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Exploring the potential of natural polymers from plants as tablet binder and accessing their release profiles: A comparative analysis

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Abstract: A tablet is a compact dosage form that includes both the active pharmaceutical ingredient (API) and various excipients, where a binder acts as an excipient, imparting cohesive quality in the powdered material. The present study aimed to extract polysaccharides from plant samples; *Plantago ovata* seeds, *Plantago ovata* husk, *Lallemantia royleana*, *Ocimum basilicum* and *Acacia nilotica* and to investigate their efficacy as tablet excipients. The wet granulation method was adopted for tablet formulation. Three different formulations (3%, 5% and 7%) were prepared by varying the binder concentration (hemicellulose extracted from plant samples). The tablets were evaluated by pre-compression tests; Angle of repose, bulk density, tapped density, Carr's Index, Hausner's ratio and post-compression tests; weight variation test, friability test, disintegration test, thickness test and dissolution test. Results were compared with binder commercially used in paracetamol drug. All 5% and 7% formulations showed friability and hardness values within range. Results of all the formulations of disintegration time are within range except 7% *Plantago ovata* seeds and 7% *Plantago ovata* husk. All the extracted hemicellulose showed good binding potential but, in all respects, the best formulation was 7% *Lallemantia royleana*, which has the potential to replace the synthetic binders in the pharmaceutical industry.

Keywords: Hemicellulose, Polysaccharides, binder, cumulative release**,** paracetamol.

INTRODUCTION

Excipients including binders, thickeners, sweeteners and glidants have the potential to alter the physicochemical characteristics of the drug's ultimate formulation and modify the pharmacodynamic and pharmacokinetic qualities correspondingly (Mishra *et al*., 2021). Binder is an important component of tablet formulation. It is used for binding inactive ingredients (other excipients) and active pharmaceutical ingredients (API) with each other in a cohesive manner. Binders are incorporated into the tablet formulation to provide plasticity and enhance the strength of inter-particulate bonding (Patel *et al*., 2012). Correspondingly, binding agents in tablet formulations results in attaining specific tablet mechanical strength and drug release characteristics (Debnath *et al*., 2019). Polymers are employed as excipients to enhance the development of polymer-based drug delivery systems aimed at precise drug targeting and distribution (Ulbrich *et al*., 2016; Yazdi *et al*., 2020). Polymers come in three primary categories: natural polymers, along with semi-synthetic and synthetic polymers (Kandar *et al*., 2021). Now-a-days commonly used binders are synthetic in nature such as polyethylene glycol (PEG), hydroxypropyl methyl cellulose (HPMC), methylcellulose, ethyl cellulose, polyvinylpyrrolidone K-30 (PVP-K30) and polyvinyl chloride (PVC) and are known for their remarkable physical, chemical, and mechanical stability. However, it is important to note that synthetic polymers can have toxic effects on cells and may not be compatible with living organisms (Nair *et al*., 2012). Synthetic polymers come with drawbacks, including limited compatibility with the patient's body, elevated expenses, and the potential to induce acute and chronic side effects. For instance, during subcutaneous injection, povidone can accumulate at the injection site, leading to the formation of granulomas. Furthermore, animal studies have indicated that oral consumption of carbomer-934P is toxic and the resulting dust has triggered allergic reactions. In tissue engineering, synthetic polymers have certain drawbacks such as low biocompatibility, the release of acidic compounds, as well as a rapid decline in mechanical strength (Deaogade *et al*., 2012). The utilization of natural polysaccharides (Darroudi *et al*., 2020; Shamasi *et al*., 2020l; Hashemzadeh *et al*., 2021) extracted from plants as excipients has been increased because they help to address formulation issues and lessen the negative effects of synthetic polymers. Natural binders have the advantage of being utilized to alter drug release (Debotton & Dahan, 2017), which affects how well the integrated pharmaceuticals are absorbed and bioavailable. Owing to their minimal toxicity, biodegradability, ready availability and cost-effectiveness, natural binders find extensive use in the pharmaceutical and food sectors as excipients and additives. They are also employed to ensure the overall stability of the drug, the precision of dosage and, if needed, enhance the organoleptic properties of the drugs to enhance patient compliance (Kumar *et al*., 2011; Rahim *et al*., 2014). Polymers extracted from plants, animals and microorganisms are called biopolymers. Cellulose is the most abundant biopolymer among plants and hemicellulose is second to cellulose in abundance. Polysaccharides from hemicelluloses being

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biodegradable are widely used in different industries especially in pharmaceutical industry. The human body decompose them into different products by hemicellulolytic enzymes (Qi *et al*., 2016; Dekker, 1985). Natural binders, including diverse starches, gums, mucilages and desiccated fruits, possess binding properties along with additional functions like acting as fillers and disintegrants. Moreover, natural polymers are considered safer and more economical than their synthetic counterparts. The present investigation was aimed to explore the binding capacity of polysaccharides extracted from different plant sources with the purpose of replacing the synthetic binders with natural ones as binder in tablet formulation.

MATERIALS AND METHODS

Chemicals and reagents

The chemicals used were paracetamol (API) (Sigma-Aldrich, CAS No. 103-90-2), microcrystalline cellulose (Sigma-Aldrich, CAS No. 9004-34-6), stearic acid (Sigma-Aldrich, CAS No. 57-11-4), sodium starch glycolate (primojel) (Sigma-Aldrich, CAS No. 9063-81-1), aerosol (Sigma-Aldrich, CAS No. 112945-52-5), magnesium stearate (Sigma-Aldrich, CAS No. 557-04-0), talc (Sigma-Aldrich, CAS No. 14807-96-6), glycerol (Sigma-Aldrich, CAS No. 56-81-5). All these chemicals are of analytical grade.

Plant material

Plantago ovata seeds (*POS*), *Lallemantia royleana seeds* (*LR*), *Ocimum basilicum seeds* (*OB*), *Plantago ovata* husk (*POH*) and *Acacia nilotica* gum (*AN*) were purchased from the local market of Lahore. *Plantago ovata PO:* The botanical classification is kingdom: Plantae; division: Magnoliophyta; class: Magnoliopsida; order: Lamiales; Family: Plantaginacea; genus: *Plantago*; species: *ovata*. (https://plants.usda.gov/home/classification/47410.).

Lallemantia royleana: LR Its botanical classification is kingdom: Plantae; division: Angiospermae; class: Eudicots; order: Lamiales; family: Lamiaceae; genus: *Lallemantia*; species: *royleana*. The Labiatae family (Lamiaceae) is one of the largest family of flowering plants, with almost 4000 species and about 220 genera existing worldwide (https://npgsweb.ars-grin.gov/gringlobal/taxon/taxonomydetail?id=21415).

Ocimum basilicum OB: Its botanical classification is: kingdom: Plantae; division: Magnoliophyta; class: Magnoliopsida; order: Lamiales; family: Labiatae; genus: *Ocimum*; species: *bacilicum* (https://florida.plantatlas.usf.edu/plant.aspx?id=1787). *Acacia nilotica: AN* Its botanical classification is: kingdom: Plantae; division: Angiosperms; class: Magnoliopsida; order: Fabales; family: Fabaceae; genus: *Acacia*; species: *nilotica* (Aslam *et al*, 2014). Plant materials (seeds and gum) were purchased on Feb 3, 2022 and used on Feb 4, 2022 to March 27, 2022 for extraction of mucilage from seeds and to purify the gum. Further studies were performed on the purified extracted freeze-dried material.

Isolation of hemicellulose from plant material

The polysaccharides from *POS, LR, OB, AN* and *POH*, were isolated by use of reported methods (Massey *et al*., 2016).

Characterization of polysaccharides

Mucilage from *POS, LR, OB, AN* and *POH* was characterized by Elemental analysis using CHNS analyzer (630-200 LECO, USA). Moisture content was determined by using KF Titrator (Mettler Toledo, USA). FTIR analyses were conducted on dehydrated hemicellulose powders using the CARY630FT-98 IR spectrophotometer from Agilent Technologies in the USA. The samples were positioned on the ATR assembly and FT-IR spectra were recorded in the range of 4000-650cm^{-1}, averaging 50 scans per sample (Smith, 2011).

Thermal analysis

Thermal analysis involved thermogravimetric analysis conducted from room temperature to 600°C using the SDT (Q600) thermal analyzer by TA Instruments in the TGA and DSC modes, with a heating rate of 10°C per minute and performed under a nitrogen atmosphere.

Swelling index

0.10 grams of the polymer were immersed in 10mL of distilled water and the wet weight of the swollen material (Wt) was measured at five-minute intervals during the initial hour and subsequently, at hourly intervals until a constant weight was achieved. Wo is the initial weight. The formula was used to compute the swelling index (Massey *et al*., 2022; Lv *et al*., 2019)

$$Swelling Index(\%) = \left[\frac{W_t - W_0}{W_0}\right] \times 100$$

Water retention

Water retention of the polymers was assessed using the centrifugation method as described by (Massey *et al*. 2016; Saghir *et al*. 2008). A precisely measured sample (ranging from 0.01 to 0.3 grams) was placed in a petri dish and soaked in approximately 10mL of water at 30°C for two hours (or 30 minutes for gums). To eliminate excess water, the swollen material was centrifuged at 4000 rpm for 15 minutes. The damp samples were subsequently dried to a constant weight in a hot-air oven maintained at 105±2°C. The water retention was computed using the following formula:

$$Water\ \mathrm{Re}tention(\%) = \left[\frac{W_w - W_d}{W_d}\right] \times 100$$

Where, W_w = weight of sample in wet state, W_d = weight of sample after drying at 105°C.

Method of granule formulation

Wet granulation method for the preparation of paracetamol tablets and the binder used was 3%, 5% and 7% mucilage in different formulations. Paracetamol, talc and microcrystalline cellulose were mixed for 20 minutes in mortal and pestle by the addition of binder solution drop wise and then passed through the granulator (screening mesh #40). These granules were then dried at 40^0C for 90 minutes. Dried granules were re-screened from mesh # 18 and converted into fine granules. After that aerosil, primojel and stearic acid were added and were geometrically mixed using a zip lock bag. At the end magnesium stearate was added. Negative and positive control was prepared for comparison purpose. Negative control formulation contained paracetamol and other excipients excluding binder. Positive control was prepared by using commercial binder. These natural binder formulations were evaluated and compared with the commercial binder formulation.

Preparation of tablets

The granules made according to the above formulations were compressed into tablets using 250mg caplet punch in a single punching tablet machine with specifications as follows: HT-TDP1.5; HENTO (China); Pressure: 15kN; Maximum tablet diameter; 12mm; Maximum tablet thickness;12mm: Filling depth: 6mm: Production capacity: 1500pcs/h.

Evaluation of tablets

Evaluation of tablets was based on pre-compression tests of tablet mixture and post-compression test of tablets.

Pre-compression tests

The purpose of pre-compression tests was to generate useful information about the flow ability and compressibility index of a mixture to develop a stable, safe and authentic dosage form with good bioavailability. Some important preformulation tests such as angle of repose (Geldart *et al*., 2006), bulk density, tap density (Shoaib *et al*., 2006) carr's index and hausner's ratio (Mcconville *et al*., 2013) were performed. Tapped density was determined using Erweka D-63150, Germany whereas to find the angle of repose, Copley scientific, UK instrument was used.

Post-compression tests

Weight variation

Twenty tablets were weighed one by one. The weight of each tablet was precisely noted. In milligram (mg) units, the results were presented as mean standard deviation (Remya *et al*., 2010).

Friability

Ten tablets are checked in a friability tester (Copley scientific, UK) for 4 minutes at 25 rpm. If the weight loss was below 1.0%, the tablet was deemed acceptable. Friability was determined using the following formula:

$$\text{Friability} = \frac{\text{wbefore - wafter}}{\text{wafter}} \times 100$$

Where W_{before} = weight of tablets before test (g), W_{after} = weight of tablets after test (g) (Bakar *et al*., 2019).

Thickness

Tablet thickness is determined using vernier caliper. Six tablets were evaluated from each formulation to determine the average thickness.

Hardness

The tablet hardness for each composition was assessed using a Monsanto hardness tester. By simply applying more force and observing the point of breaking, tablet hardness (or crushing strength) was ascertained. The tablet's hardness value was determined by measuring the maximum force necessary to break the tablet (Gabbott *et al*., 2016). The results were derived from the average values of six randomly selected tablets from the same formulation.

Disintegration time

Disintegration time was determined for six tablets from each formulation using a disintegration tester following the USP guidelines, with distilled water as the disintegration medium at 37°C. Each tablet's rate of disintegration was timed in minutes (Shirsand *et al*., 2009).

Dissolution studies

Dissolution studies were conducted on dissolution test apparatus (curio DL-0708), according to the standard USP method, using 50 rpm, 37ºC temperature and phosphate buffer of pH 6.8. 5mL solution from dissolution apparatus was taken after each specific time intervals i.e. (5, 10, 15, 30, 60, 120, 180, 240, 300, 360, 420, 480 and 1440 minutes) and measured by UV - Spectrophotometer (PG instrument, T80 Double Beam) at 273nm. Dissolution apparatus is filled with phosphate buffer solution in same amount each time.

STATISTICAL ANALYSIS

Minitab statistical software (Version 16.2.0.0) was used to perform statistical analysis to compare the effects of *LR*, *POS*, *POH*, *OB* and *AN* on the properties of paracetamol using one-way ANOVA with a Tukey's test. Differences were considered significant at $p<0.05$. Results were analysed and compared statistically with positive control.

RESULTS

The yields of the purified mucilage from *POS*, *LR*, *OB* were 32%, 28% and 25% whereas from *POH* and *AN* gum were approximately 54% and 98% respectively. In elemental analysis carbon and hydrogen percentages were similar to polysaccharides from plant hemicelluloses.

Table 2 lists the findings of the elemental analysis, moisture analysis, swelling index and water retention value of the polysaccharides extracted from hemicelluloses. The polymers' swelling indices ranged from 14.4% (*AN*) to 40.49% (*POH*) table 2. These materials are excellent options for the creation of delivery devices and controlled release tablets due to their strong swelling properties. The water content and pore size of these polymers can be used to regulate the drug's release. High water content and wide pores are necessary for quick medication release (Peppas *et al*., 2000). The water retention results (table 2) demonstrate that *POH* has the highest water-holding capacity, while for other materials, the water retention values fell within the range of 14.88% to 48.83%.

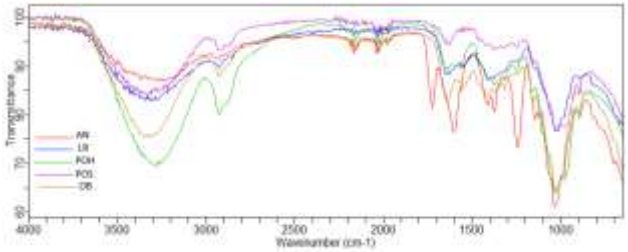

Fig. 1: FTIR Spectra of *POS*, *LR*, *OB*, *AN* and *POH*

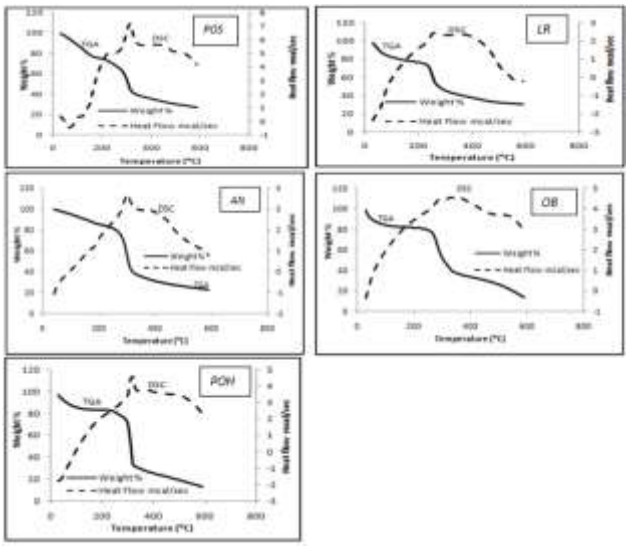

Fig. 2: TGA and DSC of *POS*, *LR*, *OB*, *AN* and *POH*

FT-IR Analysis

Our extracted polysaccharides functional groups were identified using Fourier transform infrared spectroscopy. Due to the OH stretching, these polymers exhibited a broad absorption peak in the range of 3565-3109cm^{-1}. Additional peaks were those for the saturated aldehydic unit at 2929cm^{-1}, the CO stretching of glucuronic acid at 1616cm^{-1}, the CH_2 band at 1417cm^{-1}, the CH stretching at 1373cm^{-1}, the glycosidic linkage (C-O-C) at 1244cm^{-1} and the links of sugars at 1015cm^{-1} and 840cm^{-1} (fig. 1). These common and significant peaks were seen in all of the extracted polysaccharides.

Thermal analysis

"TGA and DSC were used to examine the separated polysaccharides' thermal behavior between room temperature and 600ºC. According to several studies (Iqbal *et al*., 2011 b; Peng *et al*., 2010; Popescu *et al*., 2011; Yang *et al*., 2007), TGA of all the materials showed an endothermic weight loss of 10-15% in the 80-120ºC range. The main weight loss (35-0%) occurred between 200 and 375ºC (fig. 2) and was caused by the degradation of the structure of the polysaccharide. The DSC scan indicated that this step was connected to a significant exothermic enthalpy change (fig. 2).

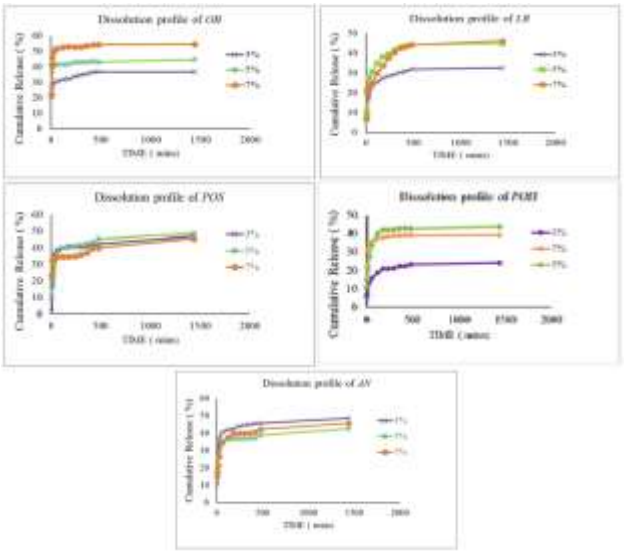

Fig. 3: Dissolution profile of *LR*, *POS*, *POH*, *OB* and *AN* as binder in tablets.

Evaluation of tablets

Pre-Compression Test

The results of the precompression tests of paracetamol granules produced with the various natural binders are shown in table 3. The angle of repose of the granules varied from 25.45±0.00525 for 7% *OB* granules to 36.59±0.010 for those made with 5% *POH* (P<0.05). With respect to angle of repose all the formulations possess values within good range. The 5% *LR*, 7% *LR*, 3% *OB*, 5% *OB*, 7% *OB*, 3% *AN* and +ve control showed the values within the excellent range of angle of repose shown in table 3.

The bulk (P<0.05) and tapped densities (P<0.05) of the granules are used to get Hausner's ratio. According to USP, all formulations have a Hausner's ratio between 1.07 and 1.10 (P>0.05) and a Carr's Index between 6.52 and 9.30 (P<0.05), all of which indicate outstanding flowability (P<0.05) according to table 1 (Goyal *et al*., 2015; Enauyatifard *et al*., 2012; Odunayo *et al*., 2021). The flow rate of the granules, which ranged from 4.81 g/s to 7.14 g/s, further supports the conclusion that granules from all formulations possessed good flow properties (Enauyatifard *et al*., 2012).

Table 1: USP standards according to Flow property (Bista, 2023)

Flow Property	Angle of Repose (%)	Hausner Ratio	Carr's Index
Excellent	25-30	1.00-1.11	≤10
Good	31-35	1.12-1.18	11-15
Fair	36-40	1.19-1.25	16-20
Passable	41-45	1.26-1.34	21-25
Poor	46-55	1.35-1.45	26-31
Very poor	56-65	1.46-1.59	32-37
Very, very poor	>66	>1.60	>38

Table 2: %Yield, elemental analysis, moisture analysis, swelling Index and water retention value of polysaccharides

Sample	Yield (%)	Carbon (%)	Hydrogen (%)	Nitrogen (%)	Moisture Analysis	Swelling Index (%)	WRV (%)
LR	28	33.006	5.060	-	11.96	16.5	29.50
POS	32	37.904	5.490	-	10.20	17.20	41.35
POH	54	38.877	5.127	-	8.24	40.49	48.83
OB	25	34.904	5.422	-	14.81	30.33	30.44
AN	98	39.208	6.252	-	4.77	14.4	14.88

Table 3: Results of pre-compression tests

Sample	Angle of repose	Tap density (g/mL)	Bulk density (g/mL)	Hausner's Ratio	Carr's index (%)	Flow rate (g/s)
3% *LR*	34.25 ± 0.010^{f}	0.35 ± 0.010^{f}	0.32 ± 0.005^{f}	1.09 ± 0.010^{a}	8.57 ± 0.005^{c}	04.68 ± 0.01^{g}
5% *LR*	30.07 ± 0.005^{l}	$0.38\pm0.010^{e,f}$	$0.35\pm0.020^{e,f}$	1.08 ± 0.010^{a}	7.89 ± 0.020^{f}	05.88 ± 0.28^{c}
7% *LR*	29.48 ± 0.010^{m}	$0.42\pm0.005^{c,d,e}$	$0.39\pm0.010^{b,c,d,e}$	1.08 ± 0.005^{a}	7.14 ± 0.010^{i}	$05.17 \pm 0.08^{d,e}$
3% *POS*	33.82 ± 0.025^{g}	$0.43\pm0.010^{b,c,d,e}$	$0.39\pm0.020^{b,c,d,e}$	1.10 ± 0.010^{a}	9.30 ± 0.020^{a}	$05.21 \pm 0.20^{d,e}$
5% *POS*	35.27 ± 0.010^{d}	$0.45\pm0.035^{a,b,c}$	$0.41\pm0.040^{a,b,c,d}$	1.10 ± 0.035^{a}	8.89 ± 0.040^{b}	$04.99 \pm 0.06^{e,f,g}$
7% *POS*	36.40 ± 0.025^{b}	$0.48\pm0.010^{a,b}$	$0.44\pm0.010^{a,b}$	1.09 ± 0.010^{a}	8.33 ± 0.010^{d}	04.25 ± 0.09^{h}
3% *POH*	36.29 ± 0.025^{c}	$0.39\pm0.005^{d,e,f}$	$0.36\pm0.010^{d,e,f}$	1.08 ± 0.005^{a}	7.69 ± 0.010^{g}	$04.81 \pm 0.05^{f,g}$
5% *POH*	36.59 ± 0.010^{a}	$0.45\pm0.040^{a,b,c}$	$0.41\pm0.040^{a,b,c,d}$	1.10 ± 0.040^{a}	8.89 ± 0.040^{b}	$05.08 \pm 0.04^{e,f}$
7% *POH*	34.37 ± 0.005^{e}	$0.44\pm0.020^{a,b,c,d}$	$0.41\pm0.020^{a,b,c,d}$	1.07 ± 0.020^{a}	6.82 ± 0.020^{j}	04.70 ± 0.20^{g}
3% *OB*	30.24 ± 0.005^{k}	$0.42\pm0.010^{c,d,e}$	$0.39\pm0.005^{b,c,d,e}$	1.08 ± 0.010^{a}	7.14 ± 0.005^{i}	07.04 ± 0.01^{b}
5% *OB*	26.61 ± 0.010^{o}	$0.44\pm0.015^{a,b,c,d}$	$0.41\pm0.025^{a,b,c,d}$	1.07 ± 0.015^{a}	6.82 ± 0.025^{j}	07.14 ± 0.02^{b}
7% *OB*	25.45 ± 0.005^{p}	0.49 ± 0.005^{a}	0.45 ± 0.020^{a}	1.09 ± 0.005^{a}	8.16 ± 0.020^{e}	06.10 ± 0.12^{c}
3% *AN*	33.54 ± 0.010^{h}	$0.41\pm0.010^{c,d,e}$	$0.38\pm0.010^{c,d,e}$	1.08 ± 0.010^{a}	7.32 ± 0.010^{h}	05.49 ± 0.15^{d}
5% *AN*	29.16 ± 0.020^{n}	$0.43\pm0.010^{b,c,d,e}$	$0.39\pm0.010^{b,c,d,e}$	1.10 ± 0.010^{a}	9.30 ± 0.010^{a}	06.19 ± 0.05^{c}
7% *AN*	33.46 ± 0.010^{i}	$0.46\pm0.020^{a,b,c}$	$0.43\pm0.005^{a,b,c}$	1.07 ± 0.020^{a}	6.52 ± 0.005^{k}	$04.92 \pm 0.03^{e,f,g}$
-ve control	36.90±0.005	0.38±0.010	0.35±0.010	1.09±0.010	7.89±0.010	05.84 ± 0.1
+ve control	32.07 ± 0.020^{j}	0.49 ± 0.005^{a}	0.46 ± 0.010^{a}	1.07 ± 0.005^{a}	6.12 ± 0.010^{l}	04.18 ± 0.04^{a}

Table 4: Results of post-compression tests

Sample	Hardness kg/cm^2) (n=3)	Friability (%)	Disintegration time (n = 6)	Weight variation (mg) (n = 5)	Thickness (mm) (n = 3)
3% *LR*	$3.99 \pm 0.42^{d,e,f}$	$1.53 \pm 0.01^{c,d}$	3.57 ± 0.02^{j}	254 ± 6.12^{a}	$4.56 \pm 0.18^{a,b,c}$
5% *LR*	$4.35 \pm 0.32^{c,d,e}$	0.89 ± 0.05^{e}	4.57 ± 0.012^{i}	252 ± 5.43^{a}	$4.67 \pm 0.24^{a,b,c}$
7% *LR*	5.88 ± 0.24^{a}	0.44 ± 0.01^{h}	10.25 ± 0.06^{g}	250 ± 5.09^{a}	$4.83 \pm 0.13^{a,b}$
3% *POS*	$5.16 \pm 0.12^{a,b,c}$	1.59 ± 0.06^{c}	4.57 ± 0.02^{i}	246 ± 6.94^{a}	$4.24 \pm 0.22^{a,b,c}$
5% *POS*	$5.33 \pm 0.58^{a,b}$	$0.52 \pm 0.02^{g,h}$	11.57 ± 0.02^{e}	258 ± 7.36^{a}	4.86 ± 0.18^{a}
7% *POS*	5.67 ± 0.58^{a}	$0.51 \pm 0.05^{g,h}$	18.01 ± 0.012^{b}	251 ± 9.44^{a}	$4.47 \pm 0.54^{a,b,c}$
3% *POH*	$3.73 \pm 0.25^{e,f,g}$	1.36 ± 0.08^{d}	10.21 ± 0.02^{g}	245 ± 8.89^{a}	$4.240 \pm 0.22^{a,b,c}$
5% *POH*	$4.67 \pm 0.21^{b,c,d}$	$0.76 \pm 0.04^{e,f}$	14.07 ± 0.015^{c}	250 ± 9.24^{a}	$4.73 \pm 0.04^{a,b,c}$
7% *POH*	$4.73 \pm 0.16^{b,c,d}$	$0.46 \pm 0.06^{g,h}$	25.09 ± 0.012^{a}	248 ± 9.36^{a}	4.14 ± 0.07^{c}
3% *OB*	$3.16 \pm 0.08^{f,g}$	3.17 ± 0.12^{a}	2.32 ± 0.08^{l}	247 ± 9.35^{a}	$4.18 \pm 0.24^{b,c}$
5% *OB*	$3.83 \pm 0.12^{d,e,f,g}$	$0.57 \pm 0.07^{g,h}$	10.56 ± 0.06^{f}	258 ± 7.36^{a}	$4.27 \pm 0.13^{a,b,c}$
7% *OB*	$4.7 \pm 0.21^{b,c,d}$	$0.62 \pm 0.01^{f,g}$	12.15 ± 0.04^{d}	252 ± 5.43^{a}	$4.42 \pm 0.12^{a,b,c}$
3% *AN*	2.95 ± 0.23^{g}	2.00 ± 0.07^{b}	1.30 ± 0.015^{m}	256 ± 9.64^{a}	$4.25 \pm 0.09^{a,b,c}$
5% *AN*	$3.3 \pm 0.16^{f,g}$	1.36 ± 0.08^{d}	2.53 ± 0.02^{k}	248 ± 9.36^{a}	$4.20 \pm 0.26^{a,b,c}$
7% *AN*	$3.5 \pm 0.27^{e,f,g}$	$0.62 \pm 0.02^{f,g}$	7.28 ± 0.04^{h}	250 ± 5.09^{a}	$4.33 \pm 0.25^{a,b,c}$
-ve control	0.9 ± 0.24	capping	0.38 ± 0.08	248 ± 9.36	4.21 ± 0.21
+ve control	$5.5 \pm 0.21^{a,b}$	0.43 ± 0.01^{h}	14.02 ± 0.09^{c}	248 ± 5.09^{a}	$4.27 \pm 0.19^{a,b,c}$

Post-hoc Tukey (95% simultaneous confidence intervals) test shows that means in a column that do not share a letter in superscript are significantly ($P<0.05$) different.

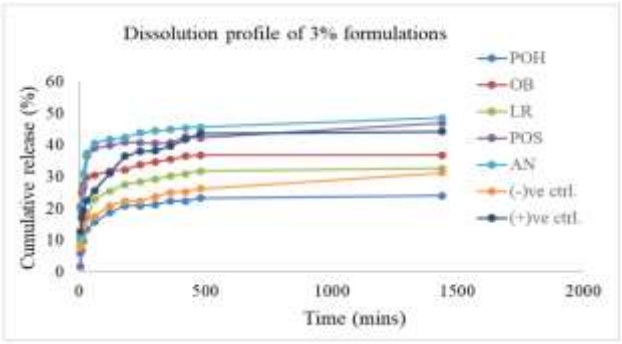

Fig. 4: Dissolution profile of 3% formulations used in tablets with (+) ve and (-) ve control

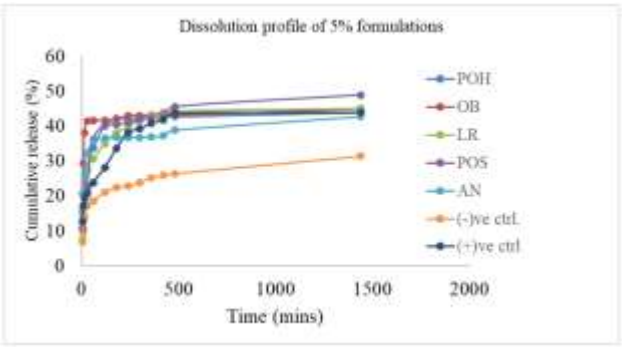

Fig. 5: Dissolution profile of 5% formulations used in tablets with (+) ve and (-) ve control

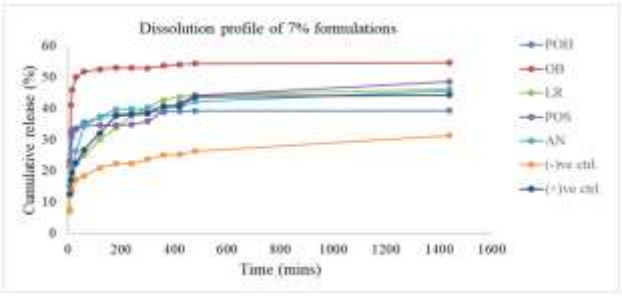

Fig. 6: Dissolution profile of 7% formulations used in tablets with (+) ve and (-) ve control

Post-compression test

The results for post compression tests of paracetamol tablets containing the various binders are shown in table 4. The mean weight of batches of tablets ($P<0.05$) ranged from 245±8.89mg for 3% *POH* tablets as binder, to 258±7.36 mg for those made with 5% *POS* and 5% *OB* as binder. According to USP if average weight of tablet is 130-324 mg, acceptable value for % weight variation is 7.5% (Bista, 2023). The hardness of all formulation tablets ranged from 2.95±0.23 for 3% *AN* to 5.88±0.24 for 7% *LR* ($P<0.05$). Each formulation's average thickness was also measured, ranging from 4.14±0.07mm to 4.86±0.18mm, as shown in table 4 (Bista, 2023). The thickness and friability of all formulation tablets was in the specified range ($P<0.05$). The hardness of tablets of all *POS* formulations and 7% *LR* was in the USP criteria range. Tablets made with 7% *LR* have the least friability of 0.44±0.01while tablets made with 3% *OB* have the highest friability of 3.17±0.12% ($P<0.05$). The disintegration times of batches of tablets varied from 1.30±0.015 min for 3% *AN* tablet, to 25.09±0.012 min for 7% *POH* ($P<0.05$).

Dissolution studies

The percentage of the active pharmaceutical component released from these tablets over time was determined by dissolution studies. The tablet formulations are compared with (-) ve and (+) ve control for 24-hours. In fig. 3, the cumulative drug release of 3% formulations of *OB*, *LR* and *POH* was less as compared to 5% and 7% formulation which was opposite to the trend found in *AN*, in which 7% formulation showed the slowest drug release. However, 3%, 5% and 7% formulations of *POS*, all showed very similar trend. This suggests that different materials and percentages have different effect on the drug release and no common pattern can be predicted. Specifically, 3% and 5% *POS* and 7% LR showed drug release trend very similar to the +ve control (fig. 4-6).

DISCUSSION

In elemental analysis, carbon and hydrogen percentages were similar to polysaccharides from plant hemicelluloses (Massey *et al*., 2022; Iqbal *et al*., 2011 a). The substantial swelling properties of these substances render them suitable choices for manufacturing delivery systems and controlled-release tablets. Among these polymers, the regulation of drug release can be achieved through adjustments in water content and pore size. A higher water content and larger pore size are essential for achieving rapid drug release (Thang *et al*., 2023; Peppas *et al*., 2000). All these materials seem to be good for making controlled release tablets. FT-IR conformed to those of typical samples of *AN* and *AM* (Massey *et al*., 2016) and that of *LR* (Massey *et al*., 2022). The observed endothermic weight loss in the 80-120°C range is attributed to the loss of trapped moisture. However, the major weight loss in the range of 200-375°C is indicative of the degradation of the polysaccharide structure. This degradation step is further supported by the exothermic enthalpy change seen in the DSC scan (Massey *et al*., 2022). According to table 1, angle of repose, ranging from 25 to 30 indicate the excellent flow of granules, 31-35 show good flow whereas 36-40 reflects fair flow and all formulations in the study fall within this range, indicating good flow (Bista, 2023). Bulk density and tapped density serve as the basis for calculating Hausner's ratio and Carr's Index, as described by Goyal *et al*. (2015). Elevated values of Hausner's ratio and Carr's Index indicate powder cohesiveness, leading to inefficient flow. As indicated in the table 1, the reported values within 1.07 to 1.10 for Hausner's ratio and 6.52 to 9.30 for Carr's Index suggest excellent flowability (Bista, 2023). The weight variation

and disintegration times of the tablets indicate important characteristics for the functionality and release profiles of the tablets. Tablets with 3% *AN* can be utilized in fast-release applications, while those with 7% *POH* can be used for sustained release. Hardness and friability values are crucial for assessing the mechanical properties of tablets, ensuring they can withstand packaging, transportation, and handling without breaking (Odunayo *et al*., 2021; Enauyatifard *et al*., 2012). Official standards for hardness are 5-8 kg/cm² for standard compressed tablets, except for chewable, effervescent, controlled, and sustained release tablets, and tablet thickness should be within 5% variation of the standard value (Bista, 2023). The 3% formulations had values greater than 1% weight loss, which is not within the friability acceptance range, while 5% and 7% formulations showed less than 1% weight loss, which is acceptable for friability. Dissolution of the drug in the medium is crucial because only dissolved drugs can be absorbed to exert their therapeutic effects. The quicker the drug is released, the greater the amount of drug that will be accessible for absorption in the gastrointestinal tract.

CONCLUSION

Five natural binders (*LR, POS, POH, OB, AN*) have been evaluated in this study for their binding properties at different concentration (3%, 5% and 7%) for paracetamol tablets. Tests, including pre- and post-compression evaluations, were conducted using wet granulation. All the extracted hemicellulose materials demonstrated their ability to bind, however 7% *LR* stood out for its exceptional ability to bind paracetamol tablets. Findings made it evident that these natural polymers which are easily accessible, affordable and nontoxic can replace the synthetic binders utilized in the pharmaceutical industry.

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