

Valorization of cocoa pod husk for sustainable binder development: comparative evaluation of cocoa pod husk-derived microcrystalline cellulose and Avicel® PH-101 in zidovudine tablet formulations

Olutayo Ademola Adeleye Ph.D.^{a*}; Mbang Nyong Femi-Oyewo Ph.D.^b; Wunia'h Bako MSc^b;
Emmanuel Adelaja Bamigbola Ph.D.^a; Emmanuel Oluwatoyin Olorunsola Ph.D.^c; Clifford Orakwe MSc^b;
Oluwatobi Oladayo Olakojo Ph.D.^d; Adepero Olubukola Awolesi MSc^e

^aPharmaceutics and Pharmaceutical Technology, Federal University Oye Ekiti; ^bPharmaceutics and Pharmaceutical Technology, Afe Babalola University; ^cPharmaceutics and Pharmaceutical Technology, University of Uyo; ^dDepartment of Pharmaceutical and Medicinal Chemistry, Federal University Oye-Ekiti, Ekiti State, Nigeria; ^eDepartment of Pharmacognosy and Herbal Medicine, Federal University Oye-Ekiti, Ekiti State, Nigeria.

Received 03 August 2025

Accepted 04 September 2025

Original Article

ABSTRACT

The high cost and dependency on imported pharmaceutical excipients such as, microcrystalline cellulose (MCC) present challenges in drug manufacturing, particularly in low- and middle-income countries (LMICs). This study investigates the potential of MCC derived from cocoa pod husk (CPH), an underutilized agro-waste, as a sustainable excipient in the formulation of zidovudine tablets. Powder blends containing varying concentrations of CPH-derived MCC (CP-MCC) and commercial Avicel® PH-101 were evaluated for flow properties, compaction behavior, and performance in direct compression. Flow characteristics such as angle of repose, Hausner's ratio, and Carr's index indicated superior flowability of CP-MCC-based blends compared to Avicel® PH-101-based blends. Compaction analysis using Heckel and Kawakita models revealed that Avicel® PH-101 exhibited lower yield pressure (Py) and better compressibility than CP-MCC. However, CP-MCC-based formulations demonstrated satisfactory compaction behavior, especially at higher binder concentrations. Mechanical strength showed increased tablet hardness and decreased friability with rising compression pressure across all formulations. CP-MCC formulations exhibited shorter disintegration times compared to Avicel® PH-101. *In vitro* dissolution studies showed that all formulations met British Pharmacopoeia requirements, releasing over 70% of zidovudine within 30 minutes. CP-MCC-based tablets displayed significantly faster drug release than Avicel® PH-101-based counterparts. Drug release kinetics followed first-order and Korsmeyer-Peppas models. CP-MCC generally demonstrated promising functionality as a pharmaceutical binder, offering good flow properties, acceptable compressibility, and enhanced drug release characteristics. These findings support the valorization of cocoa pod husk as a potential sustainable and cost-effective source of MCC for tablet production, that could contribute to reduced production costs and environmental sustainability in pharmaceutical manufacturing, especially in LMIC settings.

*Corresponding author

Olutayo Ademola Adeleye Ph.D., olutayo.adeleye@fuoye.edu.ng, Pharmaceutics and Pharmaceutical Technology, Federal University Oye Ekiti

KEY WORDS: Cocoa pod husk, microcrystalline cellulose, zidovudine tablets, binder, sustainable excipients.

INTRODUCTION

The development of pharmaceutical formulations for optimization of therapeutic effectiveness relies significantly on the selection of suitable excipients. Among the excipients used in the formulation of tablets are binders, fillers, disintegrants, lubricants, and glidants.

The choice of binder is essential to ensure optimal mechanical strength and achieve a desirable drug release profile, which has a direct impact on bioavailability (1). One of the most widely used binders in tablet production is microcrystalline cellulose (MCC). This material, derived from natural sources, exhibits excellent binding properties and enhances the compactibility of powder mixtures (2). Traditionally, MCC is obtained from fibrous wood pulp.

The search for sustainable and cost-effective pharmaceutical excipients has become increasingly important as the industry shifts toward greener and more accessible production methods. Developing local alternatives to, or sources for, conventional excipients, such as microcrystalline cellulose (MCC), offers the potential to significantly reduce product costs and enhance drug affordability, particularly in low- and middle-income countries (LMICs). Conventional MCC is expensive and largely imported, posing economic and supply chain challenges in LMIC settings such as Nigeria. Consequently, there is growing interest in natural, renewable, and biodegradable sources of MCC derived from agricultural residues. In recent years, research has increasingly focused on the valorization of agro-waste as a viable and sustainable alternative for MCC production.

Cocoa pod husk (CPH), a major byproduct of cocoa (*Theobroma cacao*) production, represents a high-volume, underutilized, agro-waste rich in cellulose and has emerged as a promising source for the possible development of pharmaceutical excipients. Due to its high cellulose content, CPH has been investigated for its potential to yield MCC with favorable physicochemical properties. Its valorization for potential pharmaceutical use aligns with the principles of green chemistry and the circular economy. Although natural sources such as walnut, corncob, rice husk and sugarcane bagasse have been extensively explored for MCC pro-

duction, (3,4), research specifically targeting the pharmaceutical application of MCC derived from CPH remains limited. Recent studies have successfully isolated and characterized alpha-cellulose and MCC from CPH, highlighting its suitability as a source of excipients for solid dosage forms (5). The utilization of agricultural by-products like CPH to produce excipients for use in drug formulation offers a sustainable approach that not only reduces the environmental burden, but also supports resource efficiency and waste minimization in pharmaceutical manufacturing (6-9).

MCC is the most widely used cellulose excipient, serving as a binder in tablet formulations and for various other pharmaceutical applications (5). In addition to binding functionality, tableting excipients should exhibit good flowability to ensure uniform die filling, tablet weight consistency, and dose accuracy. Powder flow is influenced by particle size, shape, and surface texture, and thus represents an important material attribute of MCC in tablet formulation (10).

Avicel® (a commercial source of MCC) is available in a variety of grades that differ mainly in particle size, bulk density, and flow properties, which make them suitable for different dosage forms and processing methods. The most widely used grades are Avicel® PH-101 (20 - 80 µm), Avicel® PH-102 (80 - 150µm), and Avicel® PH-200 (150 - 250 µm). Avicel® PH-101 is well recognized for its excellent compactibility, although it generally exhibits poorer flow compared with coarser grades such as Avicel® PH-200, which conversely provide superior flow but reduced compactibility. Avicel® PH-102 offers an intermediate balance between these properties. For this study the original PH-101 grade was selected based on its extensive use in the pharmaceutical industry.

Zidovudine, a nucleoside reverse transcriptase inhibitor, remains a core agent in antiretroviral therapy that is administered in various dosage forms, including an oral tablet. The use of MCC as a binder in zidovudine tablet formulations has been well-documented, with several studies evaluating the impact of different MCC grades on drug release kinetics and tablet integrity (11,12). The incorporation of MCC derived from CPH into zidovudine tablet formulations presents a promising

Table 1: Zidovudine tablet formulations (each component in mg)

	C0	C1	C2	C3	C4	C5	A1	A2	A3	A4	A5
Zidovudine	300	300	300	300	300	300	300	300	300	300	300
CP-MCC	-	120	150	180	210	240	-	-	-	-	-
Avicel® PH-101	-	-	-	-	-	-	120	150	180	210	240
Corn starch	30	30	30	30	30	30	30	30	30	30	30
Lactose	270	150	120	90	60	30	150	120	90	60	30

strategy to hopefully achieve comparable pharmaceutical performance with sustainable excipient sourcing. Although MCC from conventional sources has been extensively studied in pharmaceutical applications, research on MCC derived from alternative natural sources such as CPH remains limited, highlighting the need for further investigation.

This study investigates the material and compaction properties of MCC derived from CPH and evaluates its suitability as a binder in zidovudine tablets. The mechanical strength and dissolution profiles of the resulting tablets were compared with those prepared using commercial MCC (Avicel® PH-101). The goal was to evaluate the potential of CPH-derived MCC as a sustainable and functional alternative excipient for pharmaceutical applications, particularly in LMIC settings.

MATERIALS AND METHOD

Materials

The materials used in this study include dried cocoa pod husks, Avicel® PH-101 (Merck, Germany), sodium hydroxide (Guangdong Guanghua Sci-Tech Company, Ltd.), hydrochloric acid (BDH Lab Supplies, England), and sodium hypochlorite (Tolaram Africa Enterprise, Ltd.). All other reagents were of analytical grade.

Collection, extraction, isolation and characterization of microcrystalline cellulose

The collection, extraction, isolation and physicochemical characterization of microcrystalline cellulose from cocoa pod husk have been previously reported by Adeleye et al (5).

Preparation of zidovudine powder blends

Different batches of powder blends containing 300mg zidovudine were prepared using either CP-MCC or Avicel® PH-101 along with other excipients, as presented in Table 1. The powders were blended in a planetary mixer for 5 mins. Each batch of powder blend was subsequently

evaluated for flow properties, and Heckel and Kawakita analyses, before direct compression using a Carver hydraulic hand press (Model 38510E, Carver Inc., U.S.A).

Density and flow properties of powder blends

The bulk, tapped, and true density of each of the zidovudine powder blends were determined as previously described by Adeleye et al (5). Ten (10) grams of each powder blend were transferred into a clean, dry 50 mL measuring cylinder. The volume occupied without tapping was measured and recorded as V_b . The cylinder was then manually tapped on a soft bench surface approximately 300 times from a height of about 14mm, and the volume after tapping was measured and recorded as V_t . This procedure was performed in triplicate to ensure data reliability, and the average volume was calculated and documented. The bulk and tapped densities were then determined using equations 1 and 2 respectively:

$$\text{Bulk density} = \frac{\text{Weight of sample}}{V_b} \quad (\text{Eq. 1})$$

$$\text{Tapped density} = \frac{\text{Weight of sample}}{V_t} \quad (\text{Eq. 2})$$

The true density of each powder blend was determined by the pycnometer method with xylene as the displacement liquid (5). A 50-mL empty pycnometer bottle, along with its stopper, was weighed and recorded as W_0 . The bottle was then filled to the brim with xylene, and any excess liquid was wiped off before weighing again, recording the mass as W_1 . The difference between these weights ($W_1 - W_0$) was noted as W_2 . Then, 2 g of a powder blend was weighed and recorded as W_3 before being transferred into the pycnometer bottle. The excess solvent was wiped off, and the bottle with the stopper was weighed again, recording the mass as W_4 . The true density, D_t was then calculated using equation 3:

$$D_t = \frac{W_2 \cdot W_3}{50 (W_3 - W_4 + W_2 + W_0)} \quad (\text{Eq. 3})$$

The angle of repose, Hausner's ratio, and Carr's index of each zidovudine powder blend were determined using standard procedures, serving as indicators of the powder blend's flow characteristics.

The angle of repose (θ) was measured using the fixed-height method. A funnel was securely clamped to a retort stand with its tip positioned 2 cm (Height) above graph paper placed on a flat horizontal surface. A powder was carefully poured through the funnel until the apex of the conical pile reached the funnel's tip. The diameter of the base of the conical pile was then measured and recorded, and the radius was determined. The angle of repose (θ) was calculated using equation 4:

$$\tan \theta = \frac{\text{Height}}{\text{Radius}} \quad (\text{Eq. 4})$$

The procedure was repeated three times to ensure data reliability, and the average value was calculated and recorded.

The Hausner ratio was determined using equation 5:

$$\text{Hausner ratio} = \frac{\text{Tapped Density}}{\text{Bulk Density}} \quad (\text{Eq. 5})$$

The Carr's index was determined using equation 6:

$$\text{Carr's Index} = \frac{\text{Tapped density} - \text{Bulk Density} \times 100}{\text{Tapped Density}} \quad (\text{Eq. 6})$$

Tablet compression

A 600 mg tablet containing 300 mg of zidovudine was formulated by blending zidovudine with various excipients, as shown in Table 1, in a planetary mixer for 5 minutes. Each batch, containing different concentrations of microcrystalline cellulose, was directly compressed on a Carver hydraulic hand press (Model 38510E, Carver Inc., U.S.A.) at five different compression pressures ranging from 56.64 MN.m⁻² to 113.28 MN.m⁻² with a dwell time of 30 seconds. Compression was performed in a 12 mm die with a flat-faced punch, lubricated with a 1% dispersion of magnesium stearate in 96% ethanol before each compression. Following

ejection, the tablets were stored over silica gel for 24 hours to facilitate elastic recovery and hardening.

The compression pressure range was selected to reflect the working limits of a laboratory manual hydraulic press in small-scale studies to characterize material compactibility, which provides reproducible conditions for comparative evaluation of excipient functionality.

Weight and dimension

Tablet weights were measured using an analytical balance, while dimensions (diameter and thickness) were determined using a micrometer screw gauge. The measurements were recorded with an accuracy of ± 1 mg for weight and ± 0.01 mm for dimensions (data not shown). These data were utilized to calculate the relative density (D) of the tablets.

Kawakita analysis

The Kawakita model was employed to evaluate the compressibility of zidovudine powder blends by analyzing the relationship between the degree of volume reduction and applied pressure (13). The equation is expressed as:

$$C = \frac{V_o - V_p}{V_o} = \frac{abP}{1 + bP} \quad (\text{Eq. 7})$$

Where:

C = degree of volume reduction

V_o = initial volume of the powder bed before compression

V_p = final volume of the powder bed after compression

P = applied compression pressure

a = total compressibility constant

b = pressure term related to particle rearrangement

Rearranging the equation results in the following linear form:

$$\frac{P}{C} = \frac{P}{a} + \frac{1}{ab} \quad (\text{Eq. 8})$$

Heckel analysis

Heckel plots were generated for the various zidovudine tablet using equation 9:

$$\ln(1/(1-D)) = KP + A \quad (\text{Eq. 9})$$

Where:

D = tablet relative density

K = compression constant

P = applied compression pressure

A = Y-axis intercept

A graph of $\ln(1/(1-D))$ plotted against the applied compression pressure (P) results in a straight-line relationship with a slope of K. The yield pressure (P_y) was determined as the reciprocal of the slope ($1/K$), providing insight into the material's deformation behavior under compression.

Tablet Evaluation

Determination of tablet hardness

Tablets were randomly selected from each zidovudine tablet batch, and the force required to break them at room temperature (RT) was measured using a Monsanto hardness tester (DKB Instrument, Mumbai, Model EH 01). The reading displayed on the tester's pointer was recorded. A total of ten tablets from each formulation were evaluated, and the mean value was documented.

Determination of tablet friability

Ten tablets were randomly selected from each zidovudine tablet batch, and their initial weight (W1) was recorded. The tablets were then placed in a Friability Test Apparatus (Shivani Scientific Ind., Mumbai, India) and subjected to 25 revolutions per minute for 4 minutes. After completion, the tablets were collected, dusted, and reweighed (W2). The test was conducted in triplicate, and the mean value was recorded. The percentage friability was calculated using the following equation:

$$\text{Percentage friability} = \frac{W1 - W2 \times 100}{W1} \quad (\text{Eq. 10})$$

Determination of tablet disintegration time

The disintegration test was conducted *in vitro* using a tablet disintegration test apparatus (Biobase Model BK-BJ1, China). Distilled water was used as the disintegration medium, maintained at $37 \pm 0.5^\circ\text{C}$. The time taken for each individual tablet to completely break apart and pass through the wire mesh was recorded.

Each determination was performed in triplicate, and the mean value was noted.

Dissolution study

The *in vitro* dissolution test was conducted using a USP Type II (paddle) dissolution apparatus (Biobase Model BK-RC1 China). 900 mL of 0.1 N HCl was used as the dissolution medium, maintained at $37 \pm 0.5^\circ\text{C}$ with a paddle rotation speed of 50 rpm. Tablets from batches compressed at 84.96 MN.m^{-2} were introduced into the dissolution medium. At predetermined intervals (5, 10, 20, 30, 40, 50, and 60 minutes), 5 mL of the dissolution sample was withdrawn and immediately replaced with an equal volume (5 mL) of fresh medium to maintain sink conditions. The withdrawn samples were analyzed using a UV-Vis spectrophotometer (Model 752, Shanghai, China) at a wavelength of 267 nm. The percentage of zidovudine released at each time point was calculated using the regression equation, $y = 22.081x + 0.0593$ obtained from the calibration curve of zidovudine in 0.1 N HCl. All determinations were performed in triplicate ($n = 3$).

Statistical analysis

Data analysis was performed using Microsoft Excel and GraphPad Prism version 5.01 (GraphPad Software Inc, San Diego, CA, USA). One-way ANOVA was used to assess differences in tableting properties, with P-values < 0.05 considered statistically significant.

RESULTS

Flow properties of powder blends

The flow properties of the powder blends, as indicated by the angle of repose, Hausner's ratio, and Carr's index are presented in Table 2. The results show that formulations containing CP-MCC-based blends had lower Hausner's ratio (1.12 – 1.24), Carr's index (10.12–19.16%) and angle of repose (28.63° - 32.51°) compared to Avicel® PH-101-based blends, which had higher Hausner's ratio (1.34 – 1.44), Carr's index (22.22 – 30.56%) and angle of repose (36.73° – 42.05°) values.

Compaction and compressibility analysis

The Heckel model was employed to evaluate the densification behavior of zidovudine powder blends during compression, while the Kawakita model was used to

Table 2: Density and flow properties of formulation powder blends

Formulation	Bulk density (g/ml)	Tapped density (g/ml)	Particle density (g/ml)	Angle of repose (g/ml)	Hausner's ratio (0)	Carr's index (%)
C1	0.350	0.392	1.351	28.63	1.12	10.12
C2	0.353	0.415	1.375	32.51	1.18	16.94
C3	0.361	0.421	1.394	29.48	1.17	14.25
C4	0.367	0.454	1.416	31.52	1.24	19.16
C5	0.374	0.462	1.433	30.24	1.24	19.04
A1	0.236	0.315	1.426	38.04	1.34	22.22
A2	0.245	0.338	1.451	36.73	1.38	27.52
A3	0.256	0.352	1.465	38.22	1.37	27.27
A4	0.269	0.377	1.489	39.61	1.40	28.65
A5	0.275	0.396	1.492	42.05	1.44	30.56

assess their compressibility. Heckel plots, presented in Figure 1 and Figure 2 for CP-MCC and Avicel® PH-101-based formulations respectively, were used to determine

the yield pressure (P_y). The P_y values revealed statistically significant differences ($P < 0.05$), with Avicel® PH-101-based formulations exhibiting generally lower values

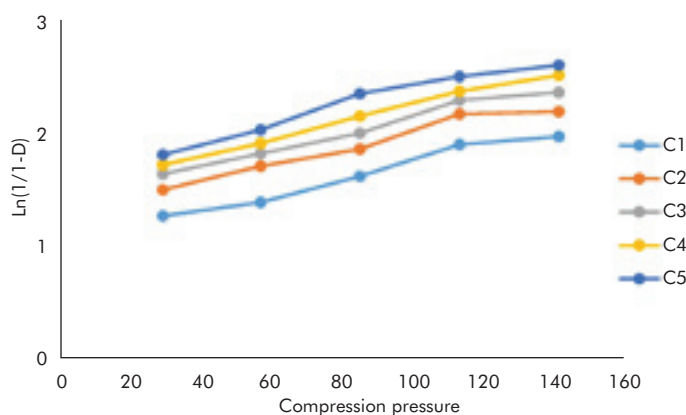
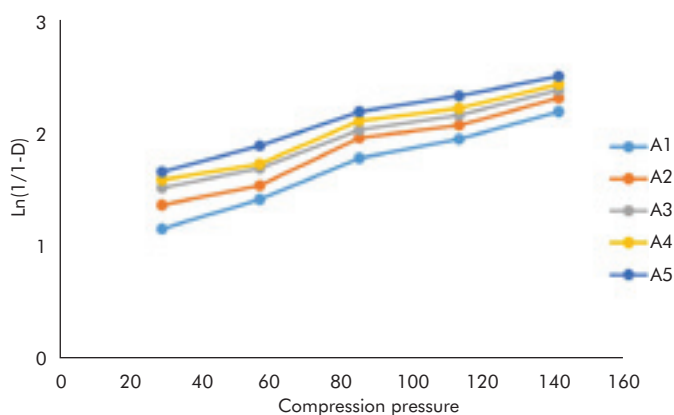
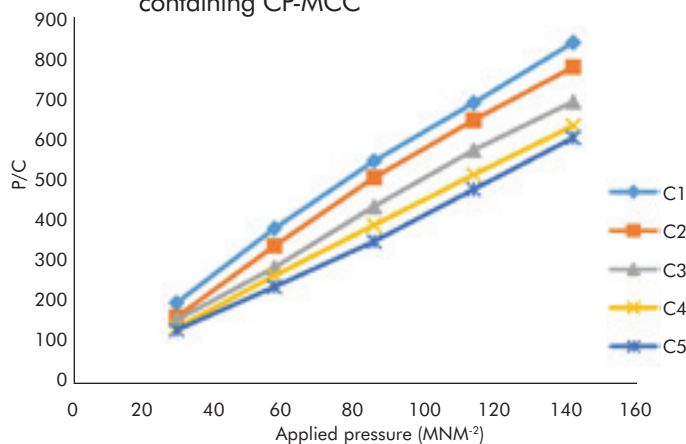
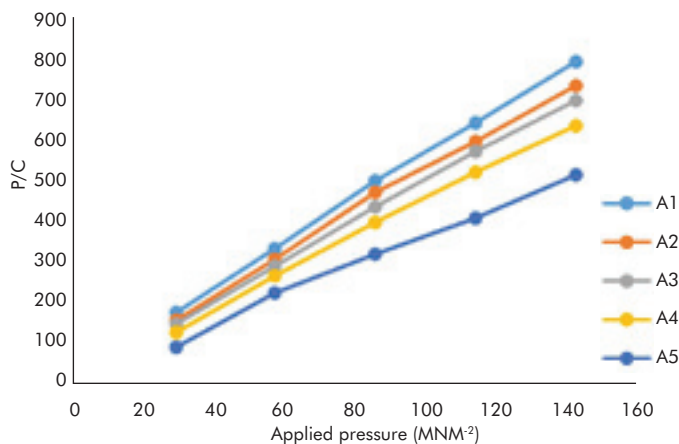
Figure 1. Heckel plots of formulations containing CP-MCC**Figure 2.** Heckel plots of formulations containing Avicel**Figure 3.** Kawakita plots of formulations containing CP-MCC**Figure 4.** Kawakita plots of formulations containing Avicel

Table 3. Parameters derived from the Heckel and Kawakita plots

Formulation			Heckel		Kawakita	
	Py	Do	Da	Db	Di	PK
C1	179.85	0.236	0.655	0.419	0.821	10.257
C2	157.06	0.245	0.739	0.494	0.816	5.273
C3	148.89	0.256	0.767	0.511	0.792	4.964
C4	144.43	0.269	0.783	0.514	0.771	4.330
C5	138.28	0.275	0.808	0.533	0.761	2.016
A1	155.33	0.350	0.597	0.247	0.816	5.021
A2	148.65	0.353	0.672	0.319	0.803	4.342
A3	139.21	0.361	0.724	0.363	0.784	3.332
A4	131.87	0.367	0.741	0.374	0.766	2.317
A5	127.92	0.374	0.769	0.395	0.725	1.315

(127.92 - 155.33 MN.m⁻²) compared to CP-MCC- based formulations (138.28 – 179.85 MN.m⁻²), as shown in Table 3. Similarly, the Kawakita analysis as presented in Figure 3 and Figure 4 for blends containing either CP-MCC or Avicel® PH-101 respectively, was used to derive the PK values, representing the pressure required to achieve a 50% reduction in powder bed volume. The results indicated that Avicel® PH-101-based formulations had lower PK values (1.315 – 5.021) than CP-MCC-based formulations (2.016 – 10.257), also detailed in Table 3.

Crushing strength and friability

Tablet crushing strength and friability results as shown in Table 4, reveal that increase in compression pressure across all Avicel® PH-101-based and CP-MCC-based formulations resulted in a progressive increase in crushing strength and a decrease in friability. For example, for-

mulation C1 exhibited a rise in crushing strength from 12.44 N at 28.82 MN.m⁻² to 51.61 N at 141.60 MN.m⁻². This trend was consistent across all formulations, emphasizing the direct relationship between compression pressure and tablet hardness. Similarly, friability decreased as compression pressure increased. For example, formulation C1 showed a reduction in friability from 2.86% at 28.82 MN.m⁻² to 0.88% at 141.60 MN.m⁻².

Disintegration time

The results of disintegration testing are shown in Table 4. The data show that the disintegration time for all formulations tends to lengthen with increased binder concentration and compression pressure. In addition, Avicel® PH-101-based tablets exhibited prolonged disintegration times compared to CP-MCC-based formulations.

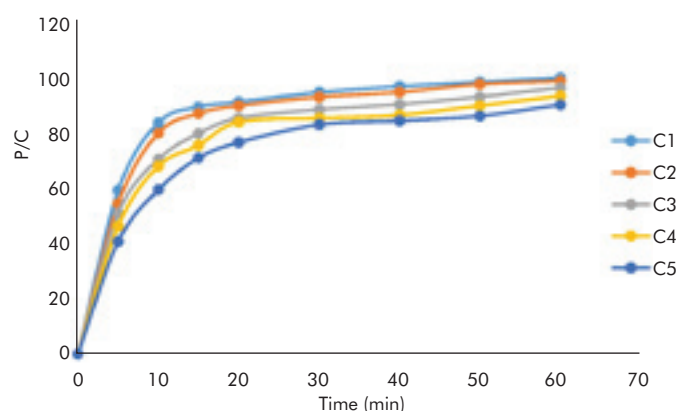
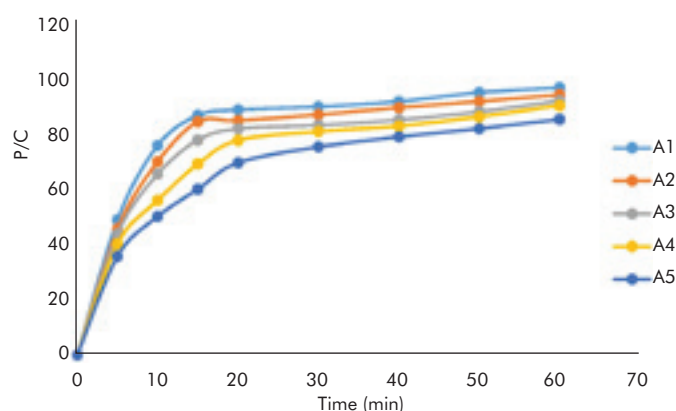
Figure 5. Percent drug release of formulations containing CP-MCC**Figure 6. Percent drug release of formulations containing Avicel**

Table 4: Physical properties of the tablets

Formulation	Compression pressure (MN.m ⁻²)	Crushing Strength (N)	Friability (%)	Disintegration time (min)
C1	28.82	12.44 ± 1.28	2.86 ± 0.09	1.28 ± 0.57
	56.64	24.08 ± 1.62	1.96 ± 1.38	2.40 ± 0.32
	84.96	31.53 ± 1.42	1.92 ± 0.52	3.46 ± 0.22
	113.28	39.46 ± 2.15	1.02 ± 1.14	5.25 ± 0.48
	141.60	51.61 ± 1.30	0.88 ± 0.29	6.18 ± 0.10
C2	28.82	19.69 ± 2.05	1.58 ± 0.09	2.85 ± 0.44
	56.64	36.04 ± 1.24	1.28 ± 1.38	3.91 ± 0.13
	84.96	48.62 ± 1.18	0.90 ± 0.52	4.22 ± 0.59
	113.28	55.28 ± 1.34	0.74 ± 1.14	6.05 ± 0.74
	141.60	64.64 ± 1.25	0.62 ± 0.29	10.21 ± 0.36
C3	28.82	25.28 ± 1.47	1.02 ± 0.14	4.02 ± 0.16
	56.64	40.26 ± 4.26	0.92 ± 0.41	5.55 ± 0.81
	84.96	54.01 ± 1.46	0.72 ± 0.15	7.12 ± 0.81
	113.28	61.45 ± 1.15	0.86 ± 1.31	9.29 ± 0.26
	141.60	70.31 ± 1.25	0.48 ± 2.07	13.64 ± 0.72
C4	28.82	31.28 ± 1.60	1.05 ± 0.32	6.28 ± 1.71
	56.64	45.42 ± 1.24	0.88 ± 2.20	7.95 ± 0.26
	84.96	60.65 ± 2.40	0.63 ± 0.31	9.28 ± 0.23
	113.28	72.74 ± 1.58	0.56 ± 0.30	11.52 ± 0.67
	141.60	84.23 ± 2.46	0.52 ± 1.22	16.47 ± 0.32
C5	28.82	38.47 ± 2.31	0.98 ± 0.12	7.96 ± 1.27
	56.64	51.81 ± 1.99	0.79 ± 1.05	10.55 ± 0.83
	84.96	65.25 ± 1.28	0.64 ± 1.26	14.72 ± 0.41
	113.28	81.37 ± 1.42	0.49 ± 0.32	15.36 ± 0.70
	141.60	96.52 ± 1.54	0.41 ± 0.23	19.12 ± 0.48
A1	28.82	20.84 ± 1.71	1.33 ± 0.38	3.67 ± 0.24
	56.64	30.20 ± 1.86	1.19 ± 0.41	4.22 ± 0.95
	84.96	42.65 ± 0.95	0.92 ± 0.25	5.20 ± 0.18
	113.28	53.38 ± 1.10	0.84 ± 0.18	7.47 ± 0.66
	141.60	71.16 ± 1.53	0.95 ± 0.11	8.30 ± 0.45
A2	28.82	29.49 ± 1.37	0.98 ± 0.81	4.80 ± 0.18
	56.64	55.04 ± 1.64	0.68 ± 0.64	6.58 ± 0.62
	84.96	68.86 ± 1.51	0.52 ± 0.93	7.62 ± 0.75
	113.28	82.82 ± 1.91	0.40 ± 0.41	8.65 ± 0.90
	141.60	98.46 ± 3.51	0.32 ± 0.58	10.73 ± 0.45
A3	28.82	34.21 ± 4.17	0.98 ± 0.42	6.15 ± 0.10
	56.64	60.84 ± 1.39	0.56 ± 0.97	7.45 ± 0.28
	84.96	72.61 ± 2.64	0.45 ± 1.15	9.10 ± 0.15
	113.28	89.45 ± 2.93	0.31 ± 0.63	10.24 ± 0.28
	141.60	104.23 ± 1.62	0.28 ± 0.28	15.52 ± 0.51
A4	28.82	41.28 ± 1.06	0.89 ± 0.24	6.98 ± 0.28
	56.64	67.84 ± 1.42	0.41 ± 0.12	10.69 ± 0.33
	84.96	80.61 ± 1.04	0.37 ± 0.36	14.02 ± 0.90
	113.28	97.14 ± 2.08	0.28 ± 1.22	15.71 ± 0.72
	141.60	112.12 ± 1.70	0.20 ± 0.25	19.46 ± 0.81
A5	28.82	48.07 ± 1.39	0.58 ± 0.21	10.10 ± 0.52
	56.64	76.18 ± 2.09	0.32 ± 0.15	15.85 ± 0.21
	84.96	89.52 ± 1.66	0.23 ± 0.42	19.08 ± 0.74
	113.28	104.42 ± 1.37	0.18 ± 0.27	25.50 ± 0.58
	141.60	131.15 ± 3.45	0.15 ± 0.22	30.25 ± 0.36

Drug release profile

Zidovudine drug release profiles, shown in Figure 5 and Figure 6, reveal that all formulations exhibited a rapid initial drug release. Furthermore, drug release from CP-MCC formulations was higher within the first 30 minutes compared to Avicel® PH-101 formulations. Increase in the concentration of the MCC in formulations C1 – C5 and A1 – A5 caused a decrease in the rate of drug release. Nevertheless, all tablet formulations released more than 70% of their drug content within the first 30 minutes of dissolution.

DISCUSSION

The flow properties of powder blends play a significant role in direct compression of tablets, as poor flowability can lead to variations in tablet weight and active pharmaceutical ingredient distribution. Powder flow behavior is influenced by factors such as particle size, shape, and surface characteristics (10). The findings from the flow properties indicate that CP-MCC-based blends have significantly better ($P < 0.05$) flow properties than Avicel® PH-101-based blends. The improved flowability of CP-MCC-based blends can be attributed primarily to their larger mean particle size as documented in previous research by Adeleye et al (5), which highlights the particle characteristics of MCC derived from cocoa pod husk. It is important to note that Avicel® grades differ in particle size distribution and functionality. Avicel® PH-101 (20–80 μm) offers superior compactibility but poorer flow, while coarser grades such as Avicel® PH-200 (150–250 μm) exhibit improved flow while demonstrating weaker binding properties. In our previous study, CP-MCC had a mean particle size of 161.32 μm (5), placing it within the range of Avicel® PH-200, suggesting that its enhanced flow properties may be attributed to this coarser particle size distribution. Additionally, studies have shown that microcrystalline cellulose sourced from alternative materials, such as rice husk and sugarcane bagasse, have enhanced flow properties due to the morphology and particle size distribution of these materials (14,15).

Tablet compaction is influenced by the deformation behavior of the active pharmaceutical ingredient (API) and excipients during compression. Lower and higher compression pressures were employed in this study to adequately model the compressional behavior of the formulations and to enable comparison of binder per-

formance across a broader pressure spectrum. This approach provides insight into how materials respond under both minimal and elevated compression pressures, which is critical for the prediction of their functionality in manufacturing. The compression pressures routinely employed in large-scale industrial tablet production using rotary presses generally fall within the pressure range explored in this study. However, the exact values applied during manufacturing are highly formulation-dependent, being influenced by drug physicochemical properties, excipient type and concentration, and the intended size and dose of the tablet. Furthermore, the choice of compression pressure is ultimately guided by the desired quality attributes of the dosage form — particularly hardness, friability, disintegration, and dissolution — which must be optimized to achieve both robust mechanical strength and acceptable biopharmaceutical performance. Evaluating compactibility across a wide pressure spectrum in small-scale studies not only simulates practical manufacturing conditions but also enables meaningful comparison of binder functionality under different compaction stresses (16). Specifically, the compaction properties of binders such as microcrystalline cellulose depend on their deformation mechanisms, which in turn impact tablet hardness and structural integrity (17–19). The P_y values obtained from Heckel plots indicated that Avicel® PH-101 undergoes greater plastic deformation upon compression, forming strong interparticle bonds that enhance tablet mechanical strength compared to CP-MCC-based formulations. The PK values from Kawakita analysis further supported the improved compressibility of Avicel® PH-101-based formulations, suggesting that Avicel® PH-101 required less applied pressure for volume reduction, thereby improving powder packing efficiency. One possible contributing factor to this effect is the mean particle size (20). As reported by Adeleye et al (5), Avicel® PH-101 has a smaller mean particle size compared to CP-MCC. Recent studies have shown that MCC primarily undergoes plastic deformation during compression, leading to stronger interparticle bonding and enhanced tablet hardness (21). In the current study, a significant overall decrease in P_y and PK values was observed with increasing binder concentration, indicating enhanced compressibility and greater plastic deformation at higher binder concentrations. Similar trends have been reported for MCC derived from alternative natural sources, such as

soybean hull, where lower P_y values and lower PK values were associated with better compressibility (22).

Tablet crushing strength is a parameter used to evaluate the mechanical integrity of compressed tablets while friability measures the ability of a tablet to withstand mechanical stress without crumbling or chipping during manufacturing, handling, and transportation. The increased crushing strength of tablets with increase in compression pressure is generally as a result of reduced porosity and enhanced particle bonding, leading to a denser and stronger tablet matrix (23). The inverse relationship of compression pressure and friability is generally attributed to the enhanced particle bonding at higher pressures, which improves tablet robustness and reduces susceptibility to abrasion (24). Tablets containing Avicel® PH-101 exhibited higher crushing strength and lower friability compared to CP-MCC containing tablets, particularly at higher compression pressures. The superior mechanical properties of Avicel® PH-101 may be attributed to its plastic deformation properties as observed in Heckel analysis data. In addition, the improved properties of Avicel® PH-101 are influenced by its particle size distribution and morphology, as previously discussed. Our findings are in agreement with previous research on MCC from other alternative sources, where improved plastic deformation contributed to stronger interparticle bonding and reduced friability (25).

Disintegration time, the duration for a tablet to break down into particles, is an important factor for drug release and subsequent absorption into the body. According to the British Pharmacopoeia (BP), the disintegration time for a conventional (uncoated) tablet should not exceed 15 minutes in water at 37 ± 0.5 °C. The disintegration time for all the formulations increased with increase in binder concentration and compression pressure. This trend is likely due to stronger interparticle bonds at higher pressures, as corroborated with increased tablet hardness, which impede water penetration and tablet disintegration (23,26). Some formulations especially at higher binder concentration and higher compression pressure exceeded 15 minutes disintegration time. Formulations containing Avicel® PH101 generally showed significantly prolonged ($P < 0.05$) disintegration times compared to formulations containing CP-MCC at equivalent concentrations and compression pressures.

The *in vitro* dissolution profile of a drug measures the rate and extent that the drug goes into solution in a specific medium under standardized conditions. It provides information about the drug release characteristics from a dosage form and provides insight on its potential *in vivo* performance, such as drug absorption in the gastrointestinal tract. In this study, the rapid release of zidovudine from the formulations can be attributed to the high solubility of zidovudine in an aqueous medium, along with the contributions of excipients that enhance wettability (27). Variations in drug release rates were apparent among formulations, which can be ascribed to differences in the type and concentration of the binder. At higher binder concentrations, the drug release was retarded, which is an indication that the rate of zidovudine release from the tablet formulation is dependent on the binder content. However, all tablet formulations released more than 70% zidovudine within the first 30 minutes of dissolution, meeting the dissolution requirements of the British Pharmacopoeia (2009).

The higher drug release of CP-MCC formulations within the first 30 minutes compared to Avicel® PH-101-based formulations may be due to the lower degree of tablet densification of CP-MCC formulations, facilitating more rapid water penetration and tablet breakdown. This can also be linked to the faster disintegration of CP-MCC formulations, leading to better drug availability. Similar trends have been reported in studies where MCC derived from other agricultural residues exhibited superior drug release kinetics compared to Avicel® PH-101 (28,29).

In-vitro cumulative release profiles of zidovudine were fitted to various mathematical models, zero-order, first-order, Higuchi, and Korsmeyer-Peppas (30-32). Goodness-of-fit was assessed by the coefficient of determination (R^2) for each model. The mechanism for drug release was obtained from the Korsmeyer-Peppas exponent (n), interpreted for cylindrical matrices as Fickian diffusion when $n < 0.45$, anomalous/non-Fickian when $0.45 \leq n < 0.89$, and case-II transport when $n \geq 0.89$ (33). The analyses showed that all formulations except A5 were best described by first-order kinetics, indicating concentration-dependent release typical of immediate-release tablets (34,35). For CP-MCC, first-order R^2 ranged from 0.9900 (C1) to 0.9239 (C5), while for Avicel® PH-101 it ranged from 0.9794 (A1) to 0.9039 (A5). Results for the

Korsmeyer-Peppas exponent n spanned 0.158 – 0.305 across all formulations, well below 0.45, indicating Fickian diffusion as the prevailing transport mechanism with diffusion through hydration dominating any erosion/relaxation contribution (33). As binder concentration increased (C1→C5; A1→A5), first-order R^2 generally decreased and the relative Korsmeyer-Peppas fit strengthened (notably A4 – A5, with A5 showing Peppas as the best model), consistent with slower release and stronger diffusion control in denser, more tortuous matrices — coherent with the results of the compaction (Heckel and Kawakita), hardness, and disintegration trends observed in this study. These findings agree with recent literature on immediate-release tablet studies reporting first-order behavior alongside diffusion-dominated mechanisms (34,35).

CONCLUSION

This study investigated the compaction characteristics and release properties of zidovudine tablets formulated with microcrystalline cellulose (MCC) derived from cocoa pod husk (CP-MCC) as a binder. Results with formulated blends demonstrated that CP-MCC exhibited superior flow properties compared to Avicel® PH-101, indicating the potential of CP-MCC as an alternative binder in tablet formulations. However, Heckel and Kawakita analyses of these blends revealed that Avicel® PH-101 displayed better compressibility and plastic deformation, leading to stronger tablets with higher mechanical strength compared to tablets made with CP-MCC formulations.

All tableted formulations showed a progressive increase in crushing strength and a decrease in friability with increasing compression pressure, confirming enhanced mechanical properties at higher pressures. Disintegration

time was found to be influenced by binder type and concentration, with Avicel® PH-101-based tablets exhibiting prolonged disintegration times compared to CP-MCC formulations. The *in vitro* drug release study showed that all formulations achieved over 70% drug release within 30 minutes, meeting the British Pharmacopoeia (2009) dissolution requirements.

Kinetic modeling provided further insight into the drug release mechanisms. The analyses showed that zidovudine release from all formulations, except A5, followed first-order kinetics, indicating a concentration-dependent release typical of immediate-release tablets. The Korsmeyer-Peppas model confirmed Fickian diffusion ($n < 0.45$) as the predominant mechanism governing drug release. These findings support the view that binder concentration and matrix density influence release rate, with denser Avicel® PH-101-based matrices exhibiting slower diffusion and reduced release compared to CP-MCC formulations.

Overall, CP-MCC demonstrated promising performance as a binder in a model direct compression formulation, offering good flow properties and acceptable tablet performance. While Avicel® PH -101-based tablets exhibited superior mechanical strength, dosage forms made with CP-MCC had acceptable mechanical properties with faster disintegration and higher drug release rates, supporting its potential as a suitable excipient in immediate-release formulations. The findings highlight the potential of cocoa pod husk as a sustainable source of MCC for potential pharmaceutical applications, that could contribute to cost reduction for pharmaceutical processing, with environmental sustainability, especially in LMIC settings.

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