



Development and evaluation of a novel, multifunctional, co-processed excipient via roller compaction of α -Lactose Monohydrate and Magnesium Silicate.

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ABSTRACT

This study investigates co-processing lactose with synthetic amorphous magnesium silicate with the aim of expanding the use of directly compressible excipients based on native lactose. The co-processing was performed using roller compaction. The co-processed excipient was characterized using particle size analysis and compression properties (Kawakita equation). The co-processed excipient demonstrated plastic behavior upon compression, good flowability and crushing strength and a shorter disintegration time. Compatibility between the different ingredients of the co-processed excipient, as well as, between the co-processed excipient and model drugs was tested using Differential Scanning Calorimetry (DSC) and Fourier Transform Infrared spectroscopy (FTIR). The interaction between lactose and magnesium silicate proved to be of a physical nature. Formulating this co-processed excipient with Mebeverine HCl and Losartan Potassium as model drugs, indicated its suitability as a single multi-functional excipient. Co-processed lactose with magnesium silicate could be used as a single direct compression excipient for tablet manufacturing.

KEY WORDS: Co-processed excipients, lactose, magnesium silicate, direct compression excipients, roller compaction

INTRODUCTION

α -lactose monohydrate is among the most widely used filler diluents in solid dosage formulations due to its cost effectiveness, availability, bland taste, low hygroscopicity, high

solubility and stability (1). However, non-agglomerated α -lactose monohydrate is not generally considered a suitable excipient for direct compression because its crystallinity causes brittle fracture behavior upon compression resulting in poor binding properties (2). This has been overcome in the industry by spray drying α -lactose monohydrate which increases the amorphous fraction thus allowing

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for better compaction, resulting in tablets with better binding properties and higher tensile strength (3, 4). Wet granulation of α -lactose monohydrate is still a popular choice for manufacturing pharmaceutical tablets. As an alternative technique, to provide a directly compressible excipient for solid dosage form manufacturing, co-processing lactose with other excipients has been widely adopted. To this effect, α -lactose monohydrate has been co-processed with e.g., cellulose (Cellactose[®]), Microcrystalline Cellulose (MicroceLac[®]), starch (StarLac[®]) and polyvinylpyrrolidone (Ludipress[®]). Such co-processed excipients can be used as filler-binders, but the formulation still requires additional excipients to add functionality to the finished solid dosage form.

Recently metal silicates, specifically calcium, magnesium and aluminum silicates, have been used to develop novel, multi-functional, directly compressible pharmaceutical excipients by co-processing them with other commonly used excipients, e.g., starch, microcrystalline cellulose or chitin (5, 6). These co-processed excipients can be used as single excipients without the need for other functional components. Thus a formulation including such a co-processed excipient together with an API and a lubricant can be compressed directly.

Among these silicates, magnesium silicate (Mg silicate) has shown to be a promising candidate for co-processing with other materials. For example, Hamid *et al.* (7) has reported that a chitin-Mg silicate composite, in comparison with other chitin-metal silicate composites (Al, Ca) indicated the best performance for tableting in terms of compaction, disintegration and dissolution properties. Additionally, in a study of the solid-state degradation of cefotaxime sodium in the presence of different chitin-metal silicates (Al, Ca, Mg), chitin-Mg silicate composite was shown to be the most suitable metal silicate by providing a neutral

surface as a compatible micro-environment for cephalosporin antibiotics (8).

Co-processing starch with Mg silicate has been found to offer a potential as a filler, a binder and a superdisintegrant in formulations prepared by direct compression or wet granulation (5, 6). Thus, Mg silicate is a reasonable choice to use as a component for co-processing with other commonly used diluent excipients.

Based on previous studies it was decided to investigate a possible improvement in the compactibility of α -lactose monohydrate, which is naturally poorly compactable, by co-processing it with Mg silicate using roller compaction (RC) which is more convenient and economical than spray-drying. The co-processed materials were characterized in terms of flowability, compactibility, compressibility and performance as a single multi-functional excipient directly compressed with two separate model drugs (Losartan potassium and Mebeverine hydrochloride).

MATERIALS AND METHODS

Materials

Aqueous sodium silicate, (46%) alkaline[®] Na₂SiO₃.5H₂O (Jordan Sulfo Chemicals Co. Zarqa, Jordan), processed Dead Sea brine (33% magnesium chloride MgCl₂.6H₂O), Pharmatose 50[®] (α -lactose monohydrate, JBICHEM Shanghai, China) and Fast Flo[®] were obtained from Foremost Farms USA (Baraboo, WI). All other reagents were donated by the Jordanian Pharmaceutical Manufacturing Co. (JPM, Naor, Jordan) and used without modification. Duspatalin[®] 135mg tablets (Mebeverine HCL, Solvay pharmaceuticals Company, Brussels, Belgium), and COZAR[®] 50 tablets (Losartan K, Merck Sharp & Dohme, USA) were purchased from local pharmacies.

Methods

Preparation of magnesium silicate

Magnesium silicate was prepared as described previously by Rashid *et al.* (5). Briefly, 200 ml of the 46% aqueous solution of sodium silicate was diluted to 2000 ml with de-ionized water. To this, 150 ml of 33% Magnesium Chloride solution was added gradually stirring continuously. The precipitated hydrated Mg silicate was filtered and the product was washed with de-ionized water until the filtrate conductivity was less than 20 $\mu\text{S}/\text{cm}$ to ensure removal of most ions. Finally the product was dried at 70°C for 14 hours, then sieved manually through a 1000 μm sieve and stored in a well closed container.

Roller compaction of α -lactose monohydrate and magnesium silicate

α -lactose monohydrate and Mg silicate were mixed manually, using suitable nylon bags filled with air, in four different weight ratios (lactose monohydrate:Mg silicate) 80:20, 70:30, 60:40, 50:50 w/w, with a total weight equivalent of 1 kg. Each weight ratio of the powders was then separately poured into a laboratory scale roller compactor (Vector TFC-Min Roller Compactor, Freund-Vector Corporation). The processing parameters were: Roll Speed 3.5 RPM, Feeding Speed 40 to 45 RPM, Roll Pressure 10 MPa and Rollers Gap 2.0 mm. The produced ribbons were passed through a 1000 μm sieve. The resultant powder was stored in a well closed container.

Particle Characterization

Determination of particle size and polydispersibility index

Particle size was determined by sieve analysis using a 50 g sample on an automatic sieve shaker (Analysette 3-Pro, Fritsch, Germany) equipped with a series of 8 sieves (38-1000 μm). The powder fractions were collected and weighed. The experiments were performed in triplicate.

The results of the sieve analysis were used to determine D_{10} , D_{50} , and D_{90} which are the equivalent diameters of particles at the 10th, 50th, and 90th percentiles of the cumulative percent undersize plot, respectively. These parameters were used to calculate the polydispersity index (PI) using Equation 1.

$$\text{PI} = \frac{D_{90} - D_{10}}{D_{50}} \quad \text{Eq. 1}$$

Determination of bulk and tapped density

Bulk density (d_b) was initially determined by pouring the powder (about 50 g) carefully into a glass cylinder. The density was then calculated by dividing the mass of the powder by the measured volume. For measuring the tap density (d_t), the powder was poured into a 100 ml cylinder mounted on an Erweka Tapped Density Tester (Stampfvolumter SVM, Erweka, Heusenstamm, Germany) with a fixed drop of 3 mm ± 0.2 at a nominal rate of 250 taps per minute. Densities were determined as the mean of five measurements.

Carr's index (CI) was then calculated using Equation 2 and Hausner's ratio (HR) using Equation 3.

$$\text{CI} = \frac{(d_t - d_b) * 100}{d_b} \quad \text{Eq. 2}$$

Where;

d_t is tap density and d_b is bulk density

$$\text{HR} = \frac{d_t}{d_b} \quad \text{Eq. 3}$$

Evaluation of compressibility

Flat-faced compacts (12 mm in diameter, 600 mg ± 5) were made from the four compositions (80:20%, 70:30%, 60:40%, and 50:50% w/w) of the compacted α -lactose monohydrate: Mg silicate mixtures. Compression was performed using the Universal Testing Machine (UTM, RKM 50, PR-F system, ABS Instruments Pvt., Ltd., Leipzig, Germany).

During the compression the lower punch was stationary whilst the upper punch movement was fixed at 3 mm/s.

Final thickness of the compacts (tablet height) and diameter were measured using Vernier Calipers. The tablet volume was calculated to determine its density.

Excipient compatibility with active pharmaceutical ingredient (API)

The compatibility of the prepared roller compacted mixtures of α -lactose monohydrate: Mg silicate in the four prepared ratios with the model drugs Mebeverine HCl (MBV) and Losartan K (LSN) was investigated using differential scanning calorimetry (DSC) and infrared spectrophotometry (IR).

Differential Scanning Calorimetry

Differential scanning calorimetry was used to characterize the thermal properties of the physical mixtures of α -lactose monohydrate:Mg silicate, the roller compacted mixtures of α -lactose monohydrate:Mg silicate, MBV, LSN and a mixture of 1:1 (w/w) drug to co-processed α -lactose monohydrate:Mg silicate using a Mettler Toledo DSC823e DSC (Mettler Toledo, Switzerland) equipped with a cooler. Samples (~5 mg) were heated over a temperature range from 25 to 250°C at a rate of 10 °C/min. in sealed aluminum pans. The tests were performed under a nitrogen purge at a rate of 80 ml/min.

Infrared spectroscopy

The IR spectra of the physical mixtures of α -lactose monohydrate:Mg silicate, the roller compacted mixtures of α -lactose monohydrate:Mg silicate, MBV, LSN and a mixture of 1:1 (w/w) drug to co-processed α -lactose monohydrate:Mg silicate were measured using a Fourier transform infrared (FTIR) spectrophotometer (Spectrum One, Perkin-Elmer, Buckinghamshire, UK) and the KBr disc method. Each sample was pulverized, gently triturated with the KBr powder in a weight ratio of 1:100, and then compressed

using a hydraulic press at a force of 10 t for 2 minutes. The disc was then placed in the sample holder and scanned from 4000 to 400 cm^{-1} at a resolution of 4 cm^{-1} .

Preparation of tablets

A single punch tableting machine (Manesty F3 single stroke tablet press, West Pharmaservices Ltd, Dorset, UK) fitted with a 12-mm flat rounded punch was used to compress separately the four different ratios of the roller compacted mixtures of α -lactose monohydrate: Mg silicate into tablets (control) at a fixed compression load of 40 kN/m^2 . The aforementioned conditions were also utilized to compress formulations of MBV or LSN using α -lactose monohydrate: Mg silicate (60: 40% w/w ratio) roll compacted mixtures. The 60: 40% w/w ratio of lactose:Mg silicate was adopted in the excipient composition because this ratio resulted in good powder and physical properties (discussed later). The formulation compositions are shown in Table 1.

Table 1 Tablet formulations of Mebeverine HCL and Losartan K

ACTIVE INGREDIENT(mg)	α -LACTOSE MONOHYDRATE: Mg SILICATE (60:40) (mg)	TABLET WEIGHT (mg)
Mebeverine HCL (135)	465	600
Losartan K (50)	100	150

Tablet characterization

Tablet crushing strength, friability, and disintegration time

Testing the tablet crushing strength, friability, and disintegration time was performed according to the methods described in USP36-NF31.

Tablet content uniformity

Ten tablets of LSN and MBV were individually weighed, crushed and placed into separate volumetric flasks to which the required amount of distilled water (for LSN) and 0.1N HCl (for MBV) was added. Suitable dilutions were prepared and sample absorbencies were measured at 205 nm and 263 nm for LSN and

MBV, respectively using the corresponding reference. Content was subsequently calculated and the data presented as mean values \pm SD.

Dissolution studies

Drug release from MBV and LSN tablets was measured using Erweka DT6 dissolution tester (Erweka AG, Heusenstamm, Germany) for 60 minutes (method II paddle, 100 RPM, 900 ml of 0.1 M HCL) for the MBV tablets, and for 45 minutes (method II paddle, 50 RPM, 900 ml of distilled water) for the LSN tablets. The dissolution tests were performed in triplicate and the mean values, as well as, standard deviations were calculated. The drug release of MBV and LSN from available brands in the market was also performed for reference.

Statistical analysis

Significance in the differences of the means of the evaluated attributes was tested using the student t-test at the 95% ($P < 0.05$) confidence level.

RESULTS AND DISCUSSION

Preliminary physico-chemical compatibility studies (DSC and IR)

Figure 1 shows the DSC thermograms of α -lactose monohydrate. A desolvation endotherm is evident in the 140–160°C region, melting endotherm at approximately 217°C and small decomposition endothermic peak at 225°C. The DSC thermogram of Mg silicate showed a broad shallow dehydration peak at about 106°C. The DSC thermograms of co-processed products showed negligible differences in terms of peak shift of the individual components.

FT-IR spectra of α -lactose monohydrate, Mg silicate, and co-processed excipients (Figure 2) showed no variation and/or shift in the position of characteristic absorption bands in the IR spectra, suggesting that no chemical interaction between α -lactose monohydrate and Mg silicate took place during the process. Furthermore, the co-processed products did not show any chemical interaction with the

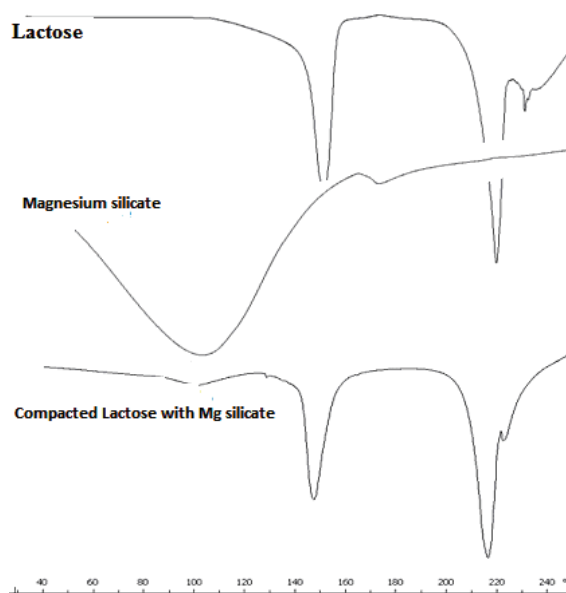


Figure 1 DSC thermograms of Lactose, Magnesium silicate and the compacted Lactose with Mg Silicate composite system

model drugs Mebeverine and LSN (as shown in Figure 3 and Figure 4, respectively). The DSC and FT-IR results show that co-processing α -lactose monohydrate with Mg silicate does not result in any immediate chemical incompatibility. The compatibility of Mg silicate with lactose confirms the report of an inert Mg silicate surface when co-processed with chitin (8).

Particle size and polydispersibility index

The PI values of the particle size distribution of the different co-processed mixtures are shown in Table 2. A comparison of compacted lactose-Mg silicate excipients with commercially spray-dried Lactose-DC, shows that spray-drying produces a slightly narrower particle size distribution as indicated by the lower PI values (9). A wider distribution of the compacted excipient is attributed to the sieving technique carried out on the compacted sheets. The lactose-Mg silicate compacts seem to undergo fragmentation upon mechanical pressure imposed between the sheets and the sieves for

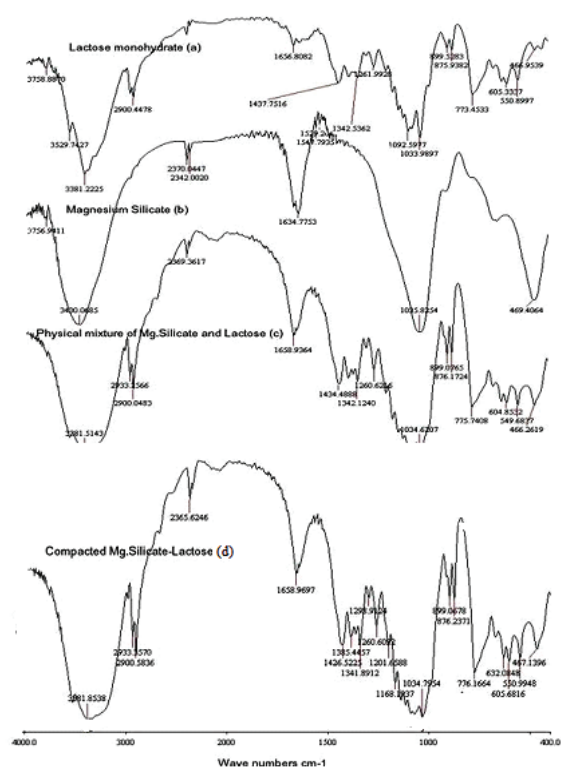


Figure 2 FTIR spectra of α -lactose monohydrate (a), Mg silicate (b), physical mixture of α -lactose monohydrate and Mg silicate (c) and compacted lactose monohydrate and Mg silicate (d)

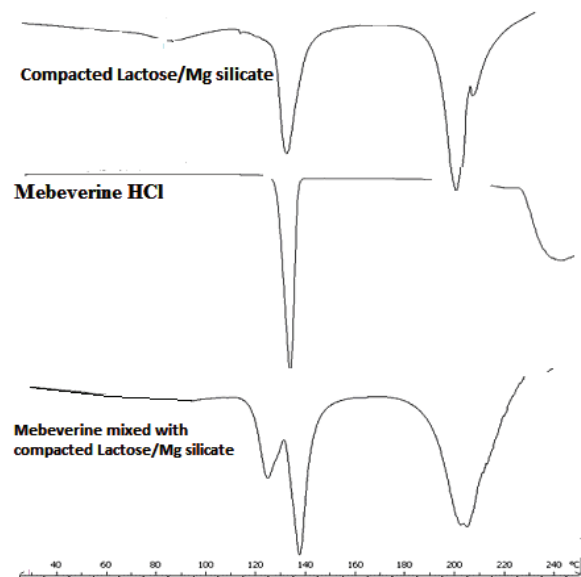


Figure 3 DSC thermograms of the compacted Lactose with Mg-Silicate, Mebeverine HCl and physical mixture of Mebeverine HCl and compacted Lactose- Mg-silicate

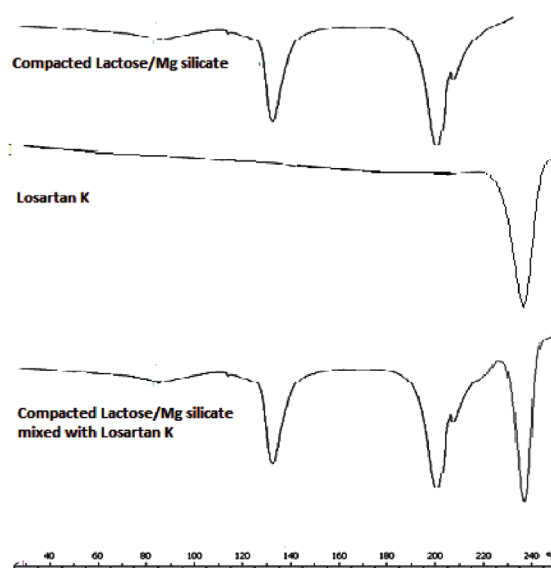


Figure 4 DSC thermograms of the compacted Lactose with Mg-Silicate, Losartan K and physical mixture of Losartan K and compacted Lactose- Mg-silicate

size reduction. Increasing the content of Mg silicate resulted in a decrease in the PI values indicating that the excipient has a lesser propensity to fragment upon sieving as the Mg silicate content increases. This is also evidenced by the D_{10} values for the 40 and 50% magnesium silicate containing coprocessed excipient, which are two times greater than those for the co-processed excipient containing

Table 2 PSD Parameters and PI of 20%, 30%, 40% and 50% (w/w) of Mg silicate compacted with α -lactose monohydrate (Mean \pm SD, n = 3)

% Mg SILICATE IN THE COMPACTED LACTOSE- Mg SILICATE (w/w)	D_{10} (μ m)	D_{50} (μ m)	D_{90} (μ m)	PI
0.2	54 \pm 2.04	483 \pm 5.4	961 \pm 5.2	1.88
0.3	64 \pm 1.01	490 \pm 4.3	940 \pm 9.3	1.79
0.4	122 \pm 2.7	490 \pm 7.2	942 \pm 6.3	1.67
0.5	127 \pm 3.2	514 \pm 3.0	942 \pm 4.5	1.59
Spray-dried Lactose-316*	79.3	180	250	0.95

*Some values for the Spray dried Lactose 316 were calculated from Reference 9

20 and 30% magnesium silicate. In the case of spray-drying lactose, spherical particles, almost uniform in size, are usually produced since lactose dries into spherical particles with no dents or folds (10). In addition, spray-drying is

capable of controlling the PSD via for e.g., the nozzle opening size (11).

Flowability and compressibility studies

The flowability of various blends of lactose-Mg silicate as physical mixtures and as co-processed composites were assessed using Carr's compressibility index (CI) and Hausner's ratio (HR) as calculated using bulk and tapped density values. Good powder flow properties are associated with Carr's index values between 5 and 25% and HR<1.25 while Carr's index values higher than 25% and HR>1.50 are indicative of poor flow (12). The co-processed products show improved flowability compared with their physical mixtures as shown by their CI and HR values (Table 3). CI values for the physical mixtures were in the range of 27-29 while HR values were in the range of 1.37-1.42 indicating high frictional and interparticle interactions, and thus "poor" flow characteristics. Roller compaction of the poorly flowable and poorly compressible α -lactose monohydrate with Mg silicate resulted in a significant improvement of powder flowability through an increase in bulk and tapped densities with 'fair' (i.e., 20 and 30 % (w/w) Mg silicate content) to 'good' (40 % and 50% (w/w) Mg silicate) flowability as shown by the excipient CI and HR values in Table 3.

Table 3 Compressibility parameters of the roller - compacted α -lactose monohydrate: Mg silicate granules, physical mixture of α -lactose monohydrate and Mg silicate and Fast flo[®].

α -lactose monohydrate: Mg silicate	d_f (bulk density) g/cm ³	d_t (tap density) g/cm ³	CI (%)	HR
physical mixture 20%	0.46(0.02)	0.65(0.02)	29.4	1.42
physical mixture 30%	0.46(0.01)	0.64(0.02)	29.0	1.41
physical mixture 40%	0.49(0.03)	0.69(0.05)	28.5	1.40
physical mixture 50%	0.52(0.04)	0.71(0.06)	27.2	1.37
Compacted 20%	0.66(0.04)	0.82(0.02)	19.6	1.24
Compacted 30%	0.67(0.03)	0.81(0.03)	17.0	1.20
Compacted 40%	0.68(0.06)	0.80(0.05)	15.0	1.18
Compacted 50%	0.70(0.03)	0.81(0.06)	14.0	1.16
Fast Flo [®]	0.56(0.04)	0.62(0.05)	9.0	1.10

Since the consolidation between lactose and Mg silicate by roller compaction provided a wide particle size distribution (Table 2) and a high bulk density compared to the physical mixtures

(Table 3), the co-processed excipient is, theoretically, expected to have a better powder flowability. It is further worth noting that, the higher the content of Mg silicate, the higher the bulk and tap densities and the better the co-processed excipient flows. This could be correlated to the previous discussion on the narrower polydispersibility index (PI) for compacted mixtures with higher Mg silicate content. Mg silicate appears to lessen the fragmentation of the compacted lactose-Mg silicate granules upon sieving, to the high bulk densities, and thus to better powder flowability.

Nevertheless, in comparison with lactose-DC (spray-dried, Fast-Flo[®]), compacted lactose with Mg silicate generally has higher CI and HR values indicating that spray-dried lactose has better flow properties. This could again be attributed to the spherical shape of the particles (13).

Analysis of compression data

Kawakita analysis

The packing characteristics of compacted α -lactose monohydrate were assessed using the Kawakita equation. The Kawakita analysis was used in the regime of the low compression forces applied in this report. The Kawakita equation depends on the degree of volume reduction representing an indirect, but simple technique that could be used to assess the packing behavior of the granules.

The Kawakita equation (Equation 4) was used to describe the relationship between the degree of volume reduction of the powder column and the applied pressure (14).

$$C = \left(\frac{V_0 - V}{V_0} \right) = \frac{abP}{1 + bP} \quad \text{Eq. 4}$$

Equation 4 can be rearranged into a linear form as:

$$\frac{P}{C} = \frac{P}{a} + \frac{1}{bP} \quad \text{Eq. 5}$$

Where;

V_0 is the initial volume of the powder bed, V is the powder volume after compression under pressure P , a is a constant corresponding to the limiting value of the relative reduction of the volume by compression and is equal to the value of the initial porosity and b is a constant that is inversely related to the yield strength of the particles and has the dimension of the reciprocal of stress.

Constant a , describes the compressibility or the amount of granules densification due to compression, and is equal to the minimum porosity of the bed prior to compression. The $1-a$ values obtained from the Kawakita analysis (Table 4) represent the initial relative density with the application of a small pressure. Therefore co-processing lactose with Mg silicate using roller compaction showed the highest degree of packing with minimum porosity when compared to lactose monohydrate and Mg silicate.

Table 4 illustrates the Kawakita parameters obtained from the Kawakita plots (Figure 5) of the binary mixtures of the compacts in addition to the individual components (lactose monohydrate and Mg silicate). Such packing tendency was almost unchanged up to a Mg silicate content of 50% (w/w) within the compacted binary mixture (Table 4 and Figure 5).

Table 4 Kawakita Parameters of Mg silicate, Lactose monohydrate, and compacted lactose with Mg-silicate

FORMULA	1-a	1/b (MPa)
Mg silicate	0.33	21.48
Lactose monohydrate	0.3	18.55
Compacted 20%	0.41	2.9
Compacted 30%	0.41	3.87
Compacted 40%	0.37	2.9
Compacted 50%	0.38	2.71

Constant b , which is known as the coefficient of compression, is related to the plasticity of the material. The reciprocal of b ($1/b$) or P_K defines the pressure required to reduce the

powder bed by 50%. P_K values are an inverse measure of the amount of plastic deformation occurring during compression. Generally, lactose monohydrate is a brittle excipient which undergoes excessive fragmentation under compression. The high P_K value (18.55 MPa) of lactose monohydrate (Table 4) determined from the Kawakita analysis reflects such a property. A similar conclusion can be drawn from Table 4 which shows that the highest P_K value (21.48 MPa) was recorded for synthetic amorphous magnesium silicate powder. Again, when there was up to 50% Mg silicate content within the compacts, the powder maintained a high amount of plastic deformation (Table 4). Consequently, as expected, magnesium silicate represents a highly fragmenting brittle material.

Co-processing lactose monohydrate with synthetic magnesium silicate using roller compaction results in a dramatic change of the mechanical behavior of the powder upon compression as shown by the Kawakita analysis (Table 4). The remarkable decrease of the calculated P_K values (to less than 4) makes the lactose-Mg silicate binary co-processed excipient a plastically deforming material. Generally, the low values of the Kawakita

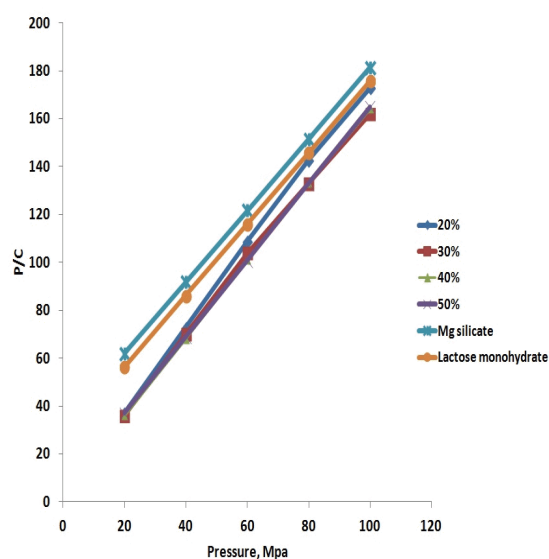


Figure 5 Kawakita plots of compacted of α -lactose monohydrate with different percentages of Mg silicate

parameter, P_K , are responsible for the high tensile strength values of compacts, as higher total plastic deformation would lead to more contact points for interparticulate bonding (15). The values of the recorded P_K parameter were 2.71-3.87 MPa for 20-50% (w/w) Mg silicate in the compacted binary mixture.

The lowest P_K value (the highest amount of plastic deformation) was obtained for the highest Mg silicate content in the compacted lactose-Mg silicate excipient. Such a trend in the increase of plasticity as the Mg silicate content increases could be the answer to the previously observed powder behavior upon particle size analysis, bulk measurement, and flowability analysis. Therefore, Mg silicate's contribution toward imparting lactose powder with a narrower polydispersibility index (due to less granule fragmentation upon sieving) and thereby higher powder bulk density and better flowability is likely due to the high amount of plastic deformation that Mg silicate imparts to the co-processed mixture upon compaction.

Physical properties and content uniformity of the Tablets

The content of active ingredients for individual tablets was found to lie in the range of 85–115%, while the relative standard deviation observed was less than 6%. The results showed no significant differences of the active content values between the products and their standard solutions ($p < 0.05$). The percentage friability (Table 5) of all tablets made from the co-processed lactose-Mg silicate as a single tablet component and for those in combination with the model drugs were within the USP acceptable 1% upper limit for pharmaceutical tablets.

On the other hand, the crushing strength results (Table 5) were considered to be acceptable (>40 N) as all values ranged from 68 to 81N. No significant effect of the content of Mg silicate (20-50 % w/w) on tablet crushing strength was observed. The disintegration time of the compacted tablets increased from 1.84 minutes ± 0.11 to 6.1 minutes ± 0.2 which

reflects the percentage increase in Mg silicate. This leads to the conclusion that the compacted lactose-Mg silicate excipient does not result in unwanted physical properties when formulated with the two model drugs.

Table 5 Tablet crushing strength (n: 10, mean \pm SD), disintegration time (n: 6, mean \pm SD) and tablet friability (mean \pm SD)

FORMULATION	CRUSHING STRENGTH (N)	FRIABILITY (%)	DISINTEGRATION TIME (min)
Compacted 20%	81 \pm 18	0.82 \pm 0.12	1.84 \pm 0.11
Compacted 30%	70 \pm 13	0.73 \pm 0.12	2.12 \pm 0.22
Compacted 40%	78 \pm 11	0.43 \pm 0.08	4.02 \pm 0.18
Compacted 50%	79 \pm 90	0.4 \pm 0.014	6.10 \pm 0.20
Mebeverine HCL Compacted	78 \pm 16	0.82 \pm 0.23	4.10 \pm 0.20
Losartan K-Compacted	68 \pm 16	0.78 \pm 0.11	6.10 \pm 0.14

Comparative dissolution profile

The dissolution profiles of the compacted lactose-Mg silicate based tablets (as single tablet filler) were compared with the dissolution profiles of selected commercial drugs. The compacted lactose-Mg silicate based tablets released 65% and 90% of MBV compared to 30% and 70% from the marketed drug (Duspatalin 135[®]) at 15 and 30 minutes, respectively (Figure 6). Figure 7 indicates that lactose-Mg silicate based LSN tablets showed no significant difference ($P < 0.05$) in the dissolution profile compared to the marketed drug Cozaar 50[®].

However, MBV required further compaction due to material characteristics while LSN did not require any further processing for the dissolution to be identical to the model drug.

CONCLUSION

Roller compaction was used successfully to produce a directly compressible multifunctional excipient by co-processing α -Lactose monohydrate with Mg Silicate. The physical properties of the tablets prepared by compaction of lactose with Mg silicate showed plastic deformation upon compression of the particles and good flowability, crushing

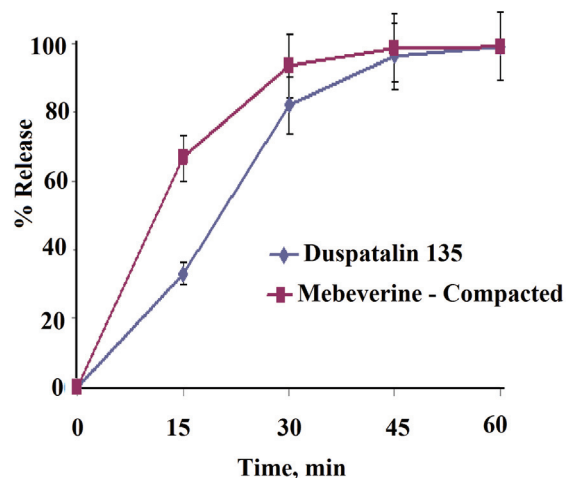


Figure 6 Dissolution profile of Mebeverine HCl compacted with Mg silicate and Duspatalin 135[®]

strength, and friability. The processed product was compatible with the model drugs. Tablets of MBV and LSN formulated with co-processed lactose-Mg silicate as single filler showed faster dissolution and disintegration times than the drugs on the market.

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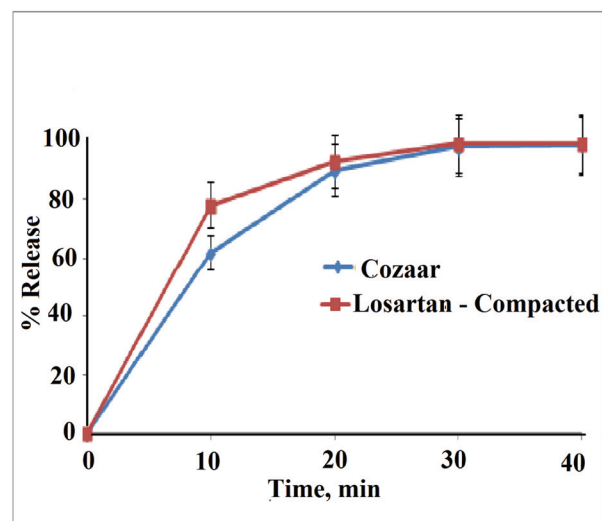


Figure 7 Dissolution profile of Losartan K compacted with Mg silicate and Cozaar 50[®]

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