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Research Paper

Insights into the Role of Electrostatic Forces on the Behavior of Dry Pharmaceutical Particulate Systems

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Purpose. Under different charging conditions, particles can be either attracted or repulsed by each other, causing powder agglomeration or segregation. Such behavior can be detrimental in many processes aimed at achieving particulate mixture homogeneity. Consequently, the effects of electrostatic charges on mixing kinetics must be well understood to insure a high level of process control, product quality, and reproducibility.

Methods. In Part 1, an electrostatic charger is used to evaluate the ability of the studied particles to develop and retain an induced charge at the surface for a fixed period of time. Part 2 assesses the natural electrostatic charge developed by powders sliding across a stainless steel, plastic, or Tyvek chute. In Part 3, 2 binary systems were formed according to an experimental design under different charging conditions, and their behavior was quantified by measuring the degree of agglomeration attained.

Results. This work has shown that each raw material develops a different charge according to its physico-chemical properties and the type of contact surface. Electrostatic charges influence the creation of agglomerates under certain conditions.

Conclusions. The presence of electrostatic charges must be accounted for in any effort to maximize mixing efficiency.

KEY WORDS: electrostatic forces; flow; lubricant; mixing; powders.

INTRODUCTION

Mixing dry pharmaceutical solids is a crucial step in the production of solid dosage forms. Two major problems are often encountered in powder-mixing operations, i.e., segregation and agglomeration, leading to content homogeneity problems (1). The extent of these phenomena depends on the physicochemical characteristics of the raw materials that are distinguished by particle size, shape, surface nature, humidity, and conductivity. Such phenomena are driven by interactions between the raw materials involved and are mainly caused by capillary, electrostatic, van der Waals, and gravitational forces. The present work focuses mainly on the effects of electrostatic forces.

Theoretical Considerations

Electrostatic charging of particles occurs via one of the following mechanisms: polarization of particles in an electric field or when two moving particles collide or via the collision of particles with a surface. Particles thus acquire a charge that can be retained when the surfaces separate, leaving both components with opposite charges (2,3). The attraction existing between two oppositely charged particles will be greater when the difference in magnitude is high (4). Therefore, this attraction initiates agglomeration. Electrostatic charging has been identified by Muzzio and Alexander (5) as a mechanism that can create agglomerates in blending operations.

During various powder-handling steps such as mixing, particles can slide, roll, and collide with each other or with container walls. These actions evoke electrostatic charge development at the level of the particle surfaces. Yurteri *et al.* (6) used an electrical single particle aerodynamic relaxation time analyzer to measure electrostatic forces and to show that the behavior (i.e., transport and deposition) of bipolar charged powders having high charge-to-mass ratio values was affected. Staniforth and Rees (4) tested a Faraday well connected to an electrometer to quantify powder electrostatic forces. They reported that most of the powders studied after contact with a glass surface were charged electronegatively, whereas after contact with a polyethylene surface, the same powders were charged electropositively. The polarity and magnitude of the charges developed depend on various parameters, including material properties and process conditions (e.g., ambient humidity and handling protocols).

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Table I. Raw Materials Studied

Compound	Manufacturer	Particle size
Zinc oxide USP/EP (ZnO)	Zochem, Brampton, ON, Canada	Mean particle size 0.2 μm (99.995% through 325 mesh)
Cupric oxide reagent grade (CuO)	J.T. Baker, Division of Mallinckrodt Baker, Inc., Phillipsburg, NJ, USA	Mean particle diameter 9.8 μm
Calcium carbonate precipitated USP (CCP)	Bihoku Funka Kogyo Co., Ltd., Niimi, Okayama, Japan	Mean particle size: 2.6 μm
Manganese sulfate monohydrate USP/FP (MnSM)	Merck KgaA, Frankfurter, Darmstadt, Germany	90% through 100 μm, 50% through 10 μm
Xylitab®100	Danisco Sweeteners Ltd., Thomson, IL, USA	Mean particle size 200 μm
Dibasic calcium phosphate USP/EP dihydrate unmilled (DCP)	Innophos, Inc., Cranbury, NJ, USA	0% on 20 mesh, 78.97% on 100 mesh, 2.27% through 325 mesh
Magnesium stearate NFDP/EP (MgSt)	Crompton Corporation, Memphis, TN, USA	99.99% through 325 mesh

To understand particle behavior during these handling stages, it is necessary to acquire information on electrostatic charges as well as the kinetics of their dissipation. Charge accumulation and dissipation at particle surfaces over time depend on the permittivity and surface resistivity of particles (2). Therefore, conductive materials will be discharged almost instantaneously, whereas insulating materials will retain the charge at its initial magnitude for many minutes or even hours, depending on whether these materials are totally insulated or grounded (7).

In this work, we focus on measuring the ability of some particles used in pharmaceutical formulations to develop and retain an induced charge at their surface for a fixed period of time (Parts 1 and 2) and on statistically evaluating the effect of electrostatic forces on the formation of agglomerates (Part 3).

MATERIALS AND METHODS

Materials

The raw materials enumerated in Table I were chosen because they are currently the components of multivitamin and multimineral formulations.

Xylitab® 100 (a sweetening agent in chewable tablets) and dibasic calcium phosphate USP/EP dihydrate unmilled (DCP, a salt in solid dosage form tablets) were the excipients chosen for the study. Magnesium stearate NFDP/EP (MgSt) was specifically selected because it is the most widely used lubricant in pharmaceutical tablets.

Methods

Prior to each experiment, all materials were stabilized at constant ambient humidity [14–16% relative humidity (RH)] and were neutralized with a DC static elimination ring (Tantec Inc., Schaumburg, IL, USA). All experiments were conducted in a laboratory at constant ambient humidity (14–16% RH).

Charging Protocol for Part 1

The goal of Part 1 was to evaluate the ability of the studied particles to develop and retain an induced charge at the surface for a fixed period of time. Particles from seven different raw materials were passed through a 12-mesh screen and subjected, by a Chargemaster BP-50 bipolar DC unit and a pinner arc-resistant bar (Simco Inc., Hatfield, PA, USA), to an electrostatic charge at different levels. Under impulsion of the electrical field created by high DC voltage, positive and negative ions moved in opposite directions. If the Pinner bar electrodes were positive, then positive ions were repulsed from them and negative ions were attracted by them. Therefore, ions were neutralized at the surface of the bar; however, the overall process charged the powder positively. The bar was placed at a distance of 0.10 m from the powder flow, and the applied voltage was either positive (+30 kV) or negative (−30 kV). The charges were based on the suggested operational limits of the Chargemaster unit. The flow of such treated particles went onto either an insulated or a grounded stainless steel pan (Fig. 1). Electrostatic charges, developing at the surface of the studied particles, were measured as a function of time, with a handheld electrostatic field meter (Tantec Inc.) for 10 min.

Charging Protocol for Part 2

The goal of Part 2 was to evaluate the natural electrostatic charge developed by powders when sliding on different material surfaces. To simulate the development of electrostatic charges during manufacturing process steps, the raw material particles were passed through a 12-mesh screen

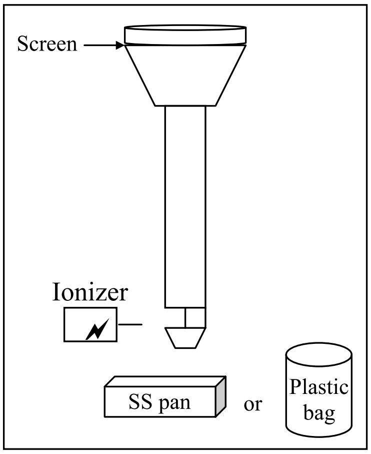


Fig. 1. Electrostatic charging setup (Parts 1 and 3).

and placed in a 1-m-long plastic, stainless steel, or Tyvek chute. These chute materials were specifically chosen to represent the equipment and materials currently employed during manufacturing steps (i.e., plastic bags containing raw materials, Tyvek used as a chute to transfer materials from one piece of equipment to another, and stainless steel, as all major equipment is made from this material). The raw materials were left to slide along the surface of the chute and developed electrostatic charges. The materials so charged slid and fell through a stainless steel, plastic, or Tyvek chute, and their flow ended in an insulated stainless steel pan. The charge developed at the particle surface while sliding on the chute surface was measured over time with the electrostatic field meter for a 10-min period.

Charging Protocol for Part 3

The goal of Part 3 was to statistically evaluate the effect of electrostatic forces on the formation of agglomerates. Two binary mixtures, each of 1 kg and composed of 99% of an excipient (Xylitab or DCP) and 1% of MgSt, were prepared. MgSt was added at the geometric middle of the excipient to prevent it from sticking to the mixing bag walls. The raw materials were all passed through a 12-mesh screen and are charged by either positive voltage (+30 kV), negative voltage (−30 kV) or neutralized with a DC static elimination ring (Tantec Inc.), according to the statistical plan shown in Tables II and III (Fig. 1) (8). The materials so treated fell into a previously neutralized plastic bag. The bag was closed, and the powders were mixed manually by shaking the bag upside down for 30 strokes. The binary mixture was then discharged into a stainless steel pan, and the agglomerates formed were withdrawn from it. These agglomerates were photographed, and their number was quantified by Sigma-Scan Pro image analyzer software.

Chemical Analysis

In Part 3, the MgSt concentration of the agglomerates was analyzed chemically in an inductively coupled plasma emission spectrophotometer (ICP-AES). The agglomerates were acidified, digested on a hot plate, filtered, and diluted with deionized water. They were then read on the ICP, which was standardized by means of a suitable preparation.

Table II. Results from DCP + MgSt Statistical Design 2^2 Plan

		Factor A	Factor B	Response
Standard order	Test order	Charge on DCP	Charge on MgSt	Number of agglomerates
1	10	−30	−30	48
2	1	−30	−30	54
3	7	30	−30	34
4	5	30	−30	94
5	8	−30	30	49
6	9	−30	30	54
7	3	30	30	83
8	6	30	30	82
9	4	0	0	96
10	2	0	0	56

Table III. Results from Xylitab + MgSt Statistical Design 2^2 Plan

		Factor A	Factor B	Response
Standard order	Test order	Charge on Xylitab	Charge on MgSt	Number of agglomerates
1	10	−30	−30	65
2	1	−30	−30	74
3	7	30	−30	38
4	5	30	−30	47
5	8	−30	30	106
6	9	−30	30	92
7	3	30	30	42
8	6	30	30	34
9	4	0	0	25
10	2	0	0	39

EXPERIMENTAL

Part 1

Figures 2A, B and 3A, B present the electrostatic charge dissipation profiles as a function of time for raw materials charged and subsequently dropped into an insulated or grounded stainless steel pan. From these figures, two observations can be made: (1) all materials dropped into the insulated pan remained charged for the 10-min test period, and (2) all materials dropped into grounded receptacles lost their charge quickly, except for Xylitab and MgSt. This can be explained by the fact that Xylitab and MgSt had lower conductivities (and, consequently, higher specific resistances) than all the other materials tested because of their less polar character.

A steep drop in charge level was detected after 0.5 min for zinc oxide (ZnO) and after 4 min for Xylitab (Fig. 2B). The cause of this sudden drop was the development of a visible arc between the field meter and the pan.

Also, it was noted that Xylitab did not always carry the charge induced during its crossing of the charging electric field. When submitted to a positive field, Xylitab either developed a positive or a negative electrostatic charge (Fig. 4). It seemed that the magnitude of its positive charge was always lower than that of its negative charge.

Part 2

Figure 5A–C displays the electrostatic charge dissipation profile as a function of time for the different raw materials studied when sliding along a plastic, stainless steel, or Tyvek chute.

From this figure, it can be seen that most of the materials tested developed a positive electrostatic charge after sliding on the surface of the stainless steel chute, except for DCP, which carried a negative electrostatic charge. The magnitude of the charge greatly depended on the material involved (Fig. 5A1 and A2). Also, most of the materials tested, with the exception of MgSt and ZnO, carried a negative electrostatic charge after their contact with the plastic chute (Fig. 5B). It was also evident that all the materials tested carried a negative or zero electrostatic charge after their

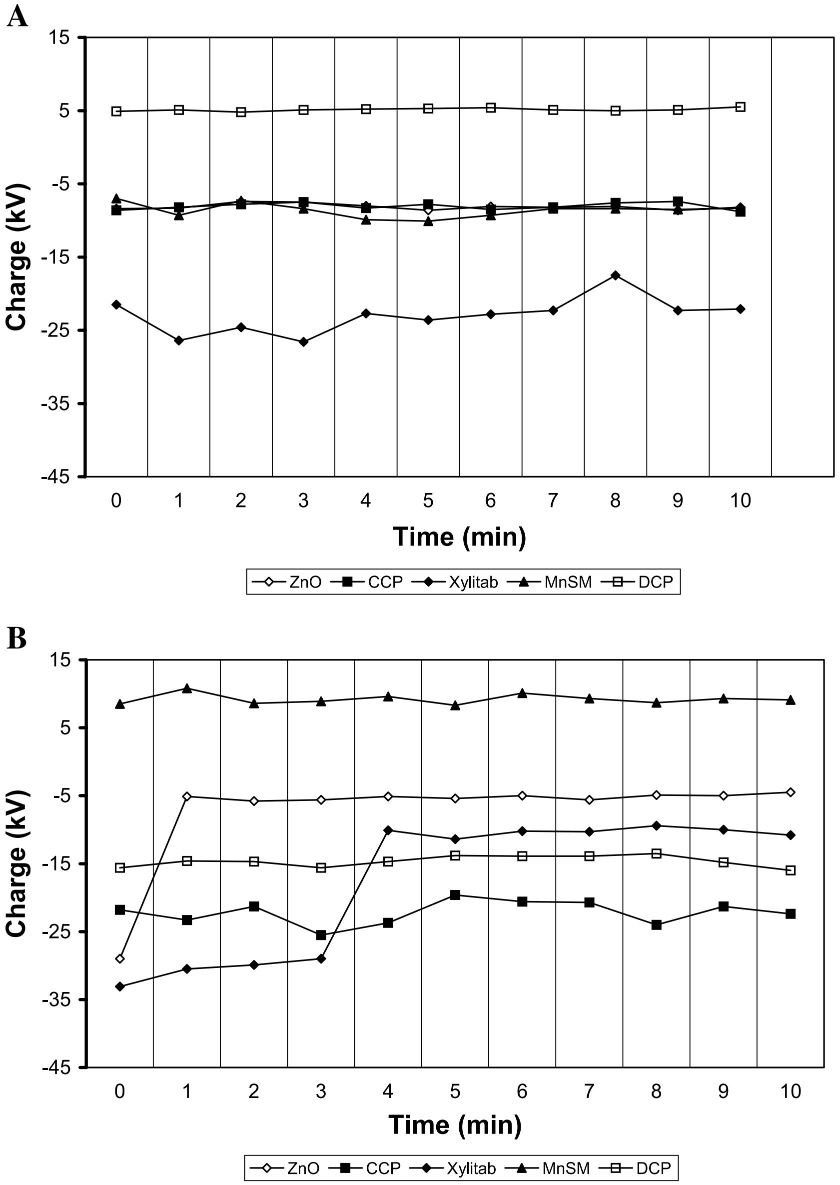


Fig. 2. (A) Profiles of charge *vs.* time for powder charged by +30 kV and dropped in an isolated stainless steel pan. (B) Profiles of charge *vs.* time for powder charged by −30 kV and dropped in an isolated stainless steel pan.

contact with the Tyvek chute. In comparison to the results obtained with the plastic chute, the magnitude of the charge was smaller in the case of the Tyvek chute (Fig. 5C1–C3).

From these findings, it is thus clear that MgSt always carried a positive electrostatic charge and that DCP always carried a negative electrostatic charge, irrespective of what material the chute was made from. All experiments were replicated to insure the qualitative evaluation of reproducibility. The mean results of our duplicated experiments are presented in Fig. 5A1, A2, B, and C1–C3. The reproducibility of the experiments is presented in this figure as error bars, calculated with Abs(Min − Max)/2. Because this study was intended to develop a qualitative understanding of how electrostatic forces affect agglomeration tendency, it was decided that full statistical evaluation of the experiments must be part of our ongoing work.

Part 3

The tests reported here were aimed at statistically analyzing the effect of electrostatic forces on the formation of agglomerates during the mixing of dry particulate systems. The experiments performed were elements of 2^2 fully replicated factorial designs for two binary systems: Xylitab + MgSt and DCP + MgSt. The factors studied were the charges applied to each of the powders. Tables II and III present statistical grid data, whereas Figs. 6 and 7 illustrate half-normal plots. Finally, Tables IV and V give analysis of variance (ANOVA) results for the number of agglomerates formed during mixing. Note that the straight line of a half-normal probability plot represents the ordered values of a sample *vs.* the expected ordered values from a true population. Thus, if the effects represent a sample from a

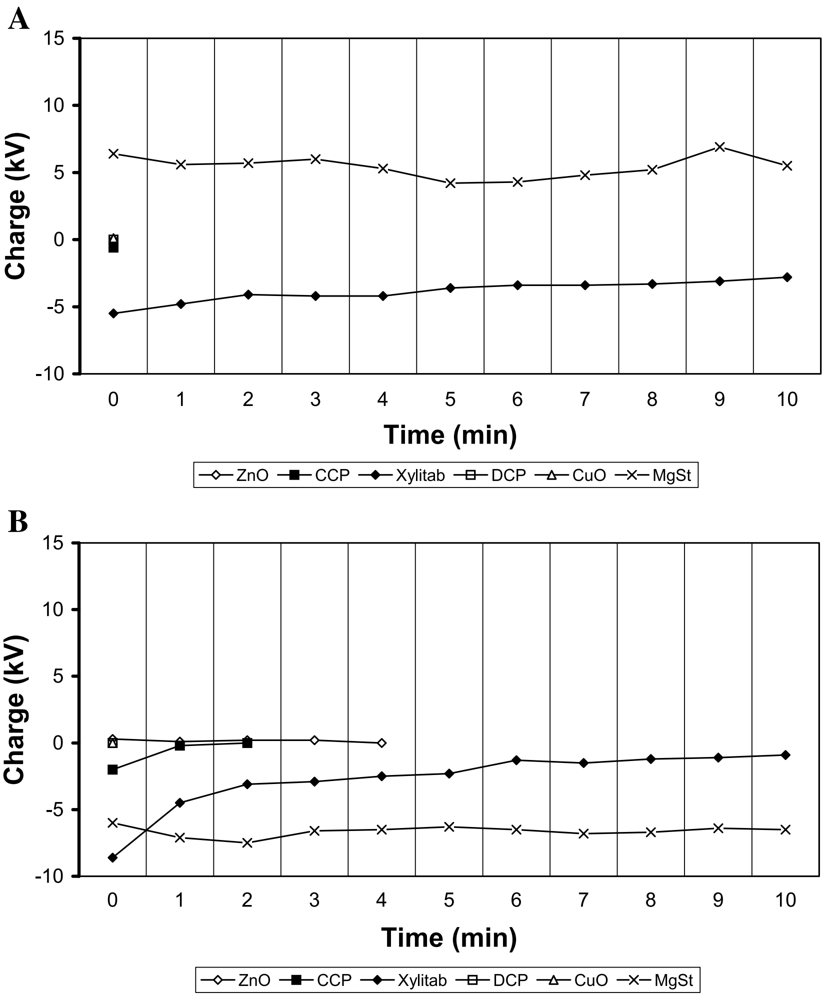


Fig. 3. (A) Profiles of charge *vs.* time for powder charged by +30 kV and dropped in a grounded stainless steel pan. (B) Profiles of charge *vs.* time for powder charged by −30 kV and dropped in a grounded stainless steel pan.

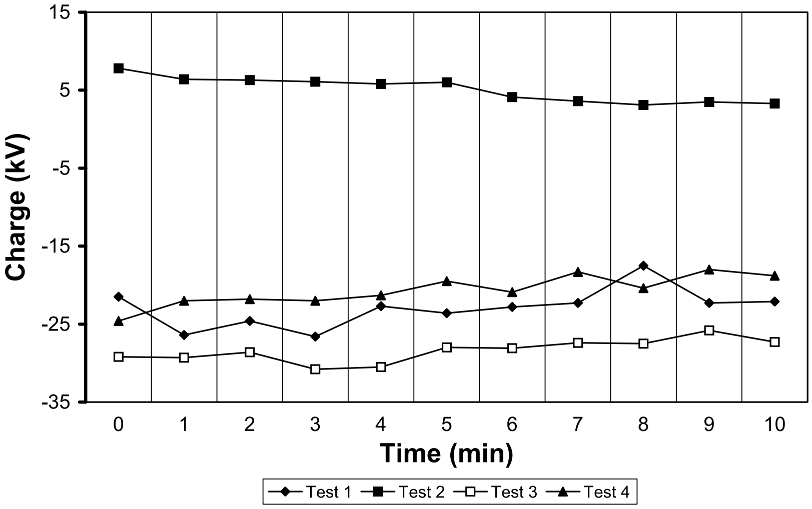
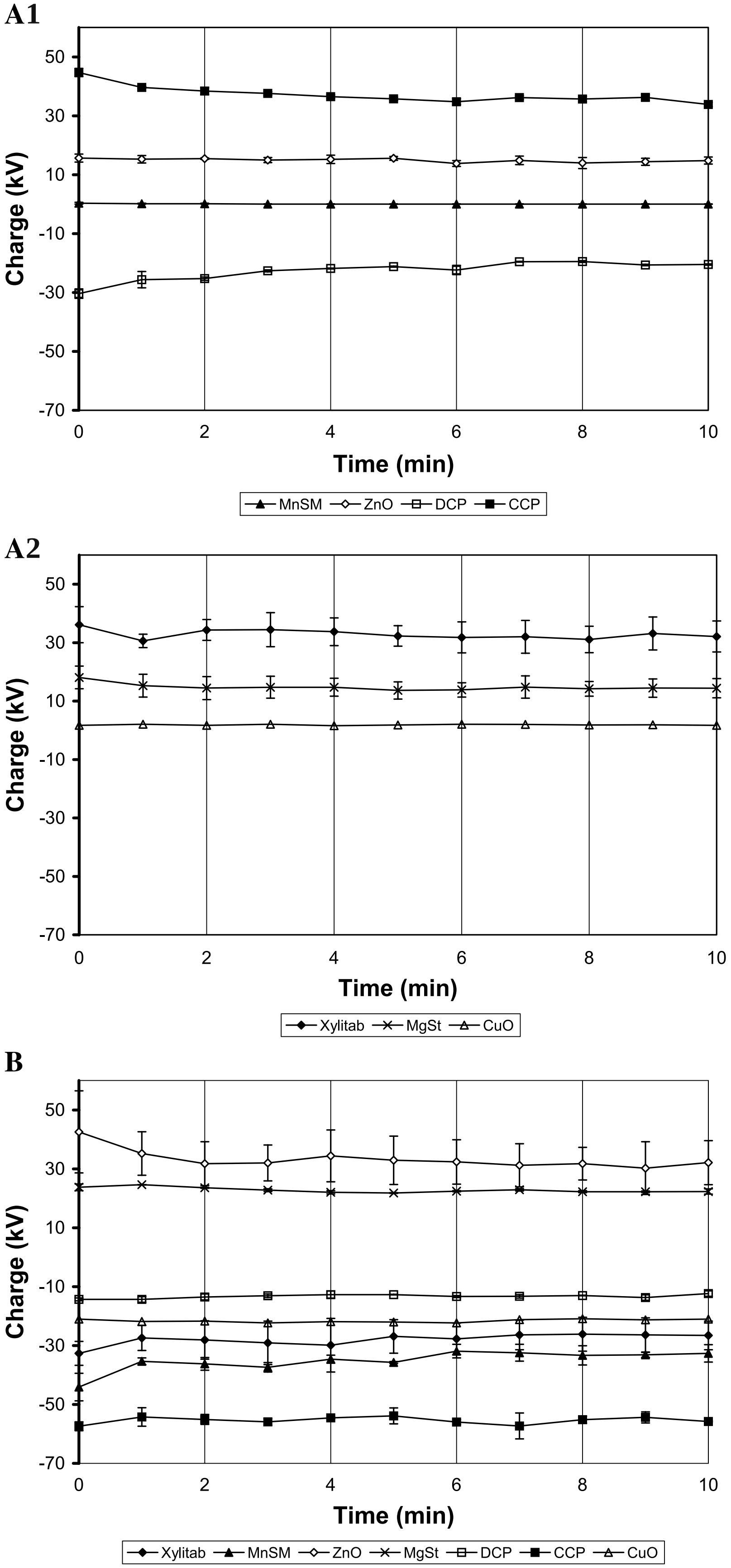
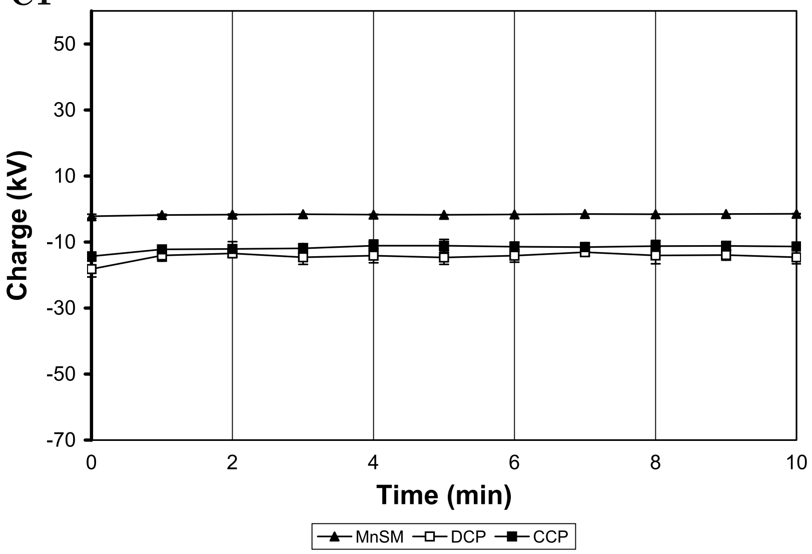


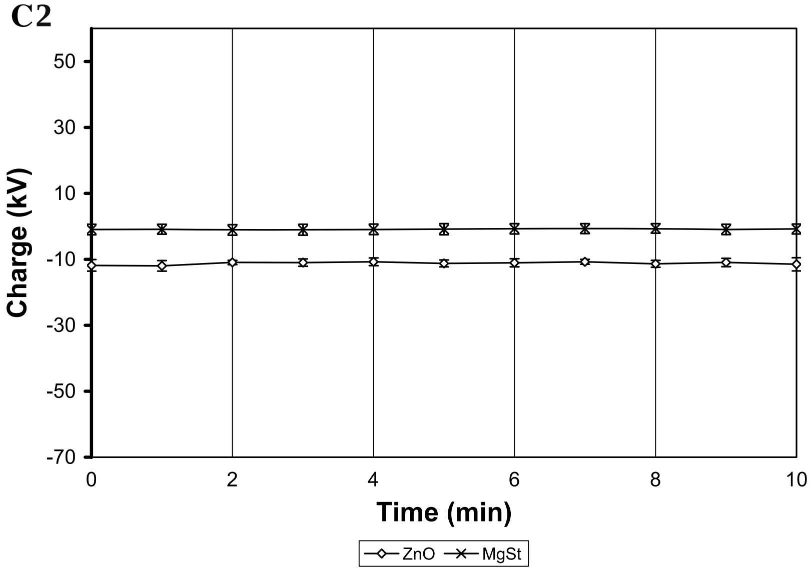
Fig. 4. Reproducibility: profiles of charge *vs.* time for Xylitab charged by +30 kV and dropped in an isolated stainless steel pan.


A1
50
30
10
-10
-30
-50
-70
0
2
4
6
8
10
Charge (kV)
Time (min)
MnSM
ZnO
DCP
CCP
A2
50
30
10
-10
-30
-50
-70
0
2
4
6
8
10
Charge (kV)
Time (min)
Xylitab
MgSt
CuO
B
50
30
10
-10
-30
-50
-70
0
2
4
6
8
10
Charge (kV)
Time (min)
Xylitab
MnSM
ZnO
MgSt
DCP
CCP
CuO

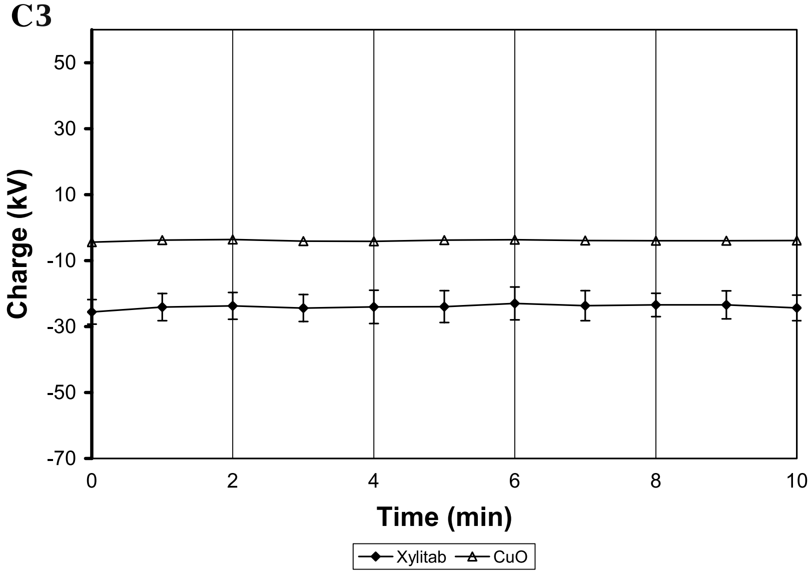
C1


Charge (kV)
50
30
10
-10
-30
-50
-70
0
2
4
6
8
10
Time (min)
MnSM
DCP
CCP

C2


Charge (kV)
50
30
10
-10
-30
-50
-70
0
2
4
6
8
10
Time (min)
ZnO
MgSt

C3


Charge (kV)
50
30
10
-10
-30
-50
-70
0
2
4
6
8
10
Time (min)
Xylitab
CuO

normal population, an approximated straight line on a half-normal probability plot of the effects would be expected. If the effects are significant, they would show up as outliers on the half-normal probability plot.

Statistical analysis of the results reported in Table II revealed that, for the ranges tested, the model for the binary mixture of DCP and MgSt was not significant; the charge level applied to each material did not affect the formation of agglomerates. Table III discloses, however, that, for the ranges tested, the model for the binary mixture of Xylitab and MgSt was significant and that the charges applied to the powders did influence the tendency to form agglomerates. It was also obvious from the half-normal probability plot in Fig. 7 that interaction between the applied charges was also significant.

Chemical Analysis

Agglomerates from the binary mixtures were analyzed chemically by ICP and found to be composed of an average of 64% MgSt.

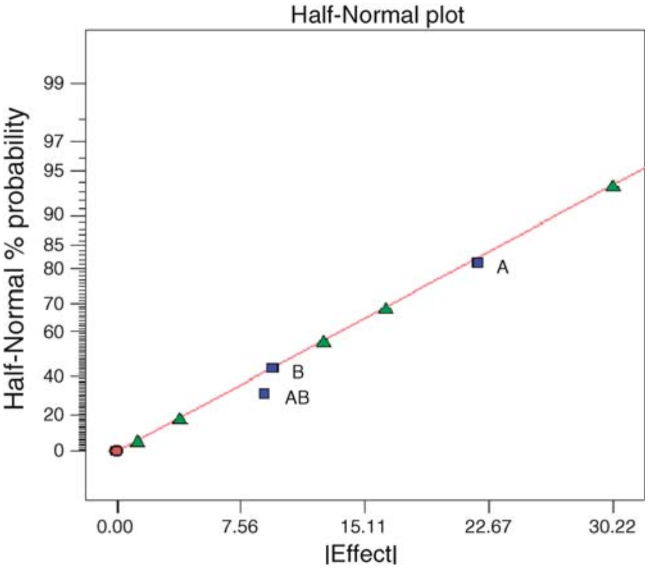


Fig. 6. Half-normal probability plot for statistical analysis of factorial design 2^2 DCP + MgSt.

DISCUSSION

Parts 1 and 2 of this work showed that the powders tested developed electrostatic charges of different polarities and magnitudes. This behavior was attributed to their different physical characteristics, conductivity, and ionic strength, as well as the material they contacted (2). Specific attention was given to Xylitab, DCP, and MgSt to explain their behavior in the agglomeration tendency observed in Part 3.

Part 1

It was apparent that Xylitab was charged negatively under a negative field but could also be charged negatively under an imposed positive field. The lack of reproducibility for Xylitab could be explained as follows: when charging positively, the Pinner bar ionizes the air surrounding the pins. The negative ions are attracted by the Pinner bar and grounded. Positive ions are directed toward the flowing particles. Positive ions are either attracted to negatively charged particles to neutralize them or to positively charge them; they could even pass through the mass of particles and land on the grounded wall of the chute. Because the chute was grounded, the generated electrons began to neutralize positive ions on the surface of the wall. Therefore, the negative flow generated by the ground enticed positive ions from the particle flow to be attracted to it, leaving the particles negatively charged. In other words, if the overall phenomenon, where positive ions created by the Pinner bar are directed and stick to the particles, is more significant than the phenomenon where positive ions entice the generation of negative ions from the grounded wall and therefore negatively charge the flowing particles, then the overall charge of the flowing particles is positive. Merle (9) reported that particle charging can be asymmetric, so that some particles under identical circumstances can be positively charged and others negatively charged, an observation that reinforces our hypothesis. The asymmetry is more significant when the particles are larger and insulated (10), i.e., the case for Xylitab. It could explain why this behavior was not seen for the other raw materials used during the experiment. Also, Kunkel (11) considered that the direction of the charge transfer between two heterogeneous surfaces was unpredictable and depended on the substance involved, explaining why, three out of four times, Xylitab charged negatively under a positive field (Fig. 4).

Another factor that could affect the charging process, although every test was conducted according to the same protocol, is the friction applied to the surface of the powder to pass it through the screen. Xylitab raw material from the supplier was compacted, and some of the powder had formed lumps. These lumps were solid; therefore, hand pressure was applied to pass them through the screen. The pressure and friction created during the screening step may have impacted further charging processes (9).

Because the goal of this study was to evaluate if electrostatic forces have an impact on particle agglomeration tendency, no further investigations were conducted to explain the Xylitab charging mechanism, but its behavior was taken into account.

Xylitab can remain charged for a few minutes when its container is grounded because of its nonionic properties, but the magnitude of the charge decreases rapidly with time. DCP charges according to the polarity of the imposed electrical field; however, the amplitude of its charge is three times higher when charged negatively. Because of its

Fig. 5. (A1) Profiles of charge *vs.* time for MnSM, ZnO, DCP, and CCP powders sliding on a stainless steel chute. (A2) Profiles of charge *vs.* time for Xylitab, MgSt, and CuO powders sliding on a stainless steel chute. (B) Profiles of charge *vs.* time for powders sliding on a plastic chute. (C1) Profiles of charge *vs.* time for MnSM, DCP, and CCP powders sliding on a Tyvek chute. (C2) Profiles of charge *vs.* time for ZnO and MgSt powders sliding on a Tyvek chute. (C3) Profiles of charge *vs.* time for Xylitab and CuO powders sliding on a Tyvek chute.

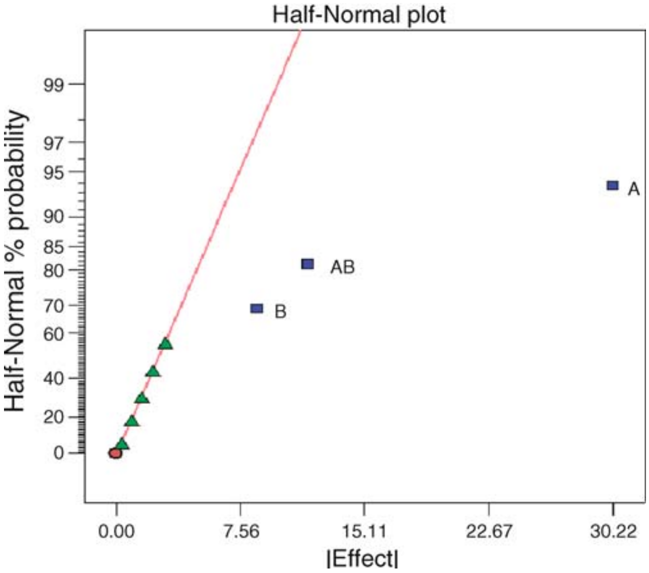


Fig. 7. Half-normal probability plot for statistical analysis of factorial design 2^2 Xylitab + MgSt.

conductive properties, DCP loses all of its electrostatic charges almost instantaneously when it comes in contact with a grounded vessel. However, MgSt can develop the same polarity with the imposed field and can retain a charge for at least 10 min when its container is grounded, as a result of its insulating properties (12).

Part 2

It was noted that the raw materials developed different electrostatic charges after their contact with the wall of different chute materials. On most tested materials, it was apparent that stainless steel chutes favored a positive particle charge, whereas Tyvek and plastic chutes favored a negative particle charge. The magnitudes of the charges acquired were higher with the plastic material than with Tyvek. As demonstrated in Part 1, DCP acquired a charge after its contact with the chutes; however, it was discharged as soon as it came into contact with a grounded material. For the purpose of the experiment, materials were dropped into an isolated pan to evaluate their potential to charge when sliding on various materials.

Table IV. ANOVA–Factorial Design 2^2 DCP + MgSt

Source	Sum of squares	DF	Mean square	*F* value	Prob > *F*
Model	1310.5	3	436.8	0.8302	0.5317
A	968	1	968.0	1.8396	0.2330
B	180.5	1	180.5	0.343	0.5835
AB	162	1	162.0	0.3079	0.6029
Curvature	302.5	1	302.5	0.5749	0.4825
Pure error	2631	5	526.2		
Cor total	4244	9			

DF = degrees of freedom; Prob = probability; Cor total = cumulative contribution of the model, curvature, and pure error.

Table V. ANOVA– Factorial Design 2^2 Xylitab + MgSt

Source	Sum of squares	DF	Mean square	*F* value	Prob > *F*
Model	4762.5	3	1587.5	25.6877	0.0018
A	3872	1	3872.0	62.6537	0.0005
B	312.5	1	312.5	5.0566	0.0744
AB	578	1	578.0	9.3528	0.0282
Curvature	1464.1	1	1464.1	23.6909	0.0046
Pure error	309	5	61.8		
Cor total	6535.6	9			

DF = degrees of freedom; Prob = probability; Cor total = cumulative contribution of the model, curvature, and pure error.

Part 3

The 2^2 design model for the Xylitab + MgSt system was found to be significant. The response measured was the number of agglomerates created when two charged components were mixed. The greatest number of agglomerates was produced when Xylitab was negatively charged and MgSt was positively charged (Fig. 8). This can be explained by the fact that oppositely charged materials are attracted to each other and thus form agglomerates. Also, according to the results of Parts 1 and 2, the most probable and natural electrostatic charge was negative for Xylitab and positive for MgSt. Two extra replicates of design point −30 kV Xylitab and +30 kV MgSt (nos. 3 and 4, respectively, in Table VI) were tested because of high agglomeration tendency. The four replicates gave a mean of 101 agglomerates, with a standard deviation of 8.4.

Although theoretically it was expected that the same phenomena would be observed when the charges were reversed, such was not the case. This can be explained by the fact that the probability of imposing a positive charge on Xylitab was low. In other words, when Xylitab was placed in a positive field, it acquired a lower magnitude of charge than what it would have acquired in a negative field. Moreover, even if Xylitab was placed in a positive field, it could acquire a negative charge, but this would be of lower intensity than if it were placed in a negative field. In contrast, when MgSt was placed in a negative field, it acquired a lower magnitude of charge than it would have acquired in a positive field. This could explain why a reduction in the number of agglomerates was observed.

The 2^2 design model for the DCP + MgSt system was not found to be statistically significant over the tested range. Even if the mix was made in a plastic bag and manipulated with plastic gloves, it seemed that DCP did not retain its electrostatic charge. Because DCP is easily discharged when grounded, it is probable that simple hand contact was sufficient to discharge it and therefore introduced a decisive bias to the design results. Such knowledge of an excipient may be of direct practical application when choosing a pharmaceutical ingredient for a specific formulation. Moreover, because the magnitude of the DCP electrostatic charge was low when compared with that of Xylitab, a small reduction in this charge could be enough to prevent attraction between particles with opposite charges. Vromans *et al.* (13) mentioned that DCP was quite insensitive to MgSt mixing.

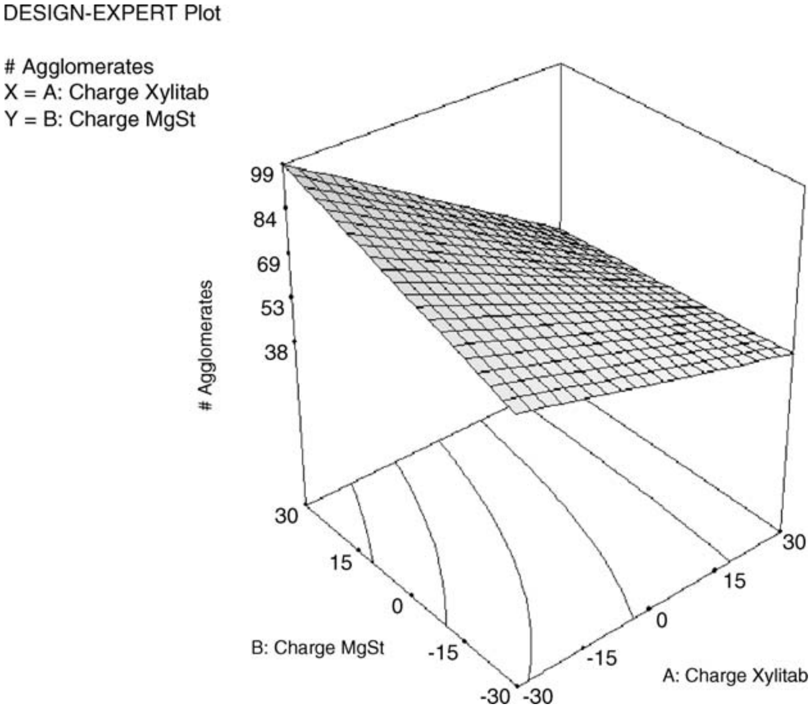


Fig. 8. Three-dimensional graphic: factorial design 2^2 Xylitab + MgSt.

It is thought that the agglomeration phenomenon, in the case of DCP, depended on other factors (humidity and van der Waals). On the other hand, the Xylitab and MgSt model showed that the tendency to agglomerate was a strong function of the electrostatic forces induced in the materials and that there was, according to the statistical analysis, significant interaction between the two applied charges that affected agglomeration tendency. Furthermore, it was demonstrated quantitatively that the number of agglomerates can double when Xylitab is negatively charged whereas MgSt is positively charged. Although the effect of electrostatic charges on the agglomeration tendency is obvious, other factors seemed to be equally important because, even when these materials were neutralized, agglomerates still formed during mixing. This is, for the moment, difficult to prove as additional testing is needed. Unfortunately, it is not possible to measure the electrostatic forces developed during the mixing process, but when particles collide with each other or with the walls of the vessel during mixing, electrostatic charges are created. This is probably why agglomerates are formed even if the raw materials have been neutralized prior to their incorporation into the mix. Nevertheless, our experiments have proved that electrostatic charges are one of the factors affecting the tendency toward agglomeration in dry powder mixing.

Table VI. Replicates of −30 kV Xylitab and +30 kV MgSt Points of Design 2^2 Xylitab + MgSt

Replicate no.	Number of agglomerates
1	106
2	92
3	96
4	110
Mean	101
SD	8.4

The Role of MgSt

From the literature (14), it is well known that MgSt is one of the most important and troublesome ingredients in frequent use because of its high surface area (micrometer powder). Although MgSt input usually accounts for less than 1% w/w of the total formulation, its surface area, per unit mass of the formulation, can be as high as 20%, depending on the other ingredients present in the formulation.

From the chemical analysis, agglomerates from the binary mixtures were found to be composed of an average of 64% MgSt. This agglomeration was caused mainly by MgSt's cohesive forces. Such MgSt autoagglomerates are able to stick to oppositely charged particles and thus form larger agglomerates of high MgSt content. This is a clear indication of the major role that MgSt plays in agglomeration phenomena. MgSt is deployed as a lubricant in formulations to reduce friction between particles by forming a film around them (13,15). The most probable distribution mechanism for MgSt covering other particles of the blend starts by partial filling of cavities, then quasi-total filling of cavities, and, finally, forming a peripheral layer of varying compositions around the particle (15). This prevents charge acquisition by reducing friction between particles and improving powder flow.

Careful attention must be given to MgSt concentration in mixtures because an excess can result in autoagglomeration and thus reduce the flowability of powders. It seems that there is no effect arising from electrostatic charges, and this conclusion is supported by the literature (16,17). Changes in the physical and chemical properties of solid dosage forms (especially the dissolution profile) can occur because of nonappropriate MgSt dispersion in the blend. Because MgSt was charged positively on contact with the three chute materials tested, it is obvious that stainless steel would be the ideal handling material when manipulating these powders. As they all develop positive electrostatic charges, agglomeration is less favored. The exception is for DCP, but as explained previously, the use of a properly grounded vessel would certainly discharge the DCP charge immediately, so that when mixed with MgSt, DCP would be already neutral. Unfortunately, during the mixing process, particles collide with the walls of the vessel, thereby creating uncontrolled electrostatic charges. This means that even if control of the electrostatic charges of raw materials entering the mixer is not completely possible, a modest decrease in attraction forces intensity between the particles greatly inhibits agglomeration tendency.

CONCLUSION

Quantitative analysis was conducted of the charging profile of selected raw materials under different controlled conditions. It was shown that the powders tested developed electrostatic charges of different polarities and magnitudes with time, according to the intrinsic properties of the raw materials and the types of surface they contacted during the various processing steps. From the mixture design of the experiment, it was demonstrated statistically that the raw materials tested remained charged when dropped in an insulated recipient and lost their charge almost instantaneously when the recipient was grounded, except for MgSt and Xylitab. Electrostatic charges influenced dry powder agglomeration tendency and even doubled the amount of agglomerates in blended powders.

Because oppositely charged particles are attracted to each other, the objective of the formulator is to reduce this attraction, thereby diminishing undesirable agglomeration phenomena. According to the results of this study, it is recommended that stainless steel equipment be used when handling the powders tested, as this material develops less attractive electrostatic forces than the plastic or Tyvek materials evaluated and can be grounded, facilitating charge dispersion from the particles, thereby decreasing agglomeration tendency. Although electrostatic forces play an important role in agglomeration phenomena, others, such as humidity and van der Waals forces, depending among other things on particle size and surface area of the particles, could also be involved.

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