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Research Article

Development and Evaluation of a Co-Processed Novel Excipient for Fast Disintegration and Direct Compression of Tablets

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Abstract

The aim of the study was to develop a novel co-processed excipient for direct compression and fast disintegration of tablets. The novel excipients were prepared by co-processing hydroxypropyl methylcellulose (HPMC) at varying concentrations with croscarmellose sodium, di-calcium phosphate, magnesium stearate and talc. Their slurry was homogenized, dried and pulverized into powder. The novel excipient powders were used to prepare batches of granules by slugging and tablets by direct compression with excipient-drug ratios of 1:1, 1:2, 1:3, 1:4 and 1:5. The novel excipient powders and granules were evaluated for their powder and flow properties while the tablets formulated were evaluated for their tablet properties. Compatibility studies on the novel excipient and with Paracetamol were carried out using FTIR analysis. The co-processed novel excipients had excellent flow properties (angle of repose $<19°$), high moisture contents (8 - 11 %), swelling indices (7.8 - 23.8) and hydration capacities (3.25 - 5.83). Their granules also showed good flow properties that increased in batches prepared with novel excipients with higher amounts of HPMC. The tablets exhibited sufficient hardness ($>$ 5.0 kp), friability values ranging from 0.29 - 2.93 %, short disintegration times (30 - 275 sec), moisture sorption (15.12 - 29.05 %), and drug content (98 - 102 %). The formulated novel excipient was compatible with Paracetamol. The co-processed excipients developed in this study was found to be a promising directly compressible vehicle for the preparation of fast disintegrating tablets of poorly compressible drugs.

Keywords: Co-processed, fast disintegration, direct compression, Paracetamol

Introduction

Particle engineering can be defined as the process of modifying a particle structure. Pharmaceutically, it is employed in modifying excipients to achieve products with improved performance and desired physical and chemical properties. Several methods such as granulation, crystallization, chemical as well as co-processing have been used in drug formulations to modify particle structure and properties [1, 2].

Co-processing, a process of combining two or more established excipients by incorporating one excipient into the particle of another, using an appropriate process, has gained much attention in the last two decades [3,4]. It was a process developed by the food industries to tackle the problems of stability, solubility, wettability, and gelling properties of food ingredients [5]. Co-processed products are simple physical mixtures at the particulate level leading to the formation of excipients with superior properties compared to the simple physical mixture of their components. The process has been used in tablet formulations to solve the problems of flowability, compressibility, disintegration potentials and filler-binder combinations, adding value to the product obtained as a bi- or multi-functional excipient [6,7]. Despite the many advantages of co-processed excipients such as the absence of chemical change after co-processing, betterflow properties, particle size distribution, physico-mechanical properties, etc., this process suffers from a major disadvantage, the fixed ratio of its constituent excipients which may not be optimum for the dose per tablet of various drugs [8]. Therefore, the maximum quantity of drug that can be accommodated by a certain amount of a co-processed excipient in a tablet and at the same time maintaining the tablets' optimal properties can be referred to as the maximum loading dose of that quantity of the excipient for that API. This means that for any co-processed excipient developed, the loading doses of various APIs must be investigated which may fall short of the drugs therapeutic dose. This drawback cannot be easily remedied by increasing the amount of the excipients used for the formulation, as this may result in a tablet of undesirable size and hence affect patient's compliance. Hence, the objectives of this study are to formulate and evaluate a novel co-processed excipient for fast disintegration and direct compression of tablets and to ascertain its loading capacity in Paracetamol tablet formulations.

Materials and Methods

Materials

Paracetamol powder (Nomagbon Pharmaceuticals, Edo State, Nigeria), croscarmellose sodium (FMC Bipolymers, USA), maize starch powder and dicalcium phosphate talc (Edo Pharmaceuticals, Benin City), hydroxypropylmethyl cellulose (Qualikems Pvt Ltd, Delhi, India), lactose monohydrate (Fluka Netherlands), hydrochloric acid (BDH Chemicals Ltd, Poole, England), acetone, magnesium stearate and talc (International Co. Ltd, Anhui, China). All other chemicals were of analytical reagent grade and used as received.

Methods

Preparation of excipient

Five grams of hydroxypropyl methyl cellulose (HPMC) was weighed and dispersed in 200 ml distilled water at 32 °C, to make a 2.5 %w/v HPMC slurry in a 500 ml beaker. The slurry was stirred continuously for about 3 min and allowed to stand for 15 min to allow for hydration and swelling of the HPMC. A mixture of 3 g of croscarmellose sodium and 2 g of di-calcium phosphate was dispersed in the swollen mass of HPMC in small quantities at a time andstirred continuously until an even mixture was formed. Another mixture of 500 mg each of magnesium stearate and talc was subsequently dispersed in the mixture with continuous stirring. The paste-like mixture was then homogenized (Silverson, UK) continuously at 500 rpm for about 30 min until a paste of uniform consistency was formed. The paste was transferred onto a transparent glass pane, spread thinly and air-dried for 48 h. The partially dried flakes were further dried using a fluidized bed dryer at 50 °C for 1 h. The resulting flakes were pulverized using a

dry mill (Philips, Switzerland) and stored in an air tight container over silica gel until use and labelled novel excipient "A". The procedures were repeated using 5.0 and 7.5 %w/v HPMC slurries and tagged novel excipients "B and C" respectively.

Evaluation of the novel excipients

The following characterizations were carried out individually on the three (3) sets of novel excipients A, B and C.

Bulk properties

Bulk density Twenty grams of the novel excipient powder was measured and poured gently into a 100 ml graduated measuring cylinder. The volume of the powder was read and the bulk density was calculated.

Tapped density The 20 g measure of the novel excipient powder was tapped against a wooden platform 100 times and the volume was noted. This value was used in calculating the tapped density.

Flow properties

Carr's index The difference between the tapped and bulk densities of the novel excipient powder was divided by the tapped density. The percentage expression of this ratio was recorded as the Carr's index.

Hausner's ratio The ratio was calculated by dividing the tapped density with the bulk density of the novel excipient powder.

Angle of repose Using the hollow tube method, a short tube with an internal diameter of 3 cm sitting on a circular horizontal base of same diameter was filled with the powders of the novel excipient. The tube was withdrawn vertically and excess powders allowed to fall off the edge of the horizontal base. The height of the heap was measured and the angle of repose was calculated using Equation 1.

$$\theta = \tan^{-1}(h/r) \quad \ldots\ldots 1$$

where h is the height of the heap of powder and r is the radius of the circular base

Flow rate This was carried out with the use of an Erweka flow tester. The time taken for 50 g of the novel excipient powder to pass through the orifice was recorded. This was done in triplicate and the mean value was recorded.

Moisture content

An initial weight (1.0 g) of the novel excipient powder was measured and dried in a hot air oven for 4 h at 105 °C to a fixed weight. The difference between the initial and final weights expressed as a percentage of the initial weight was recorded as the moisture content.

Swelling capacity

One gram of the novel excipient powder with a tapped volume (Vi) was introduced into a 50 ml measuring cylinder. The powder was dispersed with 1.0 ml of ethanol and 25 ml of distilled water and thereafter made up to volume with more water. The cylinder was firmly closed and shaken vigorously every 10 min for 1 h. The dispersion was allowed to stand for 3 h and the volume of the sediment (Vf) noted. The swelling capacity was calculated using Equation 2.

$$\text{Swelling capacity} = Vf - Vi \quad \ldots\ldots 2$$

Particle density

A 25 ml specific gravity bottle (glass pycnometer) was filled with liquid paraffin, cleaned of any residual liquid paraffin and weighed (a). The bottle was emptied, rinsed with acetone and dried. One gram (b) of the novel excipient powder was poured into the bottle and then filled with liquid paraffin. It was weighed (c) after cleaning off the residual paraffin from the bottle. The various weights recorded were used to calculate the particle density of the novel excipient using Equation 3.

$$\text{Particle density} = b / ([(a+b) - c] \times s \quad \ldots\ldots 3$$

Where, S = specific gravity of liquid paraffin

Hydration capacity

One gram of the novel excipient powder (Wi) was introduced into a 15 ml centrifuge tube and 10 ml of water was added and the tube corked. The content of the tube was shaken for about 2 min, allowed to settle for 10 min and centrifuged at 1000 rpm for 10 min using a bench centrifuge. The resulting supernatant was decanted and the sediment weighed (Wf). The hydration capacity was calculated using Equation 4.

$$\text{Hydration capacity} = Wf / Wi \quad \ldots\ldots (4)$$

Preparation of granules

A total of fifteen (15) batches (5 batches per novel excipient) were prepared. For each excipient, batches of granules containing the novel excipient and drug in the ratio of 1:1,1:2, 1:3, 1:4 and 1:5 were prepared with Paracetamol powder using the formula in Table 1.

Table 1: Formula of prepared Paracetamol granules and tablets

Ingredients	Quantity (mg/tablet)				
	1:1	1:2	1:3	1:4	1:5
Paracetamol	100	200	300	400	500
Lactose	450	350	250	150	50
Maize starch	50	50	50	50	50
Novel excipient	100	100	100	100	100
Total	700	700	700	700	700

The required quantities of the ingredients sufficient to prepare 100 tablets per batch were thoroughly dry mixed in a mixer and slugged into a large tablet using a single punch heavy duty tableting machine (Koln Niehi, Germany).The slugs were broken down into granules using a mortar and pestle and passed through a 710 µm mesh screen (BSS Endecotts, England). The resulting granules were stored in airtight containers in readiness for evaluations.

Evaluation of granules

The different batches of granules were evaluated by determining their bulk and tapped densities, compressibility index, Hausner's ratio, angle of repose, flow rate and moisture content. The same procedures employed to evaluate the novel excipients were used.

Compatibility studies

Drug-excipients compatibility studies using FTIR was carried out on the prepared granules to investigate any interaction between the novel excipient and Paracetamol. The analysis was done using FTIR-4100 Spectrophotometer (Shimadzu Co. Japan). Five milligrams granule weight was dry-mixed with potassium bromide to give a 200 mg weight powder. The mixed powder blend was compressed using a Sigma Press into a tablet. The tablet was placed in the sample compartment of the spectrophotometer and scanned over a range of 4000 - 1000 cm^{-1}.

Direct compression of granules

Paracetamol tablets were prepared by direct compressionof the granules using a single punch tableting machine (F-3 Manesty Machines, UK) at compression pressure of 30 kilonewton (KN). The die volume was adjusted to compress tablets of uniform weight by using powders weighing 700 mg. The tablets made were then kept in air tight containers and stored in a desiccator until evaluation.

Evaluation of tablets

The formulated tablets were subjected to the following evaluations: organoleptic properties, dimensions and weight uniformity, friability and crushing strength, disintegration time and moisture sorption, in comparison with a conventional commercial product.

Organoleptic properties

The tablets were examined with regard to their color, shape, taste, texture and odour. The opinion of a maximum of three out of five volunteers was recorded.

Dimensions and weight uniformity

Using a micrometre screw gauge (Gallenkamp), the thickness and diameter of 10 randomly selected tablets per in batch was measured and their mean and standard deviation values were calculated and recorded while 20 tablets per batch were selected and weighed individually using an electronic balance (College B154, Mettler Toledo, Switzerland) and the mean weight and standard deviation values recorded.

Friability and crushing strength

Ten tablets were weighed and placed in the drum of a friabilator (Erweka GmbH, Germany) revolving at 25 rpm. After 4 min, the tablets were brought out, de-dusted and reweighed. Friability was calculated as the percentage loss in weight. The force required to break each of ten (10) tablets per batch by diametrical compression using a motorized tablet hardness tester (Campbell Electronics, Model HT-30/50, India) was determined and the mean value and standard deviation were recorded as the crushing strength of the tablets.

Disintegration time

Six tablets per batch were introduced into separate tubes of a BP disintegration apparatus (MK IV, Manesty Machines, UK) containing distilled water thermostated at 37.0 ± 0.5 °C as the disintegration medium. The tablets were subjected to the upand down movements of the apparatus until all the disintegrated fragments of the tablet passed through the mesh at the bottom of the tubes. The time taken for each tablet was noted and the average time and standard deviation calculated.

Moisture sorption

The moisture sorption abilityof the tablets was determined using the static gravimetric method. A tablet per batch was dried at 80 °C for 4 h and weighed. The tablet was placed in a Petri dish and transferred to a desiccator maintained at 100% relative humidity at room temperature with distilled water. After 48 h, the tablet was taken out and re-weighed. The percentage gain in weight was used as a measure of the moisture sorption ability of the tablet. The procedures were carried out in triplicate and the mean and standard deviation values calculated.

Content of active drug

Twenty (20) tablets were randomly selected from each batch and crushed to fine powder. A quantity of the powdered tablets equivalent to 100 mg Paracetamol was weighed and dissolved in 50 ml of 0.1N HCl in a 100 ml volumetric flask and made up to volume. Necessary dilutions were carried out to obtain a final concentration of 100 µg/ml, the solution was thereafter filtered through a Whatman No. 1 filter paper and the absorbance of the filtrate determined at 245 nm using 0.1 N HCl as blank. The amount of drug was then calculated using the equation generated from the standard calibration plot obtained with the pure Paracetamol drug.

Statistical analysis

Descriptive statistics was done for all data using GraphPad InStat 3.10. Mean and standard deviations of replicate determinations were computed and reported. Differences between mean were subjected to student's t-test at 5 % level of significance.

Results and Discussion

Properties of the novel excipients

The physical properties of the co-processed novel excipient prepared with varying HPMC concentrations are shown in Table 2.

Table 2: Some physical properties of the novel excipients

Novel excipient	HPMC Concentration (%w/v)		
	2.5	5.0	7.5
Properties	**A**	**B**	**C**
Hydration capacity	5.83	4.05	3.25
Swelling capacity	23.8	9	7.8
Moisture content (%)	11	11	8
Particle density (g/cm^3)	1.860	1.968	2.038
Flow rate (g/sec)	1.786	2.308	2.727
Angle of repose (°)	18.43	15.77	12.53
Hausner's ratio	1.24	1.17	1.16
Carr's index (%)	19.05	14.29	13.97
Tapped density (g/cm^3)	0.735	0.714	0.750
Bulk density (g/cm^3)	0.595	0.612	0.645

Their bulk density values in relation with their tapped densities indicates powder particles with closer packing with increase in HPMC concentration while their Carr's indices, Hausner's ratios, angles of repose and the flow rates ranged from 19.05-13.97 %, 1.24-1.16, 18.43-12.53° and 2.73-1.79 g/sec, respectively would indicate that the excipients prepared have excellent flow properties that also improved with increase in HPMC concentration. Their particle density values of 1.86-2.04 g/cm^3 support their bulk and tapped density values and their implications as the novel excipient "C" prepared with 7.5 %w/v HPMC had the highest particle density value of 2.04 g/cm^3. This implies closer particle packing, which could be as a result of a wider particle size distribution with the smaller particles filling the void spaces created by larger ones. The low particle density of novel excipient "A"is in conformity with the study of Newman [9], who showed that low densities result when void spaces created by powder particles are not filled by smaller particles. The results showed a decrease in moisture content of the novel excipients from 11-8 % with increase in HPMC concentration. This decrease in moisture content also supports the particle size and size distribution theory that high HPMC concentration results in diverse particle sizes while at low concentrations, only large particle sizes may results, which may trap water and result in high moisture content [10]. Moisture contents as high as 3-4 % are appropriate to produce maximum disintegration and dissolution of tablets [11]. The swelling and hydration values of the novel excipients also showed a decrease from 23.8-7.8 and 5.83-3.25 respectively, with increase in HPMC concentration. These values would indicate that the novel excipients are good candidates as a disintegrant with excipient "A" possessing superior qualities as a result of its higher swelling and hydration values.

Properties of the granules

Results from the physico-chemical evaluations of the Paracetamol granules are shown in Table 3. Generally, there was an increase in the flow properties of the various batches of granules with increasing HPMC concentration in the novel excipient used in their formulation as seen in the increased granule flowability when moving from batches of granules prepared with novel excipient "A" to "C". The granules exhibited increased flow rates and bulk densities and decreased angles of repose, tapped densities, Carr's indices and Hausner's ratios moving from batches of granules A1 to C5. On the other hand, granule flow properties showed an indirect relationship with increasing amounts of the incorporated drug.

Table 3: Some physicochemical properties of the Paracetamol granules

Batch/ ratio	Bulk density (g/cm^3)	Tapped density (g/cm^3)	Carr's index (%)	Hausner's ratio	Angle of repose (°)	Flow rate (g/sec)	Moisture content (%)
A1 (1:1)	0.535 ± 0.014	0.755 ± 0.018	29.08 ± 0.04	1.41 ± 0.11	31.42 ± 1.01	4.16 ± 0.14	3.2 ± 0.16
A2 (1:2)	0.554 ± 0.012	0.776 ± 0.011	28.57 ± 0.07	1.40 ± 0.20	31.53 ± 0.85	4.13 ± 0.17	3.0 ± 0.10
A3 (1:3)	0.586 ± 0.020	0.831 ± 0.017	29.58 ± 0.06	1.42 ± 0.12	31.61 ± 0.10	4.13 ± 0.16	2.2 ± 0.12
A4 (1:4)	0.588 ± 0.012	0.834 ± 0.020	29.58 ± 0.02	1.42 ± 0.08	32.03 ± 0.04	4.12 ± 0.18	2.0 ± 0.15
A5 (1:5)	0.543 ± 0.006	0.771 ± 0.011	29.57 ± 0.05	1.42 ± 0.14	32.65 ± 0.02	4.12 ± 0.14	1.0 ± 0.08
B1 (1:1)	0.631 ± 0.010	0.846 ± 0.009	25.38 ± 0.03	1.34 ± 0.13	31.42 ± 0.06	4.38 ± 0.22	3.0 ± 0.05
B2 (1:2)	0.674 ± 0.018	0.910 ± 0.012	25.93 ± 0.02	1.35 ± 0.06	31.53 ± 0.16	4.32 ± 0.40	3.0 ± 0.03
B3 (1:3)	0.688 ± 0.014	0.942 ± 0.013	27.01 ± 0.02	1.37 ± 0.08	31.61 ± 0.20	4.18 ± 0.15	2.2 ± 0.04
B4 (1:4)	0.678 ± 0.010	0.942 ± 0.017	28.06 ± 0.01	1.39 ± 0.12	32.04 ± 0.55	4.11 ± 0.50	1.1 ± 0.88
B5 (1:5)	0.647 ± 0.017	0.906 ± 0.014	28.57 ± 0.01	1.40 ± 0.10	32.25 ± 0.38	4.08 ± 0.52	1.1 ± 0.06
C1 (1:1)	0.476 ± 0.008	0.571 ± 0.011	16.63 ± 0.02	1.20 ± 0.11	30.01 ± 0.12	4.82 ± 0.80	3.0 ± 0.07
C2 (1:2)	0.488 ± 0.011	0.580 ± 0.018	15.91 ± 0.10	1.19 ± 0.13	26.83 ± 0.48	4.80 ± 0.20	2.1 ± 0.04
C3 (1:3)	0.455 ± 0.015	0.571 ± 0.022	16.35 ± 0.01	1.26 ± 0.05	30.70 ± 0.10	4.52 ± 0.04	2.0 ± 0.02
C4 (1:4)	0.426 ± 0.011	0.502 ± 0.015	15.05 ± 0.11	1.18 ± 0.10	27.43 ± 0.20	4.43 ± 0.16	2.0 ± 0.01
C5 (1:5)	0.438 ± 0.016	0.526 ± 0.019	16.73 ± 0.01	1.20 ± 0.09	29.90 ± 0.11	4.26 ± 0.90	1.0 ± 0.01

Irrespective of the novel excipient used, granule flow decreased with increased concentrations or amounts of Paracetamol. These results are in conformity with those obtained from the flow properties evaluations of the novel excipient and it would suggest the formation of larger granules as the concentration of HPMC incorporated in the novel excipient increased leading to larger voids in between the larger granules. This increase in particle sizes would also lead to decrease in surface free energy of the powder particles and decrease in frictional forces between the particles leading to faster flow [12]. Conversely, with increase in the amounts of Paracetamol powder in the formulations, the voids in between the large granules may gradually be filled increasing the frictional forces between the particles and hence reducing granule flow.

The moisture loss of all the granules was between 1.0-3.2 %, which implies granules in excellent dry state that may be prone to taking up atmospheric moisture. This state of the granules may also be advantageous to tablets formulated with them, as they can easily take up fluid facilitating tablet disintegration ability.

Drug-excipient interactions

Figures 1 (a) and (b) shows the FTIR spectra of pure Paracetamol powder and the granule mixture of Paracetamol and the novel excipient powder. The spectrum of pure Paracetamol powder showed characteristic peaks at 1227.00 cm^{-1}, 1636.42 cm^{-1} and 3171.00 cm^{-1} (Figure 1a). These peaks observed for Paracetamol remained unchanged when compared with the spectral data of the granules (Figure 1b). This observation ruled out the possibility of chemical interaction and complex formation between Paracetamol and the novel excipient during the mixing processes.

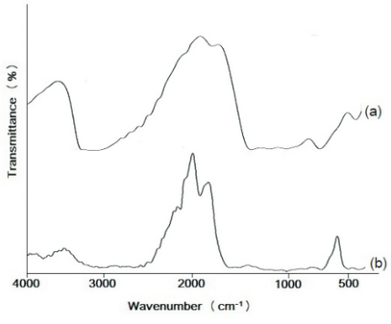

Figure 1: FTIR spectra of pure Paracetamol powder (a) and the tablet granules prepared by slugging (b).

Properties of the tablets

Results from the organoleptic examination of the formulated tablets revealed slightly off-white tablets with a slightly bitter taste, odourless and smooth in surface texture. The tablet weight uniformity results (Table 4) showed that the mean weight of the tablets prepared with the novel excipients met the British Pharmacopoeia [13] specification of not more than two of the individual weights of tablets deviating from the average weight by more than ± 5 % and none should deviate by more than ± 10 %.

There were variations in the crushing strengths, friability and disintegration times of the formulated batches of the tablets (Table 4). All the batches of tablets showed crushing strength values >5.0 kp with these values decreasing in tablets formulated with the novel excipient with increased HPMC amount and also with increased amounts of Paracetamol except the last two batches (C4 and C5) that did not follow this trend even though their increased values were not significant ($p > 0.05$). Therefore, all the tablets exhibited satisfactory tablet hardness as crushing strength value of 4.0 kp has been reported as the lower limit [14] and with values ranging from 5 - 8 kp as optimal values satisfactory tablet hardness [13]. These crushing strength values would suggest that the novel excipient developed possess acceptable/adequate binding ability, a property inherent in direct compression excipients since the hardness of a tablet is dependent on the binding ability of the tablet's excipients. Furthermore, the binding nature of the novel excipient may have facilitated the formation of inter-granular bonds between particles during tablet compression thereby allowing plastic and elastic deformations of the particles [15].

Table 4: Some physicochemical characteristics of the Paracetamol tablet

Batch	Tablet weight (g)	Tablet dimensions (mm)		Crushing strength (kp)	Friability (%)	Disintegration time (sec)	Moisture sorption (%)	Content of active (%)
		Diameter	Thickness					
A1	0.690 ± 0.009	12.46 ± 0.016	4.14 ± 0.017	7.0 ± 0.42	0.29± 0.02	274.60 ± 0.665	29.05 ± 0.12	99
A2	0.698 ± 0.008	12.45 ± 0.024	4.13 ± 0.019	7.5 ± 1.13	0.59± 0.01	181.40 ± 0.411	28.42 ± 0.24	99
A3	0.690 ± 0.025	12.45 ± 0.017	4.28 ± 0.008	7.0 ± 1.43	1.47± 0.02	150.00 ± 0.138	28.33 ± 0.10	98
A4	0.698 ± 0.024	12.47 ± 0.019	4.38 ± 0.024	6.9 ± 1.67	1.76± 0.03	123.00 ± 0.043	27.40 ± 0.44	101
A5	0.694 ± 0.021	12.12 ± 0.021	4.43 ± 0.009	6.5 ± 1.20	1.78± 0.02	109.40 ± 0.216	26.30 ± 0.22	98
B1	0.698 ± 0.007	12.41 ± 0.017	4.08 ± 0.016	7.5 ± 1.34	0.59± 0.02	156.80 ± 0.218	23.28 ± 0.34	99
B2	0.697 ± 0.009	12.35 ± 0.019	4.20 ± 0.032	7.0 ± 0.33	1.49± 0.03	115.00 ± 0.311	23.10 ± 0.20	98
B3	0.690 ± 0.021	12.39 ± 0.015	4.26 ± 0.197	6.5 ± 1.23	2.30 ± 0.02	65.00 ± 0.136	23.06 ± 0.12	99
B4	0.698 ± 0.019	12.46 ± 0.024	4.47 ± 0.056	5.0 ± 1.02	2.37 ± 0.03	60.40 ± 0.223	22.45 ± 0.14	99
B5	0.696 ± 0.017	12.48 ± 0.009	4.36 ± 0.057	5.0 ± 1.01	2.93± 0.02	55.20 ± 0.135	19.50 ± 0.24	101
C1	0.690 ± 0.009	12.46 ± 0.017	4.17 ± 0.016	5.5 ± 1.03	1.07± 0.02	77.00 ± 0.350	17.46 ± 0.11	99
C2	0.698 ± 0.007	12.07 ± 0.009	4.42 ± 0.032	5.3 ± 1.67	0.85± 0.03	32.00 ± 0.125	17.35 ± 0.22	98
C3	0.700 ± 0.024	12.11 ± 0.019	4.16 ± 0.056	5.0 ± 1.20	1.70± 0.03	29.60 ± 0.213	15.74 ± 0.23	102
C4	0.698 ± 0.008	12.05 ± 0.024	4.09 ± 0.057	5.5 ± 1.43	2.01± 0.02	38.40 ± 0.210	15.35 ± 0.22	101
C5	0.690 ± 0.021	12.03 ± 0.007	4.07 ± 0.056	6.0 ± 0.42	2.64± 0.04	37.60 ± 0.133	15.12 ± 0.18	100
CCP	0.600 ± 0.001	12.49 ± 0.003	4.50 ± 0.049	10.80 ± 0.84	0.65 ± 0.02	280.33 ± 0.122	25.10 ± 0.20	100

±Standard deviation,CCC = Commercial Conventional Product

The friability test results of the tablets revealed values ranging from 0.29 % for the A1 batches of tablets to 2.93 % with tablet batches B5 (Table 4). All the tablets therefore, did not meet the British Pharmacopoeia specification of 0.8 - 1.0 % maximum loss in the tested tablets weight, even though up to 2 % loss is permissible especially for large tablets prepared by direct compression [16]. The friability values followed a trend of increasing values as the amount of Paracetamol was increased in the various tablet batches. However, the novel excipient "A" batches of tablets exhibited lesser friability. With the crushing strength values shown by the tablets, they would have been expected to have satisfactory friability values. Since particle bond formation is key to the mechanical strength of a tablet i.e. optimal hardness and friability, it may be concluded that the introduction of Paracetamol powders in increasing amounts may have resulted in disruption of inter-particle bonds of the granules during compression leading to tablets with lesser crushing strength and higher friability values [17].

All the formulated tablets disintegrated within 5 min (Table 4) including the conventional commercial tablet product, as specified by BP [13] for immediate-release uncoated tablets. Apart from the A1 batch of tablets, all the other batches complied with the less than 3 min disintegration time specification of European Pharmacopeia for fast disintegration tablets [18]. Though tablet batches prepared with novel excipient "C" with the highest concentration of HPMC, gave the lowest disintegration times, they also appear to be the optimal batches in terms of drug loading, as the amount of Paracetamol did not appreciably affect the disintegration times of the tablets. Also, the trend of decreasing disintegration times with increase Paracetamol loading seen in all the batches of tablets makes the attribution to the novel excipient as the cause of the low disintegration times probable. Again, it can be said that the decreased tablet hardness and increased friability caused by the increased Paracetamol drug loading facilitated the fast disintegration of the tablets.

Moisture sorption, one of the indices for understanding the capacity of a tablet to disintegrate in the presence of water was found to be lower in tablets prepared with higher concentration HPMC. Since these tablets also exhibited lower disintegration times, it implies that the fast disintegration of the tablets may not be primarily attributed to moisture uptake by the tablets and swelling of the primary particles to cause a burst effect. Apart from the swelling of the tablet particles, various other tablet disintegration mechanisms such as wicking, particle-particle repulsion, deformation recovery, etc, may have contributed to the fast disintegration of the Paracetamol tablets. The content of active drug in all the tablets were within the range prescribed by the pharmacopeia [13], that is, not less than 90.0 % and not more than 110.0 % of the labelled content.

Conclusion

The developed co-processed excipients and their granules exhibited good flow properties. Their tablet formulations were of good pharmaceutical quality with short disintegration times and sufficient hardness. The novel excipient is a promising fast disintegrating and directly compressible vehicle for the preparation of compressed tablets of poorly compressible drugs.

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Conflict of interest

The authors declare no conflict of interest.

References

[1]Moreton RC. Tablet excipients to year 2001: A look into the crystal ball. Drug Dev Ind Pharm 1996; 22(1):11-23.

[2]Ochekpe NA, Kemas UC,Nep EI. Chemical modifications and their effects on binding/disintegrating properties of *Plectranthus esculentus* starch in chloroquine phosphate tablets. Am J Pharm Tech Res 2013; 3(3):867-77.

[3]Gohel MC, Jogani PD. A review of co-processed directly compressible excipients. J Pharm Pharm Sci 2005; (8):76-93.

[4]Gohel MC, Parikh RK, Brahmbhatt BK, Shah AR. Improving the tablet characteristics and dissolution profile of ibuprofen by using a novel co-processed super-disintegrant: A technical note. AAPS PharmSciTech 2007; 8(1):E94–E99.

[5]Modliszewski JJ, Ballard DA. Co-processed galactomannan-glucomannan thickener base. (FMC Corp., Philadelphia, PA, USA) United States Patent US 5 498 436.Trends Food Sci Technol 1996; 7(11):377.

[6]Bansal AK, Nachaegari SK. Co-processed excipients for solid dosage forms. Pharm Technol 2004; 28:52-64.

[7]Eraga SO, Damisah CO, Uhumwangho MU, Iwuagwu MA. Development and evaluation of novel, multifunctional co-processed excipients for direct compression of Paracetamol tablets. J Sci Pract Pharm 2014; 1(1):25-30.

[8]Bolhuis GK, Chowhan BG. Materials for direct compression. In: Alderborn G, Nystrom, C, eds. Pharmaceutical Powder Compaction Technology. New York: Marcel Dekker Inc, 1996:419-500.

[9]Newmann BS. The flow properties of powder. In: Bean HS, Beckett AH, Carless JE, eds. Advances in Pharmaceutical Sciences. London: Academic Press, 1967:181-221.

[10] Olayemi OJ, Oyi AR, Allagh TS. Comparative evaluation of maize, rice and wheat starch powders as pharmaceutical excipients. Nig J Pharm Sci 2008; 7:154-61.

[11]Pilpel N, Otuyemi SO, Kurup TR. Factors affecting the disintegration and dissolution of chloroquine phosphate starch tablets. J Pharm Pharmacol 1978; 30:214-19.

[12]Iwuagwu MA, Nwaoshai CA, Iseghohi FE. Investigations into the binding and disintegrants properties of starches from selected dioscoreaceae plants. Nig J Pharm Sci 1986; 2:10-22.

[13]British Pharmacopoeia, Vol. III. The Pharmaceutical Press, London: Her Majesty's Stationer Office, 2009:6578-85.

[14]Rudnic EM, Schwartz JB. Oral solid dosage forms. In: Troy DB, Beringer P, eds. Remington - The Science and Practice of Pharmacy, Baltimore: Lippincott Williams and Wilkins, 2006:889-928.

[15]Musa H, Muazu J, Bhatia PG (). Evaluation of fonio (*Digitalis exilis*) starch as a binder in Paracetamol tablets. Nig J Pharm Sci 2008; 7:56-66.

[16]European Pharmacopoeia. Supplement 5.0. European Pharmacopoeia Commission, Strasbourg: Council of Europe, 2005:234.

[17]Oyi AR, Allagh TS, Olayemi OJ. Comparative binding effects of wheat, rice and maize starches in chloroquine phosphate tablet formulations. Res J ApplSciEngTechnol 2009; 1:77-80.

[18]European Pharmacopoeia. Supplement 1.1. European Pharmacopoeia Commission Strasbourg: Council of Europe, 2008:748-50.