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FLOWABILITY PROPERTIES OF BINARY POWDER MIXTURES CONTAINING DATES POWDER (PHEONIX DACTYLIFERA) MIXED WITH LACTOSE MONOHYDRATE AND MICROCRYSTALLINE CELLULOSE BASED EXCIPIENTS

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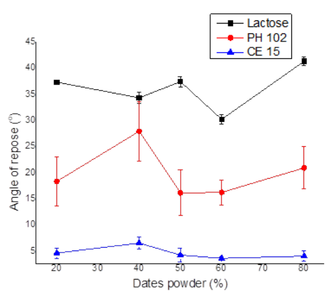
Graphical abstract



Abstract

Powder flow is important in powder processing industries to obtain a quality by design product and efficient manufacturing process. Poor powder flowability can cause problems especially during high speed tableting and capsule filling processes. In this study, dates powder (DP), lactose monohydrate powder, and two types of microcrystalline-based powder excipients evaluated for their flow properties as a binary mixture. Angle of repose (AoR), Hausner ratio (*HR*) and Carr index (*CI*) were used to characterize the extent of the powder cohesion. The results show that generally, as particle size increases, values of AoR *generally* decreases, depicting lower flowability characteristics with decreasing binary mixture particle size. However, *HR* and *CI* flowability indicators give contrasting flowability characteristics for the binary mixture containing lactose monohydrate and dates powder.

Keywords: Pheonix dactylifera dates powder, flowability, FLOWLAC 100, AVICEL PH102, AVICEL CE-15.

1.0 INTRODUCTION

Dates or *Phoenix dactylifera* is a common diet source for millions of people not only in the Middle East but to the others around the world [1]. Many research studies have been done on this plant, the most common are physiochemical and biological characterizations such as medicinal properties, chemical composition, physical properties and antioxidant activity. Of lately, there are a number of studies has been conducted on the compression of dates powder which intends to maximise the usage of the date fruits [2-5].

Tablets are the favoured dosage form because of their numerous advantages. For example, it has good patient acceptance, easy administration to patient and low price. To date, direct compression is still the easiest technology of tablet production, but some of the complexities must be addressed to achieve a successful tableting process [6]. Other than mixing, one of the most crucial parameters is powder flowability. Proper understanding of the flow behaviour of powders can change resulting in stoppages, poor quality and rejected products [7,8].

The ability of powder to flow at an optimum condition is critical in the manufacturing process of solid single dose preparations. Besides giving effect on the mixing, storage and transportation during production, coating, capsule filling and tablet die filling are commonly affected by powder flow behaviour [9-11]. Factors such as primary properties of powder (particle size, shape, bulk density and solubility), characteristics needed in powder compaction (compressibility and flowability), product stability (water), cost, availability and pharmacopoeial acceptability, giving high influence in making the right choice for selecting types of compressible adjuvant to be used in formulation of tablet [12,13].

High moisture content in fruit powder will affect the flowability of the powder. In order to improve this condition, adding excipients from various nature with higher particle size will improve in the cohesiveness of the powder. This will result in better handling and allow the powder processing to be easier [8,42,43].

There is abundance of methods that can be used to measure powder flowability. However, there is no single test that can be employed as a standard to measure powder flowability [14,8]. The compendial methods such as angle of repose [15], bulk and tapped density [16], Carr index [17], and Hausner ratio [18] are the most commonly used to measure powder flowability. While cohesive determination [19], avalanching determination [20], shear cell [21], dielectric imaging [22], atomic force microscopy [23], and penetrometry [24] are the advanced and innovative methods developed which can also be used to characterize powder flow. The drawbacks of using the advanced methods are on the reproducibility of the data, predictability and performance conditions since it is subjected to the nature of the powders and the environmental conditions where the measurements are being carried out [14,8]. To have better understanding on the powder properties, these methods can be used on a powder to obtain thorough description of flowability characteristics.

Therefore, the objective of this work was to compare the properties of binary mixture for three commercially produced excipients which are lactose monohydrate (Flowlac 100), Avicel® PH102 and Avicel® CE-15 with different percentage of dates powder. There are very limited number of study and publications done on the usage of dates powder along with commercialized excipients. Therefore, the physical and flowability properties for the binary mixtures were evaluated in terms of their angle of repose, density (bulk, tapped and absolute), Hausner ratio, Carr index, particle size measurement and moisture content.

2.0 METHODOLOGY

2.1 Materials and Methods

P. dactylifera (DP) powder supplied by A & T Ingredients, lactose monohydrate (Flowlac 100, Megggle, Germany), Avicel® PH102 (PH) and Avicel® CE-15 (CE) from DuPont, USA.

2.2 Sample Preparation

Five different compositions of the binary mixtures consisting of dates powder and the excipient were prepared for each of the commercial excipients used. The formulations are as stated in Table 1.

Table 1 Binary powder mixture composition

Sample	Dates Powder(w/w%)	Excipients (w/w%)
DP-Lac1	20	80
DP-Lac2	40	60
DP-Lac3	50	50
DP-Lac4	60	40
DP-Lac5	80	20
DP-PH1	20	80
DP-PH2	40	60
DP-PH3	50	50
DP-PH4	60	40
DP-PH5	80	20
DP-CE1	20	80
DP-CE2	40	60
DP-CE3	50	50
DP-CE4	60	40
DP-CE5	80	20

2.3 Powder Mixing

30 g of prepared powder were mixed using Glas-Col blender (Terre Haute, USA) at 80 rpm for 15 minutes to produced homogeneous mixture. The mixtures each were stored in desiccator to avoid from getting into contact with moisture.

2.4 Physical Properties Of Materials

2.4.1 Bulk, Tapped And Absolute Density

2.5 g of the powder samples was poured into a 10 mL graduated measuring glass cylinder. The bulk density was then simply evaluated through the measurement of the volume by calculating the ratio of the mass of powder to the volume occupied by the powder [25]. Tapped density was done by using by using Envelop and Tap Density Analyser (Micromeritics Geopycs 1360, USA). A gas pycnometer (AccuPyc II 1340, Micromeritics, Norcross, USA) was used to measure the absolute density of the powder samples.

2.4.2 Angle of Repose

The measurements of the powder samples angle of repose values, *α*, were evaluated according to US Pharmacopeia.

2.4.3 Moisture Content

The moisture content was determined by using oven drying method [26]. The powders in the amount of 5.0 g±0.01 g respectively, were placed into three separate sample plates and dried in an oven (Memmert, Germany) at 105ºC for 24h until a constant weight was achieved. The percentage of moisture content was calculated by:

$$M = \frac{W_{initial} - W_{final}}{W_{initial}} \times 100$$

(1)

where M is the percentage of moisture content of the sample in wet basis, $W_{initial}$ is the weight of sample before drying, and W_{final} is the weight of sample after drying.

2.4.4 Particle Size and Size Distribution

500 mg sample powder was inserted in a particle size analyser (Malvern Mastersizer 2000 Instrument Ltd, UK) via the dry dispersion method operating at 1.0 bar dispersion pressure. Therefore, the particle size and the size distribution of the powder samples were measured using the laser light diffraction technique. d_{10}, d_{50}, and d_{90} values from the instrument software were extracted to represent the particle sizes of the sample. The span value, as the measure of the particle size distribution was calculated as follows:

$$Span = \frac{D_{90} - D_{10}}{D_{50}} \tag{2}$$

2.4.5 Carr Index and Hausner ratio

The Carr index (*CI*) and the Hausner ratio (*HR*) were used to investigate the flow property of the samples [25]. *CI* and *HR* were calculated from the bulk density and tapped density as follows:

$$CI = \frac{\text{Tapped density - Bulk density}}{\text{Tapped density}} \times 100 \quad (3)$$

$$HR = \frac{\text{Tapped density}}{\text{Bulk density}} \quad (4)$$

3.0 RESULTS AND DISCUSSION

There are several important powder physical characteristics that influence powder flow behaviour such as moisture content and particle size. Flowability is the result of the influences of these material physical properties that influence the material to flow apart from the equipment utilized for processing, handling, storage and environmental conditions [27,28].

Table 2 gives the density value, moisture content and AoR reading for all the pure powder and formulations tested. The density data (bulk, tapped and absolute) obtained for Flowlac 100, Avicel® PH 102 and Avicel® CE15 are comparable with data obtained by Li et al (Flowlac 100 and Avicel® PH 102) [29] and Vodackova et al (Avicel® CE15) [6]. The same goes with AoR, particle size (D_{50}) and moisture content for Avicel® PH 102 and Avicel® CE15. However, particle size (D_{50}) and moisture content reading for Flowlac 100 is slightly lower compared to data obtained by Li et al [29]. While AoR reading obtained is higher than stated by Li but still comparable with the one obtained by van der Walt [30]. The differences occur might be due to different sample size used during the analysis for the particle size and different type of method was used for the moisture content analysis where in this study, the moisture content was measured using oven drying method. The bulk and tapped density for DP-PH and DP-CE increase with the increasing of DP percentage. However, reading given by DP-Lac showed higher density at the lowest percentage of DP, decrease at 40% and then increasing towards the percent addition. Meanwhile, the absolute density gave the same trend for all formulations where the value decreases along with higher portion of DP.

Moisture content of the formulations falls between 1.97 to 3.38% as shown in Table 1 and Figure 1. Combination of DP-Lac gave the lowest moisture when compared to DP-PH and DP-CE. Both Avicel® PH 102 and Avicel® CE15 are microcrystalline cellulose base excipients, and they have good hygroscopicity [44,45]. This explains higher reading of moisture content in the binary mixtures. Higher moisture is favourable in forming a strong bond between particles during compaction as it will increase the ability of binding between particles [31,32].

AoR data (Figure 1 and Figure 3) illustrates the decreasing trend of the particle size with the increase in the percentage of DP. Both DP-PH and DP-CE giving a very small value of AoR that categorize them under excellent flow, while AoR for DP-Lac fluctuates parallel with the size of particle in each formulation. The decrease in the powder flowability represented by relatively high values of AoR indicates the presence of high inter-particulate forces [33-35]. When a particle has a relatively smaller size, it will possess a relatively higher specific surface area and hence a relatively higher degree of inter-particulate contact areas thus creating larger inter-particle adhesion forces that may attract the particles to cohere with each other, preventing from flowing easily. Due to this, steeper slope will be formed and giving a large AoR [36-39]. DP-Lac binary mixtures possessing relatively smaller particle sizes (Figure 1 and Figure 5) display large AoR values (Table 1 and Figure 3) indicating cohesiveness and comparatively poor flow properties compared to DP-PH and DP-CE binary powder mixtures.

HR and *CI* values are two commonly used qualitative parameters in evaluation powder flowability. It is relatively simple to evaluate based upon the physical properties of powder that is the bulk and tapped density values. Theoretically, the flow of a powder sample decreases leading to bad flowability characteristics when the powder particle size decreases. This is reflected in the increase in both *HR* and *CI* values [34, 39, 40]. Powders with smaller particle size gave higher voidage during loose packing state and lower aerated bulk density compared to the powders with larger particle size [39]. The powders when subjected to tapping, will cause disruption in the inter-particle forces since the smaller particles tend to collapse, compacted and giving a large tapped density. As for the powders that consist of larger particle size, the ability to consolidate is lower, thus, lower tapped density produced (Table 2) [41]. However, inconsistencies in the flowability trends for *HR*, *CI* and AoR are reported for DP-Lac, where a poor flowability indicated by the angle of repose is not in line with the excellent and good flowability characteristics indicated by the *HR* and *CI* values (Table 3, Figure 4 and Figure 5). This might be due to that the *HR* and *CI* values are based upon the changes in the particle packing under tapping therefore, relatively lower changes observed are due to the cohesiveness of the powder samples itself preventing the consolidation of the powder during the tapping action [11]. The cohesiveness reflected by the relatively high values of the angle of repose can be caused by several factors including particle shape that was not investigated in this work.

Table 2 Densities, moisture content and angle of repose values

Sample	DB (kg/m³)	DT (kg/m³)	DA (kg/m³)	M (%)	αr (°)
DP	657.0 ± 8.4	712.3 ± 3.8	1278.5 ± 1.3	2.65 ± 0.03	27.72 ± 0.6
LACTOSE	636.2 ± 14.1	722.9 ± 2.4	1574.1 ± 2.9	0.69 ± 0.04	31.6 ± 0.6
DP-Lac1	634.5 ± 15.7	719.0 ± 10.4	1468.9 ± 0.8	1.97 ± 0.05	37.3 ± 0.2
DP-Lac2	629.5 ± 7.8	739.2 ± 21.4	1425.6 ± 0.8	2.51 ± 0.03	34.3 ± 1.1
DP-Lac3	634.3 ± 3.5	645.7 ± 9.3	1344.8 ± 0.4	2.79 ± 0.18	37.4 ± 1.0
DP-Lac4	662.0 ± 8.4	678.2 ± 2.6	1378.7 ± 1.1	2.45 ± 0.09	30.2 ± 0.9
DP-Lac5	662.2 ±17.1	696.5 ± 1.5	1299.2 ± 1.2	2.91 ± 0.09	41.3 ± 0.8
PH102	364.3 ± 5.5	452.2 ± 1.7	1565.0 ± 1.5	5.82 ± 0.02	31.0 ± 6.0
DP-PH1	383.5 ± 7.3	469.4 ± 2.8	1510.4 ± 1.0	3.34 ± 0.06	18.3 ± 4.7
DP-PH2	506.6 ± 9.5	559.0 ± 1.8	1461.9 ± 0.7	3.18 ± 0.02	27.9 ± 5.7
DP-PH3	553.3 ± 5.1	575.1 ± 2.1	1437.6 ± 1.1	3.22 ± 0.19	16.1 ± 4.6
DP-PH4	573.9 ± 6.0	602.7 ± 1.9	1400.8 ± 0.9	3.12 ± 0.02	16.2 ± 2.4

DP-PH5	626.5 ± 1.3	657.3 ± 3.1	1350.6 ± 0.7	3.26 ± 0.02	20.9 ± 4.0
CE15	551.2 ± 10.9	687.4 ± 2.8	1465.4 ± 1.2	4.66 ± 0.13	21.8 ± 2.1
DP-CE1	512.2 ± 10.3	667.3 ± 3.7	1436.3 ± 1.0	3.36 ± 0.04	4.6 ± 1.0
DP-CE2	609.7 ± 7.2	720.2 ± 1.7	1399.4 ± 0.3	3.22 ± 0.05	6.5 ± 1.3
DP-CE3	618.1 ± 14.3	722.9 ± 1.6	1385.9 ± 0.6	3.16 ± 0.04	4.2 ± 1.3
DP-CE4	630.0 ± 7.7	725.9 ± 2.6	1369.1 ± 0.7	3.23 ± 0.06	3.6 ± 0.3
DP-CE5	649.0 ± 7.3	724.4 ± 1.5	1334.0 ± 0.8	3.38 ± 0.11	4.0 ± 1.0

DB: Bulk density, DT: Tapped density, DA: Absolute density, M: Moisture content, α_r: Angle of repose.

Table 3 Hausner ratio and Carr index values

Sample	*HR*	*CI*	Flow behaviour
DP	1.08	7.76	Excellent
LACTOSE	1.14	11.99	Good
DP-Lac1	1.13	11.76	Good
DP-Lac2	1.17	14.84	Good
DP-Lac3	1.02	1.76	Excellent
DP-Lac4	1.02	2.39	Excellent
DP-Lac5	1.05	4.92	Excellent
PH102	1.24	19.44	Fair
DP-PH1	1.22	18.30	Fair
DP-PH2	1.10	9.38	Excellent
DP-PH3	1.04	3.78	Excellent
DP-PH4	1.05	4.77	Excellent
DP-PH5	1.05	4.69	Excellent
CE15	1.25	19.82	Fair
DP-CE1	1.30	23.24	Passable
DP-CE2	1.18	15.35	Good
DP-CE3	1.17	14.49	Good
DP-CE4	1.15	13.22	Good
DP-CE5	1.12	10.40	Good

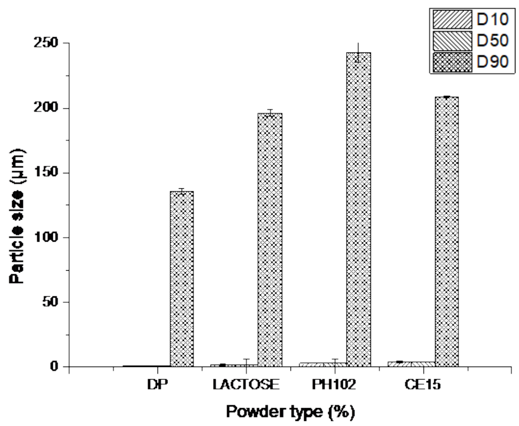


Figure 1 (a) Particle size for dates powder and excipients used

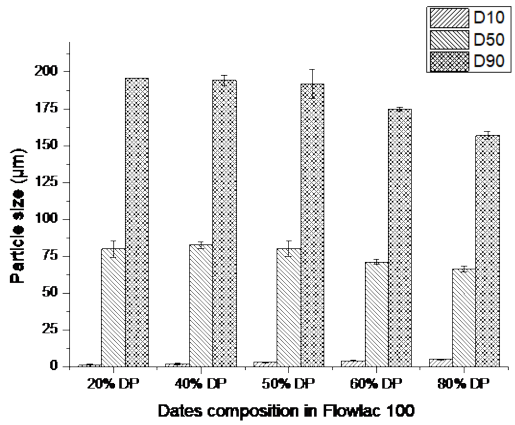


Figure 1 (a) Particle size for binary mixture of DP and Flowlac 100

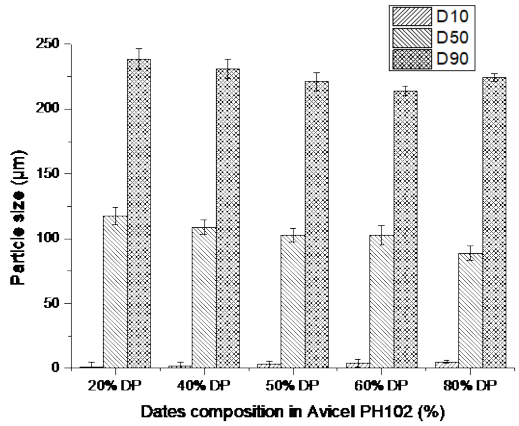


Figure 1 (c) Particles size for binary mixtures of DP and Avicel PH102

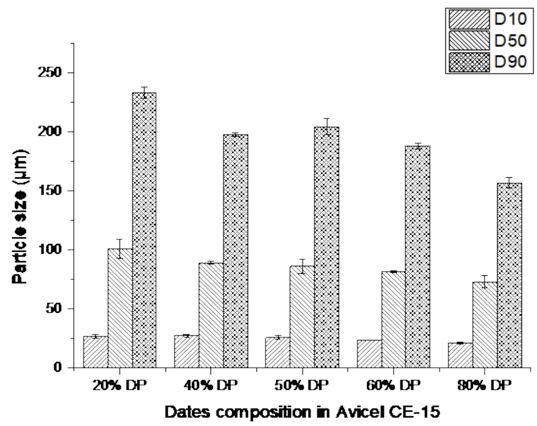


Figure 1 (d) Particles size for binary mixtures DP and Avicel CE15

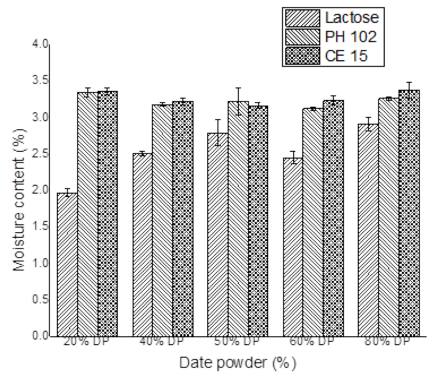


Figure 2 Moisture content variation with increasing dates powder composition

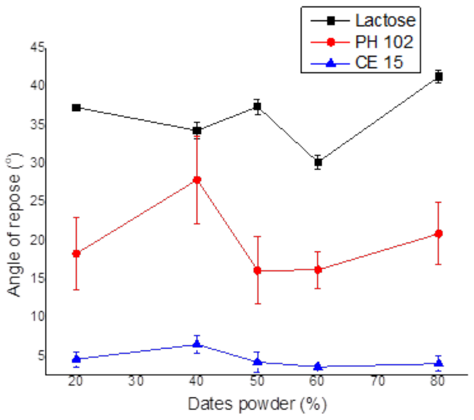


Figure 3 Variation of the angle of repose values with increasing dates powder composition

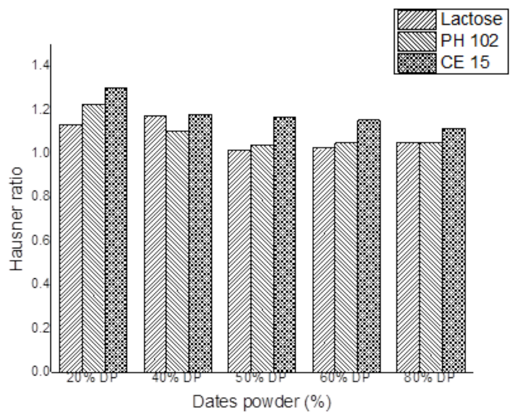


Figure 4 Variation of the Hausner ratio values with increasing dates composition

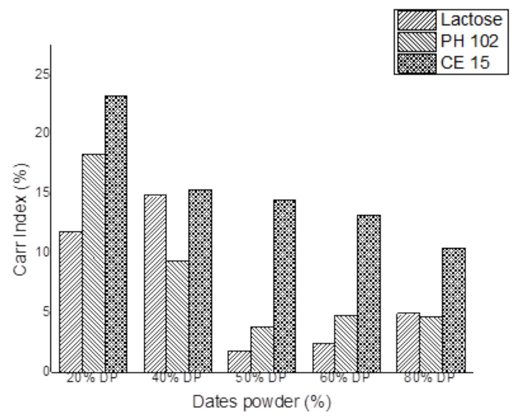


Figure 5 Variation of the Carr index values with increasing dates powder composition

4.0 CONCLUSION

Powder flowability study is useful because it measures the strength of the powder that must be overcome to cause the powder particles to move over each other and flow. Pure dates powder and three other commercial excipients were characterised in this study using a number of physical properties analysis to help define the powder properties and provide further understanding on their flow behaviour. From the findings, it was generally observed that the binary mixture particle size influences the flowability based upon the measured AoR values, where the AoR value decreases with the increase in particle size. However, the use of the *HR* and *CI* values show discrepancies, where the dates powder mixed with lactose monohydrate displays relatively good and excellent flowability characteristics, in contrast with their measured AoR, angle of repose values.

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