A novel pharmaceutical excipient: coprecipitation of calcium and magnesium silicate using brine-seawater in date palm cellulose as an absorbing host .

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ABSTRACT

The aim of this research was to develop a cost effective and innovative pharmaceutical additive for multi-purpose use in the pharmaceutical industry using Saudi Arabia's natural resources and bio-wastes. The waste substance, brine, and the naturally occurring compound, sodium silica, were reacted together to produce water insoluble calcium and magnesium silicate salts (WISS). The purity index WISS was compared with synthetic Mg silicae. The produced particle size was 1.994 μm. Date palm cellulose (DPC) with a high purity index (0.99) was produced from the biomass waste of the date palm tree. The DPC was used as a host for co-precipitation of synthetic calcium magnesium silicate within its chemical structure. The interaction between the cellulose polymer and silicates is physical in nature. The WISS-DPC was more flowable than DPC alone. SEM pictures show that the particles of the DPC were fibrous and irregular in shape, whilst the the WISS-DPC showed more regular shape than DPC. Tablets prepared using WISS-DPC were harder and had lower disintegration time at all compression forces compared to those made with DPC. The produced excipient had excellent compaction and disintegration properties and could be used as a superdisintegrant and tablet binder in pharmaceutical industries.

KEY WORDS: Date palm cellulose, brine seawater, excipient, calcium, magnesium silicate

INTRODUCTION

There are two important waste products that usually contaminate Saudi Arabia environment because of the way they are disposed of and the absence of an efficient recycling method. The first one is the waste product produced after seawater desalination and the second one is the waste product produced by date palm trees.

Desalination refers to the removal of salts and minerals from water. In Saudi Arabia there are many plants for water desalination, for example at Jubail, Rabigh, South Jeddah Corniche, Yanbu, Corniche RO and Shuaibah. The major

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problem with seawater desalination is the brine of seawater (BSW) which discharges into the seas. The concentrations of different pretreatment chemicals in Multi Stage Flash and Reverse Osmosis effluent are critical for the marine environment (1). Salts, such as, calcium, magnesium and sodium could be processed from the highly concentrated BSW thus decreasing the total costs of water desalination, as well as, solving the environmental problem.

Tanak *et al.* produced sodium chloride using BSW discharged from a reverse osmosis seawater desalination plant with a capacity of 200,000 tons per year (2). A dual-purpose desalination-salt production system was developed and the authors demonstrated that the water costs would be competitive compared with potable water produced in thermal or reverse osmosis seawater plants (3). Calcium and magnesium salts are valuable by-products that could be obtained from BSW discharge.

Another substance that could be obtained from natural resources in Saudi Arabia is sodium silicate which is available in abundance in the desert soil (4). Sodium silicate could react with calcium chloride and magnesium chloride to produce calcium and magnesium silicates, respectively. Synthetic calcium and magnesium silicates are considered water insoluble silicate salts (WISS) that have many applications in the pharmaceutical and food industries (5).

A unique pharmaceutical excipient could be prepared through the co-precipitation of WISS within the structure of natural polymers using a mineral fiber solid dispersion technology platform (6). Briefly, the technology needs trivalent or divalent cationic ion of minerals to be precipitated within the polymer structure. This research, focuses on cellulose that could be processed from the waste of the palm tree. Saudi Arabia has more than 23 million date palms and over 320 varieties providing annual earnings of more than 0.5 billion USD (7). However, during sorting and storage a high percentage of the date tree ends up as waste. This waste has traditionally been burned on the farms resulting in environmental hazards. The chemical composition of these wastes have been investigated and found to be consisting of cellulose, hemicelluloses, lignin and other compounds (8). Research into uses of these by-products has been carried out previously (9-14).

Although the date palm by-products have been investigated in different fields, only limited studies have been carried out into using the waste for developing excipients for the pharmaceutical industry. Date palm-waste is considered an important source for cellulose and other compounds such as hemicellulose and lignin. Cellulose and cellulose derivatives are largely used in food and pharmaceutical products. They can be used as thickeners, fillers and tablet binding agents, disintegrants and compressibility enhancers (15, 16).

Tablets represent 80% of all dosage form administered into man. They are primarily manufactured by direct compression or granulation. In direct compression all the ingredients are mixed together and compressed using a tableting machine to form tablets. The powder should be highly compressible to transform into compact (17). To prepare good tablets with pharmaceutically accepted characteristics the added excipients must fulfill certain requirements such as compressibility, good binding functionality, powder crystallinity and flowability. It is difficult to find one excipient that fulfills all these requirements. One of the objectives of this project was to produce a novel direct compressible pharmaceutical excipient through the inclusion of WISS within a cellulose structure. In a previous study, a directly compressible tablet excipient was developed by co-processing starch with magnesium silicate (18).

Chitin metal silicate co-precipitates were evaluated and found to have the potential to be used as filler, binder, and superdisintegrant for tablets by the direct compression and wet granulation methods (19, 20). Another natural

polymer which was co-precipitated with silica is chitosan. The precipitation process improved its powder flowability and compactability (21). From the above discussion, it is clear that the characteristics of all the investigated naturally occurring polymers were positively affected by the addition of silicates.

The aim of this project was to co-precipitate water insoluble silicates obtained from BSW and sodium silicate within cellulose obtained from the date palm in order to develop a suitable pharmaceutical excipient.

MATERIALS AND METHODS

Materials

Brine-seawater (BSW) was brought from Red Seawater after desalination from Shuaibah Desalination Plant, Jeddah, KSA. Colloidal silica was purchased from Sigma Aldrich. Date palm tree trunk, *Phoenix dactylifera* L, family (*Arecaceae*, or *Palmae*), was obtained from old trees in Taif city, KSA. All chemicals and reagents used were of analytical grade and used as received.

Determination of the content of divalent cations in BSW

BSW was obtained from the desalination plant at Shuaibah and evaporated to remove NaCl by crystallization. The obtained solution had a density of about 1.22 g/ml (sea bittern). After carrying out suitable dilutions with distilled water, measurements were taken using a Thermo Scientific (iCAP 7000 series, USA) inductively coupled plasma-atomic emission spectrometer (ICP-AES) supported by Qtera software and connected to a Cetac (ASX-520). These measurements were performed using axial mode for Pb, Cd, Ca, Mg, and radial mode for K, Na respectively, under optimized plasma parameters (RF power: 1150w, nebulizer gas and auxiliary gas flow: 0.5 l/min). For the measurements of the investigated elements, standard solutions and the samples were introduced automatically using auto-sampler to plasma under the optimized conditions and the optical system with axial and radial mode to detect the tested elements concentrations. The concentrations were determined automatically using a calibration plot.

The preparation of sodium silicate

Colloidal silica was added to the NaOH solution (1:1 mol/mol) and the mixture was heated and stirred until all the silica particles were dissolved through the conversion of the insoluble suspended silicon dioxide into the soluble sodium silicate form (21).

The preparation of synthetic Mg silicate

The magnesium silicate was prepared as described previously (18) by adding pure $MgCl_2 .6H_2O$ to sodium silicate in a molar ratio of 1: 1 as described below:

$$Na_2SiO_3 + MgCl_2.6H_2O \rightarrow MgO.nSiO_2.xH_2O + 2NaCl$$

The preparation of WISS

In order to select the appropriate proportion of BSW to sodium silicate solution, different volumes (25, 50, 75, 100,125, 150, 200, 225, 250, 275, 300, 350, 400, 500, 600 and 700 ml) of raw BSW solution were added to 100 ml of the sodium silicate solution. Sodium silicate (100 ml) was prepared by dissolving 10 g colloidal silica in an alkaline aqueous solution containing 6.6 g sodium hydroxide to produce a total volume of 100 ml. The pH was monitored after each addition, samples were withdrawn at each time interval and the particle size was determined using Malvern ZetaSizer. The best proportion was selected based on the lowest pH attained with lowest particle size.

The production of date palm cellulose (DPC)

200 g date palm tree trunk was dried in an oven at 100°C for 24 hours and cut into small pieces. The pieces were soaked in hot water for 24 hours and filtered. The remaining fibrous particles were boiled in 2 M NaOH for 1 hour, and then filtered again. The fibrous particles were bleached using a 5% sodium hypochlorite

solution. The particles were soaked in 100 ml of 2 M HCl solution for 1 hour and thoroughly washed with distilled water. The particles were dried in oven at 80°C for 8 hours resulting in palm cellulose. The powder particles were passed through a mesh of 300 μm and stored in a well-sealed container (35).

Preparation of the WISS-DPC coprecipitate

The method for the preparation of the WISS-DPC co-precipitate has been reported previously (21). Slight modifications were made in order to obtain maximum precipitation. A fixed amount (100 ml) of sodium silicate, prepared as stated above, was added to 100 grams of date palm cellulose, as prepared previously, and mixed vigorously. About 700 ml BSW was added gradually with homogenization at a rate of ~150 ml/min, which was continued for 1 hour at room temperature (25°C). The pH of the final mixture was maintained below pH 8.5. The product was washed with distilled water until the conductivity of the filtrate was close to that of water. The product was dried in an oven at 80°C to complete dryness and passed through a mesh of 300 μm. The product was stored in a sealed container with a desiccator at RH around zero.

Particle size measurement

Particle size was determined using a micro size laser diffraction analyzer Shimadzu, SALD-201V. Analysis of median particle size was carried out using the built in program WingSALD, Wing-1 standard Data Processing Ver 1.30, Shimadzu Corporation, Japan.

Purity index using FTIR

In order to investigate the chemical structure of the DPC and compare its similarity with cellulose, dry samples of the DPC were placed in the micro-sample cup of the Shimadzu Diffuse Reflectance Infrared Fourier Transform spectroscopy (DRIFT) accessory using FTIR ATR spectrometer (IR Prestige 21, Shimadzu, Japan). The transmittance mode for intensity measuring was applied in the spectrum ranging from 400 to 4000 cm^{-1}. Another reference cellulose (Avicel® PH 101) was scanned similarly as a test sample. Powdered microcrystalline cellulose is the most used cellulose for compressing tablets in the pharmaceutical industry. The purity mode calculates the similarity (purity) between a reference spectrum and a test spectrum. It judges similarity of spectra in a quantitative way. IR software was used to determine the match score by numerically calculating the similarity between the two spectra. The match score represented the square of the correlation coefficient. Similarly, FTIR purity test of the prepared WISS was compared to that of the prepared synthetic Mg silicate.

Fourier transform IR measurements

About 5 mg sample of each silica, sodium silicate, Mg silicate, DPC, WISS and WSS-DPC were mixed with 200 mg dry KBr separately. Then a small portion of the mixture was compressed in a special die to form a transparent disk. The disk was then put in the instrument beam for spectroscopic scanning 400-4000 cm^{-1}.

Loss on drying (LOD)

A fixed amount of 1 g of WISS-DPC was placed in a convection oven (Memmert Model 100 e800, Schwabach, Germany) at 110°C for 3 hours. The percent decrease in weight was calculated as LOD.

Moisture uptake of the WISS-DPC co-precipitate powder

A fixed amount of 1 g of the samples of the WISS-DPC and the DPC were spread on open plastic Petri dishes and subjected to different relative humidity (RH) conditions (33, 75 and 90%) (21). The samples were kept inside the humidity chambers at an ambient temperature

for 2 weeks. The percentage increase in weight from the original weight was recorded.

Bulk and tap densities, and Compressibility Index

Bulk and tap densities were determined after transferring a constant mass of DPC and WISS-DPC into standard graduated measuring cylinders and the initial volume was recorded using a TAP-25 tapped tester (Logan Instrument Corp., USA). The tapped densities were determined by tapping the measuring cylinder to form a constant height after tapping (22).

The Compressibility index or Carr index (CI) is used as a measurement of the flowability of a powder and can be calculated using Equation 1:

$$\text{Carr index} = \frac{\text{tapped density} - \text{bulk density}}{\text{tapped density}} \text{x}\, 100 \qquad \text{Eq. 1}$$

The Compressibility Index ranges from less than 10 up to values higher than 38 and the powder flow is considered excellent at the lowest values and very poor at the highest values (20, 40).

Scanning electron microscope (SEM)

The dried samples of Mg silicate, WISS, DPC and WISS-DPC were observed using a Quanta 250, Inspect S50, SEM microscope (FEI Czech Republic, Brno, Czech Republic) using low-vacuum mode.

Tablet preparation

Tablets were prepared using the DPC and the co-precipitated WISS-DPC powders. 500 mg of powder was filled in a special circular 15 mm die and the powder was compressed into tablets using an Instron press (Model 3367, Instron Ltd, USA) with different compression loads of 500, 1000, 1500 and 2500 kgf at maximum speed of 500 mm/min.

Disintegration time

The disintegration time of the produced tablets (n=3) was measured using an disintegration tester (QC-21 disintegration test system, Hanson Research, CA, USA).

Tablet hardness

Circular tablets (n=3) weighing 500 mg of DPC and WISS-DPC, were prepared by compression at compression loads of 500, 1000, 1500 and 2500 kgf. The tablets were subjected to crushing force using a hardness tester (TB-225, Erweka, Germany).

Compression load versus compression displacement curves and elastic stress

Compression load versus compression displacement curves were prepared using an Instron press (Model 3367, Instron Ltd, USA). Powder samples (0.5 g) were filled in a circular die with a diameter of 15 mm. The compression rate was 10 mm/min until reaching the maximum compression of 2800 kgf load (compression stage) and then the cross-head was lifted up till having zero load (decompression stage). The elastic stress was measured while the compact was left in the die. Elastic stress resulted due to the expansion of the constrained compact in the die. The stress resulted from compact expansion was used as an indicator for the matrix elastic recovery (22). Bluehill®2, ver. 2.31 software was used for the analysis.

Stress relaxation

Stress relaxation was also measured using an Instron press. The powder was directly compressed with a compression rate of 5 mm/min, until the required compression load reached 2000 kgf. Then, the load was kept stationary on the compressed powder. The decay of the compression load was measured during a holding interval to determine the compact stress relaxation (22).

Statistical treatment

One-way ANOVA test was used for comparison. The difference was considered statistically significant when the probability value (P) was less than 0.05.

RESULTS AND DISCUSSION

Content of divalent cations in BSW

The concentrations of Ca, Mg and K cations in BSW after the removal of NaCl (ppm) were 4.763, 16.994 and 6.1, while Na, Cd and Pb concentrations were almost undetectable according to the ICP analysis. Consequently, BSW contains two main divalent cations i.e., Mg and Ca. Such findings were close to the data reported by Gancy and Chester (23), where raw BSW contained impurities such as calcium compounds calculated as elemental calcium, 10 to 600 ppm and magnesium compounds calculated as elemental magnesium, 1 to 10 ppm (23).

Preparation and characterization of WISS

The BSW contains divalent cations of calcium and magnesium that could react with sodium silicate to form WISS as described previously (24, 25).

$$Na_2SiO_3 + MgCl_2 \rightarrow MgO.nSiO_2 + 2NaCl$$

$$Na_2SiO_3 + CaCl_2 \rightarrow CaO.nSiO_2 + 2NaCl$$

In this study, the BSW was used as received without treatment in order to cut off the costs of separating calcium and magnesium salts out of the BSW. Calcium and Magnesium salts could react without separation from BSW. Both Ca and Mg salts are safe to humans and can be used in pharmaceutical preparations separately or in combination.

Figure 1 shows the FTIR of silica, sodium silicate and WISS. The symmetric vibrations of

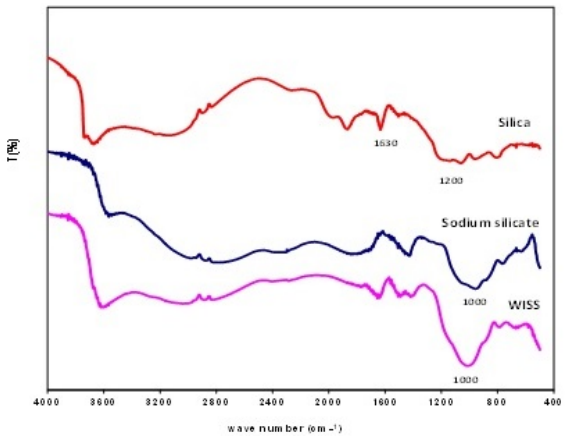

Figure 1 FTIR of silica, sodium silicate and WISS

Si-O-Si appeared at about 1200 cm^{-1} in the silica sample and at about 1000 cm^{-1} for WISS and sodium silicate and it was more intense due to the effect of metals. All bands in WISS and sodium silicate shifted to low frequency field compared to silica. Small peak in silica and silicate salts around 1630 cm^{-1} was assigned to physically bound water (26).

FTIR of WISS and pure magnesium silicate are shown in Figure 2. Two tiny peaks appeared in the spectrum of WISS due to the presence of calcium at 1400 and 1480 cm^{-1} as suggested elsewhere (27). The purity index of WISS compared to Mg silicate was calculated using FTIR software and it was 0.85 as shown in Figure 3. FTIR of Avicel® PH101 can be used

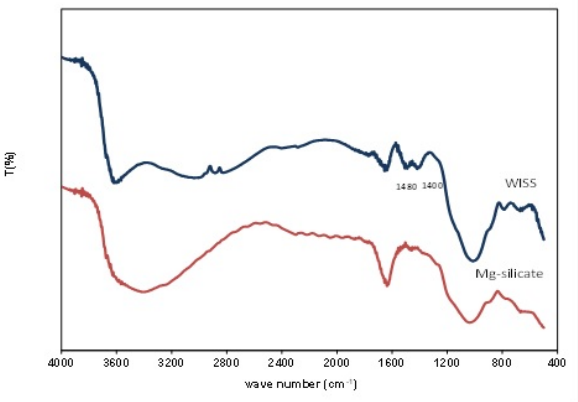

Figure 2 FTIR of Mg silicate and WISS

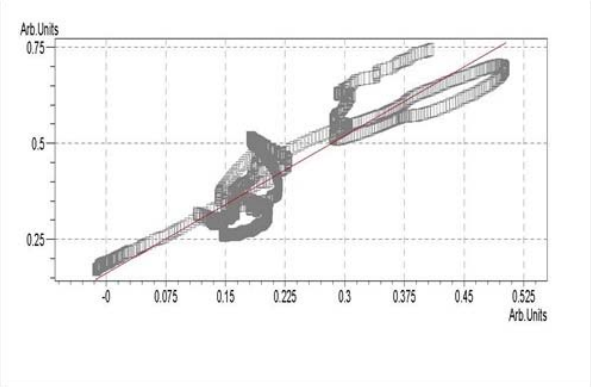

Figure 3 Purity index between WISS and Mg silicate using FTIR software 0.85

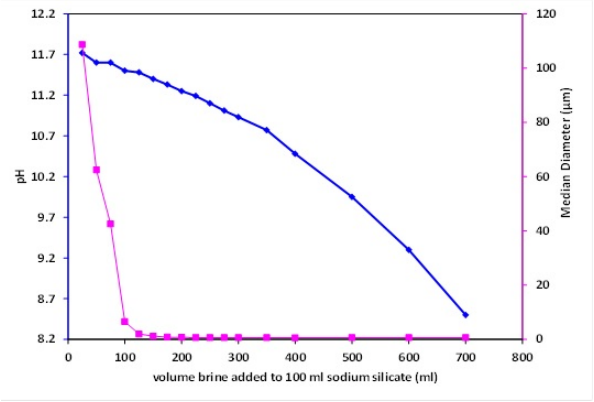

Figure 4 Change in pH and particle size upon addition of BSW to fixed volume of 100 ml sodium silicate

as a reference spectrum because it has been reported to be similar to cellulose powder. Singh and Kulkani compared the FTIR of different commercial grades of microcrystalline cellulose with cellulose powder. They found that all the peaks of Avicel® PH101, Avicel® PH102, Flocel® 101, Flocel® 102, and Cellulose Powder were comparable and there were no significant difference in the FTIR spectra of Avicel® PH101, Avicel® PH102, Flocel® 101, Flocel® 102 or celluloses powder (28).

BSW was added to sodium silicate to synthesize WISS via ion replacement reaction. Different volumes of BSW were added to 100 ml of sodium silicate and pH and particle size were monitored after each addition to select the suitable proportions.

Sodium silicate is an alkaline substance with a pH of about 12. The addition of the BSW resulted in pH reduction of sodium silicate due to formation of the salt as shown in Figure 4.

An interesting result is the tremendous reduction in particle size upon adding BSW. The initial addition of 25 ml of BSW to sodium silicate resulted in formation of WISS with a size of 108.66 µm and reached 1.994 µm with the addition of 125 ml of BSW to sodium silicate solution. After which, there was slow reduction in the particle size. In a previous study, the addition of magnesium chloride to sodium silicate solution yielded a product with a particle size of about 42 µm. The huge difference in particle size could be attributed to the difference in the initial concentration of the reactant and the feeding rate as these factors could affect the particle size and the surface area of the finished product (25). In addition, the use of the BSW, which contains magnesium and calcium chlorides, instead of the use of magnesium chloride alone, may influence particle size distribution too.

Magnesium silicate has diverse applications in the pharmaceutical, food and other industries. It is also used as an adsorbent in chromatography as rubber filler for plastic, rubber, paints, adsorbents of organic compounds and others. Most of these applications need fine particle size and high surface area (5). To obtain such particles, researchers have adopted different methods such as milling, or ultrasound-assisted precipitation (29). In this study, fine particles were obtained during synthesis without any further treatment.

Preparation and characterization of WISS-DPC

Cellulose was produced from date palm tree (*Phoenix dactylifera* L.) according to the method reported by Khiari *et al.* (30). The process employed the soda pulping method. The main objective was to facilitate the disintegration of wood into fibrous product. This was achieved

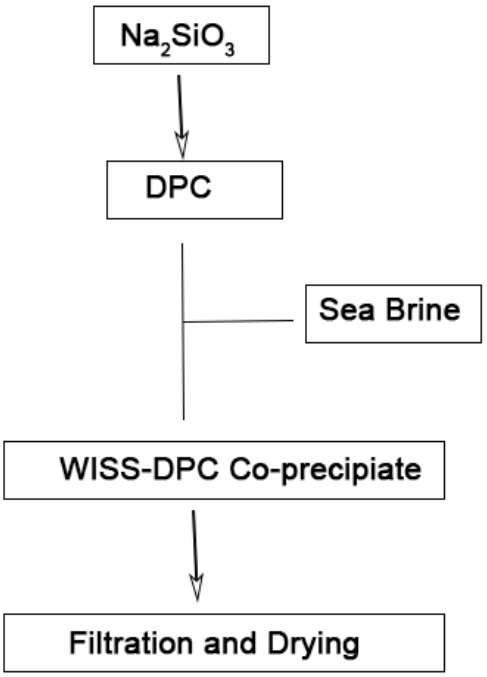

Figure 5 Overall schematic representation for the preparation of the WISS-DPC co-precipitate

by breaking the bonds in the lignin macromolecule (31). Small scale batch of WISS-DPC coprecipitate was prepared. WISS could be formed physically within the intra-porous structure of DPC forming mineral fibrous solid/solid dispersions as previously described in the published international patent (6), according to scheme shown in Figure 5.

The FTIR of date palm cellulose (DPC) is shown in Figure 6. The main features are the band around 3400 cm-1assigned to different O–H stretching vibrations, band at 2900 cm-1 corresponding to C-H vibrations. The bands at 1620 and 897 cm-1 were assigned to C =O (amide 1) and C–O–C stretching at β-glycosidic linkages, respectively (32, 33). The purity index

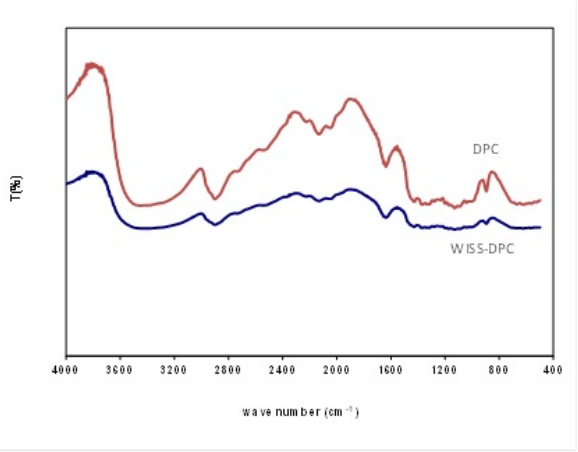

Figure 6 FTIR spectra of DPC and WISS-DPC co-precipitate

of DPC compared to microcrystalline cellulose powder was determined by FTIR software and it was 0.99 as shown in Figure 7. There was no difference in FTIR peaks position between DPC and WISS-DPC coprecipitate as shown in Figure 6. This indicates the absence of any chemical interactions between the polymer and silicates. The intensities of some peaks of the WISS-DPC copreciptate are lower than those of DPC cellulose due to dilution effect. These

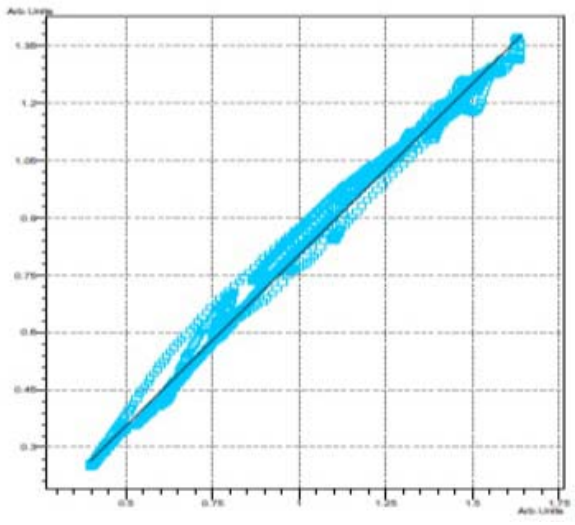

Figure 7 Purity index of DPC compared to microcrystalline cellulose (Avicel® PH 101) using FTIR software is 0.99

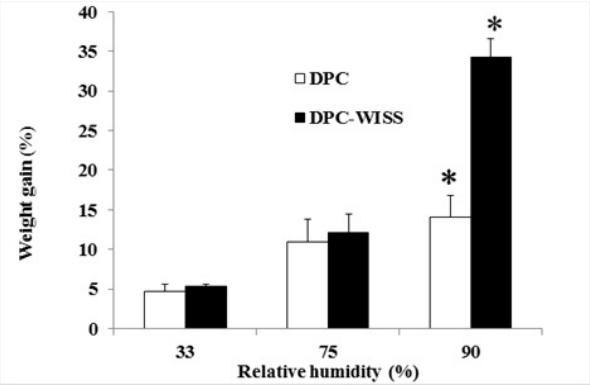

Figure 8 Percent increase in weight under different relative humidity of DPC and WISS-DPC coprecipitate (n=5). * P<0.05

observations were in accordance with a previous study where, chitin and chitin-metal silicates copreciptate showed identical bands (27).

Moisture uptake of WISS-DPC coprecipitate powder

The percent increase in weight under different relative humidity of DPC and WISS-DPC coprecipitate was indicated in Figure 8.

WISS-DPC showed a significant increase (P<0.05) in water uptake compared to DPC only under high humidity conditions i.e., above RH > 75%, however, it seems that at normal RH conditions (50-55%), WISS-DPC and DPC powders have almost close values of moisture content 5.5 ± 0.78 and 6.43 ± 0.41, respectively as shown in Table 1. Thus, the storage conditions should be similar to DPC under normal humidity conditions.

Table 1 Powder properties of DPC and WISS-DPC coprecipitate (n=6).

TEST	DPC	WISS-DPC	P-VALUES
LOD (%)	6.43 ± 0.41	5.5 ± 0.78	P<0.05
Bulk density (g/cc)	0.204 ± 0.005	0.288 ± 0.015	P<0.05
Tap density (g/cc)	0.243 ± 0.007	0.325 ±0.010	P<0.05
CI (%)	18.47 ± 5.05	13.17 ± 5.88	P>0.05
Flowability	Fair flow	Good flow	

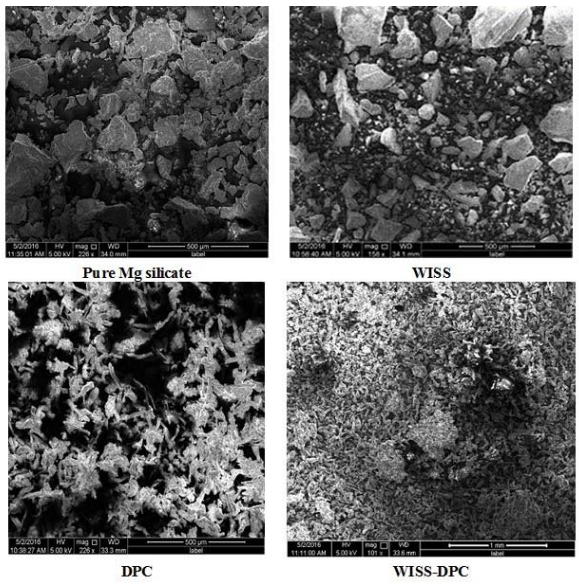

Figure 9 SEM photos of pure magnesium silicate, WISS, DPC and WISS-DPC co-precipitate

Powder properties of WISS-DPC coprecipitate

The bulk and tap densities of DPC were significantly lower (P<0.05) than that of WISS-DPC. The estimated compressibility index (%) was higher for DPC than that of WISS-DPC. However, the CI (%) did not show significant difference (P> 0.05) which could be due to the relatively higher variability between the prepared small scale batches. Such differences could be minimized under more controlled conditions on scale up batches. Thus, WISS-DPC was more flowable than DPC. This could be due to absorption and/or adsorption of WISS to DPC which improved density of the particles of DPC and improved their shape. The morphological changes of DPC upon precipitation of WISS were observed by SEM as shown in Figure 9.

The particles of the DPC were fibrous and irregular in shape because it is a cellulose polymer. WISS particles were almost similar to pure synthetic magnesium silicate particles in shape i.e. they were fluffy and amorphous structures. The coprecipitation of WISS in DPC resulted in the formation of fibrous

structures but having more regular shape than DPC which could emphasize that some of WISS may fill the pores inside and precipitate also onto the surface of DPC structures.

Consequently, such coprecipitate of WISS in DPC could densify the particles and so the particles would result in a flowable behavior. Hou and Sun studied the factors that affect powder flowability such as particle size, surface silicification, particle density and morphology (34). They found that the spherical morphology and higher particle density promoted powder flow. WISS-DPC improved morphology and increased the density of the particle and hence improved flowability which agrees with Aljaberi et al. study in which, silicification of microcrystalline cellulose (MCC) increases the surface area, improved mixing and surface morphology (35). The flowability of powder is essential parameter that affect filling of die in tableting machine and hence tablets weight.

Compact properties of WISS-DPC coprecipitate

Tablets were prepared from single component of either DPC or WISS-DPC. The produced tablets were characterized as shown in Table 2.

Table 2 Disintegration times of DPC tablets and WISS-DPC tablets compressed at different compression forces

FORCE (kgf)	HARDNESS (N)		DT (s)	
	DPC	WISS-DPC	DPC	WISS-DPC
500	40 ± 7	65±5	125	< 10
1000	62 ± 5	87 ± 6	325	< 10
1500	85 ± 4	128 ± 10	> 300	< 10
2500	110 ± 15	180 ± 12	>300	< 60

Transformation of powder into compacts (tablets) 'when a pressure is applied' involves several steps such as volume reduction, fragmentation, elastic and plastic deformations. These processes result in an increase in interparticulate bonds. The bonding areas between particles depend on moisture content, porosity, particle size, surface properties, density, and rate of flow (36). DPC and WISS-DPC showed differences in density, rate of flow and surface properties. Therefore, the compactability of these two powders would be different. WISS-DPC showed higher tablet hardness values at all compression forces compared to that of DPC. The shape of fibers of DPC was changed by precipitating minerals of WISS onto their surface as shown in Figure 10.

From SEM pictures (Figure 10) it was evident that WISS precipitated onto the surface of DPC. This result was in accordance with a study carried out by Tobyn *et al.* in which, most of the colloidal silicon dioxide was located on the surface of microcrystalline cellulose. However, this does not exclude precipitation of WISS inside the particles (37).

Thus, the surface modification of DPC by silicate resulted in a shift toward a compactable form. Similar findings were observed upon precipitating silica on chitosan. The compactability of chitosan was increased due to the decrease in the compacts' pore size and changes in chitosan surface (21).

Disintegration time is a pharmacopeial test. It is important for conventional immediate release compressed tablet to fragment into smaller parts to increase the surface area and to enhance drug dissolution which influence drug absorption and bioavailability. The WISS-DPC

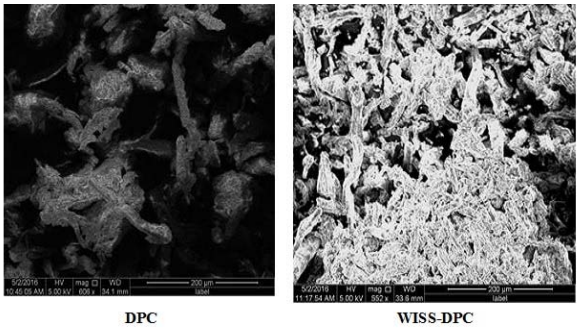

Figure 10 SEM photos of DPC and WISS-DPC co-precipitate at higher magnification

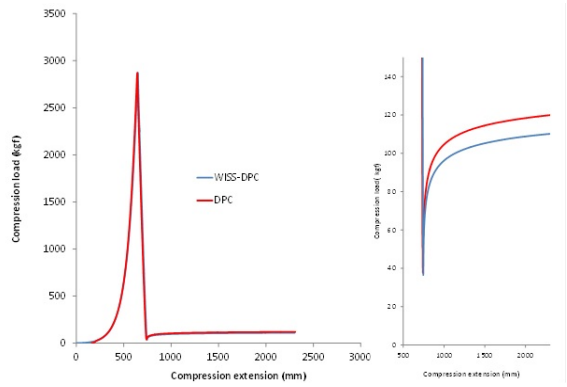

Figure 11 Compression load applied versus powder compression extension curves of DPC and WISS-DPC compressed at 2800 kgf also showing the elastic stress after zero compression load (left hand side). The developed load for constrained powder in the die of at zero applied pressure (elastic stresses) (right hand side). The compression extensions of the two curves were corrected to superimpose at the maximum compression load.

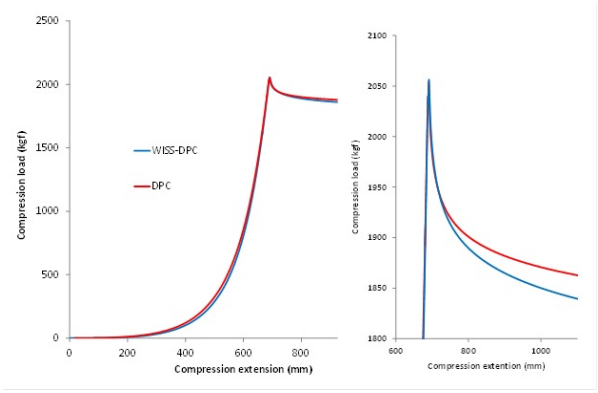

Figure 12 Compression load applied versus powder compression extenstion curves of DPC and WISS-DPC compressed at 2000 kgf also showing the stress relaxation after the maximum load (left hand side). The decrease in compression load at about 2000 kgf load of constrained compact of DPC and WISS-DPC (stress relaxation) (right hand side). The compression extensions of the two curves were corrected to superimpose at the maximum compression load.

tablets showed lower DT values at all compression forces than that of DPC. It is clear that the inclusion of WISS in DPC has a dual action i.e., DT decreased while at the same time tablet hardness increased. Such modification resulted in the production of a superdisintegrant with good tablet binding ability at the same time. Similar findings were reported elsewhere upon the inclusion of silica in chitosan polymer (21). Silica can act as a superdisintegrant upon inclusion with polymers due to its ability to absorb water and not liquefy upon absorbing water (36).

Compression process and elastic stress

In order to understand the effect of compression/decompression on WISS-DPC powder compared to DPC, the compression process was plotted against the compression displacement as shown in Figure 11. The results indicated densification and volume reduction of the powder of WISS-DPC and DPC under compression. Compression leads to permanent deformations (plastic) and recoverable deformations (elastic) of the compact (38). After the complete removal of the external load at the end of the decompression stage, the formed tablet could exert self-expansion i.e. elastic stress recovery. The degree of elastic stress depends on material physicomechanical properties (36). WISS-DPC showed lower elastic stress compared to DPC. This could be attributed to the presence of WISS which is a highly porous hollow plastic structures compared to the elastic DPC (39, 40, 41).

Stress relaxation

In order to understand the stress relaxation of WISS-DPC compared to DPC, the powder was compressed to the maximum load of 2000kgf and the compressed tablet was left to relax under the maximum applied load as shown in Figure 12.

The principal feature of stress relaxation is the decay of exerted stress within the specimen with time. The main mechanism by which this stress-relieving process can occur is through plastic flow, which could allow the movement of material in the remaining voids (41). WISS-DPC showed higher plastic flow compared to DPC. This is in agreement with the previous

results obtained from elastic stress measurement.

CONCLUSIONS

Date palm trees contain crucial substances that can be obtained easily as pure date palm cellulose (DPC) and so instead of burning the dead trees their cellulose could be used in the pharmaceutical industry. BSW contains essential divalent cations that can be used to produce water-insoluble silicate salts of calcium and magnesium (WISS) upon reacting with sodium silicate) which is inexpensive product of sand silica and soda). Thus, instead of polluting the sea with concentrated minerals, WISS could be produced as an alternative for the pharmaceutical market. It is possible to produce mineral-fiber solid dispersion through the inclusion of WISS within the structure of DPC and so improving DPC compaction and disintegration properties. The results are proof of concept indicating WISS-DPC could be used in the pharmaceutical industry as a co-processed pharmaceutical excipients during formulation of solid dosage forms.

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