Electrostatic charging of pharmaceuticals – a multifaceted phenomenon

Pharmaceutical solids are usually insulators and thus they are likely to carry an electrostatic charge during powder handling processes. Tribocharging is a popular phenomenon in pharmaceutical solids that arises from particle – particle and particle – wall collisions. Charge generation phenomena in pharmaceutical powders could be severe. However, the electrostatic charging phenomenon is complex and difficult to study and control. This is because charging of pharmaceutical powders depends on a combination of many physicochemical properties as well as the inhaler design and environmental factors (Fig. 1), making our understanding of electrostatic charging is not complete.

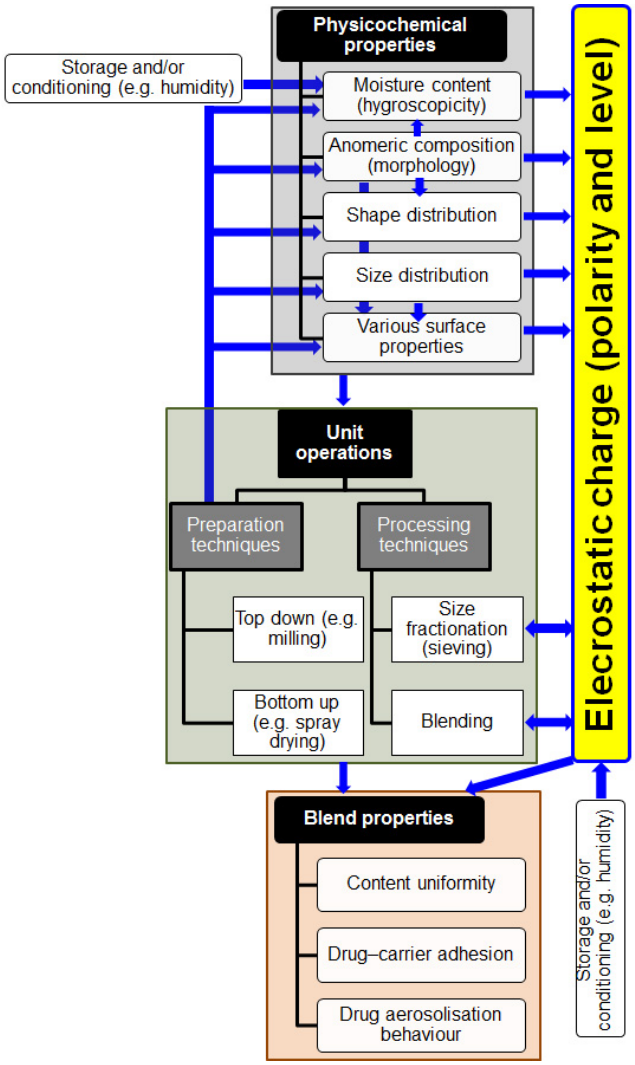

Fig. 1. Schematic presentation of some factors having an effect the electrostatic charging of pharmaceutical solids and adhesive mixtures for inhalation

In general, the electrostatic charge could be found in powders having similar or dissimilar chemical composition(s). Powders might develop different polarities and levels of charge according to their inherent ‘intrinsic’ electrical properties and types/properties (e.g., surface area) of the surfaces they contact during different processing steps. The generation and decay of electrostatic charge on the surface of charged particles also depend on their physicochemical properties, such as surface resistivity, surface roughness, surface impurities, size distribution, shape distribution, and molecular structure (Fig. 1). The electrostatic charge is furthermore influenced by environmental conditions (e.g., the relative humidity and atmospheric pressure), particle motions and binary collisions, and magnitude of the frictional forces (Fig. 1).

Since the electrostatic charging process is very sensitive to a multitude of factors, a slight difference in particle physicochemical properties or the measurement principles could lead to significant differences in the charge behaviour of pharmaceutical powders. Moreover, in addition to interactions, the linkage between variables is a main complicating element in obtaining a fundamental understanding of electrostatic charging of pharmaceutical powders. For example, although the reduction of powder electrostatic charge may improve the prospects of aerosol pharmaceutical powders, it is difficult to ascertain the influence of a single factor such as charge level/sign on dry powder inhaler (DPI) performance due to the complexity of DPI systems. Therefore, a substantial work is warranted to investigate the charging properties of drug and carrier particles of DPI systems as well as drug–carrier adhesive mixtures. The study of bipolarity in the drug–carrier inhalation powders could potentially play an important role in the technological advances in the design and development of dry powder inhalation formulations in the future. The fundamentals of charging as well as the agglomeration, deagglomeration, and deposition properties of charged drug and carrier particles have to be the subject of advanced examination. The recognition nevertheless that interactions among charging, formulations, and aerosolisation variables are pervasive is an important step towards the understanding of tribocharging of inhalation powders.

Most of the previous studies focused on the factors affecting charge one-by-one, neglecting the potential interactions between them. Therefore, there is a need for methodological evaluations and predictive in silico investigations in the future to evaluate the significance of the factors affecting charge as well as the interactions between them. Additionally, there is an increased need to separate and measure the bipolar charges (i.e., to discern positively and negatively charged particles) of inhalation powders. In time, the control of the effects of electrostatic charging in DPI devices is expected to become obligatory, although a systemic control of the charge sign and level in inhalation powders by tribocharging has not been reported yet. Additionally, up to now, the influence of electrostatic charge of aerosol particles on aerosol performance in human subjects has not been reported and therefore the role of electrostatic charge on aerosolisation performance is not yet fully ascertained. There are also concerns of the reproducibility of electrostatic charge properties, i.e., the electrostatic charge properties measured in the laboratory may not be

adaptable to the industrial scale.

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