

Evaluation of some hemicellulosic materials as an excipient for extended-release tablets

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Abstract

Cellulose-based excipients are widely used in the manufacture of pharmaceuticals. Although they are biocompatible, yet they are not digestible by human body due to absence of cellulase enzymes. Therefore, hemicelluloses were considered to be more suitable materials for development of such excipients. This work evaluates hemicelluloses isolated from *Plantago ovata* husk, *Plantago ovata* seeds, *Lallemantia royleana*, *Occimum baccilium*, *Mimosa pudica*, *Salvia plebian*, *Acacia nilotica*, *Acacia modesta*, *Astraglus tragacantha* and *Cydonia oblonga* as binders, targeted delivery and extended-release excipients for pharmaceutical tablets, using acetaminophen as a model drug. The tablets formulated through wet granulation method by using hemicelluloses from *Acacia nilotica*, *Acacia modesta*, *Lallemantia royleana*, *Occimum baccilium*, *Plantago ovata* husk afforded 6-7 kg cm⁻² hardness with 15-25 min disintegration time at pH 6.8. Others exhibited significantly lower values. Whereas, the tablets prepared by direct compression came out with poor hardness values. The longer disintegration time in case of wet granulated tablet rendered them to release acetaminophen over an extended period of time. The tablet appears to be least affected in the stomach because of the insolubility of the hemicelluloses in highly acidic medium. The tablets from wet granulation method released 45-92% paracetamol for about 7 h following non-Fickian mechanism.

Introduction

Excipients such as binders, fillers, flavors, dyes etc. are fundamental components of pharmaceutical drug dosage forms (Ahmad et al., 2021; X. Liu et al., 2018; Singh et al., 2021). The efficacy of a dosage form depends on the nature of excipients and the method of manufacture (Dürig & Karan, 2018). Most of the excipients, including the binders, being used are of synthetic nature. Efforts are being made to replace the synthetic material with natural materials, which are biocompatible and biodegradable (Amiri et al., 2021). Some of the binders considered to be biocompatible and biodegradable in current use, such as carboxymethyl cellulose and hydroxypropyl methyl cellulose, are based on cellulose (Beneke et al., 2009; Fukami et al., 2006; Gencturk et al., 2016; Karolewicz, 2016a; W. Liu et al., 2018a). It is well established fact that cellulosic materials are not digestible by humans. Therefore, there is a need to replace these materials with those which can be digested or metabolized by humans. Hemicelluloses have been shown to be suitable for this purpose as the human body can partially metabolize due to the presence of hemicelluloses in the flora of colon (Karolewicz, 2016b; W. Liu et al., 2018b; Rogers & Wallick, 2012).

Hemicelluloses are the second most abundant biomaterials on earth. Although hemicelluloses from *Plantago ovata* (PO) husk (Ispaghula husk), *Plantago ovata* (PO) seeds (Ispaghula seeds), *Lallemantia royleana* (LR) (Tukhm-e-balango), *Occimum baccilium* (OB) (Tukhm-e-rehan), *Mimosa pudica* (MP) (Tukhm-e-lajwanti), *Salvia plebian* (SP) (Samundar soakh), *Acacia nilotica* (AN) (gum kitar), *Acacia modesta* (AM) (Phulai gum), *Cydonia oblonga* (CO) (Beedana) and *Astraglus tragacantha* (AT) (Gond katira) have been investigated for their application in formulation of pharmaceutical tablets (Massey et al., 2016) but their role as binders and drug delivery agents has not been explored. In addition to their potential use as inactive ingredients in formulations they have also been shown to possess some pharmacological effects (Mukherjee et al., 2021; Zhan et al., 2020). Hemicelluloses produce sticky mucilages in contact with water. This property can be exploited in formulation of tablets where they will act as binders.

Keeping in view the abundant availability, biocompatibility and biodegradability, we hypothesize that the hemicellulosic materials could be employed as binders for formulation of tablets for human use. Therefore, the objective of this work was to evaluate some of the hemicelluloses from food materials as binding and drug delivery agents.

Materials And Methods

Materials

Plant materials including gum *Acacia nilotica* (AN), *Lallemantia royleana* (LR) seeds, *Plantago ovata* husk (POH), *Ocimum basilicum* (OB) seeds, *Salvia plebian* (SP) seeds, *Astraglus tragacantha* (AT), *Plantago ovata* seeds (POS) *Mimosa pudica* (MP) seeds, gum *Acacia modesta* (AM), *Cydonia oblonga* (CO) were purchased from a herbal shop in Lahore. Acetaminophen (PubChem CID: 1983), magnesium stearate (PubChem CID: 11177) were from Sigma-Aldrich, USA. Citric acid (PubChem CID: 311), disodium hydrogen phosphate (PubChem CID: 24203), lactose (PubChem CID: 84571) and hydrochloric acid (PubChem CID: 313) were from E. Merck, Germany. All the chemicals were used without further purification. Distilled water was used throughout this study.

Isolation and purification of hemicelluloses

The hemicelluloses were isolated and purified as per our previously reported method (Massey et al., 2016) and the analyses of the fresh samples were compared with the standards. The isolated materials were delignified by reported method (Massey et al., 2016). The molar masses, elemental and monosaccharide analyses (Table 1) were found to be significantly similar to those already reported. The analysis of the hemicellulosic material from CO matched the composition of the standard reported by others (Hakala et al., 2014).

Characterization of hemicelluloses

The elemental composition of hemicelluloses was determined by CHNS analyzer Vario MICRO V1.4.2 (Elementar Analysen Systeme, GmbH, Germany). Monosaccharide composition and molar masses of hemicelluloses were determined by following previously reported method (Iram et al., 2018; Massey et al., 2016) without any modification. Moisture content was determined by Karl-Fischer titration using 799 GPT Titrino, Karl-Fischer titrator (Metrohm, Switzerland). Fourier transform infrared spectra (FT-IR) was recorded by using IR-prestige-20 spectrophotometer (Schimadzu, Japan).

Preparation of tablets

The bill of materials for the preparation of tablets is given in Table 2. The quantities were optimized through preliminary experimentation. Acetaminophen was selected as a model drug for preparation of tablets by wet granulation and direct compression methods.

Wet granulation

Acetaminophen and lactose (diluent) were weighed for a batch of 100 tablets (Table 2), mixed and ground using stainless steel mortar and pestle and passed through a 300 mesh sieve. To the hemicellulosic material (as the binder) water (1.0 mL) was mixed thoroughly by the use of mortar and pestle. The mixture was passed through a stainless steel 40-mesh sieve (420 µm opening). The granules thus obtained were dried at 40 °C to a moisture content of 8 ± 1% and passed through a stainless steel 20-mesh sieve (840 µm opening). To granules, magnesium stearate (as the lubricant) was added and homogenized by geometric mixing.

Pre-compression evaluation of the granules was carried out by measuring flowability (angle of repose), bulk density (ρ_b), tapped density (ρ_t), Carr’s compressibility index (CI %), Hausner’s ratio (HR) and moisture content according to standard methods (Hildebrandt et al., 2019; Lindberg et al., 2004; MRPharmS, 2007; Shah et al., 2008a). The flowability (Michael E. Aulton, 2018) was determined by two methods and the results were reported in terms of angle of repose (α) and flow rate (gs^{-1}). These parameters were determined by using the flow meter (Powder Analyzer Type PTG, Pharma Test, Hainburg, Germany) according to the USP (Michael E. Aulton, 2018) using 10 g of the sample.

All the measurements were made in triplicate. The ρ_b and ρ_t were calculated by the formula: $\rho_b = m/v$ and $\rho_t = m/v_t$ respectively, where m is mass and v is volume of granules (10.0 g) without tapping according to reported method.(Iqbal et al., 2010). The CI and HR were calculated using the equations(Charagonda et al., 2016; Dev et al., 2018): $CI = [\rho_t - \rho_b] / \rho_t \times 100 = [(V_0 - V_f) / V_0] \times 100$ and $HR = \rho_t / \rho_b = V_0 / V_f$. Where V_0 and V_f are initial and final volumes. Moisture content was determined by Karl-Fisher titration using 799 GPT Titrimo,Karl-Fischer titrator (Metrohm, Switzerland), an accurately weighed amount of the sample (approx. 300 mg), pyridine-free reagent and methanol (as the solvent) were used for this analysis.

A batch of 100 tablets was compressed under 10 kN force by a single-punch tablet press fitted with 8-mm concave punch. The average weight of the tablet containing 500 mg acetaminophen was 600 ± 1 mg.

Direct compression

Acetaminophen, the hemicellulosic material, lactose and magnesium stearate were weighed according to the bill of materials for a batch of 100 tablets mixed and homogenized using mortar and pestle and passed through 20 mesh sieves (Table 2). The

Table 1
Elemental analysis and yield (%) of the hemicelluloses. The data represent mean values (n = 5) ± standard deviation.

Material	Yield (%)	Moisture (%)	Molar mass	Monosaccharide content						Elemental analysis		
				(% of total monosaccharides on anhydrous basis)						(% anhydrous)		
				Ara	Gal	Glc	Xyl	Rh	Man	C	H	N
AN	18.5 ± 0.020	7.36 ± 0.01	5.05 × 10 ⁵	74.17 ± 0.13	25.83 ± 0.17	ND	ND	ND	ND	38.78 ± 0.025	5.82 ± 0.005	0.35 ± 0.02
LR	4 ± 0.005	13.67 ± 0.04	3.5 × 10 ⁶	29.44 ± 0.31	1.41 ± 0.02	ND	ND	69.74 ± 0.51	ND	41.98 ± 0.04	6.08 ± 0.01	ND
POH	5.5 ± 0.01	6.78 ± 0.01	3.26 × 10 ⁶	23.40 ± 0.13	ND	ND	76.91 ± 0.46	ND	ND	34.43 ± 0.01	5.08 ± 0.06	ND
OB	4.2 ± 0.005	16.96 ± 0.02	4.9 × 10 ⁶	23.11 ± 0.71	ND	ND	76.89 ± 0.02	ND	ND	34.90 ± 0.025	5.42 ± 0.015	0.56 ± 0.01
SP	7.8 ± 0.03	3.41 ± 0.01	2.47 × 10 ⁶	ND	ND	ND	100 ± 0.01	ND	ND	28.4 ± 0.03	4.34 ± 0.01	0.96 ± 0.02
AT	7 ± 0.015	16.17 ± 0.01	1.61 × 10 ⁶	55 ± 1.2	6 ± 0.98	6 ± 0.72	33 ± 0.05	ND	ND	32.21 ± 0.015	5.09 ± 0.005	0.39 ± 0.005
POS	3.8 ± 0.01	10.37 ± 0.05	3.26 × 10 ⁶	21.90 ± 0.04	ND	ND	78.10 ± 0.01	ND	ND	37.90 ± 0.01	5.49 ± 0.005	0.43 ± 0.025
MP	5.1 ± 0.015	5.04 ± 0.03	2.3 × 10 ⁶	ND	ND	30.28 ± 0.41	69.13 ± 0.55	ND	ND	29.83 ± 0.05	4.63 ± 0.022	ND
AM	15 ± 0.01	7.12 ± 0.005	1.26 × 10 ⁶	68.09 ± 0.12	30.11 ± 0.31	ND	ND	1.79 ± 0.081	ND	40.76 ± 0.025	6.21 ± 0.01	0.21 ± 0.03
CO	12 ± 0.12	8.4 ± 0.043	ND	0.23 ± 0.05	3.5 ± 0.132	44.5 ± 0.01	10.06 ± 0.34	ND	0.8 ± 0.12	35.128 ± 0.017	5.388 ± 0.027	ND

Ara: Arabinose, Gal: Galactose, Glc: Glucose, Xyl: Xylose, Rh: Rhamnose, Man: mannose, ND: Not detected.

tablets were compressed under 100 kN force by a single-punch tablet press fitted with 8-mm concave punch. The average weight of the tablet containing 500 mg acetaminophen was 600 ± 1mg.

Post-compression evaluation of tablets

Post-compression parameters of the tablets including hardness, friability, weight variation, disintegration time and dissolution behavior were determined. The hardness was determined by using 20 tablets by a hardness tester (YPD-300D, Shanghai Huanghai Medicine and Drug Testing Instrument, China). The friability was determined as the percentage weight loss of 20 tablets after 100 revolutions in a friability tester (PTF-10E, Pharmatest friability tester, Germany). For disintegration testing (Model # 121-P) Galvano Scientific, Pakistan instrument was used.

For disintegration studies six tablets were allowed to disperse in water (1000 mL) on stirring at $37 \pm 2^\circ\text{C}$ and disintegration time was recorded when none of the tablet material was left in the mesh.

Assay of acetaminophen

Twenty tablets were accurately weight and powdered using a pestle and mortar. A weighed portion of acetaminophen (500 mg) was used for the spectrophotometric assay according to USP (USP30-NF25) The method was linear between $5\text{--}25\text{ }\mu\text{g mL}^{-1}$ ($r^2 = 0.9998$).

All the above measurements were three or six replicates and the average $\pm$ SD values

Table 2
Bill of materials for a batch of 500-mg acetaminophen tablets. The quantities are in grams.

Wet granulation					Direct compression				
Formulation code	Binder (Hemi Celluloses)	API (Aceto Aminophen)	Diluent/ Disintegrant (lactose)	Lubricant (magnesium stearate)	Formulation Code	Binder (Hemi Celluloses)	API (Aceto Aminophen)	Diluent/ Disintegrant (lactose)	Lub
F-1 (AN)	4	50	5.075	0.925	F-11 (AN)	10	50	4.17	0.83
F-2 (LR)	2.75	50	6.38	0.87	F-12 (LR)	10	50	4.17	0.83
F-3 (POH)	3.4	50	5.70	0.875	F-13 (POH)	10	50	4.17	0.83
F-4 (OB)	2.5	50	6.5	1.0	F-14 (OB)	10	50	4.17	0.83
F-5 (SP)	2.25	50	6.7	1.05	F-15 (SP)	10	50	4.17	0.83
F-6 (AT)	3.75	50	6.145	1.05	F-16 (AT)	10	50	4.17	0.83
F-7 (POS)	2.25	50	6.7	1.05	F-17 (POS)	10	50	4.17	0.83
F-8 (MP)	3.75	50	6.145	1.05	F-18 (MP)	10	50	4.17	0.83
F-9 (AM)	5	50	4.17	0.825	F-19 (AM)	10	50	4.17	0.83
F-10 (CO)	3.5	50	5.45	1.05	F-20 (CO)	10	50	4.17	0.83

were reported.

In vitro dissolution study

The dissolution study was carried out using USP paddle dissolution apparatus (curio DL-0708) with six tablets and phosphate buffer (pH 6.8) as dissolution medium according to USP (USP30-NF25) over a period of 7 hrs. The dissolved sample (5 mL) was drawn at 5, 10, 15, 20, 25, 30, 60, 120, 180, 240, 300, 360 and 420 min for spectrophotometric assay at 243 nm as described above (section 2.3.3). Cumulative percentage of drug released was calculated and the mean of six tablets was used for further data analysis.

Kinetic models

The drug release data was fitted into various kinetic models including zero order (Eq. 1(Möckel & Lippold, 1993), first order (Eq. 2 (Gibaldi & Feldman, 1967), Higuchi equation (Eq. 3 (Higuchi, 1961)), Hixson–Crowell cube root law (Eq. 4, (Hixson & Crowell, 1931)) and Korsmeyer-Peppas model also known as Power law (Eq. 5 (Korsmeyer et al., 1983)).

$$M = k_0 t \quad (1)$$

where k_0 is the zero-order release constant and M is the amount of acetaminophen released in time t .

$$\ln M = -k_1 t + \ln M_0 \quad (2)$$

where k_1 is the first-order release constant, M is the remaining amount of acetaminophen in the sample after time t and M_0 is the initial amount of acetaminophen in tablet.

$$M = k_H t^{1/2} \quad (3)$$

where M is the amount of acetaminophen released in time t , and k_H is the Higuchi-release constant.

$$M_0^{1/3} - M^{1/3} = -k_{HC} t \quad (4)$$

where M is the amount of acetaminophen released in time t , k_{HC} is the Hixson–Crowell release constant and M_0 is the initial amount of amount of acetaminophen in tablet.

$$\ln M/M_0 = k_k \ln t \quad (5)$$

where k_k is the Korsmeyer-Papaas release constant, M is the amount of acetaminophen remaining in tablet after time t and M_0 is the initial amount of acetaminophen.

Results And Discussion

Characterization of hemicelluloses

Monosaccharide composition and elemental analysis of the hemicelluloses used in this work are given in Table 1. The percentages of C (28.4–40.76%) and H (4.34–6.218%) on dry-substance (anhydrous) basis resembled those of the standards (Hakala et al., 2014). The moisture content ranged from 3.41–16.96 % (Table 1), which as used for calculations on dry-substance basis and explaining the mechanical properties of the materials. The highest moisture content was observed in *OB* and the lowest in *SP*. The variation in water holding capacity may be due to structural variations in the hemicelluloses.

FT-IR analysis

The characteristic bands of hemicelluloses along with their assignment are listed in Table 3. The bands in the regions $668 - 600 \text{ cm}^{-1}$ and 500 cm^{-1} due to variation in polymer backbone were observed. The region between $1200 - 800 \text{ cm}^{-1}$ provided information about glycosidic linkages and alcoholic groups (Barron & Rouau, 2008). All these analyses established the identity of the hemicellulosic materials used in this work.

Pre-compression evaluation of powders

Pre-compression evaluation of the wet granulated formulations was carried out by measuring flowability including angle of repose, bulk and tapped density, CI and HR ratio.

The knowledge of flow properties of the pharmaceutical powders is crucial in production processes including mixing, granulation, compression and filling. A good flow facilitates uniform fill weight and avoids problems encountered during tablet compression. The results of these tests for formulations prepared through wet granulations by use of hemicelluloses under investigation are given in Table 4. The angle of repose was found to be in the range $21.34 \pm 0.010 - 36.23 \pm 0.020$. A value of $< 30^\circ$ indicates 'excellent' flow, while the values in $31 - 35^\circ$ range indicates good flow properties (Shah et al., 2008b). In this work, the formulations F-1, F-6 and F-7 had excellent flow whereas the formulations F-2, F-3, F-4, F-5 and F-9 exhibited good flow property. The difference in flow is because of structural variation of the hemicelluloses. Hemicelluloses from *AN*, *AT* and *POS* used in F1, F6 and F7 appear to have compact structures due to extensive hydrogen bonding (Massey et al., 2017).

Bulk and tapped density of the materials were measured and the results are presented in Table 4. The materials with poor flow behavior, have large difference in the bulk and

tapped densities. The CI and HR were calculated by use of data obtained during bulk density and tapped density test. The CI (%) are in the range of 5.26–17.94 (Table 4). CI values are considered as > 25 (poor), $16 - 20$ (fair), $< 15 - 11$ (good) and < 10 (excellent) flow properties (Carr, 1965; Hausner, 1967).

Based on the results, F-7, F-8, F-9 & F-10 formulations with $CI < 10$, can be considered as to excellent flowability. Lower HR values indicate better flow properties. HR values < 1.11 (excellent), $1.12 - 1.18$ (good), $1.19 - 1.25$ (fair) whereas > 1.60 (very poor) flow. (Carr, 1965; Hausner, 1967). HR values of all the formulations were < 1.11 in the range of $0.84 - 0.95$ so their flow can be considered as excellent.

Post compression evaluation

Post-compression parameters including hardness, friability, weight variation, disintegration time were determined from a sample of 20 tablets. Six batches of all the formulations were prepared and subject to release study. All the batches under investigation exhibited good hardness within limits between $3 - 7 \text{ kg cm}^{-2}$ (Table 5). This demonstrates that the hemicellulosic materials provide good substitute for synthetic binders in tablet manufacturing. Tablets prepared by both WG and DC exhibited weight variation ($8 - 10\% \text{ w/w}$) and friability values ($0.11 - 1.18 \text{ w/w}$), within the limits of USP (USP 30-NF 25).

Disintegration time of hemicelluloses formed by WG method ranged from 13 to 32 min whereas tablets formed by DC method ranged from 1.18 ± 0.012 to 12.56 ± 0.041 .

Table 3
Observed FTIR bands (cm⁻¹) in hemicelluloses and their assignments

Material	$\nu(\text{O-H})$	$\nu(\text{C-H})$ Aliphatic	HOH Deformation	$\delta(\text{O-H})$ Inplane	$\delta(\text{CH}_2)$	$\delta(\text{CH})$	δ_{Asym} bridged oxygen	$\nu(\text{C-O-C})$	$\nu(\text{C-C})$ arabinosyl side chain	δ_{Asym} (out-of) β -glycosidic
AN	3410	2932	1626	1460	1421	1377	1253		1037	850
LR	3384	2923	1648		1421	1377	1244	1153	1035, 1059	896
POH	3400	2926	1650	1460	1420	1377	1250	1150	1000	890
OB	3368	2920	1638	1460	1422	1376		1153	1057	910
SP	3432	2929	1618		1421	1350	1250	1074	1042	891
AT	3368	2920	1638	1460	1422	1376		1153	1057	910
POS	3463	2926	1655	1462					1043	880,
MP	3359	2920	1605		1420	1377	1246		1047	896
AM	3422	2936	1620	1460	1421	1377	1250		1037	850
CO	3400	2920		1414	1246				1034	860

Table 4
Pre-compression test results of formulations prepared by wet granulation methods

Formulations	Angle of repose (θ)	Flow rate (g/s)	Bulk density (%)	Tap density (%)	Car's index (CI) (%)	Hausner's ratio (HR)
F-1	24.99 $\pm$ 0.010	1.25 $\pm$ 0.010	43.5 $\pm$ 0.010	39 $\pm$ 0.010	11.53 $\pm$ 0.015	0.89 $\pm$ 0.005
F-2	32.85 $\pm$ 0.020	15.48 $\pm$ 0.015	38 $\pm$ 0.005	33 $\pm$ 0.020	15.15 $\pm$ 0.015	0.86 $\pm$ 0.010
F-3	36.23 $\pm$ 0.020	6.71 $\pm$ 0.015	43 $\pm$ 0.025	38 $\pm$ 0.005	13.15 $\pm$ 0.015	0.88 $\pm$ 0.010
F-4	34.42 $\pm$ 0.015	5.14 $\pm$ 0.010	46 $\pm$ 0.015	39 $\pm$ 0.025	17.94 $\pm$ 0.005	0.84 $\pm$ 0.050
F-5	31.29 $\pm$ 0.005	0.86 $\pm$ 0.015	41 $\pm$ 0.005	36 $\pm$ 0.025	13.88 $\pm$ 0.005	0.87 $\pm$ 0.020
F-6	22.68 $\pm$ 0.020	0.73 $\pm$ 0.010	38.5 $\pm$ 0.005	35 $\pm$ 0.005	10.0 $\pm$ 0.010	0.90 $\pm$ 0.005
F-7	21.34 $\pm$ 0.010	13.22 $\pm$ 0.020	45 $\pm$ 0.035	43 $\pm$ 0.040	5.26 $\pm$ 0.015	0.95 $\pm$ 0.010
F-8	32 $\pm$ 0.011	0.12 $\pm$ 0.021	66 $\pm$ 0.024	60 $\pm$ 0.013	10 $\pm$ 0.012	0.909 $\pm$ 0.01
F-9	35.56 $\pm$ 0.010	4.05 $\pm$ 0.015	38 $\pm$ 0.030	35.5 $\pm$ 0.005	7.04 $\pm$ 0.020	0.93 $\pm$ 0.010
F-10	49.23 $\pm$ 0.025	2.24 $\pm$ 0.025	40 $\pm$ 0.100	38 $\pm$ 0.015	5.26 $\pm$ 0.015	0.95 $\pm$ 0.010

Hemicellulose tablets formed by WG method and AN, OB, AT and CO tablets prepared by DC did not fulfilled the official (IP) disintegration test of uncoated tablets. Whereas, tablets formulated by LR, POH, SP, MP and AM using DC methods disintegrated within 5 min, although their disintegration time varied from 1.18 $\pm$ 0.012 to 4.25 $\pm$ 0.021 min. Disintegration of POS and OB is 5.15 $\pm$ 0.014 and 5.22 $\pm$ 0.012 (USP30-NF25).

Dissolution studies

The dissolution profiles of WG tablets are depicted in Fig. 1. It was observed that the tablets prepared by WG (F-1 to F-10) showed a slower drug release (Table 6) than those

prepared by DC (F-11 to F-20). About 60% drug was released from DC tablets in first hour of dissolution study whereas only ~ 30% drug was released in WG tablets with the

same hemicellulose clearly highlighting the effectiveness of method of preparation. It was

observed that the release rate significantly depends upon the preparation methods and less likely by the type of hemicellulose. The release study highlights that the hemicelluloses also show a sustained release of the drug in addition acting as the binders.

The tablets prepared by DC method showed an initial burst release indicating the low

binding power of hemicelluloses in them (Missaghi & Fassihi, 2005). The F13, F15 and F16 showed only sustained release profile irrespective of the method of preparation which can be attributed to chemical features of the hemicellulose composition i.e., higher ratio of xylose. The initial burst can be beneficial, as most of the drugs need to be administered at varying rates, and for some drugs, an initial burst can provide immediate relief followed

by extended release to promote gradual healing(JB et al., 1998).

Drug release was the fastest in F-1 by DC method and the slowest in F-7 prepared by WG. 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 small pore size in the polymer can hold lower water due to capillary force, thus reducing water permeation inside the polymeric matrix and ultimately decreasing the drug diffusion through the polymer and gradual decrease in tablet size during dissolution process which indicates slow erosion and diffusion mechanisms for sustained release (Szymkiewicz, 2013).

Table 5
Post-compression test results of formulations prepared by direct compression and wet granulation methods

Formulation	Hardness (kg/cm ²)	Friability (%)	Weight variation (mg) %	Disintegration (min)	F	Hardness (kg/cm ²)	Friability (%)	Weight variation (mg) %	Disintegration (min)
F-1	6 ± 0.010	0.11 ± 0.005	9 ± 0.023	19 ± 0.041	F-11	2 ± 0.025	0.6 ± 0.021	10 ± 0.011	12.56 ± 0.041
F-2	6 ± 0.021	0.20 ± 0.015	10 ± 0.031	17 ± 0.012	F-12	4 ± 0.041	1.22 ± 0.031	10 ± 0.041	4.25 ± 0.021
F-3	6 ± 0.011	0.19 ± 0.015	10 ± 0.022	15 ± 0.024	F-13	3 ± 0.031	0.89 ± 0.036	9 ± 0.031	1.44 ± 0.043
F-4	7 ± 0.010	1.18 ± 0.024	10 ± 0.019	24 ± 0.012	F-14	3 ± 0.041	0.74 ± 0.041	10 ± 0.021	5.22 ± 0.012
F-5	4 ± 0.034	1.18 ± 0.020	8 ± 0.013	22 ± 0.035	F-15	2 ± 0.031	0.88 ± 0.021	10 ± 0.031	1.48 ± 0.014
F-6	4 ± 0.030	1.18 ± 0.010	11 ± 0.023	21 ± 0.024	F-16	2 ± 0.027	1.31 ± 0.022	8 ± 0.041	17.49 ± 0.011
F-7	3 ± 0.024	0.19 ± 0.010	12 ± 0.024	13 ± 0.016	F-17	3 ± 0.132	1.17 ± 0.025	7 ± 0.012	5.15 ± 0.014
F-8	5 ± 0.0211	0.18 ± 0.11	11 ± 0.017	18 ± 0.015	F-18	3 ± 0.031	0.11 ± 0.021	9 ± 0.11	1.18 ± 0.012
F-9	6 ± 0.020	1.12 ± 0.005	12 ± 0.02	25 ± 0.021	F-19	3 ± 0.041	0.75 ± 0.021	13 ± 0.012	6.49 ± 0.031
F-10	4 ± 0.012	0.21 ± 0.023	10 ± 0.013	32 ± 0.031	F-20	2 ± 0.021	0.81 ± 0.031	9 ± 0.12	12.16 ± 0.034

Kinetic models

The release profiles of the drug from the polymeric structure depends on several factors such as diffusion, drug dissolution, water permeation, polymer swelling and matrix erosion.

In order to determine the mechanism of drug release from the matrix tablets, the release data were fitted to different models including zero order, first order, Higuchi, Korsmeyer-Peppas and Hixon-Crowell equations. The values of model selection criteria (MSC) determine the best fitted model. The kinetic data are given in Table 6. In most of the dry compression formulations, Korsemeyer-Peppas model (Power law) was the best fit model whereas in wet granulation formulations, Higuchi model and first order were the best fit release models. As far as release mechanisms determined by Korsmeyer-Peppas model (Power law) is concerned, F1, F3, F5, F6, F7, F8, F9 and F10 (wet granulation) and F12, F13, F15, F16, F19 and F20 (dry compression) formulations were found to follow non-Fickian mechanism i. e., diffusion and swelling controlled. However, F2 and F4 (wet granulation) and F11, F14, F17 and F18 (dry compression) formulations followed Fickian mechanism, i. e., diffusion controlled. Only F16 (dry compression formulation) followed super case-II mechanism which means release of the drug from a polymeric matrix was due to diffusion, swelling and erosion. The suggested mechanism was based on the n value according to the criteria: 0.45 (Fickian), 0.45 < n < 0.89 (non-Fickian) and n > 0.89 (super case-II) (Brazel & Peppas, 2000; Markl & Zeitler, 2017).

Conclusions

This study evaluated various hemicelluloses isolated from some food materials as binders and extended-release excipients in the manufacture of pharmaceutical tablets. The tablets prepared by wet granulation method exhibited better release profile than those prepared by direct granulation method. An extended cumulative release of 45–92% was obtained for 7

Table 6
Fitness of release data into different kinetic models

Formulation	Wet Granulation							Formulation	Dry Compression						
		Zero order	First order	Higuchi	Hixson-Crowell	Power law	n			Zero order	First order	Higuchi	Hixson-Crowell	Power law	n
F1	R ²	0.802	0.608	0.929	0.683	0.931	0.458	F11	R ²	0.854	0.432	0.554	0.373	0.806	0.447
	MSC	1.218	0.537	2.246	0.749	2.268			MSC	1.355	0.006	0.236	0.104	1.066	
F2	R ²	0.941	0.972	0.992	0.8375	0.982	0.447	F12	R ²	0.931	0.963	0.990	0.371	0.983	0.580
	MSC	2.430	8.362	4.399	1.417	2.686			MSC	2.107	6.073	4.013	1.246	3.486	
F3	R ²	0.955	0.988	0.996	0.846	0.984	0.536	F13	R ²	0.502	0.551	0.669	0.438	0.767	0.494
	MSC	2.707	3.986	5.146	1.468	2.113			MSC	0.125	2.009	0.533	0.005	0.884	
F4	R ²	0.914	0.972	0.980	0.788	0.955	0.446	F14	R ²	0.130	0.402	0.232	0.133	0.854	0.448
	MSC	2.054	3.163	3.500	1.149	0.632			MSC	0.432	0.058	0.308	0.429	1.368	
F5	R ²	0.914	0.953	0.976	0.777	0.952	0.523	F15	R ²	0.986	0.951	0.983	0.996	0.986	0.783
	MSC	0.108	7.645	0.264	1.102	2.377			MSC	4.671	2.433	1.222	4.998	4.428	
F6	R ²	0.686	0.781	0.848	0.596	0.895	0.481	F16	R ²	0.843	0.896	0.948	0.696	0.913	0.971
	MSC	0.759	1.117	1.484	0.507	0.090			MSC	1.282	1.691	2.389	0.619	2.364	
F7	R ²	0.970	0.971	0.985	0.803	0.971	0.466	F17	R ²	0.488	0.530	0.657	0.438	0.759	0.450
	MSC	3.137	0.452	0.305	1.224	0.644			MSC	0.098	0.330	0.231	0.004	0.776	
F8	R ²	0.956	0.888	0.669	0.978	0.7606	0.540	F18	R ²	0.482	0.510	0.652	0.437	0.763	0.453
	MSC	1.696	1.790	0.303	0.965	0.368			MSC	0.085	0.983	0.267	1.660	0.902	
F9	R ²	0.647	0.703	0.813	0.552	0.863	0.546	F19	R ²	0.441	0.476	0.607	0.419	0.848	0.508
	MSC	0.107	0.814	0.749	0.395	0.735			MSC	0.010	0.812	0.392	0.029	1.313	
F10	R ²	0.964	0.983	0.987	0.856	0.982	0.536	F20	R ²	0.374	0.406	0.527	0.348	0.596	0.596
	MSC	1.496	7.951	0.483	0.457	2.842			MSC	0.102	0.894	0.400	1.777	0.785	

h from wet granulated acetaminophen tablets. The results showed that these materials have the potential to replace synthetic or cellulose-based excipients, such as CMC and HPMC. Hemicelluloses would be a preferred option as they are more biocompatible, biodegradable, digestible by humans and cost effective.

Declarations

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Author Contributions

I.W. performed all experimentation, S.M. supervised and performed experimentation and write-up and analysed all data. F.I. write-up and editing. M.S.I. supervised and conceptualized the work and validated the data. A.H.K. editing. N.A. supervised and validated the data.

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Conflicts of Interest

The authors declare that no conflict of interest exists in the context of this study.

Data Availability

Not applicable

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Figures

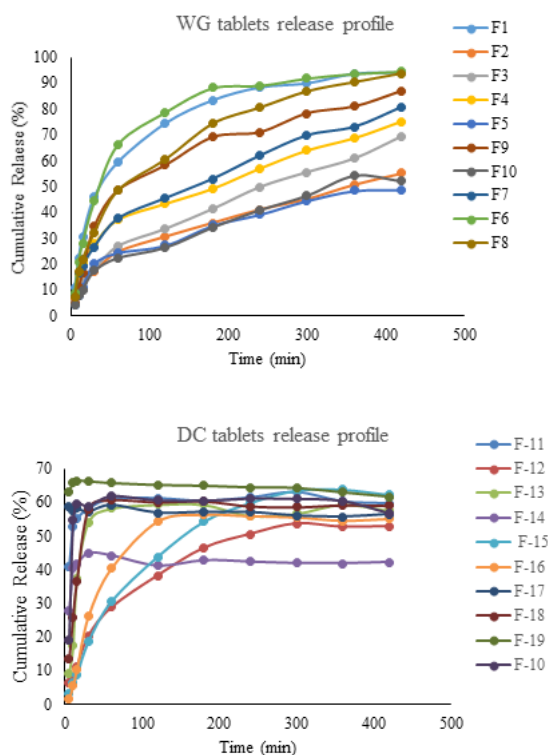


Figure 1

Drug release profiles showing cumulative drug release as a function of time