Original article

Evaluation of tableting properties of model fillers by direct compression

Evaluación de las propiedades de formación de tabletas de rellenos de modelos por compresión directa

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ABSTRACT

Introduction: There is a wide range of filler excipiences with very poor tableting properties when prepared by direct compression technique.

Objective: Tableting properties of some model filler excipiences such as kaolin (Kao), magnesium carbonate (MgCO3), and calcium carbonate (CaCO3) have been evaluated quantitatively using Kawakita equation and tabletability plot.

Methods: Kao, CaCO3, and MgCO3 were blended individually with microcrystalline cellulose (MCC) in 1:2 ratio (wt/wt), using 1 % w/w of talcum for lubrication. Accurately weighed 500 mg powder mixture was compressed into compact at different pressure in hydraulic press. Tableting parameters were estimated using Kawakita equation and tabletability plot of all the three formulations from the hardness and thickness data of each compact.

Results: Kao exhibited highest compressibility (*a* = 0,825) while, maximum inclination towards volume reduction (*b* = 2,492) has been shown by CaCO3 applying Kawakita pressure model. Tabletability quantified from the estimated area under the applied pressure vs tensile strength curve (AUTC) and found peak value in MgCO3 (1,437) compared to Kao (0,872) and CaCO3 (1,157).

Conclusion: Kaolin, magnesium carbonate, and calcium carbonate could be utilized as the filler excipiences for tablet preparation by direct compression technique. The estimated tableting parameters will definitely through light in designing directly compressible tablet formulation.

Keywords: Direct compression; Kaolin; CaCO3; MgCO3; Tabletability, Kawakita model.

RESUMEN

Introducción: Existe una amplia gama de excipientes de relleno con muy malas propiedades de formación de comprimidos cuando se preparan mediante la técnica de compresión directa.

Objetivo: Evaluar cuantitativamente, utilizando la ecuación de Kawakita y el gráfico de capacidad de formación de tabletas, las propiedades de formación de tabletas de algunos excipientes de relleno modelo, como el caolín, el carbonato de magnesio y el carbonato de calcio.

Métodos: El caolín, el carbonato de calcio y el carbonato de magnesio se mezclaron individualmente con celulosa microcristalina en una proporción de 1:2 (p/p), utilizando talco al 1 % p/p para la lubricación. La mezcla de polvo de 500 mg, pesada con precisión, se comprimió en un compacto a diferentes presiones en una prensa

hidráulica. Los parámetros de formación de comprimidos se estimaron utilizando la ecuación de Kawakita y el gráfico de capacidad de formación de comprimidos de las tres formulaciones a partir de los datos de dureza y espesor de cada compacto.
Resultados: El caolín exhibió la compresibilidad más alta (a = 0,825), mientras que el carbonato de calcio mostró la inclinación máxima hacia la reducción de volumen (b = 2,492) aplicando el modelo de presión de Kawakita. La tabletabilidad se cuantificó a partir del área estimada bajo la curva de presión aplicada frente a la resistencia a la tracción y encontró un valor máximo en el carbonato de magnesio (1,437) en comparación con el caolín (0,872) y el carbonato de calcio (1,157).
Conclusiones: El caolín, el carbonato de magnesio y el carbonato de calcio podrían utilizarse como excipientes de relleno para la preparación de comprimidos mediante la técnica de compresión directa. Los parámetros de formación de comprimidos estimados definitivamente se verán reflejados en el diseño de formulaciones de comprimidos directamente comprimibles.
Palabras clave: compresión directa; caolín; CaCO3; MgCO3; tabletabilidad, modelo Kawakita.

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Introduction

Tablets are oral unit dosage forms designed for better patient compliance and cost-effectiveness.[1] Heading deeper in this tablet formulation procedure, direct compression has claimed to be the least time, labour, and cost-effective compaction process over granulation processes. A material can only be subjected for direct compression if it possesses adequate cohesiveness with high flowability.[2] The tablet forming capacity of a material can be characterized by the determination of tabletability, compressibility and compactibility plots. There are reports of various

compaction models which are also getting widely used for characterizing a compressed mass (e.g. Kawakita Model is used for low pressures and high porosities.[3,4]

There is a wide range of drug products having poor cohesiveness for which addition of a variety of excipients are required. Incorporation of excipients in bulk allows the drug to be compressed under direct compression procedure. Microcrystalline cellulose (MCC) possesses the above-mentioned ideal properties of a direct compressible excipient. The excipients, i.e. Magnesium carbonate (MgCO3), calcium carbonate (CaCO3), and Kaolin are not properly compressible alone, hence a ratio of 1:2 (Excipient: MCC) has been used in this study of direct compression.

Mineral clays been used in pharmaceutical industries as pigments, opacifiers, emulsifying agents, thickening agents *et cetera*.[5] Kaolin is a mineral clay, used in the pharmaceutical industries as an adsorbent in the tablet formulations.[6] It has also been used for the treatment of diarrhoea, dysentery and cholera. $MgCO_3$ or 'Magnesite', as well as $CaCO_3$ are common over the counter remedies for heartburn and upset stomach caused by overproduction of acid in the stomach possessing a high absorptive ability. $CaCO_3$ also has a wide use as dissolution aid in dispersible tablets, bulking agent in tablet sugar-coating processes, opacifier in tablet film-coating and as calcium suppliment.

CaCO3 can be used as a tablet excipient for the betterment of flowability and true density when formulated with chitin, along with an acceptable tensile strength.[7,8] CaCO3 has been proved to be a useful excipient for the preparation of floating beads for gastro retentive drug delivery system.[9] When subjected to water treatment in ball milling, Kaolin can form strong agglomerates which can lead to poor compressibility unlike when treated with organic solvent (ethanol).[10] Magnesium carbonate has a considerably a capacity to exert high tensile strength in tablets along with low friability and immediate disintegration. When put in comparison against calcium carbonate, CaCO3 was proven to be better in every above-mentioned aspects.[11]

This project has been aimed toward the tabletability profile of kaolin, $MgCO_3$, and $CaCO_3$ using direct compression method, since the use of these clays as tablet excipients in direct compression has been found rarely in exhaustive literature review. To describe the tabletability and compressibility of the tablets, Kawakita model and area under the tabletability profile (AUTC) have been considered.

Methods

Materials: Microcrystalline cellulose and magnesium stearate purchased from HIMEDIA Laboratories Pvt. Ltd. (Mumbai, India). Kaolin light was obtained from Burgoyne Burbidges and Co. Pvt. Ltd. (Mumbai, India). CaCO3 and MgCO3 were purchased from Merck Life Science Pvt Ltd (Mumbai, India) and Sisco Research Laboratories Pvt Ltd (Taloja, India) respectively.

Preparation of the powder mixture: Microcrystalline cellulose and the excipients (kaolin. CaCO3, MgCO3) were weighed in a 2:1 ratio and 1 % w/w of talc was added as a lubricant. The powders were mixed to get a homogeneous mixture. The mixture was then dried in a hot air oven at 60 °C for 2 h (Universal Hot Air Oven, India).

Tablet compression: A powder mixture of 500 mg was weighed accurately and subjected to hydraulic press for compaction (Model no M-15, Technosearch Instrument). The compaction was carried out by using several applied pressure (i.e. 49, 98, 147, 196, 145 and 294 MPa) maintaining a dwelling time of 5 min.[12]

Physical properties: Weight uniformity was tested by weighing separate tablets in a digital balance. Tablets then subjected to hardness test and thickness measurement (Mitutoyo micrometer).

FTIR study: The study has been done in Jasco FT/IR 4600. The powder sample was placed on the diamond crystal in the ATR and pressed on to it by the internal pressure applicator. An average of 40 scans has been taken in the range of 600-4000 cm^{-1}.[13]

Tabletability: The capacity of a powder mixture to be compressed into the form of a tablet of specified strength, under the effect of compaction pressure, is known as

tabletability.[14] It can be determined by tensile strength versus compaction pressure plot. The formula 1 for calculating tensile strength is as follows.[15]

$$TS = \frac{2F}{\pi dh} \quad (1)$$

Where, TS is the tensile strength of the tablet, F is the crushing force in N, d and h are diameter and of the height of tablet in mm respectively. Tabletability profile has been plotted by taking applied pressure and tensile strength at X and Y axis respectively. Further, area under the tabletability curve has been calculated.

Kawakita Pressure model: The Kawakita model was used to establish the relationship between the volume change of the powder compact and the applied pressure by using the following formula 2:[12,16,17]

$$\frac{P}{C} = \frac{P}{a} + \frac{1}{ab} \quad (2)$$

The representations in the above formula 3 are applied pressure (P), Kawakita constants (a and b). The degree of volume reduction (C), can be calculated from the initial volume (V_0) of the powder and the volume under pressure (V).[12]

$$C = 1 - \frac{V}{V_0} \quad (3)$$

Results

FTIR: The homogenicity and interaction of powder in the mixture are subjected to the FTIR (ATR- Mode) and represented in fig. 1. CaCO3 has shown characteristic peaks at 1441, 872, and 712 cm^{-1} due to asymmetrical stretching vibration, out-plane and in-plane bending of O-C-O respectively.[18]

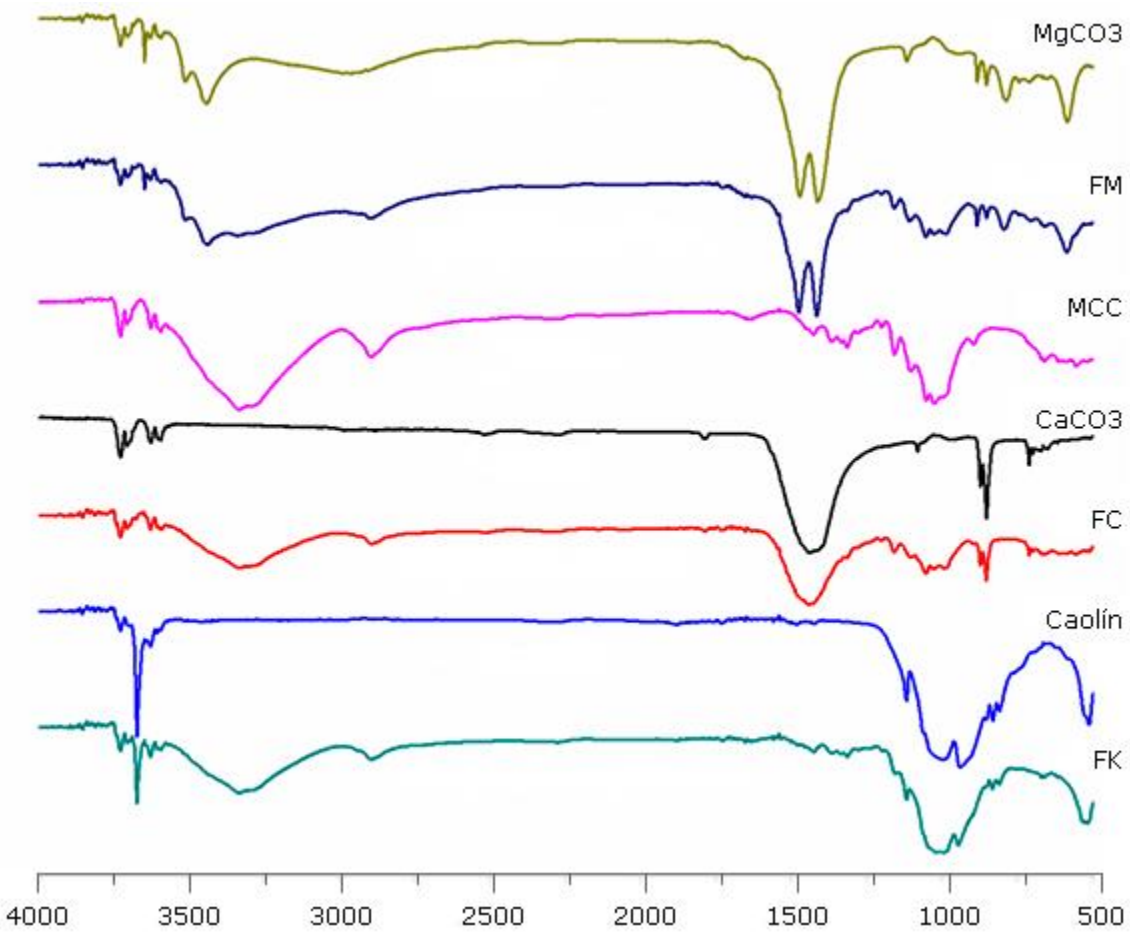

Fig. 1 - FTIR Spectra of the pure materials and the formulations.

MgCO3 has shown significant peaks at 1473 and 1412 cm^{-1} due to CO3 asymmetric stretching.[19] Kaolin has exhibited intense peaks at 3672,7 for –OH stretching vibration, 997,9 for Si-O bending vibration and 940,1 cm^{-1} for Al-OH bending vibration.[20] In MCC, typical characteristic peaks of a cellulose is evident at 1027,8, 1105, 1159 and 1200 cm^{-1} due to –CH, -C-OH , -C=O, and =CH2 respectively.

Tabletibility: As figure 2 depicts, the tensile strength has effectively increased along with the increment of applied pressure. The area under the applied pressure vs tensile strength curve has been calculated and tabulated in table 1.

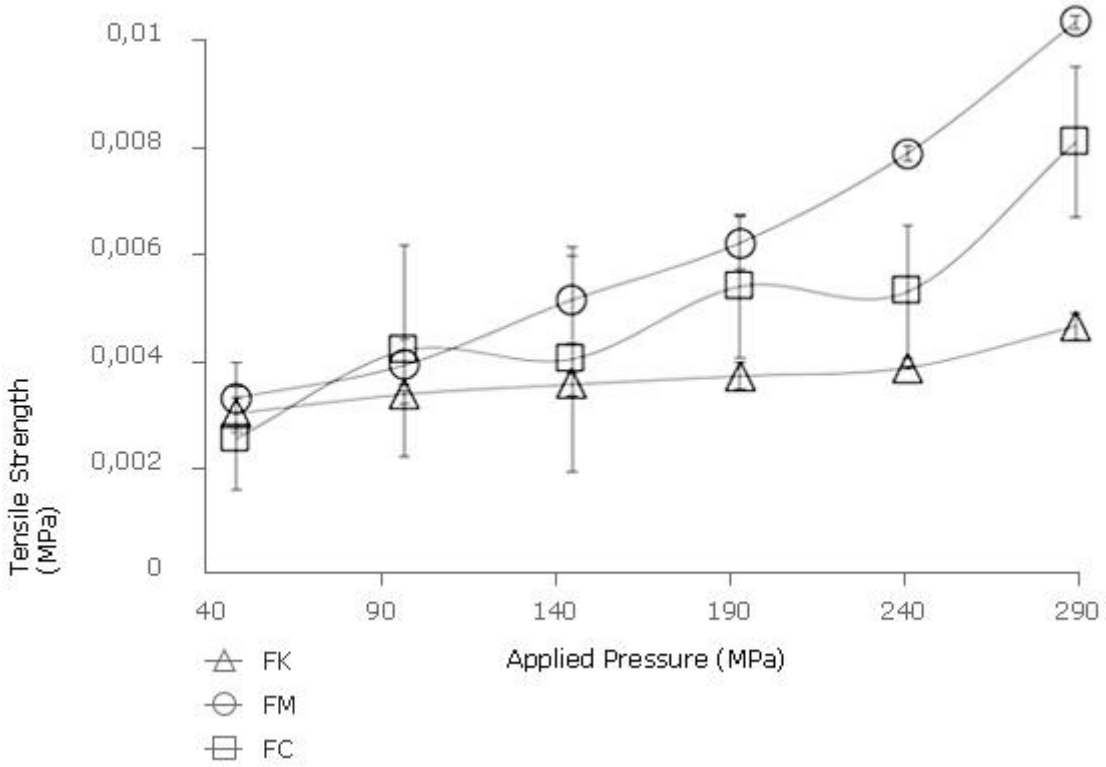

Fig. 2 - Tabletability profile of the formulation.

As per the AUTC values, FM has shown better tabletability (1,437) than the rest of the formulations where FK has shown the least (0,872). The tabletability coefficient has complied with the order of AUTC, the formulation FM has shown the highest, followed by FC and FK in that order. Kt is known as the tabletibility co-efficient, and from figure 2 it is clearly shown that FK has shown poor tabletability.

Kawakita Model: According to Kawakita analysis, the ratio of pressure (MPa) to volume decrease (C) and pressure are linearly related.[21] In an effort to understand the compression behaviour of the three manufactured filler samples, the three primary parameters (a, ab, and b) derived from Kawakita analysis were examined.

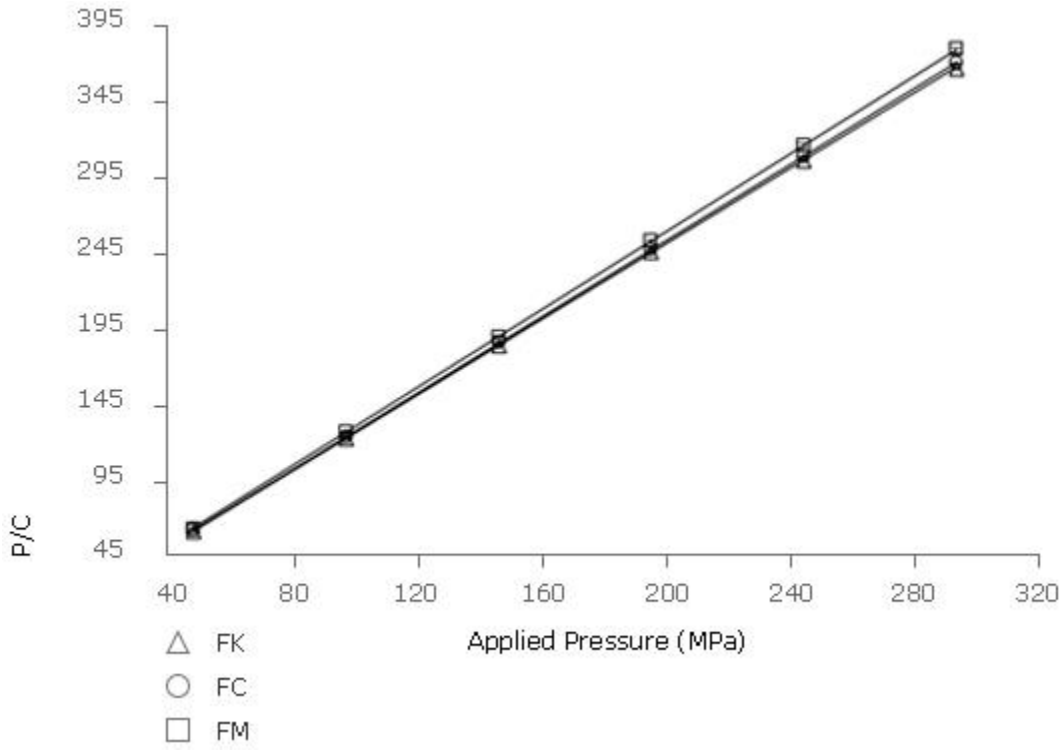

Fig. 3 - Kawakita pressure model of the formulations.

Table 1 - Kawakita parameters and Area under the Tabletability curve

Formulation Code	Filler	Filler -MCC ratio	1/a	a	ab	b	1/b	AUTC	r^2	Kt*10 $^{-5}$
FK	Kaolin	1:02	1,211	0,696	1,435	1,739	0,00058	0,872	0,977	2,8
FC	CaCO3	1:02	1,223	0,491	2,036	2,492	0,0004	1,157	0,929	1,9
FM	MgCO3	1:02	1,250	0,905	1,104	1,381	0,00072	1,437	0,950	0,5

Table 1 shows the highest volume reduction to be achieved (a), showing that FM experiences the lowest volume reduction when the same compression force was applied in comparison to FC and FK. The Kawakita parameter "1/b" was used to measure how much plastic deformation a material has undergone. The highest "1/b" value was demonstrated by FM, which nearly doubled the value of FC. In this study,

ab was employed as the Kawakita parameter to define the compression behaviour. This parameter indicates the degree of rearrangement of powder particles.[22] From the analysis it can be concluded that particle rearrangement is maximum in FC and lowest in FM.

Discussion

FTIR: From the FTIR test results, some minor changes in bond intensity and peak broadening in the formulations were observed indicating binding between the excipients through van der waals and/or dipole-dipole interactions.[23] FTIR spectra also ensured that excipient and filler doesn't change their properties after compaction. It is a good sign for the direct compression tablet.

Tabletability: A graph between tensile strength and compaction pressure is used to describe tabletability, which is the ability of a powder bed to change into a tablet of a certain strength under the effect of compaction pressure. FK has poor tabletability as well as a lower tabletibility co-efficient value, which makes direct compression challenging compared to FM and FC.[24] Since MgCO3 has a high tabletability parameter compared to other fillers. So it can be a good choice for direct compression.

Kawakita Model: The calculated value obtained from the kawakita pressure plot (P/C=P/a+1/ab) has been tabulated in Table 1. The highest compressibility (a) and the inclination towards volume reduction (b) was observed in FK and FC respectively. Degree rearrangement of powder particle (ab) was measured from Kawakita equations. Particle rearrangement is maximum in FC, which means FC has more void space. FM has shown a minimum particle rearrangement index, which indicates that it has less void space.

Conclusion: Kaolin, magnesium carbonate, and calcium carbonate could be utilized as the filler excipiences for tablet preparation by direct compression technique. The estimated tableting parameters will definitely through light in designing directly compressible tablet formulation. To estimate the tabletability quantitatively AUTC

has been determined to get the order as: FM > FC > FK. The knowledge of particle rearrangement, compressibility and the inclination towards volume reduction of the excipiences could help in designing tablet formulation by direct compression.

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Conflict of interests

The authors declared no conflict of interest.

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