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Research Article

Enhancing paracetamol compressibility using the co-drying technique: Impact on tablet release profile from direct compression

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Abstract

Direct compression is the most acceptable and preferred method for manufacturing tablets. However, the poor flow property and lack of the required compressibility of most active ingredients preclude the direct compression technique. Paracetamol is a widely used analgesic drug, usually formulated in compressed tablet dosage forms. It is a poorly compressible drug with a hefty dose, usually 300 to 500 mg. In addition, Paracetamol exhibits poor flowability and shows the tendency to cap on tableting due to its poor plasticity and compatibility. The present research work developed Paracetamol DC (Directly Compressible) by co-processing with a mixture of Potato starch and Silicon Dioxide in various ratios using co-freezing and co-drying techniques. Paracetamol DC was assessed for multiple pre-compression and post-compression tableting parameters. The marked improvement in flow behavior and compressibility of co-processed Paracetamol was observed. Results of studies showed that Paracetamol DC developed with a 10% mixture containing Potato Starch and Silicon Dioxide in a ratio of 7:3 exhibited better disintegration properties and released more than 50% of the drug within 30 min. The study concluded that the technique of coprocessing poorly compressible drugs such as Paracetamol with starch and silicon dioxide using the co-freezing co-drying technique could enhance the compressibility and flowability of active pharmaceutical ingredients.

Keywords: Poor compressibility; co-processing; flow ability; direct compression; paracetamol

Introduction

Tablets are the most preferred dosage form due to their high dosing precision, compactness, manufacturing efficiency, stability, and patient compliance. Tablets are manufactured using techniques like direct compressing, wet granulation, or dry granulation. The method selection depends upon the drug's physicochemical properties and excipients [1,2]. Paracetamol, an active pharmaceutical ingredient, presents challenges due to its poor plasticity and compactability [3,4]. Strategies such as altering the crystal lattice or changing the crystal shape have been successful in enhancing its compression behavior, but stability issues with its crystalline structure have been reported [5]. Another major challenge is the poor flowability of paracetamol, which can be overcome by suitable granulation methods [6]. However, these methods are multi-step and involve various complex processes [7].

Direct compression is usually preferred over other tableting techniques due to its simplicity, cost-effectiveness, and less processing time with fewer manufacturing steps. Direct compression is also advantageous as it is suitable for thermolabile and moisture-sensitive active pharmaceutical ingredients. However, poor flow properties and lack of the required compressibility of most of the active ingredients preclude the use of direct compression. This creates the need to incorporate a number of excipients, such as fillers, binders, lubricating agents, and flow promoters [7,8]. An Increase in excipients in the formulation blend may increase the incidence of drug-excipient and excipient-excipient interactions. It may also affect the cost of manufacture. In the case of a potent drug, improper mixing of formulation blend may result in poor content uniformity [9,10]. Although multi-functionality excipients such as starch 1500, Micro Crystalline cellulose, and Lactose DC can be used to improve the

compressibility and tablet-forming ability of the drug, improper mixing, cost of excipient development and variability in excipients may create challenges for the manufacturing of tablets [11,12]. Co-processing is a technique for the development of a multifunctional, directly compressible excipient system consisting of a combination of brittle and plastic material in a suitable ratio, which is intermixed with one another by physical processing [13,14]. Co-processing of excipients improves dilution potential, improves compressibility, and reduces lubricant sensitivity and acceptable flow properties [15].

Starch is one of the most traditional excipients of natural origin used for manufacturing compressed solid dosage forms such as tablets due to its non-toxicity, economy, ease of modification, and versatile pharmaceutical applications. Depending on the type and proportion in the formulation, Starch acts as a diluent, binder, disintegrating agent, and lubricating agent [16,17]. Potato starch is an inert, odorless, and white multifunctional excipient. Usually modified physiochemically to improve its processability [18]. Alexiou G and Itiola OA reported that the use of pre-gelatinized Starch as a binder could improve the mechanical strength of Paracetamol tablets [19]. Potato starch can be gelatinized at a lower temperature (62°C) than other Starch [20]. Gelatinization of starch results in the breakdown of hydrogen bonds between the molecules of Starch [21], and Amylose will leak [22]. Deshkar *et al.* reported increased swelling and decreased crystallinity of Native Starch on hydrothermal treatment due to the leaching of Amylose [23]. Trisopon K and Kittipongpatana OS reported that crosslinking of Starch with 10% Sodium Silicate resulted in increased flowability; however, a negative effect on swelling behavior was observed at higher concentrations of Sodium Silicate. Adsorption of Sodium Silicate on the surface of Starch resulted in increased flowability but also led to inhibition of particle binding and structural irregularities [22]. Apeji YE and co-workers observed improved mechanical strength with the rapid disintegration of tablet-compressed tablets using Starch co-processed with silicon dioxide [24,25]. Rojas J and Kumar V showed that silicification of excipients (Cellulose Microcrystalline) can help reduce lubricant sensitivity, improve flowability, and increase brittleness behavior [26]. Rashid I and co-workers also reported similar results. Improvement in mechanical strength with reduced lubricant sensitivity was observed for excipients developed by coprocessing of Starch with Magnesium Silicate [27].

Although co-processed or particle-engineered excipients offer several advantages, developing excipients separately and processing them with active ingredients is costly and time-consuming. To overcome these challenges, an attempt has been made to develop a directly compressible Active Pharmaceutical Ingredient by physical modification using the technique of co-processing.

The objective of the current research was to develop a directly compressible active ingredient using the co-processing technique. In this study, the compressibility of a poorly compressible drug, viz., paracetamol, was enhanced by co-processing it with excipients such as potato starch and silicon dioxide using a co-freezing co-drying technique. The developed Paracetamol DC (Direct Compressible) exhibited improved tableting properties.

Materials

The Paracetamol was received as a gift sample from Wallace Pharmaceuticals Pvt Ltd, located in Goa, India. The potato starch was procured from Priti Trade MEX Private Ltd in Kalol, Gujarat, India, and the silicon dioxide was obtained from Chemi Enterprises Ltd in Mumbai, India.

Development of Paracetamol DC

Paracetamol was sifted through sieve no. 80 and blended with a mixture of potato starch and silicon dioxide in varying ratios, as in Table 1. Physical Blends were dispersed in purified water to prepare 50% w/v aqueous dispersion and refrigerated for 120 min in a deep freezer. The frozen dispersion was heated at 65 ºC for 30 min and dried in a tray dryer maintained at 60 ºC. The composite obtained after drying was pulverized and then sifted through sieve no. 80. The developed paracetamol DC is assessed for pre-compression and post-compression parameters [14,15,24-27].

Table 1. Formulation table for development of Paracetamol DC.

Ingredients	PDC 1	PDC 2	PDC 3	PDC 4	PDC 5
Paracetamol	500 mg	500 mg	500 mg	500 mg	500 mg
Potato starch	45 mg	40 mg	35 mg	30 mg	25 mg
Silicon dioxide	5 mg	10 mg	15 mg	20 mg	25 mg
Final weight	550 mg	550 mg	550 mg	550 mg	550 mg

Evaluation of pre-compression parameters of developed paracetamol DC

Angle of repose

The flow rate of developed Paracetamol DC was determined as the Angle of Repose by a fixed funnel method with a constant pressure head [28-30].

Hausner's ratio

The flow behavior of Paracetamol DC was determined as Hausner's ratio using tapped and untapped density. A tapped density apparatus was used to measure the untapped and tapped volume of Paracetamol DC. The apparatus was set for 50 tapings with a time interval of 2 seconds. Untapped Densities, Tapped Densities, and Hausner's ratio were calculated using formulas as mentioned below [28-30].

$$Untapped\ Density = \frac{Weight\ of\ Sample}{Untapped\ Volume},\quad Tapped\ Density = \frac{Weight\ of\ Sample}{Tapped\ Volume},\quad Housner's\ Ratio = \frac{Tapped\ Density}{Untapped\ Density}$$

Carr's index

Compressibility of developed Paracetamol DC was determined as Carr's Index using following formula [28-30].

$$Compressibility\ Index = \frac{Tapped\ Density - Untapped\ Density}{Tapped\ Density}$$

Preparation of tablets by direct compression

The Paracetamol DC composites (PDC1 to PDC5) have been meticulously formulated and compressed using a 12-station Karnavati tablet compression machine (Table 2) (F1 to F5) with uniform concentrations of Magnesium stearate and purified talc. The speed of the turret was carefully maintained within the range of 4 to 5 rpm. A total of 300 tablets for each batch, coded from F1 to F5, were meticulously compressed and evaluated for post-compression parameters [29,31].

Table 2. Content of the Paracetamol DC (in mg), in five different formulations of tablets 570 mg.

Composition	F1	F2	F3	F4	F5
Paracetamol DC *	PDC1	PDC2	PDC3	PDC4	PDC5
	550 mg (500:45:5)	550 mg (500:40:10)	550 mg (500:35:15)	550 mg (500:30:20)	550 mg (500:25:25)
Magnesium Stearate	10 mg	10 mg	10 mg	10 mg	10 mg
Purified Talc	10 mg	10 mg	10 mg	10 mg	10 mg

* Paracetamol DC: (Paracetamol: Potato Starch: Silicon Dioxide)

Evaluation of post-compression parameters of developed paracetamol DC

Determination of tensile strength

The mechanical strength of compressed tablets of Paracetamol DC was determined by using a Monsanto Hardness tester. The compact density of tablets was determined from the thickness and radius of the tablet using vernier calipers. The tablets' thickness, diameter, and diametral crushing strength were used to calculate the tensile strength [31-34].

$$Tensile\ Strength = \frac{2F}{\pi dt}$$

Where F is the crushing strength, d is the diameter, and t is the thickness of tablets.

Test for friability

Tablets of Paracetamol DC were subjected to a friability test per Indian Pharmacopoeial specifications using a Roche Friability tester. Since the weight of each tablet (570 mg) was less than 650 mg, a random sample of whole tablets corresponding to 6.5 gm was subjected to the testing. The test was carried out at 25 rpm for 4 min, and percent friability was calculated [35].

Determination of drug content

Test for uniformity of drug content was performed as per Indian Pharmacopoeial Specifications. Randomly selected 20 tablets from each batch of Paracetamol DC were crushed and powder equivalent to 500 mg of Paracetamol was dissolved in 100 ml of distilled water. Sample was analyzed UV spectroscopically and amount of drug was calculated [35].

Disintegration test

The disintegration test was carried out as per Pharmacopoeial specifications. Randomly selected 6 tablets of Paracetamol DC from each batch were subjected to a disintegration test using distilled water as media maintained at 37 ± 20 ºC. The time required for complete disintegration was recorded [35].

In-vitro drug release studies

The in-vitro drug release studies were conducted according to the USP specifications using the USP type II paddle apparatus. The study took place in Acid Buffer with a pH of 1.2. The temperature of the dissolution medium was meticulously maintained at 37 ± 0.5 ºC, while the rotation of the paddle was kept at 50 rpm. At various time intervals, samples were withdrawn and passed through a Whatman filter, with the same volume of fresh media being replaced to ensure sink conditions. The withdrawn samples were then analyzed using a UV Visible Spectrophotometer at 243 nm [36].

Results and discussion

Pre-compression parameters

The results of precompression parameters are given in Table 3. All the composites of Paracetamol DC showed better flowability and good compressibility compared to that of untreated paracetamol. An increase in flowability could be due to the adherence of silicon dioxide onto the surface of paracetamol particles, which could result in an increased distance between two adjutant host particles. In aqueous dispersion, silicon dioxide will be rendered nonporous to form large agglomerates. During pulverization and blending, large agglomerates break down into smaller particles, possibly due to the shear force that is distributed on the surface of paracetamol [37]. Composite PDC2 and PDC3 exhibited better flowability, which could be due to the optimum proportion of glidant. At lower concentrations, the amount of glidant is insufficient to cover the surface of host particles; at higher concentrations, glidant may spread out [38]. Better compressibility was observed for Paracetamol DC, possibly due to partial pre-gelatinization of Potato starch during the co-drying step [39].

Table 3. Evaluation of pre-compression parameters.

Formulation	Untapped Density (gm/cc^3)	Tapped density (gm/cc^3)	Angle of Repose (^{o})	Compressibility Index (%)	Hausner's ratio
Untreated Paracetamol	0.40 ± 0.04	0.55 ± 0.05	35.00 ± 2.22	27.27 ± 2.33	1.38 ± 0.03
PDC 1	0.53 ± 0.07	0.58 ± 0.05	20.50 ± 3.07	8.62 ± 1.54	1.09 ± 0.05
PDC 2	0.52 ± 0.05	0.56 ± 0.04	19.66 ± 2.33	7.14 ± 1.03	1.08 ± 0.03
PDC 3	0.57 ± 0.05	0.62 ± 0.04	18.68 ± 1.63	8.06 ± 1.23	1.09 ± 0.06
PDC 4	0.55 ± 0.06	0.60 ± 0.04	21.66 ± 2.24	8.33 ± 1.45	1.09 ± 0.03
PDC 5	0.58 ± 0.03	0.64 ± 0.03	22.98 ± 1.32	9.375 ± 1.78	1.10 ± 0.02

SD: n = 3

Post compression parameters

The findings of post-compression parameters for developed Paracetamol DC are tabulated in Table 4. Tablets of Paracetamol DC showed a bonding index of less than 0.4, indicating the formation of a strong compact [40].

Table 4. Evaluation of post-compression parameters.

Average	Formulations				
	F1	F2	F3	F4	F5
Compact density (g/cm²)	0.39 ± 0.02	0.40 ± 0.04	0.39 ± 0.03	0.39 ± 0.05	0.39 ± 0.04
Tensile strength (g/cm²)	2.59 ± 0.34	2.48 ± 0.54	2.43 ± 0.47	2.26± 0.30	1.95± 0.73
Bonding index	0.32± 0.06	0.33± 0.04	0.32± 0.05	0.32± 0.06	0.32± 0.04
Tablet porosity	0.60± 0.04	0.59± 0.05	0.60± 0.06	0.60± 0.05	0.60± 0.07
Percent friability (%)	0.31 ± 0.05	0.42 ± 0.07	0.49 ± 0.05	0.53 ±0.06	0.59 ±0.04
Percent drug content (%)	98.24 ±1.53	97.36 ± 1.44	99.56 ± 0.99	98.68 ± 1.11	99.66 ±1.05
Disintegration time (seconds)	15 ± 2	27 ± 4	28 ± 3	35 ± 5	49 ± 4

SD: n=3

All formulations' tensile strength, friability, and compact density were found to be in an acceptable range, which confirmed the mechanical strength of tablets of Paracetamol DC [41]. Improvement in mechanical strength was observed, possibly due to the formation of porous agglomerates due to the pre-gelatinization of potato starch and the vaporization of water during the drying stage. Porous agglomerates of Paracetamol DC could result in better fragmentation during compression. Pre-gelatinization of potato starch could also contribute to the prepared tablets' rapid disintegration [42]. Tablets of Paracetamol DC containing higher concentrations of Potato starch disintegrated rapidly.

The results of in-vitro drug release studies are presented in Table 5 and Figure 1. More than 50% of the drug was released within the first 40 min from all the formulations. An increase in the rate of drug release was observed with an increase in the proportion of potato starch in Paracetamol DC. However, further release of the drug was negatively affected by an increased proportion of potato starch. The initial release of the drug could be due to better disintegration of the tablet, and a further decrease in release rate could be due to the formation of a swollen layer of starch [43].

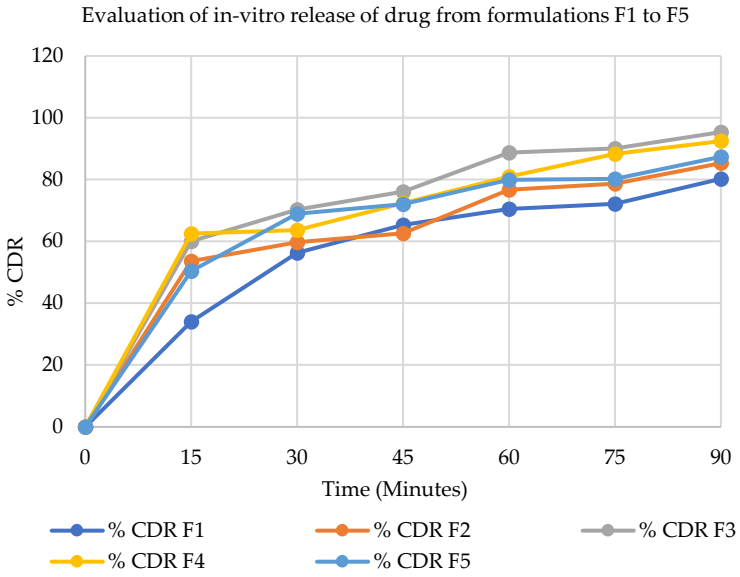

Figure 1. Evaluation of *in-vitro* release of drug from formulations F1 to F5.

Table 5. Evaluation of in-vitro release of drug from formulations F1 to F5.

Time (mins)	Cumulative % drug release				
	F1	F2	F3	F4	F5
15	34.02 ± 2.34	53.64 ± 2.33	60.02 ± 3.42	62.5 ± 2.45	50.4 ± 3.11
30	56.3 ± 2.55	59.66 ± 3.21	70.24 ± 3.21	63.66 ± 3.21	68.87 ± 4.22
45	65.31 ± 3.54	62.59 ± 2.55	76.02 ± 3.76	72.3 ± 3.46	72.02 ± 2.65
60	70.46 ± 2.21	76.66 ± 3.42	88.66 ± 2.44	80.88 ± 3.28	79.92 ± 3.42
75	72.09 ± 3.33	78.66 ± 2.63	90.08 ± 2.56	88.3 ± 3.76	80.24 ± 2.54
90	80.24 ± 3.32	85.34 ± 2.46	95.33 ± 2.11	92.52 ± 2.55	87.39 ± 3.56

SD: n=3

Based on the results of the assessment of precompression and post-compression parameters, it was observed that the Paracetamol DC (PDC3) developed with a 10% mixture containing Potato Starch and Silicon Dioxide in a ratio of 7:3 exhibited excellent flow behavior, good compaction properties, and better disintegration properties and released more than 50% of the drug within the first 30 min.

Stability studies of paracetamol DC

A stability study for PDC 3 was carried out according to ICH guidelines. The results of the study are tabulated in Table 6. No significant differences were observed in the precompression and post-compression parameters of PDC3. This indicates that the developed PDC3 exhibits satisfactory stability.

Table 6. Stability study of developed PDC 3.

Period	Angle of repose	Tensile strength	Disintegration time	% CDR at 30 min	% CDR at 60 min	% CDR at 90 min
1st Month	18.79 ± 1.25	2.44 ± 0.66	29 ± 1.64	68.34 ± 2.33	87.86 ± 1.42	93.35 ± 1.77
2nd Month	18.92 ± 1.56	2.44 ± 0.36	29 ± 1.44	67.44 ± 2.46	86.46 ± 1.67	93.37 ± 1.43
3rd Month	19.28 ± 1.22	2.43 ± 0.46	30 ± 1.57	66.27 ± 2.42	86.62 ± 1.83	92.28 ± 1.63

*Mean ± SD (n= 3)

Conclusion

Paracetamol DC was developed by co-processing Paracetamol with a blend of Potato starch and silicon dioxide using a co-freezing co-drying technique. Results showed marked improvement in flowability, possibly due to silicon dioxide's adherence onto the surface of paracetamol particles. Enhancement of compressibility with good compaction behavior of Paracetamol DC was observed. This could be due to the formation of porous agglomerates because of the pre-gelatinization of potato starch and vaporization of water during drying. An increased concentration of Potato starch showed better disintegration of the tablet; however, it hindered the drug release at higher concentrations.

The results of the studies showed that Paracetamol DC (PDC3) developed with a 10% mixture containing Potato Starch and Silicon Dioxide in a ratio of 7:3 exhibited excellent flow behavior, good compaction properties, and better disintegration properties and released more than 50% of the drug within the first 30 min. The results of accelerated stability studies on PDC3 confirmed the stability of the developed composite.

In conclusion, co-processing of poorly compressible API (Paracetamol) with Potato starch and silicon dioxide using a co-freezing co-drying technique can develop direct compressible active pharmaceutical ingredients.

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Declaration of interest

The authors declare no conflict of interest.

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References

1. Shanmugam S. Granulation techniques and technologies: recent progresses. Bioimpacts. 2015;5(1):55-63.
2. Patel S, Kaushal AM, Bansal AK. Compression physics in the formulation development of tablets. Crit Rev Ther Drug Carrier Syst. 2006;23(1):1-65.
3. Martinello T, Kaneko TM, Velasco MV, Taqueda ME, Consiglieri VO. Optimization of poorly compactable drug tablets manufactured by direct compression using the mixture experimental design. Int J Pharm. 2006;322(1-2):87-95.

4. Sáska Z, Dredán J, Balogh E, Luhn O, Shafir G, Antal I. Effect of isomalt as novel binding agent on compressibility of poorly compactable paracetamol evaluated by factorial design. Powder Technol. 2010;201(2):123-9.
5. Keshavarz L, Pishnamazi M, Khandavilli UR, Shirazian S, Collins MN, Walker GM, et al. Tailoring crystal size distributions for product performance, compaction of paracetamol. Arab J Chem. 2021;14(4):103089.
6. Szumilo M, Belniak P, Swiader K, Holody E, Poleszak E. Assessment of physical properties of granules with paracetamol and caffeine. Saudi Pharm J. 2017;25(6):900-5.
7. Somnache S, Pai KV, Godbole A, Gajare P, Pednekar A. compression vehicle: A technical review. German J Pharm Biomaterials. 2022;1(1):29-46.
8. Mirani AG, Patankar SP, Borole VS, Pawar AS, Kadam VJ. Direct compression high functionality excipient using coprocessing technique: a brief review. Curr Drug Deliv. 2011;8(4):426-35.
9. Panakanti R, Narang AS. Impact of excipient interactions on drug bioavailability from solid dosage forms. Pharm Res. 2012;29(10):2639-59.
10. Alyami H, Dahmash E, Bowen J, Mohammed AR. An investigation into the effects of excipient particle size, blending techniques and processing parameters on the homogeneity and content uniformity of a blend containing low-dose model drug. PLoS One. 2017;12(6): e0178772.
11. Badwan AA, Rashid I, Omari MM, Darras FH. Chitin and chitosan as direct compression excipients in pharmaceutical applications. Mar Drugs. 2015;13(3):1519-47.
12. Bendgude NT, Iyer VR, Poddar SS. The effects of lactose, microcrystalline cellulose and dicalcium phosphate on swelling and erosion of compressed hpmc matrix tablets: texture analyzer. Iran J Pharm Res. 2010;9(4):349-58.
13. Garg N, Dureja H, Kaushik D. Co-processed excipients: a patent review. Recent Pat Drug Deliv Formul. 2013;7(1):73-83.
14. Saha S, Shahiwala AF. Multifunctional coprocessed excipients for improved tabletting performance. Expert Opin Drug Deliv. 2009;6(2):197-208.
15. Somnache SN, Pai KV, Godbole AM, Gajare PS, Pednekar AS. Development of M3 as improved functionality composite excipient for direct compression. IJPSN;15(5):6111-20.
16. Builders PF, Arhewoh MI. Pharmaceutical applications of native starch in conventional drug delivery. Starch. 2016;68(9-10):864-73.
17. Szabó-Révész P, Szepes A. Potato starch in pharmaceutical technology-A review. Glob Sci. 2009;3:109-17.
18. Michaud J. Starch based excipients for pharmaceutical tablets. Pharmaceuticals. 2002;42-4.
19. Alebiowu G, Itiola OA. The effects of starches on mechanical properties of paracetamol tablet formulations. I. Pregelatinization of starch binders. Acta Pharm. 2003;53(3):231-7.
20. Abdullah AHD, Chalimah S, Primadona I, Hanantyo MHG. Physical and chemical properties of corn, cassava, and potato Starchs. IOP Conf. Ser.: Earth Environ. Sci. 2018: 160 012003.
21. Xu F, Zhang L, Liu W, Liu Q, Wang F, Zhang H, et al. Physicochemical and structural characterization of potato starch with different degrees of gelatinization. Foods. 2021;10(5):1104.
22. Trisopon K, Kittipongpatana OS. Development of a direct compression excipient from epichlorohydrin-crosslinked carboxymethyl rice starch with sodium silicate using a coprocessing technique. Starch. 2019;71(5-6):1800220.
23. Deshkar D, Gupta RN, Kumar KJ. Studies on effect of co-processing on palmyrah and Maize Starch mixtures using DOE approach. Int J Biol Macromol. 2019;122:417-24.
24. Apeji YE, Oyi AR, Isah AB, Allagh TS, Modi SR, Bansal AK. Development and optimization of a Starch-based co-processed excipient for direct compression using mixture design. AAPS PharmSciTech. 2018;19(2):866-80.
25. Apeji YE, Aluga D, Olayemi OJ, Oparaeche C, Anyebe SN, Gamlen MJ, et al. Comparative analysis of co-processed starches prepared by three different methods. Br J Pharm. 2017;2(1):55.
26. Rojas J, Kumar V. Comparative evaluation of silicified microcrystalline Cellulose II as a direct compression vehicle. Int J Pharm. 2011;416(1):120-8.
27. Rashid I, Al-Remawi M, Leharne SA, Chowdhry BZ, Badwan A. A novel multifunctional pharmaceutical excipient: Modification of the permeability of Starch by processing with magnesium silicate. Int J Pharm. 2011;411(1-2):18-26.
28. Fuentes-González KI, Villafuerte-Robles L. Powder flowability as a functionality parameter of the excipient GalenIQ 720. Int J Pharm Pharm Sci. 2014;1:66-74.
29. Tay JYS, Liew CV, Heng PWS. Powder flow testing: Judicious choice of test methods. AAPS PharmSciTech. 2017;18(5):1843-54.
30. Tan G, Morton DA, Larson I. On the methods to measure powder flow. Curr Pharm Des. 2015;21(40):5751-65.

31. Sandhan SB, Derle DV. A review on functionality assessment of multifunctional excipients IJPSR. 2019;10(9): 4078-89.
32. Olorunsola EO, Akpan GA, Adikwu MU. Evaluation of chitosan-microcrystalline cellulose blends as direct compression excipients. J Drug Deliv. 2017;8563858.
33. Tye CK, Sun CC, Amidon GE. Evaluation of the effects of tableting speed on the relationships between compaction pressure, tablet tensile strength, and tablet solid fraction. J Pharm Sci. 2005;94(3):465-72.
34. Kashyap S, Singh A, Godbole AM, Somnache SN. Design, development and characterization of release modulated terbutaline sulphate pulsincap device for treatment of nocturnal asthma. Res J Pharm Technol. 2018 30;11(4):1655-62.
35. Department of Indian systems of Medicine and Homoeopathy. Indian Pharmacopoeia 2014 Volume No. 1, Gaziabad. Indian Pharmacopoeia Commission (IPC).
36. Vaghela B, Kayastha R, Bhatt N, Pathak N, Rathod D. Development and validation of dissolution procedures. J Appl Pharm Sci. 2011;1(3):50-6.
37. Jonat S, Hasenzahl S, Drechsler M, Albers P, Wagner KG, Schmidt PC. Investigation of compacted hydrophilic and hydrophobic colloidal silicon dioxides as glidants for pharmaceutical excipients. Powder technol. 2004;141(1-2):31-43.
38. Abe H, Yasui S, Kuwata A, Takeuchi H. Improving powder flow properties of a direct compression formulation using a two-step glidant mixing process. Chem Pharm Bull. 2009;57(7):647-52.
39. Somnache SN, Pai KV, Godbole AM, Gajare PS, Pednekar AS. COMBILOSE: A novel lactose-based co-processed excipient for direct compression. J Appl Pharm Sci. 2023;13(04):213-9.
40. Hiestand HE, Smith DP. Indices of tableting performance. Powder Technol. 1984;38(2):145-59.
41. Newton JM, Haririan I, Podczeck F. The determination of the mechanical properties of elongated tablets of varying cross section. Eur J Pharm Biopharm. 2000;49(1):59-64.
42. Ma H, Liu M, Liang Y, Zheng X, Sun L, Dang W, et al. Research progress on properties of pre-gelatinized starch and its application in wheat flour products. Grain & Oil Science and Technology. 2022;5(2):87-97.
43. Zámostný P, Petrů J, Majerová D. Effect of maize starch excipient properties on drug release rate. Procedia Engineering. 2012;42:482-8.

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