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Research Article

A Study of Pharmaceutical Applications of Hemicelluloses From Nine Food Materials

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Objective: This study is aimed at evaluating the release-extending, film-coating, suspending, and thickening properties of various food-derived hemicelluloses, as natural alternatives to synthetic excipients for use in pharmaceutical tablets and suspensions.
Background: Hemicelluloses are partially digestible biopolymers with superior biocompatibility, biodegradability, and sustainability compared to synthetic and cellulose-based semisynthetic materials. This study focused on the evaluation of potential application of hemicelluloses as environmentally friendly, highly biocompatible pharmaceutical excipients.
Methods: The hemicelluloses were isolated from *Acacia nilotica* (*AN*), *Lallemantia royleana* (*LR*) seeds, *Plantago ovata* husk (*POh*), *Plantago ovata* seeds (*POs*), *Ocimum basilicum* (*OB*) seeds, *Salvia plebian* (*SP*) seeds, *Astragalus tragacantha* (*AT*), *Mimosa pudica* (*MP*) seeds, *Acacia modesta* (*AM*), and *Cydonia oblonga* (*CO*). Acetaminophen was used as a model drug. Tablets were prepared via wet granulation and direct compression, and various parameters, including flow, hardness, film-coating strength, and drug release characteristics, were evaluated. Rheology and sedimentation volume were determined for suspensions.
Results: The granules for tablets exhibited good flow properties, and the matrix tablets prepared through wet granulation and direct compression exhibited hardness in the range of 2–7 $kg\,cm^{-2}$, with disintegration times between 1.18 and 25.0 min at pH 6.8. Wet granulated tablets released 45%–92% of acetaminophen in ~7 h, and the film coatings showed a strength of 35–40 $kg\,m\,s^{-2}$. The suspensions demonstrated excellent stability for over 2 months without the need for redispersion, with sedimentation volumes ranging from 90% to 92%, except for those containing *AT*. The stability trend for suspensions was observed as $SP > OB > AN > AM > CO > Poh > POs > LR > MP > AT$. Notably, the prepared suspensions were more stable than the standard Calpol.
Conclusion: Hemicelluloses from natural sources show potential as effective tablet binders, extended-release agents, film-coating materials, and suspending/thickening agents in pharmaceutical formulations. These findings highlight their promise as sustainable and biocompatible alternatives to synthetic/semisynthetic excipients.

Keywords: biocompatible excipients; drug release; food hydrocolloids; hemicelluloses; pharmaceutical excipients; suspension stability

1. Introduction

Pharmaceutical excipients, such as binders, film coatings, suspending agents, thickeners, and targeted or sustained release agents, are essential components of pharmaceutical formulations [1–3]. The pharmacological activity of a formulation is influenced by the type of excipients used [4]. Currently, most excipients are synthetic or semisynthetic, making it desirable to replace them with natural materials, which offer advantages such as biocompatibility, biodegradability, and

sustainable sourcing. Materials derived from cellulose, like carboxymethyl cellulose (CMC) and hydroxypropyl methyl cellulose (HPMC), are widely regarded as biocompatible [2, 4–8]. However, compared to hemicelluloses, cellulose-based materials are less biocompatible, as cellulose is not digestible by humans. In contrast, hemicelluloses can be partially metabolized due to the presence of hemicellulases in the colonic flora [2, 8, 9]. So, this study is aimed at exploring the potential of hemicelluloses as multifunctional excipients for sustainable and biocompatible pharmaceutical formulations. The investigation focused on their capabilities as binding agents, coating materials, and sustained-release modifiers in tablet formulations. Additionally, their effectiveness as suspending and thickening agents in liquid suspensions was assessed. Acetaminophen was used as the model drug to rigorously evaluate these properties. Hemicelluloses are abundantly available biomaterials from renewable sources [10].

The hemicelluloses used in this work were isolated from *Acacia modesta* (*AM*), *Acacia nilotica* (*AN*), *Astragalus tragacantha* (*AT*), *Cydonia oblonga* (*CO*), *Lallemantia royleana* (*LR*), *Mimosa pudica* (*MP*), *Ocimum basilicum* (*OB*), *Plantago ovata husk* (*POh*), *Plantago ovata seeds* (*POs*), and *Salvia plebian* (*SP*). They have been reported as suitable binders in formulation of tablets [11], but their function as release-extending, film-coating, suspending, and thickening agents has rarely been studied [12]. These are all food materials associated with various useful pharmacological properties [13, 14]. Hemicelluloses produce sticky mucilage when in contact with water and form good films [11]. The mucilage also provides good suspending and thickening properties. These properties, uniquely combined in a material, could be exploited in formulation of various dosage forms.

Film coating of pharmaceutical tablets is generally carried out by use of synthetic/semisynthetic polymers including PVP and HPMC. Now, film-coating materials are also undergoing a transition from synthetic or semisynthetic to natural products. Hypromellose-pectin and ethyl cellulose aqueous dispersion and some combinations with chitosan are becoming popular for film coating of tablets [15].

Given their versatile functional properties, biocompatibility, and abundant availability, we hypothesize that hemicelluloses, when used as binding, release-extending, film-coating, suspending, or thickening agents, could significantly enhance the biocompatibility of pharmaceutical formulations by replacing synthetic and semisynthetic excipients. So, this study reports the use and evaluation of the hemicelluloses from widely used food materials for such applications.

2. Materials and Methods

2.1. Materials. Gum *AN*, gum *AM*, *AT*, *CO*, *LR* seeds, *MP* seeds, *OB* seeds, *POh*, *POs*, and *SP* seeds were procured from the local herbal market. Acetaminophen, L-(+)-arabinose, D-(+)-galactose, D-glucose, L-rhamnose monohydrate, magnesium stearate, and D-(+)-xylose, from Sigma-Aldrich, United States, and disodium hydrogen phosphate, sodium hydroxide, sulfuric acid, hydrochloric acid, and lactose from E. Merck, Germany, were used as received. Ferric oxide red (CI 77491, Emperor Chemical Co. Ltd., Hangzhou, China) was used as the pigment for tablet coating. Calpol pediatric suspension (GlaxoSmithKline, Pakistan) was used as a reference standard for suspensions. Purified water was used in this work.

2.2. Isolation and Purification of Hemicelluloses. The hemicelluloses were extracted and purified following our previously established method [11], and the analysis of fresh samples was benchmarked against the previously reported materials [11]. The isolated materials were delignified according to the cited method [11]. Molar masses, elemental composition, and monosaccharide analyses (see Table S1 for analytical data of the hemicellulosic materials; the data represent mean values ($n = 5$) ± standard deviation) were observed to closely resemble previously reported values [16].

2.3. Characterization of the Isolated Hemicelluloses. The CHN analysis of the isolated hemicelluloses was conducted by vario EL cube CHNS elemental analyzer (Elementar Analysensysteme, GmbH, Germany), while the monosaccharide analysis was performed according to a validated method [17] after acid hydrolysis of the sample, using a Dionex ICS 3000 HPLC system. The system comprised a CarboPacPA20 column (0.4×150 mm) and an electrochemical detector. The chromatographic conditions included isocratic elution with a mixture of 95% water and 5% 0.2 M NaOH at 25°C ± 1°C. The mobile phase flow rate was set at 0.5 mL min^{-1}, and the injection volume was 50 μL. Gel permeation chromatography (GPC), employing an Agilent 1200 series system from Germany, equipped with a PL aquagel-OH mixed column and a refractive index detector (G1362A), was carried out to determine the molar masses. Water was used as the eluent at a rate of 1.0 mL min^{-1} at 70°C, and the injection volume was 10 μL. Pullulan and dextran served as the calibration standards [11]. Karl-Fischer titration was conducted to determine water content using 799 GPT Titrino, Karl-Fischer titrator (Metrohm, Switzerland). FTIR spectra were recorded on IR-Prestige-20 spectrophotometer (Shimadzu, Japan).

2.3.1. Preparation of Hemicellulose Films. The hemicellulose films were prepared by spreading a thick paste of the mucilage in water on a polyethylene sheet and air-dried at room temperature (~25°C) for 5 days to obtain a film having thickness 0.23–0.25 mm.

2.4. Surface Morphology of Films. Surface morphology of films was studied by capturing images using the Hitachi S-3400N scanning electron microscope (SEM) after sputter coating with gold.

2.5. Rheology of Hemicellulose Suspensions. A weighed amount (2.00 g) of the dry hemicellulosic material was suspended in water and stirred at 25°C to form a homogeneous suspension; 5 mL of this was injected into the pressure cell of the Anton Paar MCR 301 rheometer (Anton Paar GmbH, Germany) using a double gap cylinder. Measurements were conducted at 25°C with shear rates in the range 0.01–1000 s^{-1} using different concentrations and at various pH values [18].

2.6. Drug–Hemicellulose Compatibility Study. In order to study the compatibility of the hemicelluloses under investigation with acetaminophen, the polymers (0.5 g) were soaked in the drug solution (10 mL of 1.0% in water) for ~5 h. After that, the drug-loaded polymer was isolated by evaporation of water under vacuum, briefly washed with methanol, and dried at 40°C. The compatibility was checked by FTIR spectroscopy.

For polymers used in drug delivery, it is crucial to understand their swelling behavior and water retention (WR) properties, as these factors influence the formulation of drug delivery devices. So, the swelling index (SI) was calculated using the following formula: $\mathrm{SI}\,(\%) = [(W_s - W_d)/W_d] \times 100$, where W_s is the weight of the swollen sample and W_d is the weight of the sample after drying at 105°C [19]. The WR was calculated by the formula $\mathrm{WR}\,(\%) = (W_t - W_d)/(W_s - W_d) \times 100\%$, where W_t is the weight of the swollen sample after 8 h [19].

2.7. Preparation of Tablets. Table 1 provides the list of materials used for formulation of tablet; the quantities were optimized through initial experimental trials. The quantity of hemicelluloses was determined to replace the commonly used excipients: disintegrant crospovidone (2%–5%), glidants (1%–2%), and binder polyvinylpyrrolidone (1%–5%), consolidating their roles into a single ingredient, that is, hemicellulose. Acetaminophen was used as a model drug for the tablets, which were prepared by wet granulation (WG) and direct compression (DC) techniques.

2.7.1. WG. For a batch of 100 tablets, acetaminophen and lactose (diluent) were weighed as per the amounts specified in Table 1. These ingredients were mixed and ground using a stainless-steel mortar and pestle. The water-triturated hemicellulosic material was then thoroughly blended into this mixture to form a damp mass, which was subsequently passed through sieve number 10/12/14. The resulting granules were sifted through a 300-mesh (300-μm openings) stainless-steel sieve. The granules were dried at 40°C before sifting until reaching a moisture content of 8% ± 1% and then sifted through 18/20/22 sieve to separate fine and coarse granules. Magnesium stearate was added to the dried granules as a lubricant and uniformly mixed through geometric blending.

Precompression evaluation of the granules included assessments of flowability [20] in terms of angle of repose and flow rate in g s^{-1}, Carr's compressibility index (CI), and Hausner's ratio (HR). Other assessments included bulk density (ρ_b), tapped density (ρ_t), and moisture content following established methods [20–23]. Flowability was measured with a Powder Analyzer Type PTG (Pharma Test, Hainburg, Germany) according to USP 43, 2020 standards, using a 10.0-g sample. Each measurement was conducted in triplicate, with results reported as the mean ± SD. The bulk and tapped densities (ρ_b and ρ_t) were calculated using the formulas $\rho_b = m/v$ and $\rho_t = m/v_t$, where m is the mass and v the volume of granules (10.0 g) before tapping. CI and HR were determined with standard formulas [24, 25]:

$$\mathrm{CI} = \frac{V_0 - V_\mathrm{f}}{V_0} \times 100 = \frac{\rho_t - \rho_b}{\rho_t} \times 100$$

$$\mathrm{HR} = \frac{V_0}{V_\mathrm{f}} = \frac{\rho_t}{\rho_b}$$

where V_0 and V_f are the initial and final volumes, respectively. Moisture content was measured by Karl-Fischer titration with pyridine-free reagents and methanol as the solvent, using an accurately weighed sample of approximately 300 mg. Compression of 100 tablets was done at a 0.010 kg m s^{-2} force using a single-punch tablet press equipped with an 8-mm concave punch. The resulting tablets, each containing 500 mg of acetaminophen, had an average weight of 600 ± 1 mg.

2.7.2. DC. For a 100-tablet batch, acetaminophen, hemicellulosic material, lactose, and magnesium stearate were weighed as specified in Table 1,then mixed and thoroughly blended with a mortar and pestle. The mixture was sifted through a 20-mesh sieve (840-μm openings). Tablets were subsequently compressed with a single-punch tablet press TDP1.5 (Qinhuangdao Shenghua Imp. & Exp. Trading Co. Ltd., China), using an 8-mm concave punch and applying a force of 10 kg m s^{-2}. Each tablet, containing 500 mg of acetaminophen, had an average weight of 600 ± 1 mg.

2.8. Postcompression Evaluation of Tablets. After compression, key parameters including hardness, friability, weight variation, and disintegration time were measured on a sample of 20 tablets for each test. Six batches of each formulation were prepared for testing. Tablet hardness was measured using a YPD-300D hardness tester (Shanghai Huanghai Medicine and Drug Testing Instrument, China). Friability was evaluated as the percentage weight loss after 100 revolutions in a PTF-10E friability tester (Pharmatest, Germany). For the disintegration test, tablets were placed in 1000 mL of water and stirred (@ 30 cycles per min) at 37°C ± 2°C using a 121-P disintegration apparatus (Galvano Scientific, Pakistan); the time was noted after all tablet material had completely passed through the mesh. These tests were performed according to USP 43, 2020, methods.

2.8.1. Assay of Acetaminophen. The USP 43, 2020, HPLC assay method for acetaminophen extended-release tablets was used to study the stability and dissolution profile of the prepared tablets. A brief description of the method is provided in the next paragraph (for suspensions). The linearity range of the method was 5–25 μg mL^{-1} ($r^2 = 0.999$) of acetaminophen. Six replicate measurements were performed, and the mean ± SD values were used in the dissolution study.

2.8.2. Stability Study of Tablets. The tablets were stored in Securitainers for 6 months at 40°C and 75% ERH and assayed for acetaminophen, as described in Section 2.7.1, at monthly intervals. The data was graphed as a scatter plot in MS Excel 365.

2.9. In Vitro Dissolution Study. This study was conducted using a USP paddle apparatus (DL-0708, Curio, Pakistan).

TABLE 1: Bill of materials for a batch of 100 acetaminophen tablets (500 mg). The quantities are in grams.

Wet granulation					Direct compression				
Formulation code	**Binder (hemicellulose)**	**Acetaminophen**	**Diluent/disintegrant (lactose)**	**Lubricant (Mg-stearate)**	**Formulation code**	**Binder (hemicellulose)**	**Acetaminophen**	**Diluent/disintegrant (lactose)**	**Lubricant (Mg-stearate)**
F-1 (*SP*)	2.25	50	6.75	1.00	F-11 (*SP*)	2.25	50	6.75	1.00
F-2 (*OB*)	2.50	50	6.50	1.00	F-12 (*OB*)	2.50	50	6.50	1.00
F-3 (*LR*)	2.75	50	6.25	1.00	F-13 (*LR*)	2.75	50	6.25	1.00
F-4 (*POh*)	3.40	50	5.60	1.00	F-14 (*POh*)	3.40	50	5.60	1.00
F-5 (*POs*)	3.40	50	5.60	1.00	F-15 (*POs*)	3.40	50	5.60	1.00
F-6 (*CO*)	3.50	50	5.50	1.00	F-16 (*CO*)	3.50	50	5.50	1.00
F-7 (*AT*)	3.75	50	5.25	1.00	F-17 (*AT*)	3.75	50	5.25	1.00
F-8 (*MP*)	3.75	50	5.25	1.00	F-18 (*MP*)	3.75	50	5.25	1.00
F-9 (*AN*)	4.00	50	5.00	1.00	F-19 (*AN*)	4.00	50	5.00	1.00
F-10 (*AM*)	5.00	50	6.75	1.00	F-20 (*AM*)	5.00	50	6.75	1.00

Bill of materials for a batch of 100-mL acetaminophen suspension (120 mg per 5 mL); hemicellulose (only one in a formulation)

Material→	Acetaminophen	*CO*	*AN*	*LR*	*PO (s and h)*	*OB*	*SP*	*AT*	*MP*	*AM*	Sucrose	Methylparaben	Ethylparaben	Propylparaben	Citric acid
Quantity → (% *w*/*v*)	2.4	2.0	1.1	0.6	1.0	0.7	1.0	0.8	3.0	0.9	45.0	0.1	0.3	0.3	0.1

Six tablets were selected from each formulation, and each tablet was placed in 900 mL of enzyme-free simulated gastric fluid (Merck, Germany) and allowed to dissolve over 7 h. Samples of 5 mL were withdrawn between 5 and 25 min (with 5-min interval) and then at 30, 60, 120, 180, 240, 300, 360, and 420 min under sink condition and filtered immediately for analysis by HPLC, as outlined in Section 2.7.1 for suspensions. The cumulative drug release data were analyzed using zero-order, first-order, Higuchi [26], Hixson–Crowell [27], and Korsmeyer–Peppas [28] models under sink conditions.

2.10. Film Coating of Tablets. The hemicellulose (1.5 g) of *OB*, *MP*, *LR*, *SP*, *PO*, *AN* gum (24 g), and *AM* gum (30 g) was suspended in distilled water (300 mL) and heated to about 60°C on hotplate with constant stirring for 1–2 h to allow the formation of mucilage. To this, ferric oxide red (1.0 g) and talc (9.0 g) were added, and the mixture was heated again to 60°C with constant stirring to get a homogenous mixture, which was used to coat the lactose tablets using Thai Coater (Zhejiang Lead Top Pharmaceutical Machinery Co. Ltd., China). The coating parameters are as listed in Table 2. The quality of coating was assessed by the film puncture test as reported by Bussemer et al. [29]. The mechanical strength was determined by using Universal Testing machine AGS-J (Shimadzu, Japan) in triplicate at 25°C ± 1°C. A metallic probe (5-mm hemispherical diameter, 15-cm length) was inserted through the dry film at a speed of 5 mm min^{-1}. The force–displacement profile was recorded using a 50 kg m s^{-2} force.

2.11. Preparation and Evaluation of Suspensions. The bill of materials for preparation of suspensions is given in Table 1. Acetaminophen (120 mg per 5 mL) suspensions were prepared as follows. Acetaminophen was triturated with the appropriate hemicellulose in water (~25 mL). The other ingredients were dissolved in water (~50 mL); to this solution, the triturate was added under stirring using an overhead mechanical stirrer (@ 1500 rpm) to obtain a homogeneous suspension.

The suspensions were evaluated according to reported methods [30]. In order to determine sedimentation volume, a well-mixed suspension (100 mL) was transferred to a glass-stoppered 100-mL graduated cylinder. It was then allowed to stand undisturbed in the dark at 25°C ± 1°C for 16 h. Sedimentation was recorded at 1, 2, 4, 8, 12, and 16 h and then 7, 15, 30, 60, and 90 days, and the results were recorded in terms of the sedimentation volume $F(\%) = (V_u/V_o) \times 100$, where V_u represents the volume of the sediment and V_o is the original volume of the suspension.

The thickening property of the hemicellulosic material was determined by measuring the viscosity (in millipascal second) of the suspension using a Brookfield Synchroelectric viscometer LVF (Brookfield Laboratories, Massachusetts) at a speed of 50 rpm.

Redispersibility was assessed by allowing the filled 120-mL bottles to stand undisturbed until the sedimentation volume (F) reached 98%. At this point, the bottles were gently shaken three times to ensure the uniform redispersion of the suspension.

TABLE 2: Coating parameters for film coating the 500-mg lactose tablets.

Parameter	Value
Batch size	100 tablets
Pan speed	14 rpm
Inlet airflow	350 cfm
Inlet temperature	90°C
Spray rate	35 g min^{-1}
Number of spray guns	1
Air pressure	40 psi
Tablet bed temperature	50°C–55°C

2.11.1. Stability Study of Suspensions. The suspensions were stored at 25°C ± 1°C in amber-colored bottles in the dark and assayed for acetaminophen for 15 months at monthly intervals. For assay, the USP 43, 2020, HPLC method for acetaminophen oral suspension was used. Briefly, the well-shaken suspension (equivalent to 100 mg of acetaminophen) was dissolved in methanol–water mixture (1:3) to make a 250-mL solution. Five milliliters of this solution was diluted to 250 mL with methanol–water mixture (1:3) and filtered through a 0.5-μm filter. The clear filtrate injected (10 μL) into an ODS column (3.9 mm × 30 cm) and chromatographed @ 1.5 mL min^{-1} using methanol–water mixture (1:3) as the mobile phase with detection at 243 nm.

3. Results

3.1. Characterization of the Isolated Hemicelluloses. The results of yield, CHN, monosaccharide, moisture, and GPC analyses of the isolated hemicellulosic materials under investigation are listed in Table S1 (for analytical data of the hemicellulosic materials, the data represent mean values (n = 5) ± standard deviation). The percentages were calculated on dry-substance basis. The yield of the pure hemicelluloses isolated from the plant materials ranged from 1.0% to 18.5%. The water content was in the range 8.0%–10.9%, which is usually present in dry polysaccharides. Characteristic absorption bands in the FTIR spectra of hemicelluloses (in the range 1200–500 cm^{-1}) were 3359–3432 ν(OH), 2920–2936 ν(CH) aliphatic, 1605–1648 δ(OH) in-plane, 1414–1460 δ(OH) in-plane, 1246–1422 $\delta(CH_2)$, 1350–1377 δ(CH), 1244–1253 δ_{asym} bridged oxygen, 1074–1153 ν(COC), 1000–1059 ν(C-C) arabinosyl side chain, 850–910 δ_{asym} out-of-plane β-glycosidic bond, and 500–668 polymer backbone. These absorptions established the identity of the hemicelluloses under investigation. The results of compatibility of acetaminophen with the polymers by FTIR are depicted in Figure 1 as a representative example. It was found that there was no significant change in the spectrum of acetaminophen after loading on the polymers.

The SI (percentage) of the polymers ranged from 24.4 (*AT*) to 40.5 (*POh*) and *WR* (percentage) was 30.1 (*AT*) to 48.9 (*POh*) (Table 3).

3.2. Precompression Evaluation of Granules. The results of precompression parameters of the granules prepared through WG are provided in Table S2 (for precompression test results of formulations prepared by WG methods). A value of < 30° for the angle of repose represents excellent flow, whereas the values in the 31°–35° range indicate good flow properties [21]. The angle of repose for the granules was in the range of 21.34 ± 0.010 to 49.23 ± 0.03. Bulk and tapped density data of the granules are presented in Table S2 (for precompression test results of formulations prepared by WG methods). The CI and HR were determined using the bulk and tapped densities. The CI (percentage) values ranged from 4.4 to 13.2 (Table S2 for precompression test results of formulations prepared by WG methods). The CI values categorize flow as > 25 (poor), 16–20 (fair), < 15–11 (good), and < 10 (excellent) [31, 32].

3.3. Postcompression Evaluation of Tablets. Hardness, weight variation, friability, and disintegration data are presented in Table S3 (for postcompression test results of formulations prepared by WG (F-1 to F-10) and DC (F-11 to F-20) methods). The tablets prepared by both the WG and DC methods exhibited weight variation (8%–10% *w*/*w*) and friability values (0.11%–1.18% *w*/*w*) close to the standard limits (USP 43, 2020). Tablets prepared by both WG and DC exhibited weight variation within the limits of USP. The disintegration time of the tablets prepared by the WG method ranged from 13 to 32 min, whereas those prepared by DC method ranged from 1.18 ± 0.012 to 12.56 ± 0.041 min. The tablets prepared by DC using *LR*, *PO*, *SP*, *MP*, and *AM* disintegrated within 5 min; the range was 1.18 ± 0.012 to 4.25 ± 0.021 min.

3.3.1. Stability of Tablets. The assay of the acetaminophen in the tablets (both DC and WG) remained > 93% (Figure 2, a typical profile) as determined by the HPLC method for 6 months at 40°C and 75% ERH.

3.4. Dissolution Study. Figure 3 illustrates the dissolution profiles of the tablets. It was noted that the tablets produced by WG (F-1 to F-10) exhibited a slower release of the drug compared to those made by DC (F-11 to F-20). Approximately 60% of the drug was released within the first hour from the DC tablets, while only around 30% was released from the WG tablets containing the same hemicellulose, highlighting the impact of the preparation technique. The tablets manufactured via DC displayed an initial burst release, indicating the relatively lower binding capacity of hemicelluloses [33] in these formulations. Formulations F-12, F-15, and F-16 showed a sustained release profile regardless of the preparation method, likely due to specific structural characteristics of the hemicelluloses. This initial burst release can be advantageous, as several drugs require varied release rates, and for certain medications, an initial surge can provide immediate relief, followed by a gradual, sustained effect [34].

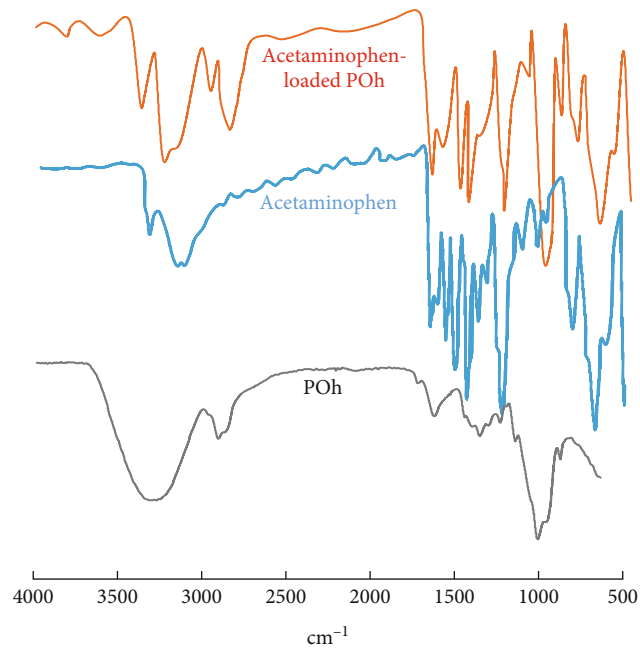


FIGURE 1: FTIR spectra of *POh*, acetaminophen, and acetaminophen-loaded *POh*.

3.5. Surface Morphology of Films. The SEM images of the prepared films depicting their morphology are shown in Figure 4. Generally, the films were found to contain voids.

3.6. Evaluation as Film-Coating Materials. The film coating of sample tablets, prepared from lactose, was conducted without the use of any plasticizer and was assessed using the film puncture test. The images of the coated tablets are presented in Figure 5. A typical force–displacement curve of *OB* film is shown in Figure 6. The maximum force ranged from 35 to 40 kg m s^{-2} with displacement in the range 2–2.5 mm at 25°C ± 1°C. The trend was *AT* < *OB* < *SP* < *AN* < *AM* < *CO* < *POh* < *POs* < *LR* < *MP*.

3.7. Evaluation of Suspensions. The results of sedimentation analysis are given in Table 3. All, except that of Calpol, the suspension samples remained stable for more than 2 months' time and readily redispersible after 2 months.

The trend of stability was found to be *SP* > *OB* > *AN* > *AM* > CO > *POh* > *POs* > *LR* > *MP* > *AT*. It can be noted that all the hemicelluloses under investigation produced more stable suspension than Calpol. The viscosity of the prepared suspensions (25°C ± 1°C) lay in the standard range of 800–1600 mPa·s and the pH at 4.50–6.90 [35].

3.7.1. Stability of Suspensions. The stability curve (assay of the API vs. time) is shown in Figure 7. It was observed that the acetaminophen assay remained ~93% after the suspensions were stored at 25°C ± 1°C in amber-colored bottles in the dark for 15 months. Figure 8 presents representative picture of the suspensions prepared from *OB* 1 h and 15 months after the storage.

TABLE 3: Swelling index and water retention value.

Sample code	SI (%)	WR (%)
SP	25.5 ± 1.4	30.4 ± 1.0
OB	30.3 ± 1.2	30.5 ± 1.1
LR	26.5 ± 0.6	37.5 ± 0.9
POh	40.5 ± 1.1	48.9 ± 1.5
POs	27.2 ± 0.9	41.3 ± 1.1
CO	39.9 ± 1.3	47.8 ± 1.6
AT	24.3 ± 0.3	30.1 ± 0.1
MP	37.5 ± 1.5	79.4 ± 1.7
AN	24.4 ± 0.7	30.2 ± 0.9
AM	25.4 ± 1.2	30.4 ± 0.9

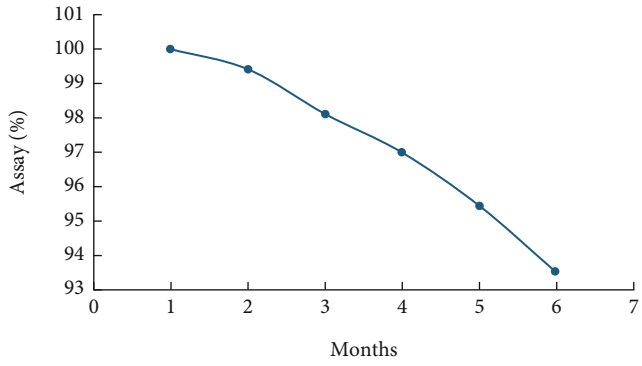


FIGURE 2: Assay (percentage) versus time (months) graph of acetaminophen in the WG tablets prepared using *OB* as the binder and coating agent. The tablets were stored in Securitainers for 6 months at 40°C and 75% ERH.

3.7.2. Rheology of Suspensions. The results of the rheological analysis in the shear rate 10.0 s^{-1} at 1.0% concentration level and viscosity data are presented in Table 4. The viscosity ranged from 1500 to 1600 mPa·s. The viscosity values of 1% suspension in H_2O at shear rate 10 s^{-1} fell in the range 0.002–0.16 mPa·s showing the pH value around 5.

4. Discussion

4.1. Characterization of Hemicelluloses. Monosaccharide composition and elemental analysis of the hemicelluloses on dry-substance basis resembled those of the standards [16]. The FTIR absorptions in the region 910–850 cm^{-1} provided evidence for the presence of glycosidic linkages and alcoholic groups. These absorptions are characteristic of polysaccharides [36]. In addition to these, other absorptions were also indicative of the polysaccharide structure. The comparative FTIR spectra regarding drug compatibility provided clear evidence of lack of chemical interaction (covalent bonding) of the drug with the polymers. These analyses confirmed the identity of the hemicellulosic materials employed in this study. The high swelling characteristics of these materials (Table 3) indicated that they are suitable for drug delivery [37, 38]. From these polymers, release of drug can be controlled by the water content and pore size.

4.2. Precompression Evaluation of Granules. The angle of repose, CI, and HR are crucial precompression parameters used to assess the flow properties of powders, which directly impact their suitability for tablet compression. The angle of repose measures the maximum angle at which a pile of powder remains stable, indicating flowability; a lower angle suggests better flow. CI and HR are derived from bulk and tapped densities, offering insights into powder compressibility and cohesiveness. A lower CI (less than 15%) and HR (close to 1) indicate good flow properties (USP 43, 2020), essential for uniform die filling and optimal tablet production. According to the results (Table S2), the formulations F-1, F-6, and F-7 exhibited excellent flow, while formulations F-2, F-3, F-4, F-5, and F-9 demonstrated good flow properties. The difference in flow is because of structural variation of the hemicelluloses. Hemicelluloses from *AN*, *AT*, and *PO* used in F1, F6, and F7 are known to have compact structures due to extensive hydrogen bonding in them [39]. It was observed that granules having relatively poor flow had significant difference in the bulk and tapped densities. Based on these results, formulations F-6, F-7, F-8, F-9, and F-10 with CI < 10 can be considered as having excellent flowability. The HR values of all the formulations under investigation were < 1.11, that is, in the range of 0.84–0.95, so their flow can be considered excellent. These results indicate the diversity of hemicelluloses, which is a desired feature in formulation of pharmaceutical products.

4.3. Postcompression Evaluation. Hardness, weight variation, friability, and disintegration time are key parameters that assess a tablet's quality [40]. Hardness indicates the tablet's strength and resistance to breaking under pressure, influencing its durability during handling and storage. Weight variation ensures uniformity in dosage, critical for maintaining consistent therapeutic effects. Friability measures a tablet's tendency to crumble, affecting its stability and appearance. Disintegration time reflects how quickly the tablet breaks down in the body, impacting the drug's availability. Together, these parameters ensure that tablets meet the required quality standards for safe and effective use.

All the prepared tablets that exhibited hardness in the range 2–7 kg cm^{-2} (Table S3 for postcompression test results of formulations prepared by WG (F-1 to F-10) and DC (F-11 to F-20) methods), that is, within the typical range of 1.02–40.80 kg cm^{-2} (0.1–4 MPa), are typically desired for tablets [40]. These results demonstrate that the hemicelluloses under investigation can be good substitutes for synthetic binders in tablets. The weight variation (8.3%–13.1%), friability (0.11%–1.22%), and disintegration time (5.1–32.1 min) largely complied with the USP 43, 2020, limits specified for similar tablets. The friability value of formulations F-4, F-5, F-6, F-12, and F-17 was slightly higher than 1%, which may be considered as close to the limit taking into account the experimental errors. A variety of trends in disintegration time, ranging from 5.1 to 32.1, of the tablets was observed due to different nature of the hemicelluloses used.

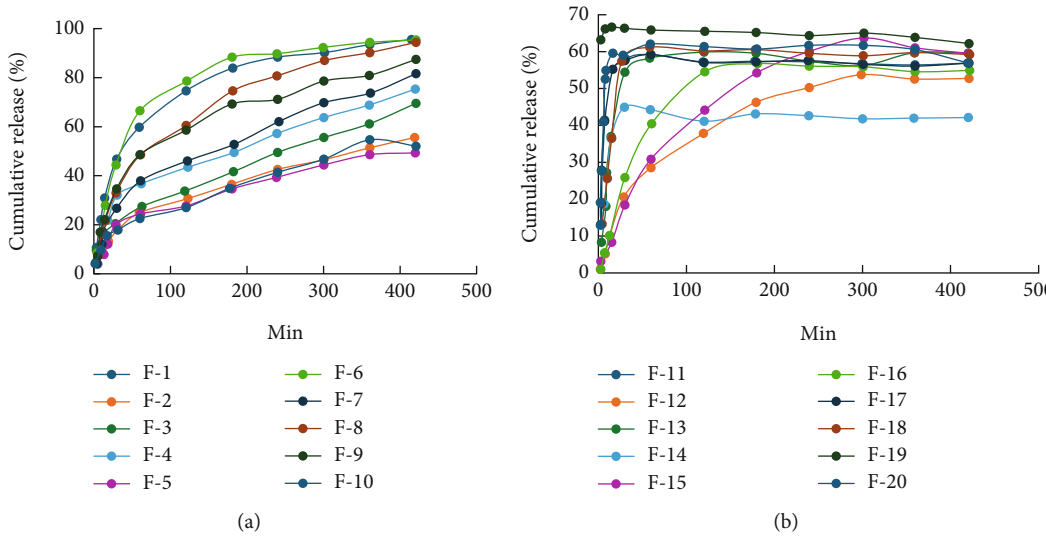


Figure 3: Drug release profiles showing cumulative drug release as a function of time: (a) WG and (b) DC.

This again reflects the versatility of hemicelluloses as binders.

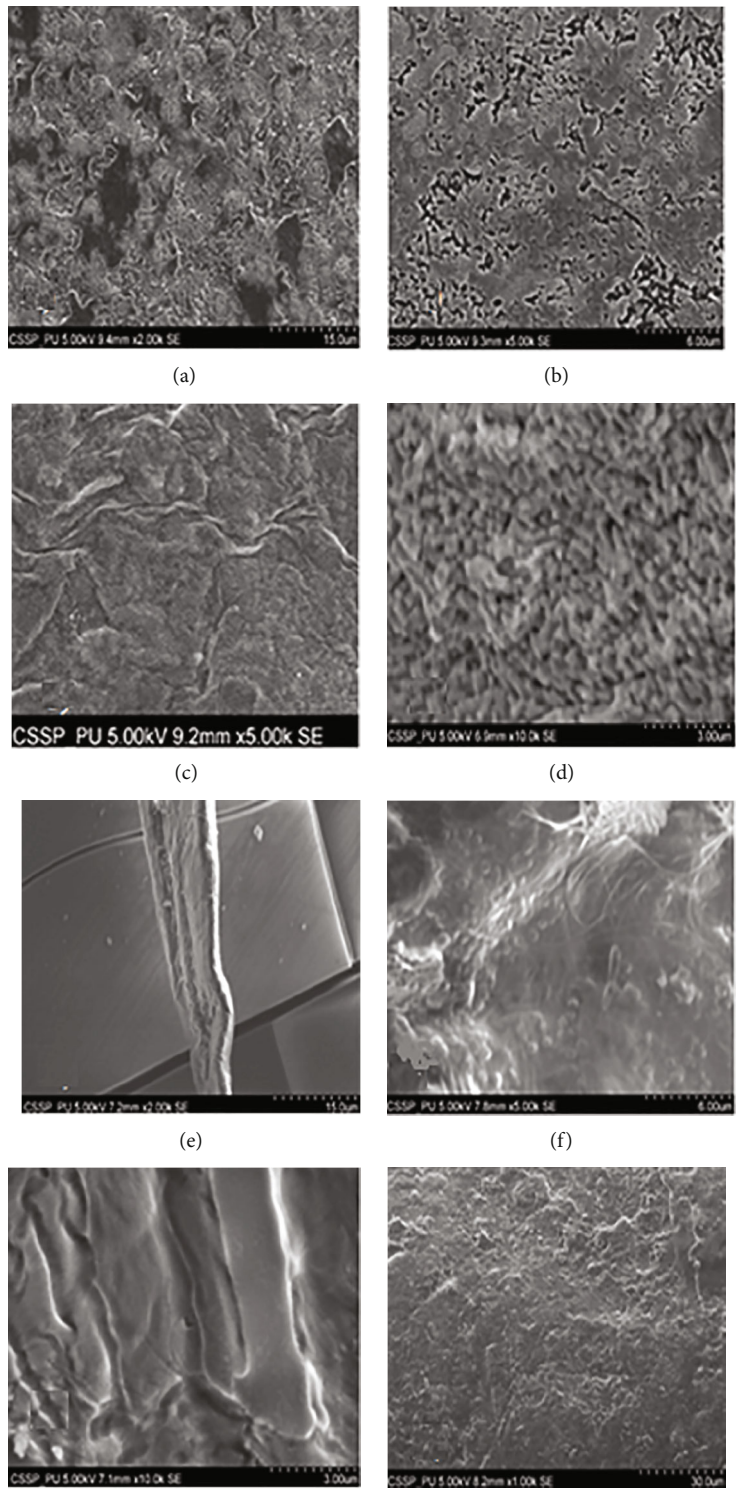
The friability, hardness, and disintegration time of tablets are critical quality attributes that significantly influence the sustained release of a drug. High friability can lead to tablet fragmentation during handling or within the gastrointestinal (GI) tract, increasing the surface area exposed to the dissolution media. This fragmentation accelerates drug release, potentially compromising the sustained-release mechanism. Conversely, if a tablet is too hard, it may resist penetration by the dissolution media, slowing drug release. Excessive hardness can also hinder proper disintegration, particularly in matrix-based sustained-release systems.

Sustained-release tablets often rely on polymers or matrix systems to control the disintegration process. If disintegration occurs too quickly, the sustained release mechanism may fail, resulting in a burst release. Polymers play a central role in these tablets by forming a matrix or coating that regulates drug diffusion or erosion. The effectiveness of friability, hardness, and disintegration time depends on how well these polymers encapsulate the granules. Properly encapsulated granules offer better control over drug release, as the polymer barrier modulates the rate of water penetration and drug diffusion. Achieving the desired release profile without compromising the mechanical integrity of the tablet requires a delicate balance between these attributes. This balance is validated through an in vitro dissolution profile, which determines the optimal values for these parameters.

The assay of the acetaminophen in the tablets (both DC and WG) remained within the standard limit (90%–110%) as determined by the HPLC method for 6 months at 40°C and 75% ERH suggesting a standard shelf life of 3 years for these tablets if stored at a cool and dry place as recommended for such products.

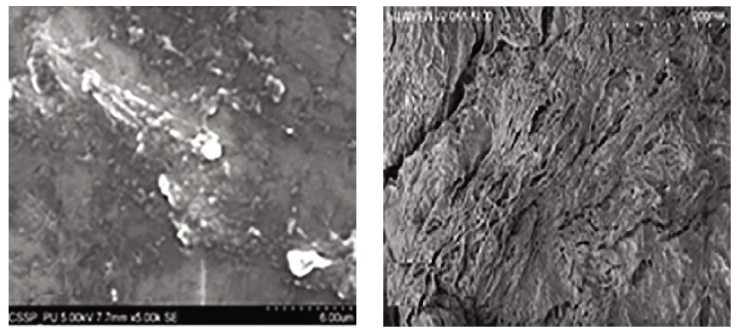
4.4. Dissolution Study. The tablets prepared by WG (F-1 to F-10) exhibited a slower drug release than those prepared by DC because of their higher hardness. The fastest drug release was observed in F-1, and F-7 exhibited the slowest release rate; these formulations were prepared using WG method. The possible explanation may be that the pores in the tablets prepared by WG are smaller than those in the tablets prepared by DC. The smaller pore size in the polymer structure will hold lesser amount of water resulting in reduced permeation inside the polymeric matrix and reduced drug diffusion affording a sustained release [41]. Dissolution profiles of WG and DC tablets prepared using the same hemicellulose show that release rate also depends upon the method of preparation in addition to the nature of the hemicellulose used. The results of this study confirm that the postcompression parameter values are appropriate for achieving the observed release profiles of the prepared formulations. Further, the release profiles of the tablets prepared by WG suggest that they can meet the requirement of twice daily administration, which has rarely been achieved for acetaminophen [42].

4.4.1. Kinetic Models. The drug release profiles from the polymeric matrix depend on various factors such as diffusion, drug solubility, water permeability, swelling index, and matrix erosion. To determine the drug release mechanism from the matrix tablets, the release data were analyzed using zero-order, first-order, Higuchi, Korsmeyer–Peppas, and Hixon–Crowell models. The most suitable model was selected based on model selection criteria (MSC) [43]. The kinetic analysis (Table S4 for fitness of drug release data (R^2, MSC, and n) into different kinetic models) revealed that, for most of the DC formulations, the Korsmeyer–Peppas (Power Law) model provided the best fit, whereas for the WG formulations, the Higuchi and first-order models were more appropriate. In terms of the release mechanisms identified by the Korsmeyer–Peppas model, formulations F-1, F-3, F-5, F-6, F-7, F-8, F-9, and F-10 (WG), as well as F-12, F-13, F-15, F-16, F-19, and F-20 (DC), followed a non-Fickian mechanism, indicating that the drug release was controlled by both diffusion and



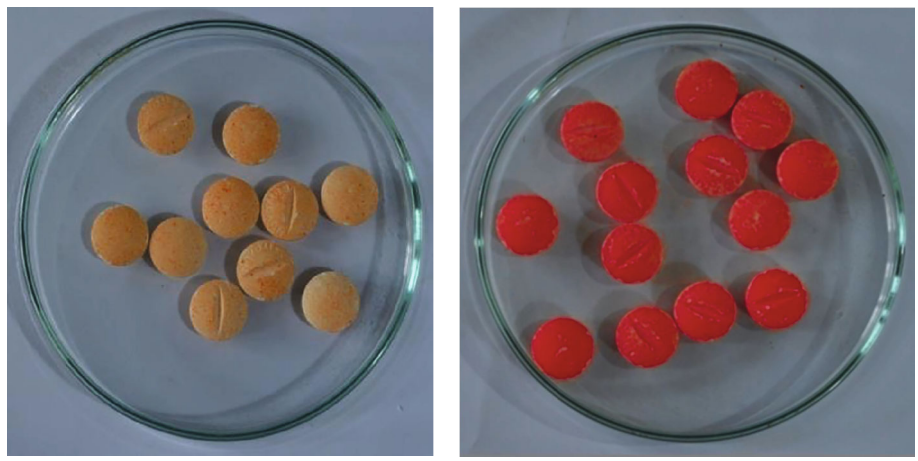
(a) (b) (c) (d) (e) (f) (g) (h)

Figure 4: Continued.



(i) (j)

Figure 4: SEM images of films of (a) *OB*, (b) *LR*, (c) *POh*, (d) *SP*, (e) *AN*, (f) *MP*, (g) *AM*, (h) *AT*, (i) *CO* and (j) *POs*.



(a) (b)

Figure 5: Images of (a) cores and (b) coated tablets.

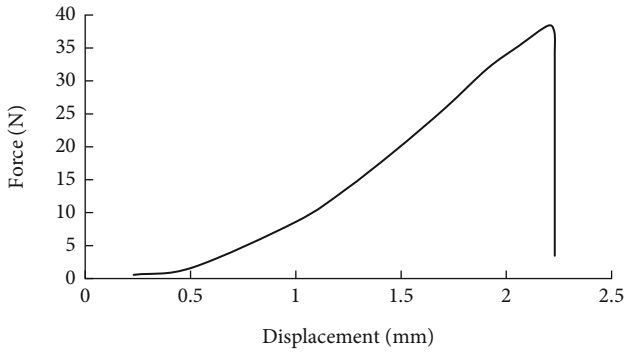


Figure 6: Force–displacement curve of *OB* film ($7 \times 7\,cm^2$) at $25°C \pm 1°C$.

swelling properties. In contrast, formulations F-2 and F-4 (WG) and F-11, F-14, F-17, and F-18 (DC) adhered to a Fickian (diffusion-controlled) mechanism. Formulation F-16 (DC) uniquely exhibited a Super Case II release mechanism, indicating that the drug release was influenced by a combination of diffusion, swelling, and erosion. These findings are based on the "n" value criteria: 0.45 for Fickian, $0.45 < n < 0.89$ for non-Fickian, and $n > 0.89$ for Super Case II mechanisms [44, 45]. The varied release behaviors of the hemicelluloses suggest their potential as versatile materials for designing controlled-release formulations.

4.5. Surface Morphology. Surface morphology of film-coating polymers plays a crucial role in controlled-release formulations, as it directly impacts the release rate and overall stability of the encapsulated active ingredients. A well-suited surface morphology, characterized by factors such as porosity, roughness, and particle size, can ensure a more sustained and predictable release profile. Smooth surfaces may slow down the release by limiting the diffusion of the active ingredient, while porous surfaces can accelerate the release. Additionally, surface morphology influences the interaction with biological environments, affecting bioavailability and the therapeutic efficacy of the formulation. The SEM images (Figure 4) of the films of the hemicelluloses under investigation showed that they are porous and contain voids, so they are suitable for drug coating to make sustained-release formulations.

4.6. Evaluation as Film-Coating Materials. Film coating is a critical requirement in the manufacturing of some

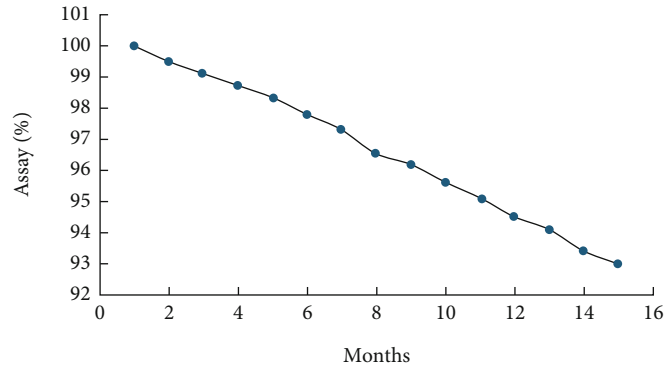


Figure 7: Assay versus time graph of acetaminophen in the suspension prepared by use of *OB* as the suspending and thickening agent. The suspension was stored at 25°C ± 1°C in amber-colored bottles in the dark.

Aftter 1 h After 15 months

Figure 8: Pictures of the suspensions prepared from *OB* 1 h and 15 months after preparation.

pharmaceutical tablets [46]. The applied film coat serves multiple purposes: it shields the active ingredient (API) within the tablet from environmental factors, masks undesirable tastes and odors, and enhances the tablet's palatability. Additionally, the coating may also serve to protect the API in the stomach and facilitate the production of controlled-release tablets. Remarkably, even in the absence of a plasticizer, these materials exhibited good strength (Figure 6) required for coating pharmaceutical tablets, leaving room for further enhancement with the incorporation of a plasticizer. In contrast to this, studies reporting use of plant mucilages as coating material also add polyethylene glycol or HPMC as auxiliaries [47]. The effectiveness of the film coat was demonstrated by the stability profile of the prepared tablets as discussed in Section 4.3.

4.7. Evaluation of Suspensions. The viscosity (800–1600 mPa·s and the pH at 4.50–6.90) of the prepared suspensions demonstrated that all the hemicelluloses under investigation are good thickening/suspending agents. The results were compared with Calpol pediatric suspension (GlaxoSmithKline, Pakistan), a standard preparation; the prepared suspensions were found to exhibit exceptional stability. The stability of the API in the suspensions was evidenced by the acetaminophen assay that remained within the standard limit (90%–110%) as determined by the HPLC for more than 15 months (Figure 7, a typical profile). The suspensions were stored at 25°C ± 1°C in amber-colored bottles in the dark. It is important to note that Calpol contains sorbitol, glycerol, polysorbate 80, dispersible cellulose, and xanthan gum to achieve the claimed stability in contrast to only one hemicellulosic material affording much better performance. Thus, the materials used in the present work have a great potential to replace the currently used suspending and thickening agents.

4.7.1. Rheology of Suspensions. Rheological study is an important aspect in characterization of polymers. In the case of polysaccharides, they behave akin to flexible coils in dilute solutions [48]. The successful coating of pharmaceutical tablets with polymers hinges on the viscosity and elasticity of the polymer used. Hence, a comprehensive investigation into the rheological properties of the hemicellulosic polymers under study was essential. This aimed at evaluating their potential application as film-coating agents, enhancers of viscosity and suspension agents. These polymers were subjected to rheological analysis in the shear rate $10.0\,s^{-1}$ at 1.0% concentration level (Table 4). The sample of *AT* could not be studied due to its inability to form the requisite homogeneous solution for the analysis. While *AN*, *MP*, *OB*, and *AM* demonstrated Newtonian flow, the other materials exhibited non-Newtonian characteristics. In the case of *SP*, *PO*, *OB*, *LR*, and *MP*, the structural integrity remained relatively constant, as evidenced by the repetitive nature of the reverse rheogram within the same range. A view of the viscosity data at 1% concentration level and shear rate $10\,s^{-1}$ (Table 4) revealed that *PO* possesses the highest viscosity and *AN* the lowest; the trend was *POs/h* > *LR* > *SP* > *AM* > *MP* > *OB* > *AN*. It is conceivable that *AN* and AM polymers hold promise for applications where Newtonian flow is required.

TABLE 4: Sedimentation volume (F), viscosity, and pH of the suspensions.

Material	F (%)											Viscosity (mPa·s)	pH
	Hours						Days						
	1	2	4	8	12	16	7	15	30	60	90	of 1% in H_2O at shear rate 10 s^{-1}	
SP	100	100	100	100	99	99	97	97	96	95	92	1600	0.017	5.0
AN	100	100	100	99	99	98	96	96	95	94	91	1594	0.002	5.1
MP	100	100	100	98	97	95	94	93	92	90	90	1582	0.004	5.0
POh	100	100	100	99	99	96	95	94	94	92	91	1590	0.16	5.2
POs	100	100	100	99	99	96	95	94	94	92	91	1590	0.16	5.2
CO	100	100	100	99	99	96	95	94	94	92	91	1590	0.16	5.2
AM	100	100	100	99	99	97	96	95	95	93	91	1590	0.005	5.1
LR	100	100	100	99	98	96	95	94	94	91	90	1585	0.079	5.0
OB	100	100	100	99	99	97	97	96	96	94	92	1595	0.003	5.1
AT	100	93	91	90	88	81	56	49	38	37	37	1500	0.002	5.0
Calpol	100	94	93	92	89	85	60	50	40	40	40	1500	—	5.0

5. Conclusions

Hemicelluloses derived from food materials demonstrated significant potential as multifunctional pharmaceutical excipients, offering environmentally friendly and biocompatible alternatives to synthetic and semisynthetic counterparts. The granules prepared for tablet formulation exhibited excellent flow properties, ensuring efficient manufacturing. Moreover, the matrix tablets showed desirable mechanical strength, with hardness values ranging between 2 and 7 kg cm^{-2} and disintegration times ranging from 1.18 to 25.0 min at pH 6.8, making them suitable for various pharmaceutical applications. Importantly, the wet granulated tablets achieved controlled drug release, with 45%–92% of acetaminophen released over approximately 7 h, confirming their effectiveness as extended-release agents.

In suspensions, the hemicelluloses displayed exceptional stability, with sedimentation volumes ranging from 90% to 92% over 2 months, surpassing the performance of standard formulations like Calpol. The stability of suspensions followed the trend $SP > OB > AN > AM > CO > Poh > POs > LR > MP > AT$. Additionally, the film coatings prepared using hemicelluloses exhibited impressive strength (35–40 kg m s^{-2}), further underscoring their utility in pharmaceutical coatings.

These findings highlight the versatility, superior biocompatibility, efficacy, and sustainability of hemicelluloses for their choice in pharmaceutical formulation. We feel that a more comprehensive parameter optimization should be the target of future work, which may reveal greater versatility of hemicelluloses from the investigated sources and other plant materials.

Data Availability Statement

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

Conflicts of Interest

The authors declare no conflicts of interest.

Author Contributions

Irva Waqar: investigation, formal analysis, characterization, data analysis, writing–original draft. Shazma Massey: supervision, validation, writing, review, and editing. Fozia Iram: supervision, validation, writing, review, and editing. Mohammad Saeed Iqbal: conceptualization, supervision, validation, writing, review, and editing. Naila Perveen: investigation, formal analysis, characterization, data analysis. Abdul H. Khan: supervision, writing, review, and editing.

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Supporting Information

Additional supporting information can be found online in the Supporting Information section. *(Supporting Information)* Supporting information to this article (Tables S1–S4) can be found online.

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