



# The influence of electrostatic properties on the punch sticking propensity of pharmaceutical blends



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## ABSTRACT

**Purpose:** The present study details characterisation of the electrostatic properties of a range of active pharmaceutical ingredients (APIs) and blends and investigates the role of electrostatics as a potential root cause of punch sticking during tableting.

**Methods:** Microcrystalline cellulose (AVICEL® PH-102) and magnesium stearate were used to prepare blends of constant drug loading (10% w/w) with a range of APIs. The electrostatic properties of the APIs and blends were then determined using a JCI Chilworth 155v6 Charge Decay Time Analyser (CDTA) under controlled environmental conditions. The measurements recorded were then correlated to a punch sticking assessment of each blend, which was obtained utilising a Material Adhesion Screen for Sticking (MASS) Punch.

**Results:** The APIs became electrostatically charged to a higher extent than the blends. The linear relationship between particle punch sticking and the maximum surface voltage (Vs) attained post charging was poor ( $R^2 = 0.58$ ). However, a reduction in the susceptibility of the blend to retain electrostatic charge, as determined by the measurement of charge decay times (Time 1/e and Time 10%), was found to be linearly proportional ( $R^2 = 0.89$  and  $0.88$  respectively) to the sticking propensity.

**Conclusion:** Despite the excipients significantly damping the charging propensity of the API in a formulation, the electrostatic behaviour and punch sticking propensity of the majority of the formulated blends were shown to be dominated by the API (even at only 10% w/w). It is anticipated that the use of formulations with fast charge decay rates may reduce sticking problems during tablet production.

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## 1. Introduction

Tablets are the most popular oral solid dosage form in the pharmaceutical industry due to their convenience to the patient, ease of manufacture and their ability to deliver a wide range of therapeutic doses [1–4]. The most efficient tableting process is direct compression (DC), in which the excipients and active pharmaceutical ingredient (API) are thoroughly mixed to form a homogenous blend and then compacted without the need for granulation [1,3]. For this process to be successful, the excipients and API need to possess suitable physical properties including low punch sticking propensity [1,5]. However, as new drugs are developed, instances often arise where failures in the manufacturing process occur due to high punch sticking propensity of

the input materials [1,6]. The sticking of tablets to punch faces is a serious problem in tablet production, causing considerable loss of time and money [6–10]. In the worse cases, strong adhesion to the upper punch may lead to complete sticking of a tablet to the punch. Subsequent compression of the tablet with a new filling of the die may lead to a breakdown of the tableting machine. However, in most cases the outcome is less severe as sticking only leads to adhesion of a powder layer onto the punch surface. Nevertheless, it may result in early termination of the tableting process for cleaning purposes. In addition, sorting and disposal of tablets exhibiting rough surfaces and incomplete or missing debossing is wasteful and costly [8]. Despite the fact that numerous studies have already been conducted to elucidate the fundamental causes of tablet sticking [11–24], it is still one of the most common problems observed during production-scale tableting [6]. Therefore, tablet manufacturers are still searching for universally applicable measures to prevent and/or solve sticking problems more efficiently.

During pharmaceutical powder processing operations, powder particles frequently come into contact with each other and with the walls of the processing equipment and become electrostatically charged by a process known as triboelectrification [1,25–34]. Particle triboelectrification has been suggested as a potential cause of punch sticking [32,35],

**Abbreviations:** API, active pharmaceutical ingredient; CDTA, Charge Decay Time Analyser; DC, direct compression; Hz, Hertz; MASS, Material Adhesion Screen for Sticking; MgSt, magnesium stearate; nC, nanoCoulomb; N/R, not reached; RH, relative humidity; RPM, revolutions per minute; SD, standard deviation;  $t_{1/e}$ , time taken for the surface potential to decay to 1/e (36.8%) of the initial value;  $t_{10\%}$ , time taken for the surface potential to decay to 10% of the initial value; Vs, initial surface potential difference.

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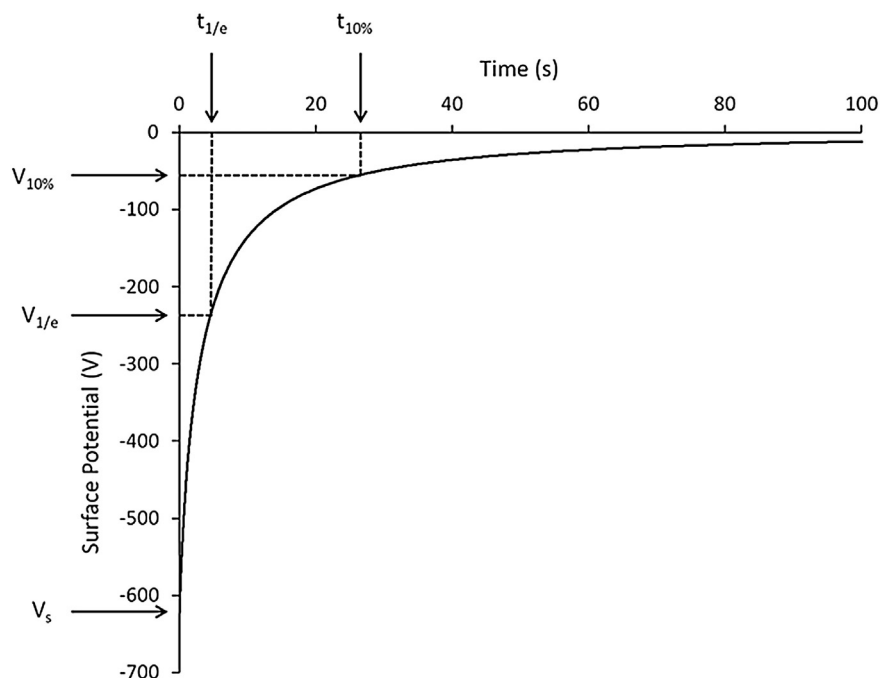


Fig. 1. Typical surface potential versus time decay profile generated with a Charge Decay Time Analyser (CDTA). This figure has been adopted from [38].

however, little work has been reported in this area. Ghori et al. recently studied the relationship between triboelectric charging and surface adhesion for binary mixtures of flurbiprofen and different cellulose ethers in powders with varying particle size [36]. A reduction in susceptibility towards triboelectric charging showed a linear relationship ( $R^2 = 0.81–0.98$ ) with surface adhesion. However, most triboelectric studies reported in the literature including the study highlighted above, used a triboelectric charge measurement apparatus based on a shaking concept [37]. Triboelectrification of powder samples inside a horizontally shaking container was achieved by particles impacting and sliding against the surfaces for certain time periods at a vibration frequency of 20 Hz with the amplitude of vibrations fixed at 8.9 mm. The triboelectric charge was then measured by pouring the charged powder particles into a Faraday cup, connected to an electrometer [36]. However, a limitation of the study is that pouring itself may result in additional triboelectrification of the powders [38].

A Charge Decay Time Analyser (CDTA) (JCI155 v6, Chilworth Technology Ltd. Southampton, UK) is an instrument which has been suggested as a robust, operator independent means of determining the electrostatic charging propensity of materials [38–41]. A high voltage corona discharge is used to deposit charge onto the surface of a sample to be tested. A fast response electrostatic field meter measures the surface potential difference generated by this charge and how quickly the resultant voltage falls as charge decays from the sample over time as shown in Fig. 1 [38]. If the corona discharge is kept at a constant value,

the initial surface potential post corona charging ( $V_s$ ) will indicate the susceptibility of a powder to pick up static charge, with the greater the initial value, the greater the charging propensity [38]. In addition, the charge decay rate, as quantified by the Time to 10% ( $t_{10\%}$ ) and Time to 1/e ( $t_{1/e}$ ) values as shown in Fig. 1, will provide an indication of how long a powder will remain statically charged for after it has undergone a tribocharging event [42]. Consequently, the electrostatic properties of powders can be ranked according to their charge decay profile, from the best behaving samples (i.e. those exhibiting the lowest values for  $V_s$ ,  $t_{1/e}$  and  $t_{10\%}$ ) to the worst behaving samples (i.e. those exhibiting the highest values for  $V_s$ ,  $t_{1/e}$  and  $t_{10\%}$ ).

It is not always clear whether it is the excipients or API that causes failures in the manufacturing process due to punch sticking [1]. Šupuk et al. compared the magnitude of triboelectric charge in a number of excipients and APIs. As the excipients exhibited lower charge levels, it was hypothesised that the extent of electrostatic charging of the APIs is the predominant contributor to the electrostatic charging behaviour of pharmaceutical blends and to any related formulation issues [1]. The main drawback of the study was the lack of control of the environmental conditions. Charge decay characteristics have been shown to be

Table 1

Settings of the JCI155 v6 Charge Decay Time Analyser (CDTA) used for electrostatic charge decay measurements.

Run settings	
Pretest voltage (V)	$\leq \pm 5$
Corona voltage (V)	8000
Corona time (s)	0.02
Analysis start (s)	0.07
Plate speed	Slow
Temperature ( $^{\circ}\text{C}$ )	20

Table 2

Initial surface voltage ( $V_s$ ), times from  $V_s$  to 1/e and 10% of this value and amount of charge remaining on the sample after 9 h (as a percentage of initial surface potential) for the APIs at 45% relative humidity (RH) and temperature = 20  $^{\circ}\text{C}$  ( $n = 3$ , mean  $\pm$  SD).

API	$V_s$ (V)	Time 1/e (s)	Time 10% (s)	Charge remaining after 9 h (% of $V_s$ )
API 1	$-1596 \pm 109$	N/R <sup>a</sup>	N/R	$87.3 \pm 1.1$
API 2	$-1660 \pm 65$	N/R	N/R	$81.5 \pm 1.2$
API 3	$-1880 \pm 45$	N/R	N/R	$96.4 \pm 0.0$
API 4	$-1809 \pm 40$	N/R	N/R	$65.1 \pm 3.9$
API 5	$-1092 \pm 24$	$130 \pm 13$	$1983 \pm 137$	$0.0 \pm 0.0$
API 6	$-1650 \pm 22$	N/R	N/R	$70.0 \pm 0.5$
API 7	$-1241 \pm 80$	N/R	N/R	$67.9 \pm 0.7$
API 8	$-1582 \pm 39$	N/R	N/R	$89.2 \pm 0.5$
API 9	$-1691 \pm 16$	N/R	N/R	$99.0 \pm 0.2$

<sup>a</sup> Not reached.

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