

Applicability of Specific Surface Area Determination on Pharmaceuticals by Inverse Gas Chromatography

Shasad Sharif, Lynn DiMemmo, Martha Davidovich, Beth Sarsfield

Solid-State Analysis Group, Analytical and Bioanalytical Development (ABD), Bristol-Myers Squibb Company, 1 Squibb Dr, New Brunswick, NJ 08902, USA.

Nitrogen adsorption (B.E.T. method) is the most commonly applied technique to measure the specific surface area (SSA) of active pharmaceutical ingredient (API) and excipient powders. The major limitation of the B.E.T. method is the requirement of large sample amounts for low surface area materials. Since the majority of APIs and excipients used in the pharmaceutical industry exhibit low surface areas this greatly limits the utility of the general B.E.T. method for pharmaceutical applications. The aim of this work was to evaluate the applicability of an alternative method for measuring SSA of API and excipients by inverse gas chromatography (IGC). With this technique, the SSA was measured in situ by injections of a single solute (suitable nonpolar probe) of increasing concentrations at constant temperature using finite dilution (IGC-FC). The solutes used for this investigation were n-alkanes: hexane, heptane, and octane. A model material, spherical glass beads, was selected to develop this technique, and evaluated by comparing the results with those obtained using the general B.E.T. method. Further, the developed method was validated by calculating the geometrical surface area of the glass beads from the true density and the surface weighted mean diameter, $D[3,2]$, as determined by optical microscopy. Lastly, a variety of excipients that exhibit a wide range of specific surface areas were selected to validate the IGC method and the resulting SSA data was compared to the results obtained by the general B.E.T. method. The IGC results obtained are in very good agreement with those obtained by the general B.E.T. method. In conclusion, the applicability of using IGC to determine SSA and its possible applications within the pharmaceutical industry was evaluated. The results demonstrated the utility of IGC to determine SSA, particularly during the early phase of development when materials are in short supply, by requiring at least 10-fold reduction in the quantity of sample required without sacrificing the data quality.