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COMBILOSE: A novel lactose-based co-processed excipient for direct compression

Sandesh Narayan Somnache[1*], Karkala Vasantakumar Pai[2], Ajeet Madhukar Godbole[1], Pankaj Sadashiv Gajare[1], Arti Shashikant Pednekar[1]

[1]Department of Pharmaceutics, PESs Rajaram and Tarabai Bandekar College of Pharmacy, Ponda, India.
[2]Department of Industrial Chemistry, KUVEMPU University, Shimoga, India.

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ABSTRACT

Lactose is the commonly used diluent in the manufacturing of tablets dosage form. However, the poor flowability and compressibility of lactose limit its use as direct compressible filler binder. In this research work, composite excipient COMBILOSE was developed as directly compressible filler binder by coprocessing technique. Lactose monohydrate was co-processed with maltose monohydrate and maize starch by co-freezing and co-drying technique. Physical blends of lactose monohydrate and maize starch were prepared in ratio of 20:1. Prepared physical blends were dispersed in 5% w/v, 10% w/v, and 15% w/v aqueous solutions of maltose monohydrate. Dispersions were subjected to co-freezing followed by co-drying. Microfine granules of COMBILOSE were obtained by comminution and sifting of the dried composites. The developed composite excipients were evaluated for various excipient functionalities. The results of studies showed that coprocessing of lactose monohydrate with maize starch and maltose monohydrate can improve flowability and tabletability. COMBILOSE containing 10% w/v of maltose monohydrate showed better dilution potential and reduced lubricant sensitivity. Improvement in compressibility was observed, which could be due to pre-gelatinization of maize starch during development process. In conclusion, a blend of lactose monohydrate and maize starch in a ratio of 20:1 when processed with 10% of maltose monohydrate could provide good compressibility and better dilution potential with a reduced lubricant sensitivity.

INTRODUCTION

Lactose is the most commonly used pharmaceutical diluent for the development of compressed solid dosage forms. However, poor flow property and compressibility of lactose limits its use as a direct compressible filler and binder (Patel *et al*., 2011; Ugoeze and Idris, 2020). Modification of shape and size of its particle usually improves flowability and compressibility of this excipient (Kudo *et al*., 2020). The compressibility of adjuvant developed by co-granulation of brittle and ductile material was found to be highly influenced by proportion of poorly fragmenting brittle material such as lactose (Gohel *et al*., 2003). Study on various techniques of granulation of lactose showed that freezing and subsequent drying of lactose with aqueous dispersions of starch can improve compressibility and exhibit lower ejection forces (Patel *et al*., 2011). However, a poor improvement in compressibility and dilution potential was observed in case of modified grades of lactose. Similarly, commercially available lactose-based co-processed excipients showed higher compactability, but with a poor tensile strength (TS)and high ejection force (Dominik *et al*., 2021; Hauschild and Picker, 2004; Rani and Begum, 2014).

Tablets compressed using developed excipient composite by co-granulation of highly compressible saccharides such as maltose with poorly compressible saccharides such as lactose

**Corresponding Author*
Sandesh Narayan Somnache, PESs Rajaram and Tarabai Bandekar College of Pharmacy, Ponda, India.
E-mail: sandeshsomnache @ gmail.com

showed marked improvement in mechanical strength without affecting disintegration, due to very high surface free energy and amorphous state of highly compressible saccharides (Mizumoto *et al*., 2005). Microgranules of lactose developed by coprocessing with microcrystalline cellulose and corn starch in a ratio of 7:2:1 gave excellent flow property, good compressibility with better binding property, and reduced disintegration time (Akram *et al*., 2011). Improved mechanical strength and disintegration property was observed for tablets compressed by using StarLac containing lactose and starch in the ratio of 85:15 (Hauschild and Picker, 2004; Schwarz *et al*., 2022). However, there was a negative impact on flowability of co-processed excipients observed with excipient formulation containing excess quantity of starch (Akram *et al*., 2011; Chang *et al*., 2008). A comparative study using fully gelatinized starch and pregelatinized starch showed that the tablet formulation compressed using pre-gelatinized starch exhibited better crushing strength and friability, which could be due to enlargement of the particles because of formation of agglomerates during process of pre-gelatinization (Olowosulu *et al*., 2011). Increase in swelling behavior was observed in case of pre-gelatinized starch. This could be due to increase in amylase content because of structural deterioration and molecular disarrangement during hydrothermal exposure of starch (Deshkar *et al*., 2019).

The study reported herein aims to develop COMBILOSE as a lactose-based composite excipient by coprocessing it with maltose and maize starch.

MATERIALS

Paracetamol IP was received as a gift sample from Wallace Pharmaceuticals Pvt Ltd Goa, India. Lactose monohydrate (SD Fine Chem, Mumbai, India), maize starch (Ozone International, Mumbai, India), maltose monohydrate (Molychem, Mumbai, India), purified talc (SD Fine Chem, Mumbai, India), and magnesium stearate (Molychem, Mumbai, India) were procured from Shri Venkatesh Enterprises, Dharwad, India.

Design and development of excipient composite: COMBILOSE

Aqueous solutions of maltose monohydrate in varying concentrations were prepared by dissolving the weighed quantity of maltose monohydrate (Table 1) in 100 ml of distilled water. The physical blends of lactose monohydrate and maize starch were prepared as per Table 1 and were added to respective solutions of maltose monohydrate with continuous stirring using a mechanical stirrer with rotational speed maintained at 500 rpm. The resultant dispersions were refrigerated overnight. The frozen dispersions were pre-heated for 15 minutes at 60°C to initiate pre-gelatinization of maize starch and then dried for 120 minutes at 50°C in a tray dryer. The dried composites were size reduced and sifted to obtain micro-fine granules of the required size. The developed granules were subjected to the assessment of various excipient functionality parameters.

Evaluation of pre-compression parameters

Flow properties

The rate of flow of sample of the developed COMBILOSE was determined using the angle of repose and Hausner's ratio. A fixed funnel with a constant pressure head method was used to determine the angle of repose (Fuentes-Gonzalez and Villafuerte-Robles, 2014). Hausner's ratio was calculated using tapped and untapped densities of COMBILOSE (Moondra *et al*., 2018). Carr index was determined as an indicative of compressibility of COMBILOSE. Ratio of difference in tapped density and untapped density against tapped density was determined (Moondra *et al*., 2018).

Moisture sorption capacity and swelling behavior

The moisture content of developed COMBILOSE was determined by exposing weighed quantity of COMBILOSE in a Petri plate to 60°C in a tray dryer till a constant weight was obtained and the percentage moisture loss against the total weight of COMBILOSE was recorded (Olorunsola *et al*., 2017). Moisture sorption capacity was determined by exposing the weighed amount of COMBILOSE to 75%RH for 120 hours at room temperature. The percent weight of water absorbed against the dry weight of the sample was determined (Olorunsola *et al*., 2017). The percent rise in the volume of wet powder of COMBILOSE due to swelling was used to calculate the percentage swelling index (Olorunsola *et al*., 2017).

True density and porosity

The true density of COMBILOSE was determined using a specific gravity bottle. Ortho-Xylene was used as displacement fluid (Hasan *et al*., 2012). The obtained values of bulk volume and true volume were used to calculate porosity of the sample of COMBILOSE (Hasan *et al*., 2012).

Evaluation of post-compression parameters

Evaluation of mechanical properties

Mechanical properties of the developed COMBILOSE were evaluated by compressing the blend of COMBILOSE with 2% magnesium stearate as a lubricating agent and 2% purified talc as a glidant on 12 station Karnavati tablet press. Three batches of 250 tablets each (average weight of 500 mg and 3–5 mm thickness) containing COMBILOSE 05, COMBILOSE 10, and COMBILOSE 15 were compressed by direct compression method using 10-mm D tooling with a turret speed of 4.5–5.5 RPM. The compressed tablets were evaluated for compact density (CD), Tensile Strength (TS) and bonding index, solid fraction (SF), and porosity (Table 2) (Olorunsola *et al*., 2017; Sandhan and Derle, 2019; Tye *et al*., 2005).

Table 1. Formulation of COMBILOSE as co-processed excipient.

	COMBILOSE 05	COMBILOSE 10	COMBILOSE 15
Lactose monohydrate	100 g	100 g	100 g
Maltose monohydrate	5 g	10 g	15 g
Maize starch	5 g	5 g	5 g
Distilled water	100 ml	100 ml	100 ml

Table 2. Evaluation of mechanical properties of COMBILOSE.

Evaluation parameter	Formula	Particulars	References
CD	$CD = \frac{M}{\pi r^2 t}$	m is the weight of tablet r is the radius of tablet t is the thickness of tablet F is diametrical crushing strength (permanent deformation pressure) of tablet d is the diameter of tablet TS is tensile strength of tablets	Olorunsola *et al*. (2017); Sandhan and Derle (2019)
TS	Tensile strength $= \frac{2F}{\pi dt}$		
Bonding index	Bonding index $= \frac{TS}{F}$		
SF	Solid fraction $= \frac{CD}{D_t}$ -	CD is compact (tablet) density D_t is true density of the powder blend	Tye *et al*. (2005)
Tablet porosity	Tablet porosity $= \left(1 - \frac{CD}{D_t}\right)$		

Table 3. Evaluation of dilution potential.

	Drug: excipient ratio					
Paracetamol	0	1	2	3	4	5
COMBILOSE	5	4	3	2	1	0

Table 4. Flow properties of developed excipient formulations (n = 3*).

Precompression parameter	COMBILOSE 05	COMBILOSE 10	COMBILOSE 15
Angle of repose	25.46 ± 1.43	21.20 ± 1.22	32.27 ± 1.35
Hausner's ratio	1.27 ± 0.04	1.30 ± 0.06	1.41 ± 0.06
Carr's index compressibility index	21.81 ± 1.34	23.07 ± 1.78	28.57 ± 1.70

Determination of dilution potential

The dilution potential of the developed COMBILOSE was determined using paracetamol as a model for a poorly compressible drug. The formulation blends containing COMBILOSE 05, COMBILOSE 10, and COMBILOSE 15 were prepared separately with an increasing ratio of paracetamol (Table 3). The prepared blends were mixed with 2% of purified talc and 2% of magnesium stearate as a processing aid and were compressed as a tablet with an average weight of 500 mg using a direct compression method on 12 station Karnavati tablet press. TS of compressed tablets were calculated for each formulation blend using the measured diameter, thickness, and diametrical crushing strength of tablets. TS of compressed tablets were plotted against respective percentage drug content (Gohel *et al*., 2012; Haruna *et al*., 2020).

Determination of lubricant sensitivity

The effect of an increased proportion of magnesium stearate on the percentage friability of the COMBILOSE tablet was evaluated to determine the lubricant sensitivity. Tablets of COMBILOSE with an average weight of 500 mg were compressed using increasing proportions (0%–5%) of magnesium stearate and 2% of purified talc. The percentage friability of tablets from each batch was analyzed against the proportion of magnesium stearate (Daraghmeh *et al*., 2010; Haruna *et al*., 2020).

RESULT AND DISCUSSION

Flow properties

The developed excipient COMBILOSE exhibited fair to excellent flow properties. This may possibly be due to uniformity in the size of micro-fine granules. The results are tabulated in Table 4. The decrease in flowability was observed with an increase in the concentration of maltose. This could be due to the tendency of maltose to form aggregate by absorbing moisture (Crouter and Briens, 2014; Lamy *et al*., 2019). COMBILOSE 05 with 5% of maltose exhibited better flow behavior compared to that of COMBILOSE 10 and COMBILOSE 15.

Moisture sorption capacity and swelling behavior

Moisture content is one of the critical parameters which affects the process of compression. (Patel *et al*., 2006). About 4%–5% of moisture content in filler binder is usually considered ideal for direct compression (Tomar *et al*., 2017). The moisture sorption capacity of excipients affects the TS of tablets during storage (Malamataris *et al*., 1991). Hence, it could be one of the parameters of critical consideration for direct compressible excipient.

High moisture content and moisture sorption capacity were observed for COMBILOSE containing a higher proportion of maltose. This may be due to the solubility behavior and hygroscopic nature of maltose. The aqueous solubility of maltose also affected results of swelling capacity of the excipient formulation. In aqueous medium, maize starch could swell due to pre-gelatinization during the co-drying step of excipient development. However, negative results for the percentage swelling index were observed, which could be due to the solubilization of maltose. The results are presented in Table 5.

True density and porosity

Higher true density with a low porosity was observed for COMBILOSE containing a higher proportion of maltose. This could be due to the filling up of voids of agglomerates of maize starch with soluble entities of maltose. The results of the study are presented in Table 6.

CD, TS, and bonding index

The developed excipients COMBILOSE were assessed for tabletability using various evaluation parameters such as CD,

Table 5. Moisture sorption capacity and swelling behavior of developed excipient formulations (n = 3*).

Precompression parameter	COMBILOSE 05	COMBILOSE 10	COMBILOSE 15
% Moisture content	3.15 ± 0.3	4.31 ± 0.5	6.53 ± 0. 4
% Moisture sorption capacity	46.31 ± 5.3	51.21 ± 3.4	57.42 ± 5.1
% Swelling index	−12.5 ± 0.3	−21.77 ± 0.6	−31.57 ± 0.5

Table 6: True density and porosity of developed excipient formulations (n = 3*).

Precompression parameter	COMBILOSE 05	COMBILOSE 10	COMBILOSE 15
True density	1.42 ± 0.42	1.48 ± 0.52	1.52 ± 0.36
Porosity	0.88 ± 0.03	0.86 ± 0.06	0.85 ± 0.07

Table 7. Evaluation of CD, TS, and bonding index (n = 3*).

Post compression parameters	COMBILOSE 05	COMBILOSE 10	COMBILOSE 15
CD g/cm^3	0.33 ± 0.07	0.35 ± 0.04	0.40 ± 0.03
TS g/cm^2	1.14 ± 0.02	1.40 ± 0.05	1.70 ± 0.03
Bonding index	0.34 ± 0.05	0.35 ± 0.02	0.37 ± 0.04
SF	0.22 ± 0.03	0.23 ± 0.05	0.28 ± 0.07
Porosity	0.78 ± 0.02	0.76 ± 0.06	0.72 ± 0.05

Table 8. Determination of dilution potential (n = 3*).

Formulation no.	Drug excipient ratio	% Drug content	CD g/cm^3	TS Kg/cm^2
COMBILOSE 05	00:05	0	0.33 ± 0.07	1.15 ± 0.02
	01:04	20	0.32 ± 0.05	0.81 ± 0.04
	02:03	40	0.35 ± 0.06	0.55 ± 0.05
	03:02	60	Capping of tablet	
	04:01	80		
	05:00	100	Tablets could not compressed*	
COMBILOSE 10	00:05	0	0.35 ± 0.04	1.41 ± 0.02
	01:04	20	0.34 ± 0.05	1.24 ± 0.03
	02:03	40	0.36 ± 0.06	0.68 ± 0.02
	03:02	60	0.37 ± 0.04	0.48 ± 0.05
	04:01	80	Capping of tablet	
	05:00	100	Tablets could not compressed*	
COMBILOSE 15	00:05	0	0.40 ± 0.03	1.71 ± 0.06
	01:04	20	0.38 ± 0.04	1.33 ± 0.04
	02:03	40	0.33 ± 0.07	0.77 ± 0.07
	03:02	60	0.36 ± 0.04	0.47 ± 0.05
	04:01	80	0.32± 0.06	0.35 ± 0.04
	05:00	100	Tablets could not compressed*	

* The formulation blend containing 100% of drug could not be compressed due to poor compressibility of paracetamol.

porosity, TS, and bonding index (Table 7). The tablets prepared with COMBILOSE containing an increased proportion of maltose exhibited a higher bonding index and CD. The increase in TS of tablets could be due to the pre-gelatinization of maize starch during the excipient development stage (Odeku *et al*., 2008). In addition to this, loss of water of crystallization also contributes for better fragmentation of COMBILOSE on application of compression force. The SF was found to be increased with a decreased porosity.

Dilution potential and lubricant sensitivity

Results of dilution potential and lubricant sensitivity of COMBILOSE showed that an increase in the percentage of maltose in COMBILOSE provides a better dilution potential; however, the same exhibited high sensitivity for hydrophobic lubricants such as magnesium stearate. The results of the study are tabulated in Tables 8 and 9. The tablets of paracetamol with COMBILOSE 15 exhibited better dilution potential. Tablets with COMBILOSE 5 and COMBILOSE 10 showed acceptable TS at a lower proportion of paracetamol; however, capping was observed for tablets with a higher proportion of paracetamol (Table 8). This could be possibly due to high post-ejection elastic recovery. High lubricant sensitivity was observed for COMBILOSE containing a higher proportion of maltose, which could be due to poor fragmentation during compression (Table 9).

TS for COMBILOSE containing 0%, 20%, 25%, and 30% of maltose were determined mathematically from equations obtained from the graph of TS of COMBILOSE 05, 10, and 15 against respective percentage drug content (Tables 8 and 10, Fig. 1). Effects of an incremental increase in maltose content of COMBILOSE on TS were derived mathematically (Table 11, Figs. 2 and 3). The results indicated that maltose monohydrate in

Table 9. Determination of lubricant sensitivity ($n = 3$*).

% Lubricant Content	COMBILOSE 05	COMBILOSE 10	COMBILOSE 15
1	0.55 ± 0.02	0.64 ± 0.02	0.65 ± 0.03
2	0.67 ± 0.03	0.73 ± 0.03	0.75 ± 0.03
3	0.72 ± 0.02	0.80 ±0.03	0.85 ± 0.03
4	0.79 ± 0.04	0.86 ± 0.03	Capping and Lamination
5	0.88 ± 0.03	0.92 ± 0.03	

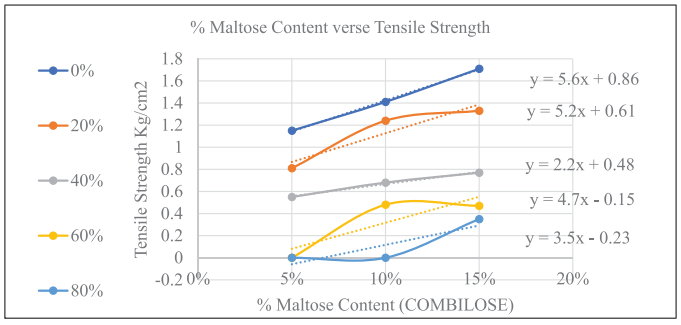

Figure 1. Graph of % maltose content in COMBILOSE versus TS.

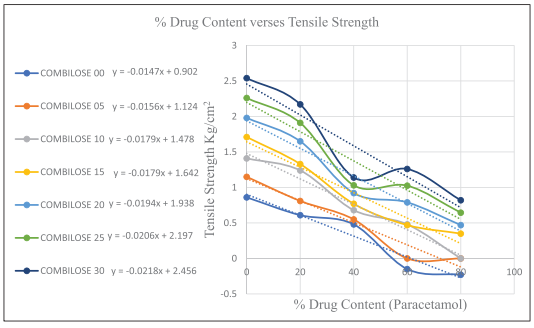

Figure 2. Graph of % drug content versus TS.

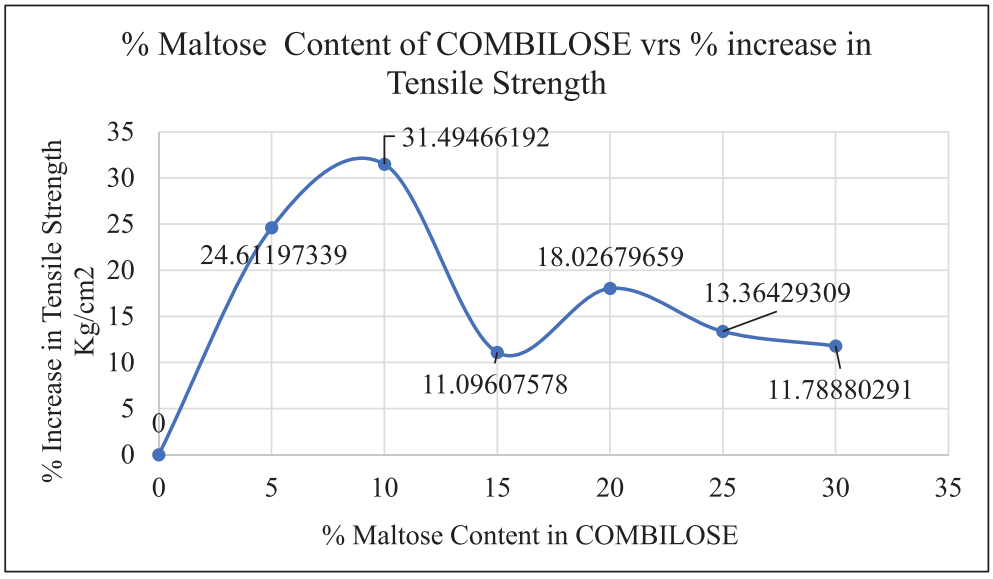

Figure 3. Increase in TS per 5% increase in maltose content of COMBILOSE.

Table 10. Determination of tensile strength.

% Drug content	Equation of line	TS for COMBILOSE (Kg/cm$^{2)}$						
		00*	05	10	15	20*	25*	30*
00	$y = 5.6\times + 0.86$	0.86	1.15	1.41	1.71	1.98	2.26	2.54
20	$y = 5.2\times + 0.61$	0.61	0.81	1.24	1.33	1.65	1.91	2.17
40	$y = 2.2\times + 0.48$	0.48	0.55	0.68	0.77	0.92	1.03	1.14
60	$y = 4.7\times - 0.15$	−0.15	0	0.48	0.47	0.79	1.025	1.26
80	$y = 3.5\times - 0.23$	−023	0	0	0.35	0.47	0.645	0.82

*Calculated values of tensile strength.

Table 11. Effect of incremental increase in maltose content of COMBILOSE on TS.

% Maltose content of COMBILOSE	TS (Kg/cm^2)	Percent increase in TS
0	0.90 Kg/cm^2	0.00
5	1.12 Kg/cm^2	24.61
10	1.47 Kg/cm^2	31.49
15	1.64 Kg/cm^2	11.09
20	1.93 Kg/cm^2	18.02
25	2.19 Kg/cm^2	13.3
30	2.45 Kg/cm^2	11.78

10% concentration in COMBILOSE substantially improved the dilution potential when compared to other concentrations.

CONCLUSION

COMBILOSE was developed as a novel lactose-based co-processed excipient by co-drying of an aqueous dispersion of lactose monohydrate with maize starch and maltose monohydrate. The aqueous dispersions of lactose monohydrate, maltose monohydrate, and maize starch were prepared in varying ratios and refrigerated for 12 hours. Frozen dispersions were pre-heated at 60°C and then dried at 50°C using a tray dryer. The composites that were obtained were size reduced and sifted to obtain micro-fine granules.

The developed excipient, COMBILOSE, showed better flowability, which could be due to uniformity in the size of microfine granules. An increase in CD and bonding index was observed, which could be due to the development of an increased number of contact points between the particles of composite because of better fragmentation of composite excipient. Pre-gelatinization of maize starch during drying could be another reason for the improved TS of the tablets. COMBILOSE with an increased proportion of high compressible saccharide exhibited good compressibility with better dilution potential. This could be attributed to the formation of porous agglomerates of maize starch with lactose. However, COMBILOSE containing a higher proportion of maltose exhibited high lubricant sensitivity and leads to capping and lamination of tablets. This may be due to poor fragmentation and higher elastic recovery. In conclusion, the results of the study revealed that the coprocessing of lactose monohydrate using 10% of maltose monohydrate can improve dilution potential. The compressibility of the excipient can be improved by co-treatment with a plastically deforming form of starch developed by pre-gelatinization.

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AUTHOR CONTRIBUTIONS

All authors made substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; took part in drafting the article or revising it critically for important intellectual content; agreed to submit to the current journal; gave final approval of the version to be published; and agree to be accountable for all aspects of the work. All the authors are eligible to be an author as per the international committee of medical journal editors (ICMJE) requirements/guidelines.

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The authors have no conflicts of interest regarding this investigation.

ETHICAL APPROVALS

This study does not involve experiments on animals or human subjects.

DATA AVAILABILITY

All data generated and analyzed are included in this research article.

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REFERENCES

Akram M, Naqvi SBS, Gauhar S. Development of co-processed micro granules for direct compression. Int J Pharm Pharm Sci, 2011; 3(Suppl 2):64–9.

Chang CK, Alvarez-Nunez FA, Rinella JV Jr, Magnusson LE, Sueda K. Roller compaction, granulation and capsule product dissolution of drug formulations containing a lactose or mannitol filler, starch, and talc. AAPS PharmSciTech, 2008; 9(2):597–604.

Crouter A, Briens L. The effect of moisture on the flowability of pharmaceutical excipients. AAPS PharmSciTech, 2014; 15:65–74.

Daraghmeh N, Rashid I, Al Omari MM, Leharne SA, Chowdhry BZ, Badwan A. Preparation and characterization of a novel co-processed excipient of chitin and crystalline mannitol. AAPS PharmSciTech, 2010; 11(4):1558–71.

Deshkar D, Gupta RN, Jayaram Kumar K. Studies on effect of co-processing on palmyrah and maize starch mixtures using DOE approach. Int J Biol Macromol, 2019; 122:417–24.

Dominik M, Vraníková B, Svačinová P, Elbl J, Pavloková S, Prudilová BB, Šklubalová Z, Franc A. Comparison of flow and compression properties of four lactose-based co-processed excipients: Cellactose® 80, CombiLac®, MicroceLac® 100, and StarLac®. Pharmaceutics, 2021; 13(9):1486.

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.

Gohel MC, Jogani PD, Bariya SH. Development of agglomerated directly compressible diluent consisting of brittle and ductile materials. Pharm Dev Technol, 2003; 8(2):143–51.

Gohel MC, Patel TM, Parikh RK, Parejiya PB, Barot BS, Ramkishan A. Exploration of novel co-processed multifunctional diluent for the development of tablet dosage form. Indian J Pharm Sci, 2012; 74(5):381–6.

Haruna F, Apeji YE, Oparaeche C, Oyi AR, Gamlen M. Compaction and tableting properties of composite particles of microcrystalline cellulose and crospovidone engineered for direct compression. Futur J Pharm Sci, 2020; 6(35):9.

Hasan MM, Chowdhury SS, Lina SM, Bhoumik NC, Ashab I. Comparative evaluation of *Zea* mays (L.) and *Ipomoea batatas* (L.) as a pharmaceutical excipient. IOSR-JPBS, 2012; 3:31–6.

Hauschild K, Picker KM. Evaluation of a new coprocessed compound based on lactose and maize starch for tablet formulation. AAPS J, 2004; 6(2):27–38.

Kudo Y, Yasuda M, Matsusaka S. Effect of particle size distribution on flowability of granulated lactose. Adv Powder Technol, 2020; 31(1):121–7.

Lamy B, Serrano DR, O'connell P, Couet W, Marchand S, Healy AM, Tewes F. Use of leucine to improve aerodynamic properties of ciprofloxacin-loaded maltose microparticles for inhalation. EJPR, 2019; 1(1):2–11.

Malamataris S, Goidas P, Dimitriou A. Moisture sorption and tensile strength of some tableted direct compression excipients. Int J Pharm, 1991; 68(1–3):51–60.

Mizumoto T, Masuda Y, Yamamoto T, Yonemochi E, Terada K. Formulation design of a novel fast-disintegrating tablet. Int J Pharm, 2005; 306(1–2):83–90.

Moondra S, Maheshwari R, Taneja N, Tekade M, Tekade RK. Bulk level properties and its role in formulation development and processing. In: Tekadle RK (ed.). Advances in pharmaceutical product development and research, dosage form design parameters. vol. II. Academic Press, London, UK, pp 221–56, 2018.

Odeku OA, Schmid W, Picker-Freyer KM. Material and tablet properties of pregelatinized (thermally modified) *Dioscorea* starches. Eur J Pharm Biopharm, 2008; 70(1):357–71.

Olorunsola EO, Akpan GA, Adikwu MU. Evaluation of chitosan-microcrystalline cellulose blends as direct compression excipients. J Drug Deliv, 2017; 2017:8.

Olowosulu AK, Oyi A, Isah AB, Ibrahim MA. Formulation and evaluation of novel coprocessed excipients of maize starch and *acacia* gum (StarAc) for direct compression tabletting. IJPRI, 2011; 2:39–45.

Patel P, Telange D, Sharma N. Comparison of different granulation techniques for lactose monohydrate. Int J Pharm Sci Drug Res, 2011; 3(3):222–5.

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

Rani U, Begum N. Overview of co processed excipients used to improve tabletting performance. JADD, 2014; 1(6):8.

Sandhan SB, Derle DV. A review on functionality assessment of multifunctional excipients. IJPSR, 2019; 10(9):4078–89.

Schwarz E, Fichtner V, Luhn O, Häusler O. Case study: properties of a co-processed compound versus the physical blend based on lactose and starch. Available via https://www.roquette.com/media-center/resources/pharma-poster-properties-of-a-co-processed-compound-vs-blend-lactose-starch (Accessed 08 May 2022).

Tomar M, Kumar SA, Raj SA. Effect of moisture content of exicipient (microcrystalline cellulose) on direct compressible solid dosage forms. IJPSR, 2017; 8(1):282.

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.

Ugoeze KC, Idris MEJ. Development of co-processed powders containing lactose, *Mucuna flagellipes* seed gum and *Ipomoea batatas* tuber starch. Int J Appl Biol Pharm, 2020; 11(4):256–75.

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