride tablets and evaluated the tableting properties.

Department of Pharmaceutical Chemistry, Faculty of Pharmacy, University of Dhaka, Dhaka 1000, Bangladesh.

Corresponding Author: Abu A. Chowdhury, Department of Pharmaceutical Chemistry, Faculty of Pharmacy, University of Dhaka, Dhaka 1000, Bangladesh, Email: asaddg27@du.ac.bd

How to cite this article: Rana MS, Haque MR, Amran MS, Chowdhury AA. Preparation of Microcrystalline Cellulose from Dissolving Cellulose Obtained from Jute Fibers and Its Application in the Formulation of Fexofenadine Hydrochloride Tablet Dosage Form. Journal of Applied Pharmaceutical Sciences and Research. 2022; 5(4):28-32

Source of support: CRG, DU

Conflict of interest: None

Materials And Methods

Materials

Jute fibers were collected from local market. Cupriethylenediamine hydroxide solution, Anthraquinone and hydrogen peroxide (30%) were purchased from authentic

supplier of Sigma-Aldrich, Germany. All other reagents used in these experiments were in analytical grade.

Preparation of Dissolving Cellulose from Jute Fibers

The jute fibers were cut into small pieces (2-3 cm), soaked in 0.1 N HCl solution, and heated at 150°C in a high pressure reactor (Model IV, CarlRoth, Germany) for 2 hours. After washing with hot water it was again treated with 20% w/w sodium hydroxide solution with 0.5% anthraquinone for 2 hours at 170°C. Treated fibers were washed with hot water till neutralization followed by several steps of bleaching and alkali extraction with ClO_2 at 65°C for 1-hour, H_2O_2 for 1-hour at 60°C. The bleached fibers after washing were dried at 60°C for a period of 24 hours. The cellulose content of the dissolving cellulose was then determined by TAPPI method described earlier.[15]

Preparation of Microcrystalline Cellulose

For the synthesis of MCC, 15 gm of dissolving cellulose was soaked with 300 mL of 1.5 N hydrochloric acid and the mixture was heated at 100°C for 1-hour. The powder MCC was filtered to remove the acid solution, washed with water till neutralization and dried at 60°C overnight. The MCC powder was then sieved through 120 mesh. The fraction that passed through 120 mesh sieve and retained on the 200 mesh sieve was collected.

Identification of MCC

Identification of MCC by Degree of Polymerization

The MCC powder's polymerization degree was determined by method described earlier with some modification.[16] Different concentration (1, 0.5, 0.25, 0.125, 0.625%) of MCC solution was prepared in Cupriethylene diamine solution. The relative viscosity of these solutions were determined compared with the CUEN solution using Ostwald Viscometer 1831. Reduced viscosity was calculated from the relative density. A plot of reduced viscosity vs. concentration indicated the reduced visocity from the Y-intercept value of the straight line. The degree of polymerization was then calculated from the following equation.

$$(DP)^{0.85} = 1.1 \times \eta$$

Identification of MCC by Fourier Transform Infrared Spectroscopy (FTIR)

A small amount of MCC powder was placed on the sample holder of FTIR instrument and analyzed by LabSolution software in frequency range of 4000–600 cm^{-1} in transmission mode with a resolution of 2 cm^{-1}.

Characterization of Prepared MCC

Determination of bulk density and tapped density

The MCC powder's bulk density and tapped density were determined using methods described earlier. A total of 10 gm of MCC powder was seived to breakdown lump (if any) and transferred to a 50 mL measuring cylinder. After determining the volume (V_o) occupied by the powder, the sample was tapped 200 times with the healp a tap densitometer. The volume (V_{200}) of the powder after 200 times tapping was determined. The bulk density and tapped density of the powder were calculated by dividing the weight (10 gm) of the powder by bulk volume (V_o) and tapped volume (V_{200}), respectively.[17] The Hausner and Carr indexes were also calculated using the following equation.[18]

$$\text{Hausner Index} = \frac{\text{Tapped density}}{\text{Bulk density}}$$

$$Carr's\ Index = \frac{(\text{Tapped density} - \text{Bulk density}) * 100}{\text{Tapped density}}$$

Analysis of flow property by measuring angle of repose

The prepared MCC powder's angle of repose (AoR) was determined by Powder Angle of Repose measuring tester as described earlier. [19] A total of 10 gm of MCC powder was passed through funnel and allowed to fall on surface of the protractor. The height of the powder and the diameter of the base of powder were determined. The angle of repose was calculated from the following equation.

$$tan\theta = \frac{2h}{D}$$

Where h is the height of the MCC powder pile, D is the diameter of the base of powder, and θ is the angle of repose

Application of MCC in Fexofenadine hydrochloride Tablet Formulation

Preparation of fexofenadine hydrochloride tablets

Approximately, 120 mg fexofenadine hydrochloride powder was mixed with 262 mg of prepared MCC or Avicel PH102, 15 mg of sodiumstarch glycolate and 3 mg of Mg-stearate and subjected to compression in single punch machine to form the tablet.

Evaluation of hardness of the fexofenadine hydrochloride tablets

The hardness of ten tablets was determined using a hardness tester (Veego, India). The average force essential to crush the tablets was calculated in kilograms.

Friability test

For the friability test, twenty tablets were taken, weighed and transferred to the chamber of Friabilator (Veego, India). The chamber was rotated at 25 rpm for 4 minutes. The remaining total weight of twenty tablets were measured and % weight loss was calculated.

Disintegration of fexofenadine hydrochloride tablets

Disintegration of the tablets was measured in 0.001 N HCl solution at 37 ± 2°C with rpm of 50 using USP disintegration test apparatus. The assemblies were moved up and down at

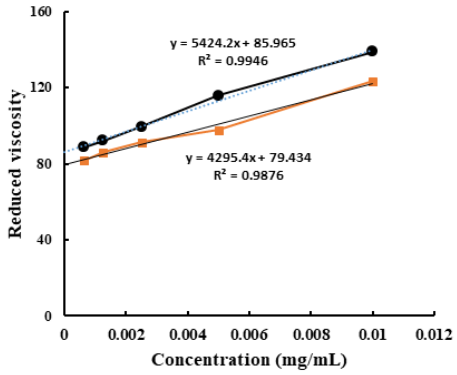

Figure 1: Reduced viscosity versus concentration curve for the determination of degree of polymerization of prepared MCC and Avicel PH102.

a rate of 30 cycles/minute. The time necessary to disintegrate tablet was measured.

In vitro dissolution of the formulated fexofenadine hydrochloride tablets

In vitro dissolution of fexofenadine hydrochloride tablets was measured by USP dissolution type II apparatus using 900 mL of 0.001 HCl solution at 37 ± 0.5°C. The speed of the stirrer was 50 rpm. Each tablet was placed in the basket and after 30 min period 5 mL of the medium from each basket was removed, filtered and diluted 10-fold and; determined the absorbance at 220 nm using UV-vis spectrophotometer (Model: UV 1700, Shimadzu). The amount of drug released in the dissolution medium after 30 min was calculated from the standard curve of fexofenadine hydrochloride prepared by measuring the absorbance of fexofenadine hydrochloride solution having different concentrations.

Results and Discussion

The jute fibers were treated with 0.1 N hydrochloric acid at 150°C for 1-hour followed by 20% w/w sodium hydroxide treatment and bleaching with chlorine dioxide and hydrogen peroxide to remove the hemicellulose and lignin and to isolate the pure cellulose known as dissolving cellulose. The dissolving cellulose contains more than 90% α-cellulose.[20] In our case, we got 94.67% of α-cellulose in the sample. This confirms that we were able to prepare to dissolve pulp or cellulose. The hydrolysis of this dissolving cellulose by 2 N hydrochloric acid at 100°C for 1 h produced MCC powder which was white in color, tasteless, odorless and free-flowing.

Identification of the MCC

The prepared MCC and standard Avicel PH102 were evaluated to determine the degree of polymerization by determining the relative viscosity using Ostwald Viscometer 1831. The Y-intercept of the straight line obtained from the reduced viscosity vs. concentration for different solutions of MCC indicates the intrinsic viscosity. A shown in Figure 1, the intrinsic viscosity of prepared MCC and Avicel PH102 is 79.434 and 85.965, respectively. From the intrinsic viscosity, the DP

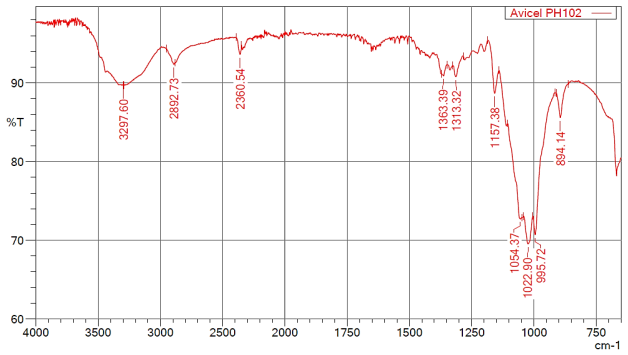

Figure 2A: FTIR spectrum of Avicel PH102

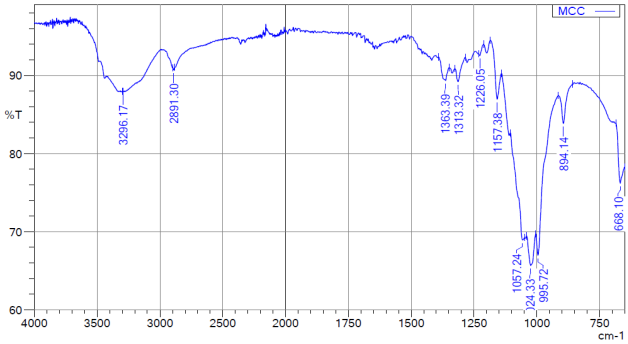

Figure 2B: FTIR spectrum of prepared MCC

of the prepared MCC and Avicel PH102 was calculated 191 and 211, respectively. According to USP, the DP of MCC must be lower than 350.[1] This confirms that our prepared powder is MCC in nature.

The prepared MCC was further identified by FTIR analysis. The FTIR spectrum of the prepared MCC and Avicel PH102 in Figure 2(A-B) reveals that all the peak position at different wave number are same. This indicates the similarity of the two sample. Both sample showed O-H absorption around 3297 cm^{-1}, C-H stretching absorption within 2800 to 3000 cm^{-1}, and C-O-C absorptions around 1024 and 1157 cm^{-1}. All these peaks are similar with those of the typical cellulose backbone.[21] Moreover, there was no peak at 1740 and 1595 cm^{-1} in the spectrum. Absence of this absorption peak in the spectrum indicates the absence of hemicellulose and lignin in the prepared MCC.[22,23] This clearly confirms the high level purity of prepared MCC which is comparable to Avicel PH102.

Characterization of Prepared MCC

A crucial factor for a pharmacological excipient is flow property. To be utilized as an excipient, the powder needs to have the best flow characteristics. In general, a material has a better chance of flowing and rearranging under compression the higher its bulk and tapped densities are. Bulk density provides an estimate of a powder material's flowability, whereas tapped density measures how well a powder may be packed in a small area after repeated tapping. In the present study, the prepared MCC's bulk density and tapped density are 0.21 ± 0.01, 0.31 ± 0.03 gm/mL. Once more, the

Table 1: Bulk density, tapped density, Hausner index, Carr's index and angle of repose of prepared MCC and Avicel PH102

Sample	*Bulk Density (gm/mL)*	*Tapped Density (gm/mL)*	*Hausner Index*	*Carr's Index*	*AoR*
MCC	0.21 ± 0.01	0.31 ± 0.03	1.47 ± 0.14	31.40 ± 6.78	38.67 ± 1.91
Avicel PH102	0.31 ± 0.02	0.40 ± 0.02	1.28 ± 0.05	22.11 ± 2.87	32.63 ± 1.45

*Average of three experiments has been shown for all samples

Table 2: Hardness, friability, disintegration, and dissolution of the tablets from MCC and Avicel PH102.

Sample	*Hardness (Kg) ± SD*	*Friability (%)*	*Disintegration time (Sec) ± SD*	*Dissolution (%Dissolved in 30 min) ± SD*
MCC	5.6 ± 0.38	0.34	178.17 ± 11.87	83.89 ± 2.95
Avicel PH102	5.9 ± 0.15	0.27	166.83 ± 11.81	85.22 ± 2.97
Marketed Tablet	6.4 ± 0.25	0.18	122.67 ± 10.81	94.41 ± 2.97

interparticle friction-related Hausner index can be used to predict the powder flow. The prepared MCC has a Hausner index that is comparable to that of Avicel PH102, and its value is 1.47, indicating that it has passable flowability compared to the Avicel PH102 that has the Hausner Index value of 1.28 ± 0.05 (Table 1). Another indicator of powder flowability is Carr's index. Typically, powder flowability is indicated by Carr's index values of 5–15, 16–18, 19–21, 22–35, and 36–40, respectively, for excellent, decent, reasonably passable, poor, and extremely poor powder flowability.[24,25] The Carr's index of the prepared MCC and Avicel PH102 are 31.40 and 22.11, respectively indicating the flow property of prepared MCC is low compared to the Avicel PH102.

On the other hand, because of their connection to interparticle cohesion, the angle of repose is an indirect means of evaluating powder flowability. Powders with an angle of repose less than 30 degrees exhibit outstanding flow properties, whereas those with 31°-35° and 36°-40° exhibit acceptable and passable flow capabilities, respectively.[18] A repose angle greater than 65 degrees denotes extremely poor flowability. The AoR value of the prepared MCC also indicates passable flow property while that of Avicel PH102 indicates good flow property (Table-1). The lower flow property of the prepared MCC might be due to the particles' rod shape or surface roughness.

Tableting Property of the MCC

We prepared fexofenadine hydrochloride tablets by direct compression technique using prepared MCC or Avicel PH102 and evaluated different parameters. The harness of the fexofenadine tablets prepared from MCC and Avicel PH102 is 5.6 and 5.9 kg, slightly lower than that of marketed fexofebadine tablets (Table 2). According to the United States Pharmacopoeia, the hardness should be within 4 to 8 kg and the friability is lower than 1%. Both the parameters are within the range of USP specifications.[26,27]

The MCC-formulated tablets underwent *in vitro* disintegration using the USP disintegration device. The fact that all of the prepared tablets dissolve in 178 seconds indicates that the tablets have a very good disintegration property. Again, the prepared tablets were subjected to an *in vitro* dissolution study using the USP dissolution apparatus II. We generated the fexofenadine HCl curve in order to measure the released fexofenadine HCl in the dissolving medium after the designated time. The square of the straight line's correlation coefficient indicates an excellent connection between the concentration and absorbance value, which is > 0.99. In 900 mL of 0.01 N HCl at 50 rpm, the tablet formulation made from MCC demonstrated more than 80% drug release in less than 30 minutes. Considering the aforementioned factors collectively, we may draw the conclusion that the MCC made from jute fibers is comparable to the commercial Avicel PH102 in terms of several factors including identity and flow property.

Conclusion

The current effort aimed to utilize jute fibers to produce MCC, a highly useful immediately compressible excipient. Using the hydrolysis process, we extracted the MCC from the dissolving cellulose of jute fibers. Regarding identification and other metrics including bulk density and flow property the resulting MCC was quite comparable to the commercial Avicel PH102. By creating and testing fexofenadine HCl tablets, we further demonstrated the derived MCC's appropriate performance as a directly compressible agent in tablet formulation.

Acknowledgement

The authors thank Incepta Pharmaceuticals Ltd., Bangladesh, for giving Fexofenadine hydrochloride and Avicel PH102 as gifts.

Funding

The research work has been supported financially by the Centennial Research Grant (CRG Project No.: Reg./Admin-3/47856) funded by the University of Dhaka, Dhaka-1000, Bangladesh.

References

1. USP 36-NF 31. Monograph: microcrystalline cellulose, p 643. Rockville, MD.
2. Marianna L, Svetlana C. Obtaining microcrystalline cellulose from softwood and hardwood pulp. Bioresources. 2007;2;4-10..
3. Jain JK, Dixit VK, Varma KC. Preparation of microcrystalline cellulose from cereal straw and its evaluation as a tablet

excipient. Indian J Pharm Sci 1983;45:83-5.
4. Azubuike CP, Okhamafe AO. Physiochemical, spectroscopic and thermal properties of microcrystalline cellulose derived from corn cobs. Int J Recycl Org Waste Agric 2012;1:1-9.
5. Paralikar KM, Bhatawdekar SP. Microcrystalline cellulose from bagasse pulp. Biol Wastes 1988;24:75-7.
6. Cherian BM, Leao AL, de Souza SF, Thomas S, Pothan LA, Kottaisamy M. Isolation of nanocellulose from pineapple leaf fibres by steam explosion. Carbohydr Polym 2010;81:720-5.
7. Uesu NY, Pineda FA, Hechenleitner AA. Microcrystalline cellulose from soybean husk effects of solvent treatments on its properties as acetyl-salicyclic acid carrier. Int J Pharm 2000;206:85-96.
8. Rosa M, Medeiros E, Malmonge J, Gregorski K, Wood D, Mattoso L, et al. Cellulose nanowhiskers from coconut husk fibers: Effect of preparation conditions on their thermal and morphological behavior. Carbohydr Polym 2010;81:83-92.
9. Bochek AM, Shevchuk IL, Lavrentev VN. Fabrication of microcrystalline and powdered cellulose from short flax fiber and flax straw. Russ J Appl Chem 2003;76:1679-82.
10. Setu NI, Mia MY, Lubna NJ, Chowdhury AA. Preparation of microcrystalline cellulose from cotton and its evaluation as direct compressible excipient in the formulation of naproxen tablets. Dhaka Univ. J. Pharm. Sci. 13(2): 187-192, 2014
11. Rana RH, Rana MS, Tasnim S, Haque MR, Kabir S, Amran MS, Chowdhury AA. Characterization and tableting properties of microcrystalline cellulose derived from waste paper via hydrothermal method. J Appl Pharm Sci, 2022; 12(06):140–147
12. Alemdar A, Sain M. Biocomposites from wheat straw nanofibers: Morphology, thermal and mechanical properties. Compost Sci Tech 2008;68:557-65.
13. Arun M, Vincent S, .Karthikeyan R, Development and characterization of sisal and jute cellulose reinforced polymer composite. 2020, 28, 556-561.
14. Jahan MS, Saeed A, He Z, Ni, Y. (2011). Jute as raw material for the preparation of microcrystalline cellulose. Cellulose. 2011;18:451- 459.
15. Hamilton, F. and B. Leopold. 1987. Pulp and Paper Manufacture: Volume 3 Secondary Fiber and Non-Wood Pulping. 3rd ed. The Joint Textbook Committee of the Paper Industry, TAPPI (. TAPPI 203 cm-99), Atlanta, GA, USA and CPPA, Quebec, Canada
16. Sihtola H, Kyrklund B, Laamanen L, Palenius I. Comparison and conversion of viscosity and DP-values determined by different methods. Paperi ja Puu, 1963; 45(4a):225–32.
17. Azubuike CP, Okhamafe AO. Physicochemical, spectroscopic and thermal properties of microcrystalline cellulose derived from corn cobs. Int J Recycl Org Waste Agric, 2012; 1:1–7.
18. Aulton ME. Tablet. In: Pharmaceutics- the science of dosage form design, Churchill Livingston, New York, 1996.
19. Train D. Some aspects of the property of angle of repose of powders. *J Pharm Pharmacol*, 1958; 10(1):127T–35T.
20. Chen C, Duan C, Li J, Liu Y, Ma X, Zheng L, Stavik J, and Ni Y. **Cellulose (dissolving pulp) manufacturing processes and properties: A mini-review,"** *BioRes. 2016;1*1:5553-5564.
21. Chen LM., Wilson RH. and McCann MC. Investigation of macromolecule orientation in dry and hydrated walls of single onion epidermal cells by FTIR microspectroscopy. J. Mol. Struct. 1997;408:257-260.
22. Revol, JF, Stewart D, Wilson HM, Hendra PJ, and Morrison IM. On the cross-sectional shape of cellulose crystallites in Valonia ventricosa. Carbohyd. Polym. 1982;2: 123-134.
23. Diana C, Florin C and Valentin IP. Amrorphous Cellulose–Structure and Characterization. *Cellulose Chem. Technol*. 2011;45:13-21.
24. Carr RI Jr. Classifying flow properties of solids. Chem Eng, 1965; 1:69–74.
25. Shlieout G, Arnold K, Muller G. Powder and mechanical properties of microcrystalline cellulose with different degrees of polymerization. AAPS Pharm Sci Tech, 2002;3:E11.
26. Sharma K, Bhatia R, Anghore D, Singh V, Khare R, Rawal RK. Development and Validation of UV-Spectrophotometric and RP-HPLC Methods for Simultaneous Estimation of Fexofenadine Hydrochloride, Montelukast Sodium and Ambroxol Hydrochloride in Tablet Dosage Form. Analytical Chemistry Letters 2018;8:829-843.
27. Safila N, Qamar F, Zainab S, Ghulam S, and Tanweer MA. Assay of fexofenadine brands using UV Spectrophotometer. The American Journal of Innovative Research and Applied Sciences. 2015; 1(1): 10-13.