EFFECTS OF STATIC ON PLASTICS USED IN DRUG DELIVERY DEVICES

Drug delivery in dry-powder and aerosol inhalers can be hindered by static attraction of the drug substance to plastics used in the drug flow path. Here, Joel R Bell, PhD, International Technology Manager, and Josh Blackmore, MBA, Global Market Manager, Healthcare, both of RTP Company, report a series of projects to characterise this interaction, measure the effect of static build up and create new conductive plastic solutions to reduce the static charge in plastics used in the drug flow path of delivery devices.

INTRODUCTION

Dry-powder inhalers (DPIs) and pressurised metered-dose inhalers (pMDI) have been around for many decades. Both drug delivery technologies face some of the same challenges when compared to oral medication or injections. One of the key challenges for inhalers is effectively to measure the amount of drug that is dispensed *versus* the amount of drug that reaches the patient through their lungs. Drug formulations can stick in the drug packaging, the drug flow path, the back of the throat or tongue, and some may not reach deep enough in the lung to provide maximum effectiveness. Each variable is critical and must be accounted for and managed to improve consistent drug delivery.

This paper focuses on improving drug dosage accuracy by eliminating the static attraction between the drug formulation and the plastics used in the drug flow path of the device.

BACKGROUND ON STATIC ELECTRICITY

Everyone is familiar with static electricity and has experienced its effects from a young age. Simply rub a balloon on your head and watch as your hair stands on end as the balloon is slowly moved away. This happens because electrons from your hair are transferred to the balloon surface during rubbing (called tribocharging) and the difference in charge on the two surfaces causes attraction. Simply put, static electricity is the accumulation of charge (positive or negative) on a non-conducting surface.

Polymers (plastic) are inherently insulative and thus components made of plastic can easily accumulate charge on their surfaces. This charge can attract dust to the surface of the part; in medical drug delivery devices such as inhalers this surface attraction can cause particles of drug formulation (or other particles) to adhere to the surface resulting in reduced and inconsistent dosage. In more severe cases, an electrostatic discharge (ESD) event can take place when the charged surface comes in contact with a highly conductive object (ground) and the charge is rapidly released. Touching a metal doorknob and receiving a mild shock is a common everyday occurrence of ESD, but in certain situations ESD can damage or destroy sensitive electronic components, erase or alter magnetic media, or set off explosions or fires in flammable environments. Each year, many billions of dollars in losses due to ESD damage occur in the electronics industry alone.[1-2]

CONDUCTIVE STANDARDS, SPECIFICATIONS & TESTS

Three performance characteristics, surface resistance, resistivity, and static decay rate, are typically evaluated for conductive thermoplastic compounds. Surface resist-

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ance and static decay are directly measured, while volume or surface resistivity is derived from the measured surface resistance. There are standards in place to measure each of these properties and the measured values are only meaningful if the test procedures (equipment, geometry, environmental conditions, etc) are referenced.

Surface resistance is the ratio of direct current (DC) voltage to the current flowing between two electrodes and is expressed in ohms (measured value is dimensional). The US American Society for Testing and Materials' ASTM D257 and the UD Electrostatic Discharge Association's ESD STM 11.11 are the methods utilised in measuring surface resistance of plastic materials. There are several types of equipment that can be used to measure this property; typically RTP Company uses a Prostat PRS-801, operating at 100 Volts, equipped with a two-point probe, and all surface resistance values in this paper were obtained using this equipment.

Surface resistivity is the surface resistance measured between two electrodes that form opposite sides of a square and is independent of the size of the square or its dimensional units. Surface resistivity is typically measured using a Voyager meter or a guarded ring and the units are ohms/square.

Volume Resistivity is the ratio of DC voltage per unit thickness to amount of current per unit area passing through a material and the units are ohm-cm.

Static decay rate is a measure of a highly resistive material's ability to dissipate static charge under controlled conditions. FTMS 101C/4046.1 describes the protocol for static decay rate testing. In the test, a 3x5 inch (7.62x12.7 cm) plaque of the material is charged to 5,000 Volts and then the amount of time to dissipate 99% of the voltage is measured. According to the MIL PRF 81705D specification for antistatic materials used in packaging, the time measured must be less than two seconds.

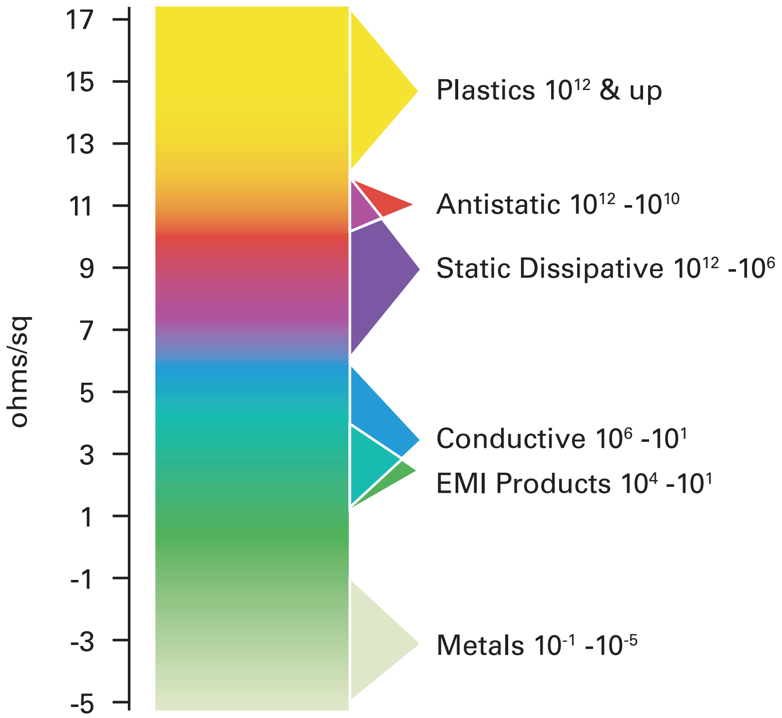

Figure 1: Surface resistivity spectrum for conductive materials.

CONDUCTIVE TECHNOLOGIES

Through the use of additive technologies, polymers can be made more or less conductive. Figure 1 shows a classification of materials based on their surface resistivity (inverse of conductivity). The type of additive technology will dictate the attainable level of conductivity, and Figure 2 shows the pros and cons for a selection of conductive technologies.

Conductive Technology	Pros	Cons
Migratory Antistats	• Economical • Non-permanent	• Process temperature limited
Inherently Dissipative Polymers (aka PermaStat®)	• Permanent • Transparent availability • Colourable • No loss of mechanical properties	• Limited to dissipative range • Process temperature limited
Carbon Black	• Economical • Dissipative or conductive • Resists tribocharging	• Sloughing • Black only • Lower impact strength
Carbon Fiber	• Dissipative or conductive • Reinforcing • Non-sloughing	• Anistropy • Poor triobcharging
Carbon Nanotubes	• Dissipative or conductive • Superior tribocharging performance • Minimal effect on mechanical properties and resin viscosity • Low LPC	• Cost • Black only
Metallic Additives	• EMI-FRI shielding • Highly conductive	• Limited colorability • Higher specific gravity

Figure 2: Table Summarising Conductive Technologies, and their pros and cons.

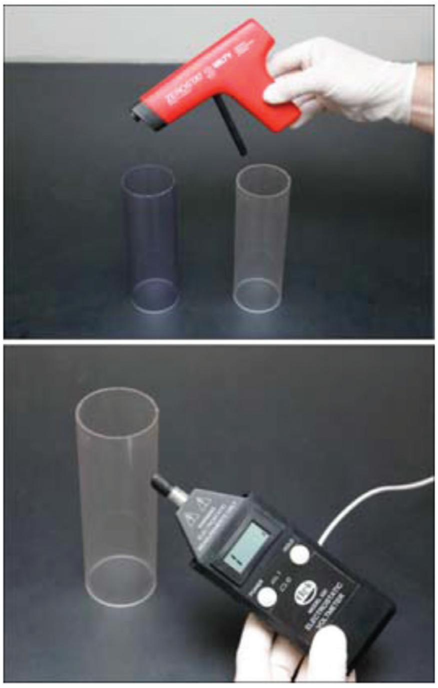

Figure 3: Top – tubes of the PermaStat® ABS (left-violet) and base ABS (right-clear) along with the Milty Antistatic Gun used to charge the tubes. Bottom – the voltmeter used to measure surface charge on a positively charged ABS tube.

As stated previously, plastics are inherently insulative and typically have surface resistivity values greater than 10^{12} ohm/sq. Antistatic compounds have surface resistivity values of 10^{10}-10^{12} ohm/sq and provide a relatively slow decay of static charge – from just hundredths of seconds to several seconds – thus preventing accumulations that may discharge or initiate other nearby electrical events. These compounds can be made one of two ways: by addition of a low-molecular-weight antistatic additive that migrates to the surface of the part, absorbs water, and then dissipates surface charge, or by the addition of an inherently dissipative polymer into the compound that forms a network structure with the base polymer. The first option is not permanent while the latter permanent option is the basis for RTP Company's PermaStat® antistatic technology.

> "Often, it is the interaction between the carrier material and the plastic component that needs to be controlled in DPIs"

Static dissipative compounds allow for dissipation or decay of static charges at a faster rate than anti-static materials (on the order of milliseconds) and are generally considered "optimal" for ESD protection. Compounds can be obtained using carbon particulate additives or by the addition of an inherently dissipative polymer.

Conductive compounds have surface resistivity values of 10^{1}-10^{6} ohm/sq and static decay rates on the order of nanoseconds. These compounds are achieved by addition of carbon fibre, high levels of carbon powder, carbon nanotubes, or other metallic additives. Performance is achieved by the charge being transferred through a percolated network of the conductive additive.

EXPERIMENTAL SETUP

A test was designed that simulated drugs coming into contact with the plastic walls in a drug delivery device, such as an inhaler. The effects static charge has on drugs sticking to the device were measured for antistatic and non-antistatic compounds. Materials were chosen to ensure that visual as well as quantitative comparisons could be measured.

MATERIALS

Acrylonitrile butadiene styrene (ABS) has good impact properties and is economical. It offers a good material for inhaler applications. In addition, PermaStat® ABS can be made transparent, which aids in visualisation. For the experiments presented here, RTP Company's clear PermaStat® ABS is compared with the base ABS resin.

Often, it is the interaction between the carrier material and the plastic component that needs to be controlled in DPIs. Lactose powder is a typical carrier material for the pharmaceuticals used in DPIs and therefore was used in this experiment. The specific lactose powder used was InhaLac® 230 (Meggle, Wasserburg, Germany).

DEVICE DESIGN

A tube was used to simulate the chamber in a DPI. The dimensions for the tube were 2 inches (5.08 cm) diameter by 6 inches (15.24 cm) long, with a 1/16 inch (0.16 cm) thick wall. This geometry allowed for maximum surface area without unwanted interactions with part corners. The tubes were extruded by Thermoplastic Processes (Stirling, NJ, US).

Figure 4: Top – tubes of the PermaStat® ABS (left-violet) and ABS (right-clear) prior to testing. Bottom – powder retention in the two materials after testing.

TEST PROCEDURE

All tubes were cleaned and conditioned at 50% humidity prior to testing. For the test, each individual tube was weighed using an A&D Balance (FR-200 MKII, ± 0.0001g). A positive or negative charge was then placed on the tube using a Milty Zerostat 3 Antistatic Gun. The charge was confirmed using a Trek Electrostatic Voltmeter (Model 520) (Figure 3).

Lactose powder, 400 mg, was then inserted into the tube and then ends were sealed. The tube was continuously rotated to ensure the powder contacted the entire inside surface area of the tube. All free flowing lactose powder was then removed and the tube was reweighed. The powder retained in the tube was then calculated and percentage powder retention (weight of powder left in tube/initial weight of powder x 100%) was determined. A minimum of five tubes for each set of conditions (charge and plastic type) was measured for statistical accuracy.

RESULTS

Figure 4 shows the typical appearance of the tubes after testing. From the picture it is clear that there is more lactose powder stuck to the surface of the non-PermaStat® tube (clear tube). Quantitative results showed that <2.5% of the lactose powder was retained in the PermaStat® ABS tubes regardless of charge while >20% of the lactose powder stuck to the positively charged ABS tubes. The amount of powder that stuck to the negatively charged ABS tubes was reduced, but >8% was still retained. During testing, the surface charges on the tubes were monitored using the voltmeter and the PermaStat® tubes were able to dissipate the charge while a charge remained on the ABS tubes throughout the experiment. This inability to dissipate static surface charge caused the ABS tubes to perform less favourably.

Results from this experiment agree with previous experiments that show electrostatic charge affects drug delivery in inhaler type devices.[3-4]

Another key result is that the variability in the results for the ABS tubes is far greater than for the PermaStat® tubes. The standard deviation for the ABS tubes was ±8.9% for the positively charged tubes while it was only ±0.7% for the PermaStat® tubes. This could mean that drug delivery devices with less conductive surfaces in the drug flow path exhibit greater dose variability than those with more conductive surfaces, which will affect the ability of a drug delivery device to deliver consistent doses to a patient.

> "Results from this experiment agree with previous experiments that show electrostatic charge affects drug delivery in inhaler type devices"

CONCLUSIONS

Static charges that build up on the plastics used in the drug flow path and housing materials in pMDIs and DPIs have demonstrated the ability to attract the drug formulation and therefore potentially reduce the amount of drug delivered. A decrease in dose consistency is also a potential problem. Antistatic plastics would help to eliminate these effects in both pMDI and DPI devices.

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