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Spherical Composite Particles of Rice Starch and Microcrystalline Cellulose: A New Coprocessed Excipient for Direct Compression

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ABSTRACT

Composite particles of rice starch (RS) and microcrystalline cellulose were fabricated by spray-drying technique to be used as a directly compressible excipient. Two size fractions of microcrystalline cellulose, sieved (MCS) and jet milled (MCJ), having volumetric mean diameter (D_{50}) of 13.61 and 40.51 μm, respectively, were used to form composite particles with RS in various mixing ratios. The composite particles produced were evaluated for their powder and compression properties. Although an increase in the microcrystalline cellulose proportion imparted greater compressibility of the composite particles, the shape of the particles was typically less spherical with rougher surface resulting in a decrease in the degree of flowability. Compressibility of composite particles made from different size fractions of microcrystalline cellulose was not different; however, using MCJ, which had a particle size range close to the size of RS (D_{50} = 13.57 μm), provided more spherical particles than using MCS. Spherical composite particles between RS and MCJ in the ratio of 7:3 (RS-MCJ-73) were then evaluated for powder properties and compressibility in comparison with some marketed directly compressible diluents. Compressibility of RS-MCJ-73 was greater than commercial spray-dried RS (Eratab), coprocessed lactose and microcrystalline cellulose (Cellactose), and agglomerated lactose (Tablettose), but, as expected, lower than microcrystalline cellulose (Vivapur 101). Flowability index of RS-MCJ-73 appeared to be slightly lower than Eratab but higher than Vivapur 101, Cellactose, and Tablettose. Tablets of RS-MCJ-73 exhibited low friability and good self-disintegrating property. It was concluded that these developed composite particles could be introduced as a new coprocessed direct compression excipient.

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KEYWORDS: rice starch, microcrystalline cellulose, spray drying, coprocessed excipient, direct compression

INTRODUCTION

Direct compression technique has been one of the well-accepted methods of tablet manufacture. A wide range of materials from various sources has been developed and marketed as directly compressible vehicles such as lactose, starch, cellulose derivatives, inorganic substance, polyalcohols, and sugar-based materials. In addition to the development of directly compressible excipients by the modification of a single substance, coprocessing of 2 or more components was applied to produce composite particles or coprocessed excipient. The composite particles or coprocessed multicomponent-based excipients are introduced to achieve better powder characteristics and tableting properties than a single substance or the physical mixture. Several of these excipients are commercially available; eg, Ludipress(lactose, polyvinylpyrrolidone, and crosspovidone),[1] Cellactose and Microlac (lactose and cellulose),[2-3] Cel-O-Cal(cellulose and calcium sulfate),[4] and Prosolv (microcrystalline cellulose and silicon dioxide).[5]

Starches from many sources have long been used in tablet formulations as a diluent, binder, and disintegrant depending on the method of incorporation and the quantity used. The starch, *United States Pharmacopeia (USP)* grade, may be obtained from either the grain of corn, rice, or wheat, or from tubers of tapioca or potato.[6] Starches from different botanical sources do not have identical properties with respect to their uses as additives in tablet formulations. Among various native starches without subjection to any modifications or further treatments, RS is the most compressible.[7] But the flowability of RS is very poor because of the small size range of starch grains (2-8 μm). Spherical agglomerated RS has been developed by spray-drying process to improve its fluidity, making it suitable for direct tableting process. This spray-dried RS is marketed in Thailand as Eratab and is distributed in The Netherlands as Primotab ET.[8]

Among directly compressible fillers, microcrystalline cellulose is the most compressible and has the highest dilution potential. However, because of the high cost and poor fluidity when compared with that of most other direct compression vehicles, it is generally not used as the only diluent in tablet formulations but is usually combined with other direct compression vehicles to improve the flowability and reduce the cost of the product. Because of its high binding and good disintegrating properties, microcrystalline cellulose is of interest to be combined with other less compressible excipients as an added component in coprocessed direct tableting excipients as mentioned above.

Although spray-dried RS possesses some degree of compressibility and applied well in direct compression process, the incorporation of microcrystalline cellulose to rice-starch-based excipient would enhance more consolidated compacts. Therefore, it was of interest to develop coprocessed particles of RS grains and microcrystalline cellulose. The prime objective of the project was to develop the composite particles between these 2 materials, having the RS as the main component as it is plentiful and inexpensive.

A review of the literature yielded no report on the combination of RS and microcrystalline cellulose used to form a coprocessed excipient. In the past, there were attempts to produce coprocessed excipient of starch and microcrystalline cellulose.[9-12] However, in those studies, corn starch or hydroxypropyl starch was used to combine with microcrystalline cellulose. Bavitz and Schwartz[9] and Schwartz and Bavitz[10] introduced a coprocessed excipient of corn starch and microcrystalline cellulose (84:16) that could not provide tablets with an acceptable hardness when drug ingredients were incorporated in formulations. This result might be because of the poor compressibility of corn starch. Ohno and Ikeda combined cellulose and hydroxypropyl starch in ratios from 9:1 to 4:6. These invented products were reported to have good tableting properties.[11-12] However, the starch needed to be chemically modified, hence increasing the cost and steps required for preparation.

This report describes the preparation of new composite particles between rice grains and microcrystalline cellulose fibers by using the spray-drying technique. Microcrystalline cellulose was employed to form the composite particles in various mixing ratios with RS. The composite particles produced were evaluated for their powder and tableting properties.

MATERIALS AND METHODS

Materials

RS was obtained from the domestic source (Cho Heng Rice Vermicelli Factory Co, Nakhon Pathom, Thailand). Microcrystalline cellulose was also obtained from a commercial source (Vivapur101, lot no. 5610102917, J. Rettenmaier and Söhne, Rosenberg, Germany). The following marketed directly compressible vehicles were used for comparative studies: Eratab (lot no. T440219, Erawan Pharmaceutical Research and Laboratory Co, Bangkok, Thailand) and Tablettose (lot no. L0021A4003) and Cellactose (lot no. L0016A4901) (Meggle Gmbh, Wasserburg, Germany).

Methods

Preparation of Composite Particles

Feed suspensions for spray-drying process were prepared to have different ratios of RS grains and microcrystalline cellulose of 9:1, 8:2, 7:3, 6:4, and 5:5. RS was used as received without further modification. It was dried at 80°C for 2 hours before use in the preparations. Two different size fractions of microcrystalline cellulose were applied and categorized as microcrystalline cellulose sieved (MCS) and microcrystalline cellulose jet milled (MCJ). MCS was prepared by screening microcrystalline cellulose from commercial source (Vivapur101) through a 325-mesh sieve with an opening aperture of 45 μm (Endecotts Ltd, London, UK). MCJ was microcrystalline cellulose that had particle size reduced by jet mill (Current Jet Crusher, CJ-10, Isekyu Co, Nagoya, Japan).

Two liters of feed suspension were prepared for each combination. The required proportions of RS together with MCS or MCJ were dispersed in the amount of deionized water necessary to have the final solid content of feed suspensions of 20% wt/wt. Then, suspensions were mixed thoroughly with the aid of a disperser for 10 minutes to obtain homogeneous feed liquid. Suspensions were subsequently spray dried on spray-drying apparatus (Niro Atomizer, Mobile Minor Unit, Soeborg, Denmark). The feed liquids were atomized using a rotating centrifugal wheel atomizer. The spray-drying conditions were inlet temperature of 130°C, atomizing pressure of 2 bars, and feed rate of 28 g/min. Spray-dried RS without microcrystalline cellulose was also produced using the same conditions as described.

Physical Properties of Powder

Powder Morphology

Shape and surface topography of spray-dried formulations were observed by scanning electron microscopy (SEM) (JSM-5410LV, Jeol, Tokyo, Japan).

Powder Characteristics

Angle of repose, angle of spatula, compressibility, and cohesion of spray-dried formulations were determined using

Table 1. Particle Size Distribution of Rice Starch, Vivapur 101, Sieved Microcrystalline Cellulose, and Jet-Milled Microcrystalline Cellulose*

Material	D_{10} (μm) Mean (SD)	D_{50} (μm) Mean (SD)	D_{90} (μm) Mean (SD)	Span $(D_{90}-D_{10})/D_{50}$ Mean (SD)
RS	0.56 (0.01)	13.57 (0.11)	77.51 (2.16)	5.67 (0.11)
Vivapur 101	24.25 (0.12)	69.05 (0.91)	142.77 (5.17)	1.72 (0.05)
MCS	12.92 (0.11)	40.51 (0.08)	86.90 (0.47)	1.83 (0.02)
MCJ	2.98 (0.11)	13.61 (0.51)	33.84 (1.98)	2.27 (0.05)

*RS indicates rice starch; MCS, sieved microcrystalline cellulose; and MCJ, jet-milled microcrystalline cellulose.

Powder Characteristics Tester (model PT-N, Hosokawa Micron Corporation, Osaka, Japan). These 4 parameters were converted into flowability indices for numerical evaluations of powder flow properties.

Particle Size Measurement

Particle size and size distribution of the starting materials and spray-dried powders were determined using laser light scattering method (Metasizer 13, Malvern Instruments Ltd, Worcestershire, UK). Absolute ethanol was used as dispersion medium. Three readings were performed for each measurement.

Tableting Properties

Compressibility of the composite particles was assessed by direct compression of powder sample (~500 ± 5 mg), with no additive, on a hydraulic press, using round, flat-faced punch and die assembly (12.7 mm in diameter). All powders were compressed at the force of 8.8 kN. The tablets produced were evaluated as follows.

Hardness, Thickness, and Diameter

Hardness, thickness, and diameter of tablets prepared were determined using Tablet Hardness Tester (TBH30, Erweka, Heusenstamm, Germany). The results are the average of 10 determinations.

Friability

The friability of 20 tablets was determined using the Roche Friabilator (TAR-20, Erweka, Heusenstamm, Germany) at rotation of 25 rpm for 4 minutes. Percentage of weight loss was determined.

Disintegration Time

The disintegration time of tablet was determined in deionized water at 37°C ± 1°C using *USP* disintegration test apparatus (ZT31, Erweka, Heusenstamm, Germany). The disintegration test was performed without disc. The data given are the average of 6 determinations.

RESULTS AND DISCUSSION

Particulate morphology and particle size determination of starting materials before coprocessing by spray-drying technique to form the composite particles are presented in Figure 1 and Table 1, respectively. SEM photomicrographs of RS show the polygonal shape of rice grain. Each grain size was apparently smaller than 10 μm; however, this finding might be due to the aggregate formations, as the particle size measurements of RS by particle size analyzer gave the volumetric mean size (D_{50}) of 13.57 and 90% undersize (D_{90}) of 77.51 μm.

Vivapur 101 was used as a cellulose component in preparing the composite particles with RS. As shown in Figure 1, microcrystalline cellulose from commercial source was in fibril aggregates with the D_{50} of 69.05 μm. The rather large particle size of microcrystalline cellulose might clog up the nozzle of the atomizer during the spray-drying process. Therefore, it was necessary to reduce the particle size of microcrystalline cellulose to a proper size range suitable for the process. As described in the experimental section, 2 particle size fractions of microcrystalline cellulose, MCS and MCJ, were prepared. MCS and MCJ had the D_{50} of 40.51 and 13.61 μm, respectively. Examination of the photomicrographs showed that MCJ exhibited less fibril aggregates than original microcrystalline cellulose (Vivapur 101), most appeared in short, discrete, cellulose fragments.

Figures 2 and 3 illustrate the morphology of composite particles between RS and MCS or MCJ in different ratios (9:1, 8:2, 7:3, 6:4, and 5:5) in comparison with RS, which was spray dried without incorporation of cellulose component. RS, after subjection to spray drying process, was in spherical shape particles of various sizes when compared with native RS, which consisted of irregular shape aggregates. A granular particle of spray-dried RS was made up of a large number of rice grains attached together. During the spray-drying process, the heat could induce partial gelatinization of the surface of starch grains, resulting in the formation of solid bridges when water in a spraying droplet was evapo-

rated; these solid bridges assisted starch particles in adhering together to form granular particles. By means of SEM photomicrographs at high magnification, the welding of starch grains at the contact regions could be observed.

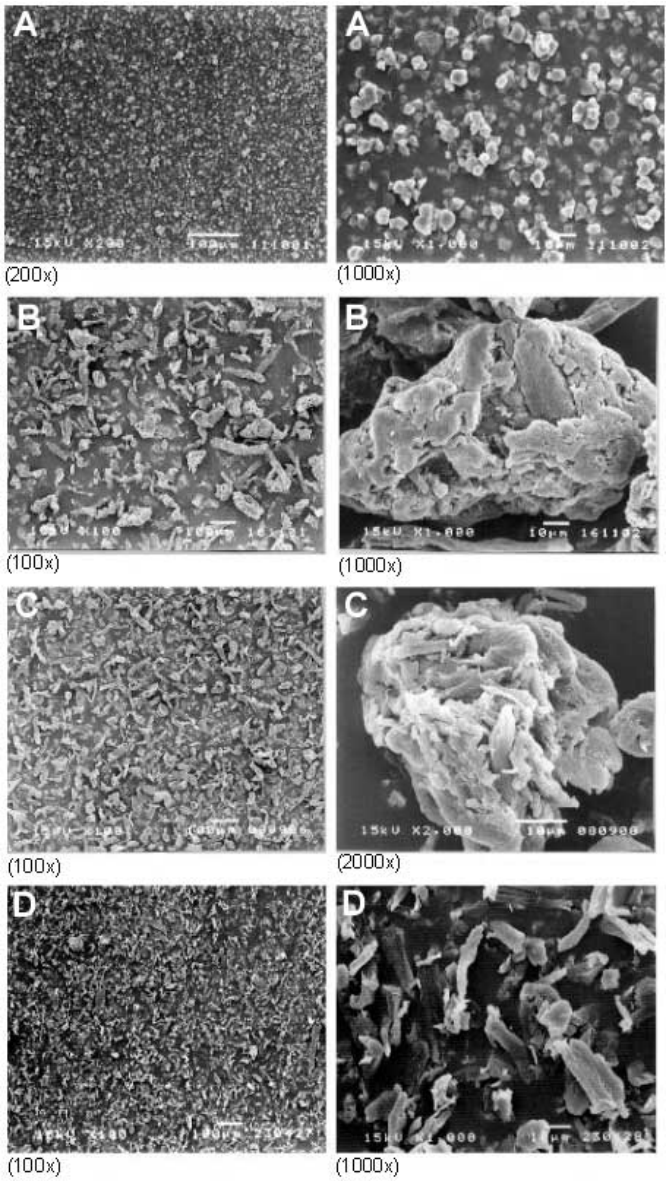

Figure 1. Scanning electron photomicrographs of (A) RS, (B) Vivapur 101, (C) MCS, and (D) MCJ.

It was demonstrated that the composite particles between RS grains and microcrystalline cellulose fibers could be formed via spray-drying technique. The photomicrographs revealed the composite particle consisting of cellulose fibers embedded in aggregate of the starch grains forming a one-body particle. As previously described, gelatinization of starch grains might be responsible for binding rice grains and cellulose fibers together to form composite granular particles.

Particle size of microcrystalline cellulose had a pronounced effect on the shape of composite particles produced. When MCS was used, an increase in the quantity of MCS in composite particles not only provided the larger size of the particles but also produced more shape irregularity of the composite particles (Figure 2). It was also noted that, at MCS concentrations between 10% and 30%, the spray-dried powders obtained were composed of both round- and oval-shaped particles (Figures 2B-D). The formation of oval-shaped particles was probably the result of the greater size of the cellulose fiber in comparison with the starch grain resulting in the deposition of smaller starch grains along the cellulose fiber to form the aforementioned particle shape. When the amount of MCS in formulations was greater than 30%, the shape of composite particles became more irregular (Figures 2E and 2F).

However, it was observed that MCJ gave more spherical-shaped composite particles than did MCS even at high proportions (Figure 3), possibly because the MCJ particle size range was similar to the grain of RS. But a high amount of MCJ (40%-50%) in the formulations seemed to reduce particle sphericity, with more irregular surface texture of the particles.

The composite particles of all mixing ratios between RS and MCS or MCJ were evaluated for their compressibility by compressing the powders at the force of 8.8 kN. Physical properties of tablets prepared from composite particles of RS and MCS or MCJ formulations are presented in Table 2. RS, before and after the spray-drying process, gave similar tablet hardness. The spray-drying process had an effect on the shape of the particulate agglomerates but not on the compactability of RS. As was expected, MCS and MCJ had such high compressibility, forming strong compacts, that the hardness could not be measured by hardness tester. The coprocessed composite particles of RS and MCS or MCJ exhibited greater compactability when compared with spray-dried RS without cellulose component. When the quantity of microcrystalline cellulose was increased, the hardness of the resultant tablets was increased. Tablets with high hardness values, low percentage friability (less than 1%), and good self-disintegration could be obtained at all proportions of these 2 components. It should be noted that different size ranges of microcrystalline cellulose (MCS and MCJ) in preparations apparently had no effect on the compressibility and other physical properties of the tablets (ie, hardness, friability, and disintegration time) but affected the shape formation of composite particles. Also, according to the results described, the process of spray drying did not improve the compactability of these systems but was a tool for particle engineering of the composite particles.

Good flowability is an important requirement for a direct compression excipient. A material developed for direct

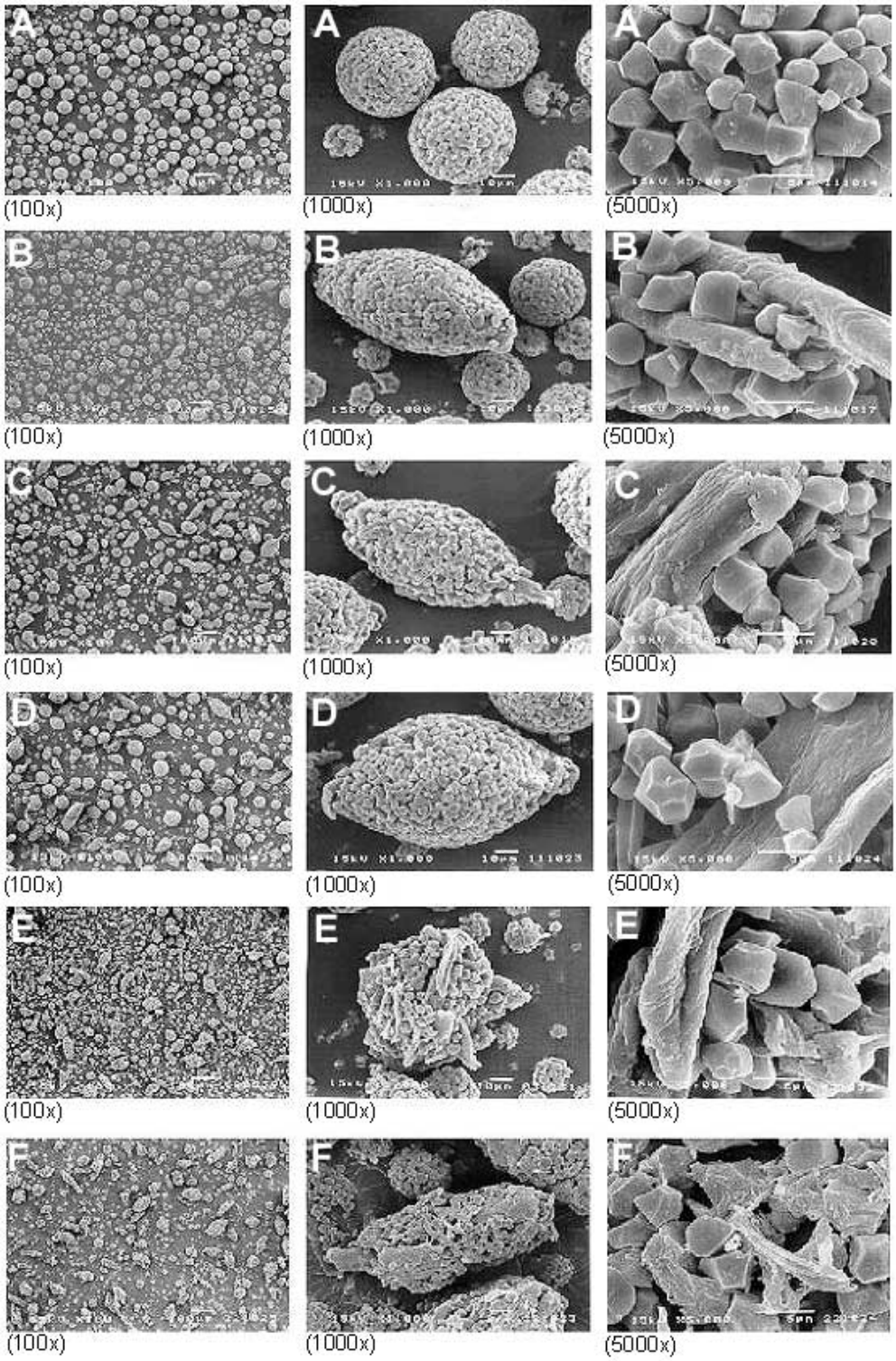

Figure 2. Scanning electron photomicrographs of spray-dried RS (A) and composite particles of RS and MCS in various ratios from 9:1 (B), 8:2 (C), 7:3 (D), 6:4 (E), to 5:5 (F).

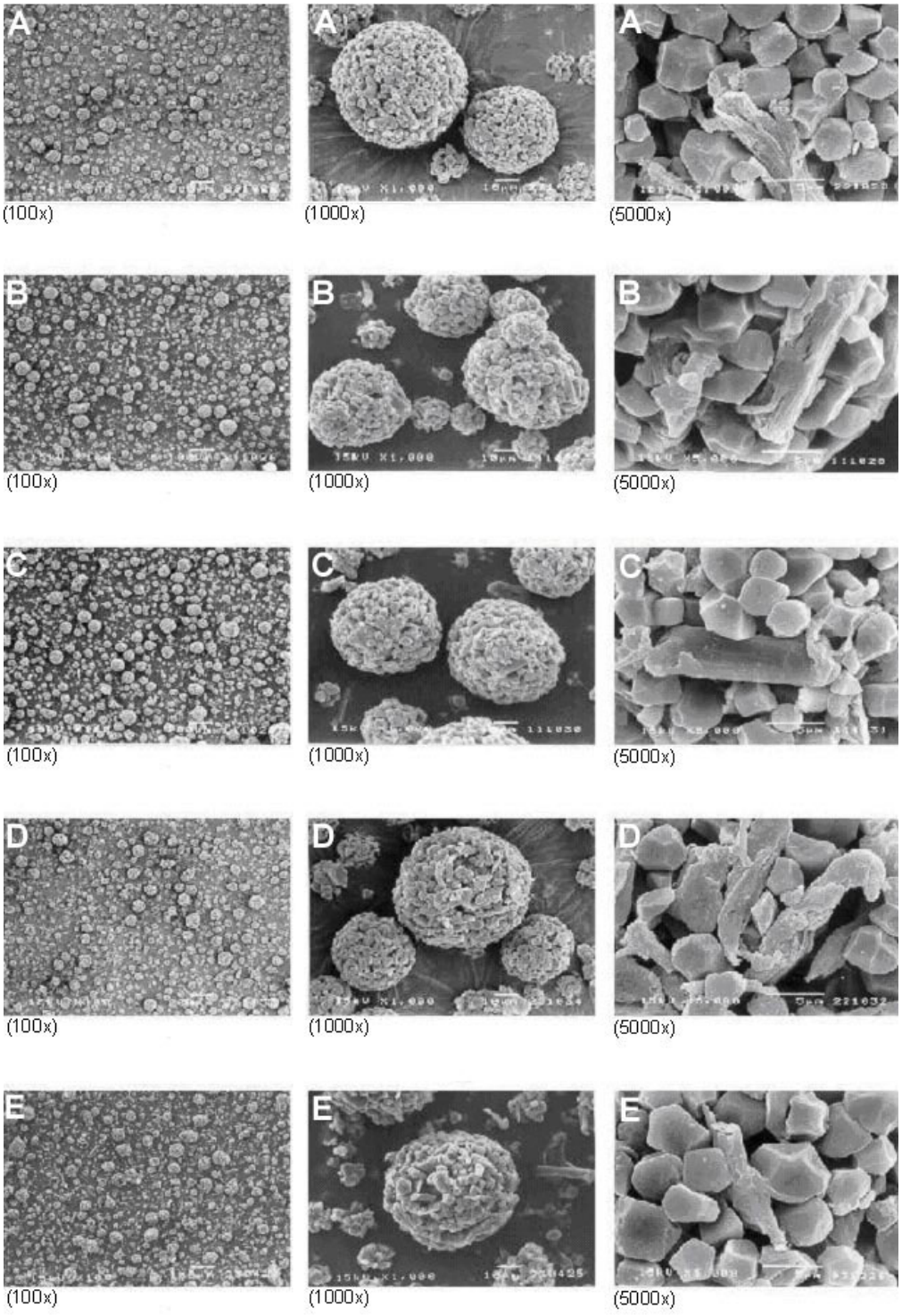

Figure 3. Scanning electron photomicrographs of composite particles of RS and MCJ in various ratios from 9:1 (A), 8:2 (B), 7:3 (C), 6:4 (D), to 5:5 (E).

Table 2. Physical Properties of Tablets Made From Spray-Dried Formulations of Rice Starch and Microcrystalline Cellulose Using Compression Force of 8.8 kN*

Material	Hardness (N) Mean (SD)	Diameter (mm) Mean (SD)	Thickness (mm) Mean (SD)	Friability (%)	DT (minutes) Mean (SD)
RS	131.4 (8.8)	12.87 (0.02)	3.46 (0.04)	0.60	1.88 (0.09)
MCS	†	12.83 (0.01)	3.26 (0.02)	0.00	>30
MCJ	†	12.82 (0.04)	3.24 (0.02)	0.00	>30
Spray-dried RS	128.2 (16.0)	12.89 (0.04)	3.60 (0.05)	0.77	2.06 (0.15)
RS-MCS-91	160.6 (11.3)	12.83 (0.02)	3.56 (0.07)	0.59	2.47 (0.21)
RS-MCS-82	164.6 (18.7)	12.86 (0.04)	3.58 (0.06)	0.40	3.16 (0.25)
RS-MCS-73	189.8 (10.6)	12.87 (0.03)	3.50 (0.04)	0.30	2.77 (0.34)
RS-MCS-64	201.2 (7.1)	12.87 (0.02)	3.46 (0.05)	0.20	2.40 (0.46)
RS-MCS-55	228.0 (10.2)	12.85 (0.01)	3.49 (0.04)	0.10	0.92 (0.15)
RS-MCJ-91	141.5 (10.7)	12.87 (0.02)	3.63 (0.06)	0.69	2.80 (0.21)
RS–MCJ-82	172.2 (14.5)	12.90 (0.04)	3.57 (0.07)	0.40	3.04 (0.24)
RS-MCJ-73	188.7 (8.6)	12.89 (0.03)	3.47 (0.06)	0.60	2.56 (0.22)
RS-MCJ-64	220.8 (14.4)	12.86 (0.02)	3.48 (0.03)	0.10	2.07 (0.76)
RS-MCJ-55	229.6 (12.7)	12.87 (0.02)	3.48 (0.03)	0.20	1.09 (0.13)

*DT indicates disintegration time; RS indicates rice starch; MCS, sieved microcrystalline cellulose; and MCJ, jet-milled microcrystalline cellulose. RS-MCS-91 or RS-MCJ-91 indicates the combination of RS and MCS or MCJ in the ratio of 9:1.
†Very hard tablets; could not be measured by hardness tester.

Table 3. Powder Characteristics of Starting Materials and Composite Particles of Rice Starch and Microcrystalline Cellulose

Material	Angle of Repose (degree) Mean (SD)	Angle of Spatula (degree) Mean (SD)	Compressibility (%) Mean (SD)	Cohesion (%) Mean (SD)	Flowability Index Mean (SD)
RS	†	†	44.6 (3.3)	†	1.3 (1.1)
MCS	46.3 (0.6)	66.3 (3.9)	38.3 (0.5)	0.5 (0.0)	45.2 (1.4)
Spray-dried RS	30.8 (0.5)	55.6 (2.6)	10.7 (0.3)	14.4 (0.0)	72.3 (0.3)
RS-MCS-91	29.8 (0.8)	55.6 (2.9)	13.9 (1.0)	8.8 (0.0)	74.0 (1.5)
RS-MCS-82	31.1 (0.2)	60.8 (1.0)	18.1 (0.9)	7.3 (0.0)	68.3 (1.6)
RS-MCS-73	36.4 (1.4)	62.1 (3.6)	19.1 (0.5)	3.4 (0.0)	65.3 (2.8)
RS-MCS-64	36.0 (1.8)	66.2 (2.0)	20.5 (0.4)	3.4 (0.0)	63.5 (1.3)
RS-MCS-55	35.8 (0.9)	67.3 (3.6)	21.4 (0.7)	4.9 (0.0)	63.3 (0.8)
RS-MCJ-91	29.4 (1.7)	58.5 (2.2)	14.7 (0.5)	9.3 (0.0)	73.5 (1.7)
RS-MCJ-82	32.9 (0.4)	61.8 (3.0)	18.0 (1.3)	8.4 (0.0)	67.7 (2.0)
RS-MCJ-73	37.2 (2.1)	57.9 (2.1)	19.2 (1.6)	3.2 (0.0)	67.0 (1.7)
RS-MCJ-64	36.9 (0.1)	62.7 (2.7)	21.0 (1.4)	4.4 (0.0)	63.3 (2.2)
RS-MCJ-55	39.4 (0.7)	66.6 (2.5)	24.2 (1.9)	4.7 (0.0)	59.5 (1.7)

* RS indicates rice starch; MCS, sieved microcrystalline cellulose; and MCJ, jet-milled microcrystalline cellulose.
†Could not be determined due to poor fluidity.

compression process should possess an adequate level of flowability when blending with other ingredients in formulation to ensure a uniform die filling of a powder blend during tableting. Several bulk powder characteristics have been employed for indirect estimation of the degree of powder flow. To evaluate the flow properties of composite particles prepared in comparison with the starting materials, the 4 powder behaviors were examined: angle of repose, angle of spatula, compressibility, and cohesion (see Table 3). Measurements were made using a powder characteristics tester, which is a single instrument able to provide all 4 parameters. Angle of repose, angle of spatula, and cohesion of RS could not be measured because powder plug occurred during testing. MCS had the highest angle of repose and angle of spatula, which indicated poor flowability. Powder characterizations of MCJ could not be done as electrostatic charges induced during size reduction caused the powder to be very cohesive, and it stuck to all surfaces contacted.

Angle of repose values tended to increase when the cellulose components in composite particles were increased from 10% to 30%. However, when cellulose proportions were increased to 40% and 50%, only RS-MCJ-55 showed increased angle of repose values. The increase in angle of

Table 4. Particle Size Distributions of RS-MCJ-73 and Commercial Direct Compression Diluents*

Material	D_{10} (μm) Mean (SD)	D_{50} (μm) Mean (SD)	D_{90} (μm) Mean (SD)	Span $(D_{90}-D_{10})/D_{50}$ Mean (SD)
RS-MCJ-73	18.06 (0.12)	52.55 (0.19)	108.20 (1.27)	1.72 (0.02)
Eratab	19.20 (0.71)	62.21(1.40)	116.45 (3.44)	1.56 (0.02)
Vivapur101	24.25 (0.12)	69.05 (0.91)	142.77 (5.17)	1.72 (0.05)
Tablettose	60.54 (2.95)	202.88 (2.90)	411.08 (2.14)	1.73 (0.10)
Cellactose	68.83(1.74)	214.51(2.53)	371.61(2.10)	1.41(0.02)

*RS indicates rice starch; and MCJ, jet-milled microcrystalline cellulose.

spatula values seemed to fluctuate when the cellulose proportions were increased, in particular for the composite particles of RS and MCJ. However, it seemed that high cellulose content in composite particles resulted in an increase of angle of repose and spatula, which were indicative of less flowability. When using the percentage compressibility to assess the flowability of a bulk powder, a lower value indicates a better flow. Percentage compressibility was calculated from aerated bulk density and packed bulk density, which were also the measurements provided by this instrument. Percentage compressibility of native RS and MCS were much higher than of coprocessing powders of these 2 components. Increasing cellulose content gave an increase of percentage compressibility. Cohesion is a descriptive indication of interparticulate bonding behavior of powders. Powders with a higher cohesion value are less flowable. Cohesion values were obtained by determining the weight of residual powder remaining on the mesh after having applied constant amplitude of vibrations for a certain period to the sample powder on screen. RS is more cohesive than microcrystalline cellulose. Adding more cellulose component to RS would, therefore, reduce the cohesiveness of composite particles as compared with spray-dried RS. In this study, the cohesiveness of composite particles reached the minimum value at RS and MCS or MCJ in the ratio of 7:3. When increasing cellulose component to 40% to 50%, cohesion values seemed to increase. This result might have been caused by the shape of the particles, which became less spherical and had a rougher surface texture. Less spherical and rougher surface texture of particles could induce particle-particle interlocking and friction resulting in a larger amount of residual powder on the screen, hence increasing cohesion values.

Carr has described the index system to compare the flow behaviors of powder materials by using a scoring system to convert the measurements of angle of repose, angle of spatula, percentage compressibility, and percentage cohesion into index numbers.[13] The overall summation of these index numbers yields the flowability index, which could be used as a parameter to predict the relative degree of fluidity of the bulk power. A higher value of flowability index indicates better flow property of powder. A flowability index number higher than 70 indicates a good degree of flowability; a number below 60 indicates that flowability is poor. RS was composed of both irregular shape aggregates and isolated grain, which would have resulted in poor flowability, while spray-dried RS was in spherical form resulting in a high flowability index. MCS also exhibited a rather low flowability index, in spite of having the lowest cohesion; as a fibrous particle, it was resistant to the flow due to interlocking of the particles. It was clearly indicated that an increasing percentage amount of microcrystalline cellulose would reduce the flowability index of composite particles. Ten percent of cellulose component in composite particle did not affect its flowability index compared with spray-dried RS.

Incorporation of microcrystalline cellulose would enhance the compressibility property of the system and better compressibility than single RS-based direct compression excipient. Although an increase in microcrystalline cellulose proportion improved the compressibility of the system, use of starch as the major component in the composite particles is preferred because of the tremendous supply of inexpensive RS. In addition, using a higher proportion of microcrystalline cellulose will increase the cost of the system. For economic reasons and because it has the appropriate required tableting properties (eg, hardness, friability), the formulation consisting of RS and cellulose in the ratio of 7:3 is considered to be suitable. Both MCS and MCJ yielded composite particles (RS-MCS-73 and RS-MCJ-73) of similar compressibility. But powder consisting of more spherical-shaped particles tends to have better fluidity (see Figures 2D and 3C). RS-MCJ-73 was, therefore, chosen for further evaluations of powder and tableting characteristics in comparison with some commercially available excipients.

Table 4 shows the particle size distributions of RS-MCJ-73 and commercial excipients. D_{50} of RS/MCJ-73 was in a size range similar to Vivapur 101 and Eratab (a commercial spray-dried RS) but smaller than that of Tablettose and Cellactose. RS-MCJ-73 exhibited a similar span to Vivapur 101 and Tablettose but a wider span than Eratab and Cellactose.

Table 5. Powder Characteristics of RS-MCJ-73 and Commercial Direct Compression Diluents

Materials	Angle of Repose (degree) Mean (SD)	Angle of Spatula (degree) Mean (SD)	Compressibility (%) Mean (SD)	Cohesion (%) Mean (SD)	Flowability Index Mean (SD)
RS-MCJ-73	37.2 (2.1)	57.9 (2.1)	19.2 (1.6)	3.2 (0.0)	67.0 (1.7)
Vivapur 101	39.5 (0.7)	64.7 (1.3)	32.6 (0.6)	0.0 (0.0)	52.5 (1.7)
Eratab	33.2 (1.8)	55.5 (2.9)	13.0 (0.4)	12.3 (0.0)	70.0 (0.0)
Tablettose	36.6 (1.1)	59.3 (1.8)	23.5 (0.2)	47.2 (0.1)	57.2 (1.8)
Cellactose	39.6 (1.6)	57.3 (2.0)	21.5 (0.5)	45.3 (0.0)	57.0 (0.0)

*RS indicates rice starch; and MCJ, jet-milled microcrystalline cellulose.

Table 6. Physical Properties of Tablets Made From RS-MCJ-73 and Some Commercial Diluents Using Compression Force of 8.8 kN

Materials	Hardness (N) Mean (SD)	Diameter (mm) Mean (SD)	Thickness (mm) Mean (SD)	Friability (%)	DT (minutes) Mean (SD)
RS-MCJ-73	188.7 (8.6)	12.89 (0.03)	3.47 (0.06)	0.60	2.56 (0.22)
Vivapur 101	†	12.81 (0.01)	3.61 (0.03)	0.00	>30
Eratab	131.6 (11.1)	12.86 (0.03)	3.34 (0.04)	1.42	2.11 (0.05)
Tablettose	30.9 (1.7)	12.78 (0.02)	3.12 (0.03)	‡	§
Cellactose	72.2 (4.3)	12.83 (0.01)	3.30 (0.01)	1.20	0.31 (0.06)

*RS indicates rice starch; MCJ, jet-milled microcrystalline cellulose; and DT, disintegration time.
†Very hard tablets; could not be measured by hardness tester.
‡All tablets were broken during testing.
§Not determined due to friable tablets.

Comparative powder characteristics of composite particles and commercial directly compressible vehicles are shown in Table 5. Based on flowability indices, flow property of RS-MCJ-73 and other direct compression diluents might be ranked in decreasing order as follows: Eratab > RS-MCJ-73 > Tablettose ≈ Cellactose > Vivapur 101. Round-shaped particles of Eratab and RS-MCJ-73 provided more fluidity than other diluents.

Figure 4 illustrates the appearances of tablets prepared from RS-MCJ-73. Physical properties of tablets made from RS-MCJ-73 and various commercial diluents are presented in Table 6. Hardness of tablets prepared could be ranked in the following order: Vivapur 101 > RS-MCJ-73 > Eratab > Cellactose > Tablettose. Vivapur 101 gave very hard compacts, which could not be measured by hardness tester; disintegration times were consequently longer than 30 minutes. Composite particles of rice grains and microcrystalline cellulose exhibited higher hardness tablets than Eratab. This finding demonstrates an advantage of adding cellulose component to RS based diluent. Cellactose gave higher hardness tablets than Tablettose because Cellactose is the spray-dried mixture of 75 parts lactose monohydrate and 25 parts cellulose powder, while Tablettose is composed of only lactose monohydrate agglomerates. RS-MCJ-73 and Cellactose had similar level of cellulose content, but RS-MCJ-73 gave higher hardness tablets than Cellactose. Because of higher hardness, RS-MCJ-73 tablets were less friable than Eratab, Cellactose, and Tablettose.

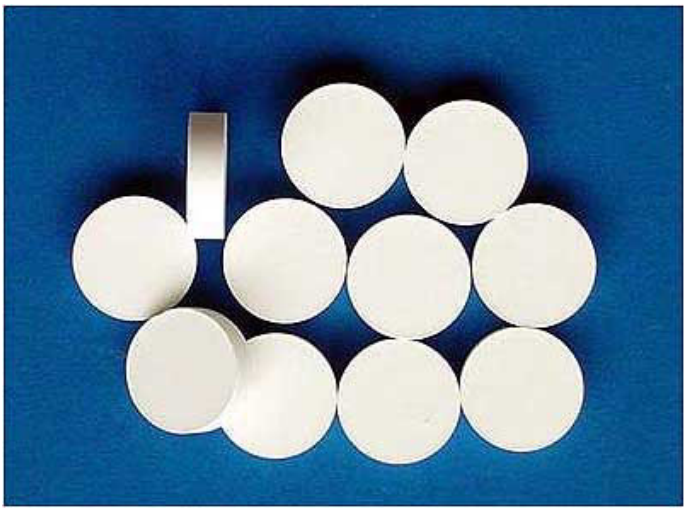

Figure 4. Tablets made from RS-MCJ-73..

CONCLUSION

RS and microcrystalline cellulose in the ratio of 7:3 is proposed to be a proper combination with respect to its properties for use as the vehicle for direct tableting process and the cost of the system. This developed material possessed fundamental characteristics and can be introduced as a new

coprocessed directly compressible excipient. The tablets made from this coprocessed composite particles exhibited high compressibility, good flowability, and self-disintegration.

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