Surface Characterization of API Using Inverse Gas Chromatography

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Inverse gas chromatography (iGC) represents a highly adaptable and robust methodology for assessing the interfacial and surface characteristics of various solid materials, including powders, nanostructures, films, and fibers. This contribution presents a review of iGC applications, experimental methodology, and underlying principles.

Unlike traditional gas chromatography, iGC reverses the conventional setup by employing the investigated material as the stationary phase, which then interacts with injected gas-phase probe molecules. By measuring the resulting retention volumes, it is possible to accurately determine key material properties such as both the dispersive and specific (acid-base) components of surface energy, thermodynamic characteristics (including the work of cohesion and adhesion), surface heterogeneity and BET surface area.

$$\gamma_S^T = \gamma_S^d + \gamma_S^{ab} \qquad (1)$$

We provide a detailed outline of the iGC experimental workflow, ranging from sample preparation and measurement protocols to the extraction of essential parameters like the distribution coefficient and net retention volume. Furthermore, the presentation highlights the evaluation of surface energy components (Eq. 1) using the Dorris-Gray and Schultz approaches, alongside the analysis of surface heterogeneity profiles.
To illustrate the technique's practical utility, we show case studies focusing on active pharmaceutical ingredients (APIs). Specifically, we examine how surface properties are influenced by mechanical processing, such as sieving, and how various crystallization strategies affect the overall surface energy of APIs. These examples underscore the capacity of iGC to detect minute surface variations that ultimately dictate the processing behavior and performance of the materials.

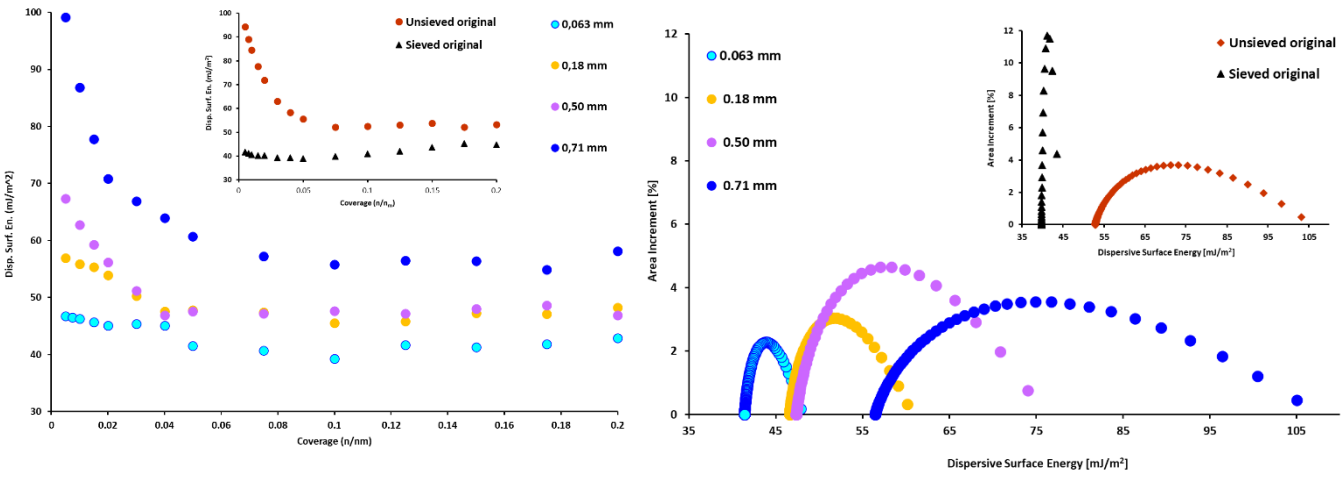

Figure 1 – Dispersive surface energy (profile – left; and distribution – right) of sieved and unsieved sample, larger graphs are for samples sieved through different sized sieves (0,063; 0,18; 0,50; 0,71 mm)

Ultimately, iGC stands out as a highly reproducible, sensitive, and versatile analytical instrument in surface science, capable of unlocking complex insights into surface chemistry that conventional techniques frequently fail to capture.

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