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Nanotechnologies — Silica nanomaterials — Specification of characteristics and measurement methods for nanoporous silica microparticles applied in liquid chromatography

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Contents

Page

Foreword

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Introduction

Owing to their excellent physicochemical properties, silica-based materials have been used in various fields, such as electronics, optics, and materials.[1] Silica materials with nanopores (1-100 nm) have widely been applied in separation due to their chemical inertness, naturally porous structure, large surface area, and reversible adsorption-desorption ability under certain circumstances.[2] These features also make it an ideal candidate as liquid chromatography packing materials since liquid chromatography is essentially based on selective adsorption and desorption of molecules in nanopores of stationary phases to achieve desired separation of target molecules.[3]

Originally, nanoporous silica materials as liquid chromatography media were mainly produced by sol-gel methodology.[4] The particles produced by this method had an irregular shape and broad size distribution, from nanometres to millimetres. Typically, those particles needed to be further separated by passing through a series of sieves with different meshes; thus irregular nanoporous silica particles, when used as liquid chromatography media, were usually labelled with mesh size to indicate their particle size distribution.[5] Nowadays, more advanced synthetic techniques enable the production of spherical silica particles for a new generation of liquid chromatography media. Compared to the irregular silica particles, spherical silica particles exhibit narrower size distribution, leading to more even column packing and better separation efficiency.[6] Also, the packing of spherical silica particles minimizes voids and variability inside the column bed, which can endure higher column pressure and flow rates and, consequently, are welcomed by engineers who desire higher throughput of products when using liquid chromatography for preparative purposes. Despite these advancements in particle morphology and packing performance, pure silica faces limitations in chemical stability under extreme pH conditions. Ongoing research has led to the development of spherical hybrid silica-based phases integrating organic moieties within the silica framework, offering enhanced chemical stability, reduced silanol interactions, and greater mechanical robustness. This represents an active technological direction aimed at expanding the operational range of silica materials. Currently, major chromatography suppliers offer hybrid silica products as part of their portfolio. Nevertheless, pure silica materials continue to be extensively utilized across diverse separation scenarios due to their well-established manufacturing processes, consistent performance profiles, and cost efficiency.

The particle size of nanoporous silica microparticles determine the separation efficiency when the particles are packed in liquid chromatography columns. Smaller particles provide better efficiency. Nevertheless, the column back pressure is inversely proportional to the size of the particles. So, when high resolution for complex samples or high-speed separation is desired, smaller particles packed in high-pressure columns are the best candidates. When loading capacity is of high importance, e.g. in preparative chromatography, larger particles are used to pack columns with larger volume and slower flow speed. The nanopores in silica microparticles play a key role in separation processes. Most of the surface area of silica particles used as liquid chromatography media is provided by the internal nanopores of the particles. Spherical particles will have larger surface area when the pore size decreases, which is more suitable for the separation of smaller molecules. Other factors influencing the chromatographic performance of nanoporous silica microparticles include bulk density, water content, surface silanol group density, etc.[7]

In common with other nanostructured materials, the manufacturing and material specification of nanoporous silica microparticles are complex. Small variations in the synthesis conditions during manufacturing and functionalization can lead to dramatic shifts in chromatographic properties. Moreover, characterization methods can vary between different manufacturers and are typically not mentioned in the document provided along with commercial products. Standardization of nanoporous silica microparticles for liquid chromatography is therefore critical to harmonize test methodologies and specifications across both pure and hybrid silica materials. Such standardization will enable users to compare or select the most suitable and qualified silica microparticles for their applications.