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Comparison of the surface properties of salbutamol sulphate prepared by micronization and a supercritical fluid technique

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As materials for drug delivery via the pulmonary route are rarely crystallised to provide the requirements of particle size and size distribution to reach the deep lung region (i.e. 1-5 microns), secondary processing such as milling by micronisation is often required. However, this processing is usually sufficiently energetic to cause varying and uncontrolled degrees of disruption to the crystal structure. This disruption will most likely predominate at the surfaces which have interfaced with the processing stress, producing amorphous domains on the particle surfaces.

A new process called Solution Enhanced Dispersion by Supercritical Fluids (SEDS) has been developed at Bradford University to overcome some of these problems. The process involves rapid dispersion and extraction of the drug solution solvent by a supercritical fluid, typically carbon dioxide. An oven and back-pressure regulator control the temperature and pressure, which together with precise flow rates and metering of the drug solution, provides uniform conditions for particle formation and control of particle size (York et al., 1996).

In this study Inverse Gas Chromatography (IGC) has been used to quantify changes in the surface thermodynamic properties of a batch of unprocessed salbutamol sulphate (U1) after micronisation (M1) and after preparation by the SEDS process (S1). M1 and S1 have similar particle size distributions.

In IGC the surface characteristics of a sample are determined by injecting a range of liquid probes with differing polarities into a column which contains the sample as the stationary phase. The retention times and volumes of these probes reveal information about surface thermodynamic properties (Ticehurst et al., 1994).

Table 1 gives the surface free energies of the samples and all standard errors are less than 4%. Micronisation has increased γ_s^d (the dispersive component of surface free energy) implying that the surface of M1 has a more energetic surface for non-polar surface interactions. The specific component of surface free energy ($-\Delta G_A^{SP}$) of the acidic probe (chloroform) has also increased, in contrast to the amphoteric (acetone) and basic (tetrahydrofuran) polar probes. This suggests stronger basic (electron donor) interactions at the surface of M1, resulting from exposure of more basic functional groups after particle breakage on micronisation. The SEDS product exhibits lower γ_s^d and $-\Delta G_A^{SP}$ suggesting that S1 has a generally less energetic surface than U1.

Batch	γ_s^d (mNm^{-1})	$-\Delta G_A^{SP}$ ($KJmol^{-1}$)		
		Chloro-form	Acetone	Tetrahydro-furan
U1	49.07	1.53	10.22	9.52
M1	58.57	1.98	8.19	6.58
S1	38.45	0.71	5.77	4.96

Table 1: Surface thermodynamic properties of U1, M1 and S1.

Feeley et al. (1997) have shown that surface energy differences detected by IGC influence important secondary processing properties such as powder flow, with less energetic samples having better flow properties. Thus, the SEDS process provides an attractive alternative to size reduction by micronisation with lower energetic surfaces and potentially improved processing and pulmonary product performance characteristics.

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