Saudi Pharmaceutical Journal (2010) **18**, 81–89

King Saud University

Saudi Pharmaceutical Journal

www.ksu.edu.sa
www.sciencedirect.com

ORIGINAL ARTICLE

Utilization of date syrup as a tablet binder, comparative study

Fars Kaed Alanazi

Kayyali Chair for Pharmaceutical Industry, Department of Pharmaceutics, College of Pharmacy, King Saud University, P.O. Box 2457, Riyadh 11451, Saudi Arabia

Received 18 October 2009; accepted 30 January 2010
Available online 14 February 2010

KEYWORDS

Dates syrup;
Tablet binder;
Masking taste;
Tablets' sweetener;
Tablets' flavorings

Abstract The aim of this study was to investigate the possibility of using dates syrup as a tablet binder. Dates syrup (40%, 50%, 60% w/w dates syrup:water) was utilized for the granulation of sodium bicarbonate and calcium carbonate as examples for water-soluble and water-insoluble materials; correspondingly. Those two materials represent examples of bulky drugs as well. Starch paste (10% w/w starch in water) and sucrose syrup (50% w/w sucrose in water), the well-known tablet binders, were used in the granulation of the same materials for the sake of comparison. The granulations were evaluated with regard to particle size and particle size distribution, granule strength, bulk density, flowability, moisture content and compression behavior. In addition, tablets prepared and evaluated from these granules. Taste and flavor of the prepared tablet have been tested by seven healthy volunteers. Within the scope of this work, dates syrup showed excellent properties as a tablet binder in comparison to starch paste or sucrose syrup for the granulation of both water-soluble and water-insoluble materials. Also, better flavoring and masking taste have been noticed from an evaluation by human volunteers demonstrating the usefulness of the date syrup as sweetener and flavoring the tablets in addition to its use as binder.

1. Introduction

Most powders cannot be compressed directly into tablets, even after the addition of an appropriate lubricant, mainly because they lack the proper characteristics of binding or bonding together into a compact entity. Granulation of those non-compressible powders is the most frequently adopted solution to render them tablet-able. Granulation is any process of size enlargement whereby small particles are gathered together into larger permanent aggregates to render them into a free-flowing state similar to that of dry sand (Bandelin, 1989).

Binders are the "glue" that hold powders together to form granules. They also provide the cohesiveness required for the bonding together of the granules under compression to form a tablet. Although, a number of process variables have been considered to influence granule quality in the wet granulation process, only binder solution was found to be the determining

E-mail address: afars@ksu.edu.sa

1319-0164 Peer-review under responsibility of King Saud University.
doi:10.1016/j.jsps.2010.02.003

ELSEVIER Production and hosting by Elsevier

factor (Miyamoto et al., 1995). Binder efficiency depends on its type, concentration and the method of incorporation (Rue et al., 1980; Reading and Spring, 1984). It also depends on the type of solvent (Phadke and Anderson, 1990).

Binders are either sugars or polymeric materials (Bandelin et al., 1989). The latter fall into two classes: (a) natural polymers such as starches or gums including acacia, tragacanth, and gelatin and (b) synthetic polymers such as polyvinylpyrrolidone, methyl and ethyl cellulose and hydroxypropyl cellulose.

Although binders could be added, in the solid state, to the powder mix and the mixture wetted with water, yet in practice, solutions of binders are usually used in tablet production. The efficiency of binders is augmented when used in the solution state (Saleh et al., 2001).

Date syrup is thick-dark brown syrup extracted from dates. There are many types of dates which are cultivated and be using in production of date syrup. Khalasah is one of the most famous palm cultivars in Saudi Arabia, famous for its sweetness level that is neither high nor low thus, suits most people. The production of the date syrup in the east side of Saudi Arabia is about 1200 ton in 2008 (Algazail, 2008) which reflects its economical importance.

Al-Hooti et al. (2002) reported that glucose and fructose are the major sugars presented in date syrup and total sugar contents were reaching 88%. Date syrup contains in addition to sugar, macro and micro elements (Table 1) which may play important role of considering the date syrup as a rich nourishment (Al-Khateeb, 2008).

Thinking of date syrup as a possible tablet binder provokes its advantages over a corresponding binder like sucrose syrup. Contrary to sucrose syrup, date syrup is a natural product and it does not necessitate solution preparation manipulations since it produces in a nice fluid form. In addition, it has a richer nutrition value which is considered valuable source of minerals such as potassium, magnesium and calcium (Al-Khateeb, 2008). Furthermore, dates syrup tastes sweeter than sucrose and has a unique good flavor. Also, date syrup, as investigated in the current study, gives granules and tablets a nice yellowish color with excellent date flavor. This could be used in manufacturing to mask undesirable taste and odor especially in pediatric tablets like chewable multivitamins tablets.

Table 1 The constitution of date palm syrup.

Components	Value
Moisture content (%)	16
Ash content (%)	6.8
Total solids on dry weight (%)	84.0
Total sugar (%)	79.45
Reduced sugar (%)	4.87
Invert sugar (%)	74.83
Total proteins (as N) (%)	0.83
Total lipids (fats) (%)	1.98
Pectin content (as calcium pectate) (%)	1.46
Vit. C. content (mg/100 g)	0.185
Minerals (mg/100 g)	
Sodium	13
Potassium	202.8
Iron	7.8
Magnesium	143
Calcium	338

The aim of this work was to investigate the possibility of using date syrup as a tablet binder and evaluating it against two well-known binders; namely sucrose syrup and starch paste. Sodium bicarbonate and calcium carbonate were used as water-soluble and water-insoluble materials, respectively, for granulation.

The granulations were evaluated with regard to particle size and particle size distribution, granule strength, bulk density, flowability, moisture content and compression behavior. In addition, tablets were prepared and evaluated from these granules. Taste and flavor of the prepared tablet have been tested by seven healthy volunteers.

2. Materials and methods

2.1. Material

Khalas date syrup was kindly gifted from Al-Hussa Saudi Dates Manufacture, Al-Hussa, Saudi Arabia. Sucrose was purchased from BDH (Poole, England). Starch, sodium bicarbonate and calcium carbonate were purchased from Pace Grove Limited (Leicestershire, UK). Magnesium stearate was purchased from Merck (Darmstadt, Germany). All other chemicals and solvents were of pharmaceutical grade.

2.2. Methods

The binders, their concentrations, and their amounts used in the granulation of 750 g of either calcium carbonate or sodium bicarbonate were shown in Table 2. Date syrup was diluted with water because preliminary trials in the study with undiluted date syrup were not successful. The same dilution approach was kept for sucrose syrup for comparison. Three diluted concentrations of date syrups have been used 40%, 50% and 60% (v/v, date syrup/ water). To avoid microbial contamination, the diluted solutions were immediately used post the preparation and neither stock nor storage solutions have been used. It should be noted that the date syrup has brown color and its dilute are yellowish to brownish.

2.3. Preparation of starch paste

The calculated amount of starch (to make 10% w/w paste) was suspended in an equal amount of water. The rest of water was then added in the boiling state with constant stirring till the paste was formed (Ringard and Guyot-Hermann, 1981).

2.4. Preparation of sucrose syrup

Sucrose syrup was prepared by stirring the calculated amounts of sucrose (to make 50% w/w solution) and warm water until dissolved (Peck and Baley, 1989).

2.5. Elemental analysis of dates syrup

The studied date syrup was analyzed and the results were provided with help of Soil Research Center, King Saud University using elemental analysis method utilizing inductive coupled plasma atomic emission instrument (ICP-AE) (Alanazi et al., 2003).

Table 2 Quantities of binders used in the granulation of 750 g of either calcium carbonate or sodium bicarbonate.

Formula no	Materials		Binders		
	Name	Weight (g)	Name	Concentration (%)	Quantity of binder (g)
C1	Calcium carbonate	750	Starch	10	487.50
C2			Sucrose	50	450.00
C3			DS 40%[a]	40	369.38
C4			DS 50%	50	367.50
C5			DS 60%	60	348.75
N1	Sodium bicarbonate	750	Starch	10	123.75
N2			Sucrose	50	150.00
N3			DS 40%	40	133.13
N4			DS 50%	50	125.63
N5			DS 60%	60	121.88

[a] DS = dates syrup.

The specific gravity (weight/ml) and the viscosity of the binders solutions used in this study (diluted dates syrup, diluted sucrose syrup and starch paste) were determined to characterize those binders.

The specific gravity was determined by taking the average weight of five samples (l ml each) of each of the diluted binder solutions. The viscosity of the diluted binder solutions was determined by using an AND vibro viscometer SV-10 (A&D company limited). The test was carried out in triplicate and the mean viscosity was calculated.

2.6. Preparation of granules

Granulation was conveniently carried out using a Planetary mixer (Erweka-Apparatebau, Germany) at a speed of 30 rpm. Binder solutions were gradually added to the powder till the formation of a coherent mass. The obtained mass was passed through 10 mesh sieve then dried on trays at 40° for 24 h. The obtained granules were passed through 20-mesh sieve then kept in well closed non-transparent containers till studied and used in the compression of tablets.

2.7. Evaluation of calcium carbonate, sodium bicarbonate and their produced granules

Calcium carbonate and sodium bicarbonate powders as well as the prepared granules were evaluated with regard to mean particle size, bulk density, angle of repose, granule strength and moisture content according to the methods described below.

2.8. Particle size analysis

Particle size distribution of each was determined by sieve analysis using 100 g of the test material and series of US standard sieves range in screen opening from 1000 μm to 180 μm. The test material was placed on the top sieve and mechanically shaken for 10 min on a shaker (Rota C 30, Germany). The fraction retained on each screen was weighed and the average particle size was calculated accordingly (Abdel Rahman and Alanazi, 2008a).

2.9. Bulk density

The bulk density was determined by filling the material into a graduated cylinder to the 100 ml mark. The graduated cylinder was weighed and the bulk density (VB) calculated as the ratio of the sample weight to sample volume (Alanazi, 2007a). The graduated cylinder was then tapped by Tapped density tester (Erweka, Type SVM 102) till constant volume was achieved.

The tap density (VI) was calculated as the ratio of the sample weight to the final (constant) sample volume. The changes occurring in packing arrangement during the tapping procedure are expressed as the Carr's Index (I) as shown by our previous study (Alanazi, 2007b). The test was repeated three times and the mean values were calculated.

3. Angle of repose

The angle of repose is a common way of expressing flow properties of powders and granules. It was simply measured using a glass funnel and a graph paper (Abdel Rahman and Alanazi, 2008b). The funnel, 10 cm in diameter with a stem of 5 cm long and 1 cm in diameter, was suspended on a stand, in a way to make the distance between the flat lower end of the funnel stem and surface of the graph paper equals 2.5 cm. The funnel was filled to the top with each of the test material.

The material was allowed to flow through the funnel onto the graph paper. The reading of the radius (r) at the base of the cone formed by the powder on the graph paper and the height (h, 2.5 cm) of the cone permitted the determination of the angle of repose (Ø) as follows:

$$\mathrm{Tan}\,\text{ø} = h/r.$$

The mean angle of repose was calculated after three determinations.

3.1. Granule strength

The granule strength was determined by testing the friability of a certain size fraction of the granules using the Roche friability tester (T A3R, Erweka, Apparatebau, Germany). The size fraction, of the granulation, passing through 1000 μm sieve and retained on 600 μm sieve was used in this test. The drum of the friabilator was charged with 20 g of the granulation under test and the tester was put on for 8 min at 25 r.p.m. (Saleh et al., 2001).

The worked sample was shaken through a 600-μm sieve for 2 min, with the help of the shaker, and the weight of the retained granules was assessed. The granule strength, which was considered as the opposite of friability (Abdel Rahman and Alanazi, 2008b), was calculated as percentage according to the following equation:

(1 − Final weight/Initial weight) × 100.

3.2. Moisture content

Weight loss on drying was determined using a Mettler moisture balance (Mettler PM 480 Delta Range, Switzerland). About 5 g of each granulation was put on the pan of the balance. Heating temperature was set at 100 °C and the time mode was set at 30 s which means continuous heating of the sample after removal of the free water content for 30 s. The percentage moisture content was directly read (Alanazi, 2007b). The test was carried out on each of three samples of the granules under test and the mean values were calculated.

3.3. Compression of tablets

EKO laboratory model eccentric tablet press (Korsch, Berlin, Germany) was used to press flat face tablets, 10 mm in diameter with beveled edges, weighing about 800–900 mg. The tablets contain 750 mg of either calcium carbonate or sodium bicarbonate and using Mg Stearate as lubricants (0.8–1%), Talc as glident (1.5–1.8%) and Starch as disintegrant (8–9.5%). This big size of tablets was tried having in mind the big tablets of calcium carbonate (sometimes chewable) but also smaller tablets were also studied during the course of this investigation. Ease of compression and compression problems, if any, were also noted.

3.4. Tablet evaluation

The obtained tablets were evaluated with regard to uniformity of weight, friability and disintegration time according to the USP XXII requirements. The crushing strength was determined on ten tablets of each batch using an Erweka hardness tester (Type T.B.H. 28, Erweka, Apparatebau, Germany).

3.5. Scanning electron microscopic (SEM) examination for the granules and tablets

The investigated granules and tablets' morphologies were further examined under the scanning electron microscope (Jeol, JSM-6360LV scanning microscope, Tokyo, Japan). Before microscopy, the samples were mounted at carbon tape and were sputter-coated using gold (Jeol, JFC-1100 fine coat ion sputter, Tokyo, Japan). The photomicrographs were taken at an acceleration voltage of 20 kV (Alanazi et al., 2007).

4. Tablet sensation tests

The tablet sensation tests were performed with human volunteers according to a previously described method (Miyanaga et al., 2002; Indow, 1966; Katsuragi et al., 1997). The composition of the tested tablets was shown in Table 10 and the corresponding tastes were recorded. Before testing, the volunteers ($n = 7$) were asked to keep the tested tablets in their mouths, and were not told the constituent for each tested tablets. After tasting the tablet, they were asked to give precisely their taste-sensation. All samples were chewed and kept in the mouth for 15 s. After tasting the sample, subjects gargled well and waited for at least 15 min before tasting the next sample.

5. Statistical analysis

One-way analysis of variance (ANOVA) and *t*-test were performed using Statgraphics® plus 2 software to compare the mean values. Multiple Range Test (Fisher's least significant difference procedure, LSD) was used to determine which means are significantly different from others (Alanazi, 2007b). The level of confidence was 95%.

6. Results and discussion

The analysis of a sample of the studied date syrups (by ICP-AE) gave the following concentrations of some important contents: 345.1, 6.6, 138.8 and 194 w/w (mg/100 g) for total calcium, iron, magnesium and potassium, respectively (Table 3). These figures shows that the studied date syrup is genuine and its main constituents are comparable with those of the average date syrup cited in the introduction of this paper (Al-Khateeb, 2008).

Table 4 shows the specific gravity and the viscosity of the binders' solutions tested. It indicates the similarity between the diluted date syrup, the diluted sucrose syrup and starch paste in their specific gravity. However, starch paste showed a noticeably higher viscosity than dates syrup or sucrose syrup (more than 12 times of their values). Also, the relationship between concentrations of date syrups and the viscosity

Table 3 Elemental analysis of the studied date syrup.

Constituents	Contents in mg/100 g
Ca	345.1 ± 10
Cd	–
Cu	0.34 ± 0.01
Fe	6.6 ± 0.36
Mg	138.8 ± 8
Mn	0.203 ± 0.01
P	–
Pb	0.26 ± 0.01
Zn	104.1 ± 6.8
K	194 ± 11

–, means that the value is minute.

Table 4 The specific gravity, the viscosity and pH values of the diluted solutions of the different binders used.

Binder	Specific gravity[a] (g/ml)	Viscosity[a] (CP)	pH value
Starch paste (10%)	1.096 ± 0.0005	202.3 ± 4.163	–
Sucrose syrup (50%)	1.112 ± 0.0080	16.13 ± 0.208	5.7
Dates syrup (40%)	1.03 ± 0.0014	5.517 ± 0.424	4.67
Dates syrup (50%)	1.081 ± 0.0011	9.07 ± 0.845	4.59
Dates syrup (60%)	1.112 ± 0.0066	17.7 ± 0.265	4.55

All reading results presented as mean ± S.D.
–, means is not available.
[a] The means are calculated from at least of three determinations.

generated a linear line with high correlation value ($r^2 = 0.945$). The rheological properties of the date syrups seem to be either pseudoplastic or plastic due to the high negative value of the intercept (−19) which indicates the presence of the yield value of 32.33. This is could be explained by the presence of date particles in a suspension (plastic) and/or the presence of natural date solution (pseudoplastic).

The pH values show that the date syrups are slightly acidic ranging from 4.67 to 4.5 in their pH values. This is because of the natural composition of sugars in date syrup. This was confirmed when compared with sucrose that has pH value of 5.7. pH value is an important determinate to binder evaluation which play important role in the pH-microenvironment around the dissoluted particles. As sequences may facilitate or hinder the dissolution of tablet-drugs.

Table 5 Characteristics of calcium carbonate and sodium bicarbonate powders.

Parameter	Calcium carbonate	Sodium bicarbonate
Mean particle size, μm	< 63	< 63
Angle of repose, Ø ± S.D.	53 ± 5	55 ± 4
Bulk density, VB g/cm^3 ± S.D	0.330 ± .012	0.503 ± 0.022
Tapped density, V_T g/cm^3 ± S.D	0.570 ± .030	1.001 ± 0.051
Carr's Index, I	42.1	49.7

* The means are calculated from at least of three determinations.

Table 5 shows the characteristics of calcium carbonate and those of sodium bicarbonate powders. It shows that both of the two materials suffer from small particle size, poor flowability and low bulk density; characteristics which are to be improved upon granulation.

The morphologies of sodium bicarbonate and calcium carbonate granules prepared with the help of different binders are shown in Figs. 1 and 2, respectively. The morphology of the granules and the form of the binder on the granular structure play an important role in the pharmaceutical behavior of the granules and tablets as sequence.

Sodium bicarbonate granules were appeared as small particles bond together forming a granular structure, while the calcium carbonate granules appeared as single granular structure. In case of sodium bicarbonate, granules came into view as the particles bond together composed of large particles (sodium bicarbonate) and small particles (binders). This applied to

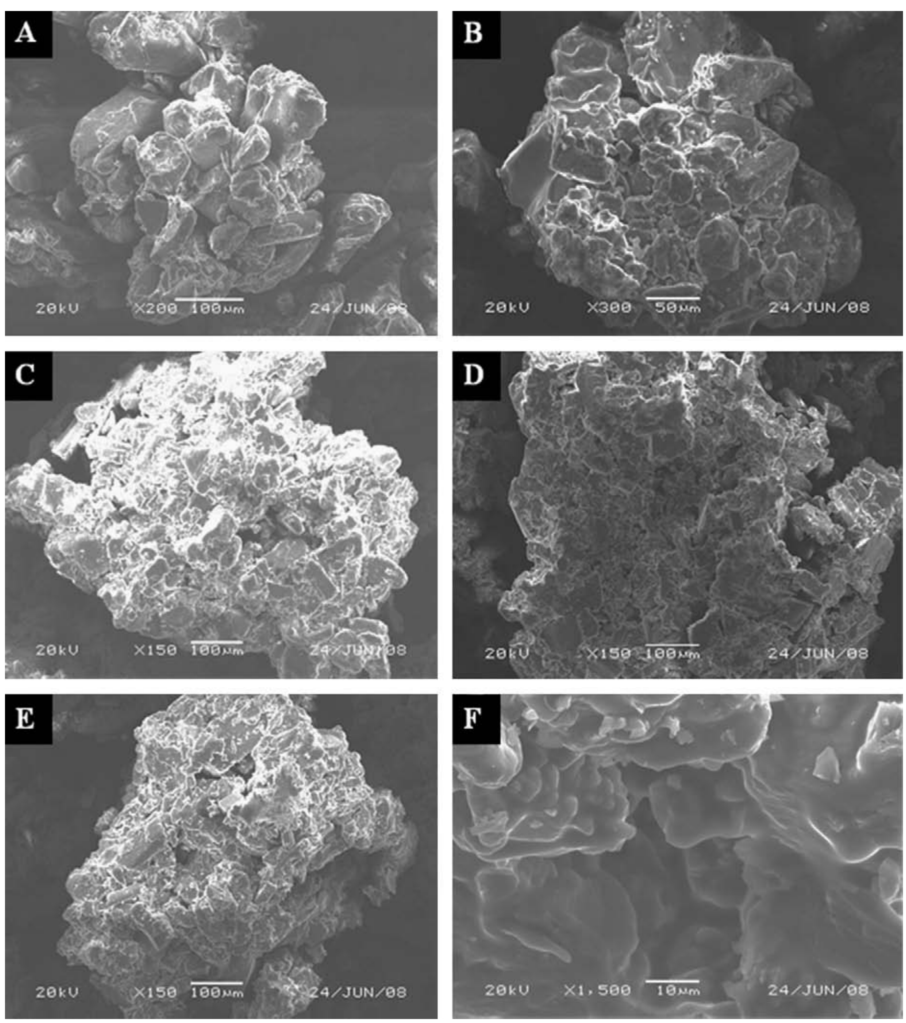

Figure 1 Photomicrographs taken by scanning electron microscope for the sodium bicarbonate granules prepared with different binders as follows: starch (A); sucrose (B); date syrup 40% (C); date syrup 50% (D); date syrup 60% (E) and (F).

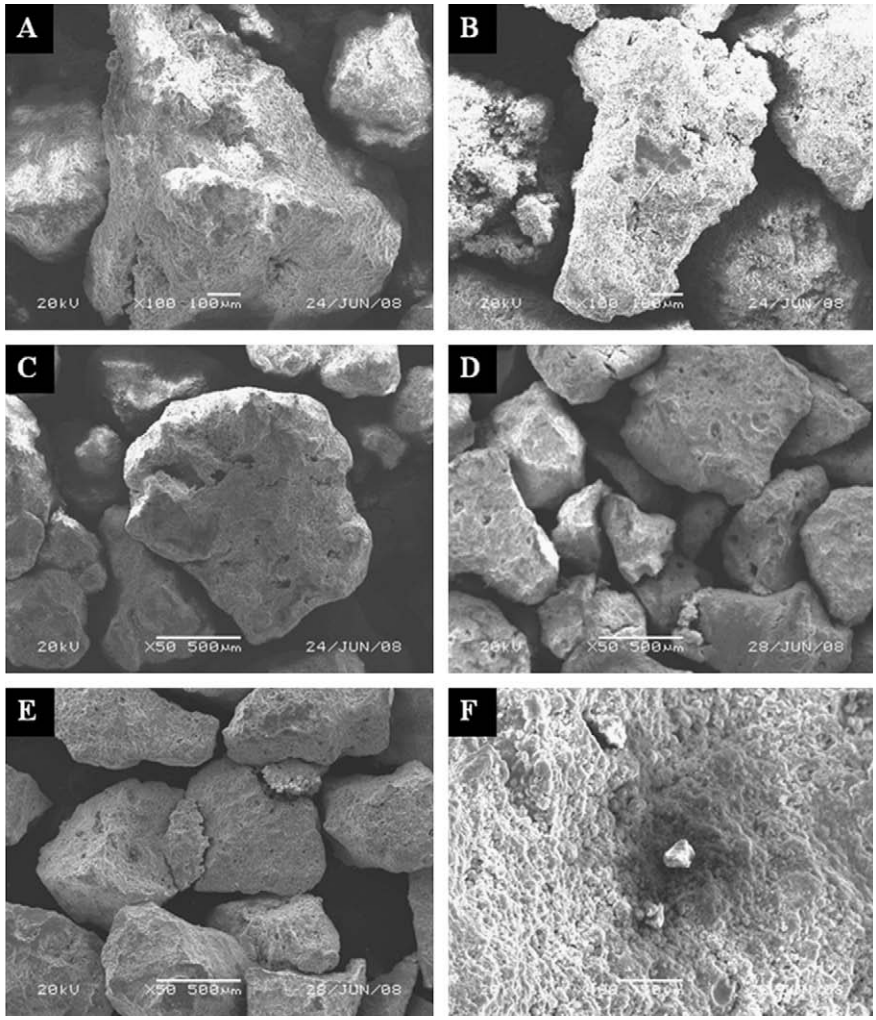

Figure 2 Photomicrographs taken by scanning electron microscope for the Calcium carbonate granules prepared with different binders as follows: starch (A); sucrose (B); date syrup 40% (C); date syrup 50% (D); date syrup 60% (E) and (F).

Table 6 Characteristics of calcium carbonate granules.

Binder	Particle size (μm)	Ø	Bulk density (g/cm^3)	Tapped density (g/cm^3)	Carr's Index	Moisture content (%)	Friability (%)
Starch paste	519.3	34.62 ± 0.33	0.709 ± 0.025	0.797 ± 0.024	11.01 ± 1.12	0.63	1.44 ± 0.24
Sucrose	549.2	34.44 ± 0.65	0.757 ± 0.030	0.826 ± 0.027	8.38 ± 1.20	0.59	1.41 ± 0.27
DS 40%	614.5	33.4 ± 0.18	0.892 ± 0.030	0.928 ± 0.016	3.92 ± 1.55	0.40	1.22 ± 0.05
DS 50%	608.4	33.8 ± 0.29	0.874 ± 0.015	0.928 ± 0.016	5.83 ± 0.10	0.74	0.66 ± 0.21
DS 60%	610.9	32.87 ± 0.78	0.958 ± 0.036	1.001 ± 0.033	4.24 ± 1.75	0.46	1.23 ± 0.47

The results of angle of repose, moisture content and bulk density are the means of three determinations.
Ø = Angle of repose (mean ± S.D.)

starch and sucrose (in the percentage used) (Fig. 1A and B). However, in the case of date syrups, the granules appeared as large particles coated with binder (date syrup) and this phenomenon became clear with the increase of the binder concentration from 40% to 60% (Fig. 1C–E). It can be observed clearly with large magnification (X1500) (Fig. 1F).

In contrast, the effect of binder types on granular morphology was minimum for calcium carbonate (no difference noticed during observation) due to their presence as single granular structure and may be due to the water-insolubility nature of the calcium carbonate (Fig. 2A–E).

Table 6 shows the characteristics of calcium carbonate granulations. Granulation led to a global improvement of the physical characteristics of the calcium carbonate powder. Date syrup granulated calcium carbonate in the study showed higher average particle size to that of both sucrose syrup and

Table 7 Characteristics of sodium bicarbonate granules.

Binder	Particle size (μm)	Ø	Bulk density (g/cm^3)	Tapped density (g/cm^3)	Carr's index	Moisture content (%)	Friability (%)
Starch paste	517.8	38.14 ± 0.32	0.699 ± 0.033	0.756 ± 0.011	7.66 ± 3.17	0.47	3.70 ± 1.6
Sucrose	526.9	34.59 ± 0.47	0.715 ± 0.034	0.784 ± 0.044	8.74 ± 1.46	0.10	2.22 ± 0.66
DS 40%	559.4	34.59 ± 0.47	0.688 ± 0.024	0.777 ± 0.031	11.46 ± 0.41	0.10	1.50 ± 0.82
DS 50%	563.4	34.93 ± 0.14	0.710 ± 0.036	0.784 ± 0.044	9.46 ± 0.48	0.20	1.25 ± 0.30
DS 60%	557.4	35.16 ± 0.63	0.652 ± 0.014	0.738 ± 0.011	11.58 ± 1.03	0.57	1.63 ± 0.22

The results of angle of repose, moisture content and bulk density are the means of three determinations.
Ø = angle of repose (mean ± S.D.)

starch paste granulation which reflects higher binding efficiency. On the other hand, calcium carbonate granules prepared using starch paste showed the least average particle size which indicates weaker binding efficiency of starch paste compared to date syrup or sucrose syrup. These results neglected the high viscosity of starch paste solution to have played a role in this respect. This finding is supported by the data obtained from date syrup. The relation between the viscosity of date syrup and the particle size yielded in no direct relationship between the viscosity of the binder and the particle size. Date syrup gave rise to granules with a relatively better flowability as shown from the angle of repose values, when compared to sucrose and starch paste granules.

Date syrup granulated with calcium carbonate showed the best granular strength among all the different studied granules based on the friability value. Strong granules are advantageous for subsequent steps in the production process, such as final mixing and transport, because powdery, friable granulate has a detrimental effect on flow properties and can cause demixing (Alanazi et al., 2007).

Moisture content of the different granulations was smaller; reading less than 1%. The bulk density, tapped density and Carr's Index show once again the inferior characteristics of starch paste granulated calcium carbonate, especially if we look at the difference between the bulk and tapped density (Table 6). The large difference in case of starch paste granulation is due to the weak granule strength leading to easy packing. Date and sucrose syrups gave similar results in this respect.

Table 7 shows the characteristics of sodium bicarbonate granules. In general, granulation improved the physical characteristics of sodium bicarbonate powder. The utilization of date syrup gave rise to the greatest average particle size reflecting higher binding efficiency. Date and sucrose binders showed almost similar angle of repose values indicating similar flowability. On the other hand, starch paste showed the highest angle of repose value indicating the poor flowability. Date syrup led to the formation of granules having the best granular strength based on the friability value. The value of friability % is suggesting that starch paste is the least in granular strength followed by the sucrose syrup. All granulated sodium bicarbonate showed smaller moisture content value; reading less than 1%.

Table 8 shows the characteristics of calcium carbonate tablets compressed from granules prepared using the different binders. All tablets complied with the USP XXII requirements for weight uniformity. Interestingly, calcium carbonate tablets compressed from date syrup granules gave acceptable friability values (less than 1%, USP XXII). Nevertheless, calcium carbonate granulated with starch paste and sucrose syrup gave the most friable tablets. Date syrup granulated calcium carbonate produced the strongest tablets as shown by their crushing strength whereas, starch paste produced tablets with the lowest crushing strength. Disintegration of the tablets depends on many factors including the compression force, nature of the binder, method of tableting, water-solubility of the filler and mechanism of tablet disintegration. So, starch paste granulated calcium carbonate tablets and that with sucrose gave the longest disintegration time (more than 10 min), whereas those with date syrup gave the shortest disintegration time (less than 5 min).

Table 9 shows the characteristics of sodium bicarbonate tablets compressed using the different granules. All tablets complied with the pharmacopeia (USP XXII) requirements for weight variation. On the other hand, all tablets failed to comply with the friability limit (USP XXII) except those based

Table 8 Characteristics of calcium carbonate tablets.

Binder	Moisture content (%)	Hardness	Friability (%)	Disintegration (min)
Starch paste	0.63	5.05 ± 0.30	f*	17.00 ± 4.33
Sucrose	0.59	7.46 ± 0.40	f*	16.00 ± 1.09
DS 40%	0.40	9.58 ± 0.20	2.68 ± 1.75	5.11 ± 1.24
DS 50%	0.74	11.12 ± 1.34[a]	0.80 ± 0.34[b]	4.42 ± 0.63
DS 60%	0.46	11.44 ± 1.7[a]	1.20 ± 0.45[b]	4.76 ± 1.22

f* = tablet is friable (few tablets were breakdown).
a and b = with the consideration of standard deviation, this increase in the hardness with increase in friability is considered statistically insignificant.

Table 9 Characteristics of sodium bicarbonate tablets.

Binder	Moisture content (%)	Hardness	Friability	Disintegration
Starch paste	0.47	3.22 ± .20	f*	0.88 ± 0.19
Sucrose	0.10	5.03 ± 0.30	f*	5.21 ± 1.68
DS 40%	0.10	8.19 ± 1.85	0.52 ± 0.1	3.79 ± 0.88
DS 50%	0.20	8.43 ± 1.72[a]	1.89 ± 0.07	2.85 ± 0.61
DS 60%	0.57	7.52 ± 3.05[a]	1.32 ± 0.49	3.08 ± 0.40

f* = tablet is friable (few tablets breakdown).
a = with the consideration of standard deviation, this increase in the hardness with increase in friability is considered statistically insignificant.

on date syrup 40% which gave the acceptable value less than <1%. Sodium bicarbonate tablets based on date syrup 50% and 60% showed also lower loss% values (1.98 ± 0.07 and 1.32 ± 0.49, respectively). It seems from the investigation of the binders with the extent of dilution, that they were unable to provide the enough cohesiveness to sodium bicarbonate granules and tablets thereof. Tablets based on starch paste granules showed the highest percentage loss. However, date syrup tablets showed the best strength as indicated by the crushing strength values. Alternatively, all tablets gave low disintegration time; starch paste granulated sodium bicarbonate tablets gave the shortest disintegration time (less than 1 min).

Table 10 Testing the prepared tablet in term of taste and flavor by human volunteers (n = 7).

Tablet	Binder	Flavor	Taste
Sodium bicarbonate	Starch (10%)	No	Salty
	Sucrose (50%)	No	Less salty
	Date syrup (50%)	Yes[a]	Slight salty
Calcium carbonate	Starch (10%)	No	No
	Sucrose (50%)	No	Sweet
	Date syrup (50%)	Yes[a]	Sweet

[a] Meaning = date flavor.

The tablet sensation tests which were performed with human volunteers (n = 7) is shown in Table 10. Naturally, sodium bicarbonate has salty taste; however, calcium bicarbonate has no taste at all. This is mainly because of water-solubility of sodium bicarbonate and water-insolubility of calcium carbonate. Sodium bicarbonate tablets prepared with starch paste granules gave a salty taste and have no flavor. Changing the binder to sucrose makes tablets less salty yet, still have no flavor. Using date syrup as a binder makes tablet slightly salty and date flavored. These results are in agreement with the results obtained by SEM for the granules. Date syrup appears as coating material for the granules which gave yellowish color for the granules and tablets (Fig. 3).

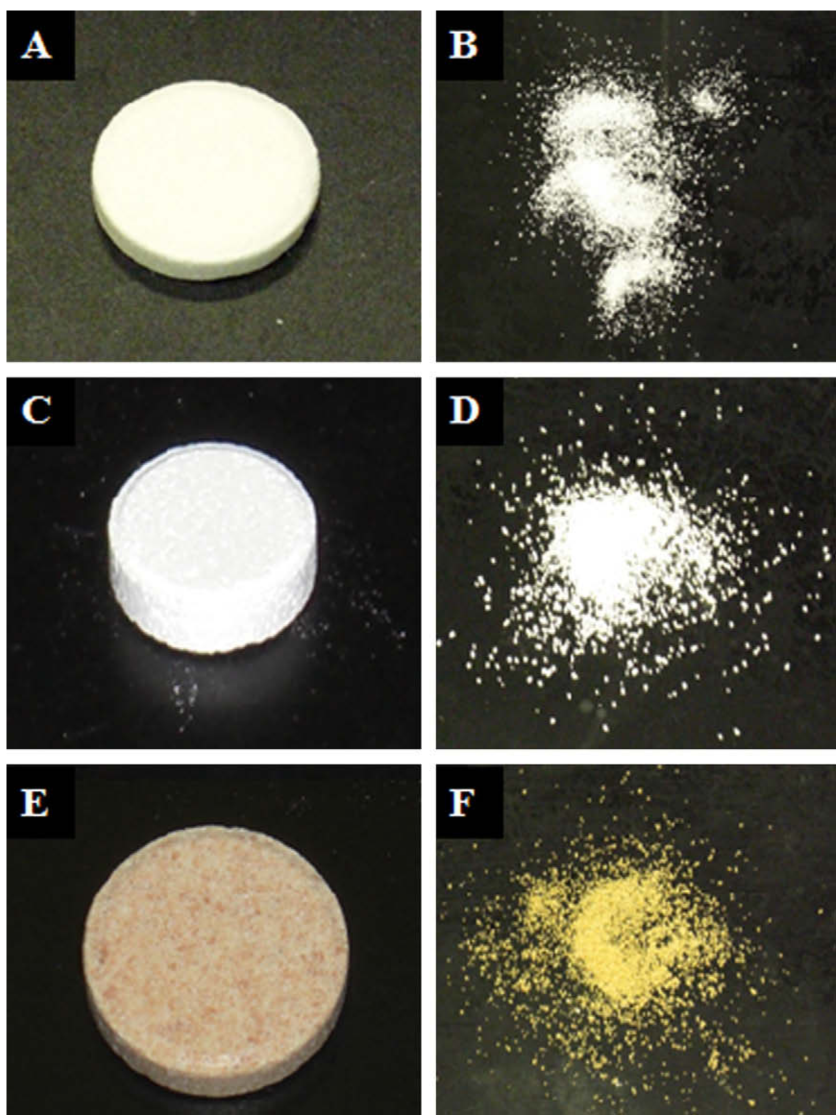

Figure 3 Photomicrographs for the sodium bicarbonate tablets and granules prepared with different binders as follows: starch (A; tablet); starch (B; granules); sucrose (C; tablet); sucrose (D; granules); date syrup 50% (E; tablet); date syrup 50% (F; granules).

In case of calcium carbonate tablets, sucrose and date syrup make the tablets sweetener than those of starch paste. In addition to that, tablets prepared from date syrup as a binder gives the tablets date flavor. These findings strongly support the advantages of date syrup in masking the taste and in giving acceptable flavor.

Generally speaking, the tested date syrup succeeded as a tablet binder for water-soluble (e.g. sodium bicarbonate) or water-insoluble (e.g. calcium carbonate) materials. In the same time, date syrup of different sources may give a similar result; because the main constituents of date syrup, the reducing or the inverted sugars, which represent about 79.45%, by weight, do not change remarkably by changing the source. In a simple trial conducted in the present study, it is worthy to mention that date syrup from different sources also gave almost similar results. Nevertheless, a further investigation of the effect of date syrup source and composition on its outcomes seems interesting.

Within the scope of this work, we can conclude that date syrup may represent a promising binder or granulating agent for both water-soluble and water-insoluble materials. It is advisable to use date syrup diluted with water in a 40:60 to 60:40 (v/v) ratio to get better granules and tablets thereof. Within the present study date syrup is found to be highly efficient binder, compared to starch paste or sucrose syrup, the well-known binders, it has other merits. Its nutritional value, sweetening power and preference to sucrose in case of diabetes and avoidance of dental caries make it a valuable candidate as a binder not only for conventional tablets but also for chewable ones. In the same time, the preliminary findings require more investigations on the details of the behavior of date syrup during densification with respect to deformation, breaking and packing of the granules. Three month storage at room temperature (25 °C) gave almost no significant change based on the current study.

Acknowledgements

The author would like to thank Dr. Diaa Zidan for his technical help. This work is fully supported by Kayyali Chair for Pharmaceutical Industry, Department of Pharmaceutics, College of Pharmacy, King Saud University.

References

Abdel Rahman, A.A., Alanazi, F., 2008a. Particle size analysis of powders and granules (Chapter 9). In: Bases of Industrial Pharmacy. Al-kayalli Chair for Pharmaceutical Technology (Publisher), p. 127.

Abdel Rahman A.A., Alanazi F., 2008b. Tablets and tableting (Chapter 13). In: Bases of Industrial Pharmacy. Al-kayalli Chair for Pharmaceutical Technology (publisher), p. 177.

Alanazi, F.K., 2007a. Evaluation of certain amino acids as tablet excipients: accelerated disintegration effects in tablets containing propranolol. Alex. J. Pharm. Sci. 21, 135–146.

Alanazi, F.K., 2007b. Evaluation of spray and freeze dried excipient bases containing disintegration accelerators for the formulation of metoclopramide orally disintegrating tablets. Saudi Pharm. J. 15, 105–119.

Alanazi, F., 2003. Density gradient separation of carborane-containing liposome from LDL and detection by inductively coupled plasma spectrometry. Thesis: Application of Lipoprotein as Drug Delivery System for Anticancer Drug and DNA-based Vaccine. The University of Georgia, USA.

Alanazi F.K., El-Badry M., Ahmed M.O., Alsarra I.A., 2007. Improvement of albendazole dissolution by preparing microparticles using spray-drying technique. Scientia Pharmaceutica (Sci. Pharm.) 75, 63–79.

Algazail, Zohair, 2008. Twelve Million Riyals the Cost of the Depis this Year in Al-Hussa Provenance, Al-Jazirah News Paper, Thursday, 02/10/2008 G, Issue 13153.

Al-Hooti, S.N., Sidhu, J.S., Al-Saqer, J.M., Amani, A., 2002. Chemical composition and quality of date syrup as affected by pectinase/cellulose enzyme treatment. Food Chem. 79, 215–220.

Al-Khateeb, A.A., 2008. Enhancing the growth of date palm (Phoenix Dactylifera) in vitro tissue by adding date syrup to the culture medium. Sci. J. King Faisal University (Basic Appl. Sci.) 19, 71–85.

Bandelin, F., 1989. In: Pharmaceutical Dosage Forms: Tablets. vol. 1, 2nd ed. Marcel Dekker, Inc., New York, p. 148.

Bandelin, F., 1989. In: Pharmaceutical Dosage Forms: Tablets, vol. 1, 2nd ed. Marcel Dekker, Inc., New York, p. 160.

Indow, T., 1966. A general equi-distance scale of the four qualities of taste. Jpn. Psychol. Res. 8, 136–150.

Katsuragi, Y., Mitsui, Y., Umeda, T., Sugiura, Y., Otsuji, K., Kurihara, K., 1997. Basic studies for the practical use of bitterness inhibitors: selective inhibition of bitterness by phospholipids. Pharm. Res. 14, 720–724.

Miyamoto, Y., Ogawa, S., Miyajima, M., Sato, H., Takayama, K., Nagai, T., 1995. An evaluation of process variables in wet granulation. Drug Dev. Ind. Pharm. 21 (19), 2213–2225.

Miyanaga, Y., Tanigake, A., Nakamura, T., Kobayashi, Y., Ikezaki, H., Taniguchi, A., Matsuyama, K., Uchida, T., 2002. Prediction of the bitterness of single, binary- and multiple-component amino acid solutions using a taste sensor. Int. J. Pharm. 248(1–2), 207–218.

Peck, Garnet E., Baley, George J., McCurdy, Vincent E., Banker, Gilbert S., 1989. Tablet formulation and design. In: Lieberman, Herbert A., Lachman, Leon, Schwartz, Joseph B. (Eds.), Pharmaceutical Dosage Forms: Tablets, 2nd ed. Marcel Dekker, Inc., New York, p. 106.

Phadke, D.S., Anderson, N.R., 1990. Effect of crosspovidone on the wet granulation aspects of acetaminophen. Drug Dev. Ind. Pharm. 16, 983–994.

Reading, S.J., Spring, M.S., 1984. The effect of binder film characteristics on granule and tablet properties. J. Pharm. Pharmacol. 36, 421–426.

Ringard, J., Guyot-Hermann, A.M., 1981. Disintegration mechanisms of tablets containing starches: hypothesis about the particle–particle repulsive forces. Drug Dev. Ind. Pharm. 7, 155–177.

Rue, P.J., Seager, H., Ryder, J., Burt, I., 1980. The relationship between granule structure, process of manufacture and tableting properties of a granulated product II. Compression properties of the granules. Int. J. Pharm. Tech. Prod. Mfg. 1, 2–6.

Saleh, S.I., El-Helw, A., Al-Angary, A., Mahrous, G.M., 2001. Utilization of honey as a tablet binder: a preliminary study. Saudi Pharm. J. 9 (1), 26–33.