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Comparison of small size fully porous particles and superficially porous particles of chiral anion-exchange type stationary phases in ultra-high performance liquid chromatography: effect of particle and pore size on chromatographic efficiency and kinetic performance☆

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ABSTRACT

Recent advancements in particle design are common in reversed-phase liquid chromatography (RPLC), but in chiral separations their use is still sporadic in commercially available chiral stationary phases (CSPs). Due to reported lower mass transfer resistance, they might be a promising opportunity to increase efficiency and reduce time of analysis since the relatively higher mass transfer resistance term of CSPs caused by slow adsorption-desorption kinetics is the most performance-limiting factor in enantioselective chromatography. This study was dedicated to the evaluation of new support materials for *tert*-butylcarbamoylquinine (tBuCQN) based CSP to provide highly efficient and fast enantioseparations. As the main focus of this study, the chiral selector tBuCQN was immobilized on sub-2 μm fully porous particles (FPPs) and 2.7 μm superficially porous particles (SPPs) and their column performance in enantioseparation was evaluated in comparison to 5 μm FPPs by van Deemter and Knox analyses as well as kinetic plots using racemic Fmoc-Phe. Both new particle types outperformed the 5 μm FPP benchmark in terms of speed and efficiency, with wider pore materials (160 or 200 Å) being advantageous (over 90 or 120 Å). Basically decisive for the performance gain was the 10-times smaller mass transfer resistance. Furthermore, 2.7 μm 160 Å SPPs outperformed their fully porous sub-2 μm 120 Å counterpart (H_{minR} = 4.64 μm vs. H_{minR} = 8.94 μm) due to various parameters affording reduced plate height *h* of 1.7. Caused by the inaccessible core, separations were about 2-times faster. Packing of 2.7 μm core-shell particles provided a very homogeneous column bed, and, owing to its higher permeability, the column backpressure was much lower. It enables packing of longer columns providing theoretically separation efficiencies of up to 10^6 plates per m (as indicated by kinetic plots) and versatile use without the necessity of UHPLC systems. Investigating the effect of particle size reduction (FPPs: 5 μm, 3 μm, 1.7 μm; SPPs: 2.7 μm, 2 μm) and wider pores (FPPs: 120 Å, 200 Å; SPPs: 90 Å, 160 Å), a significantly reduced mass transfer resistance was the driving force for performance gain. Individual contributions of peak dispersion were deconvoluted for 5 μm FPP CSP and confirmed that slow adsorption-desorption kinetics is the most significant contribution to peak broadening in this chromatographic system.

1. Introduction

The surface chemistries of modern chiral stationary phases (CSPs) have essentially been developed in 1980s and early 1990s [1]. Amongst others, polysaccharides [2], plasma proteins [3,4], macrocyclic antibiotics [5], cyclodextrins [6], chiral crown ethers [7,8], low-molecular synthetic selectors such as Whelk O1 [9], cin-

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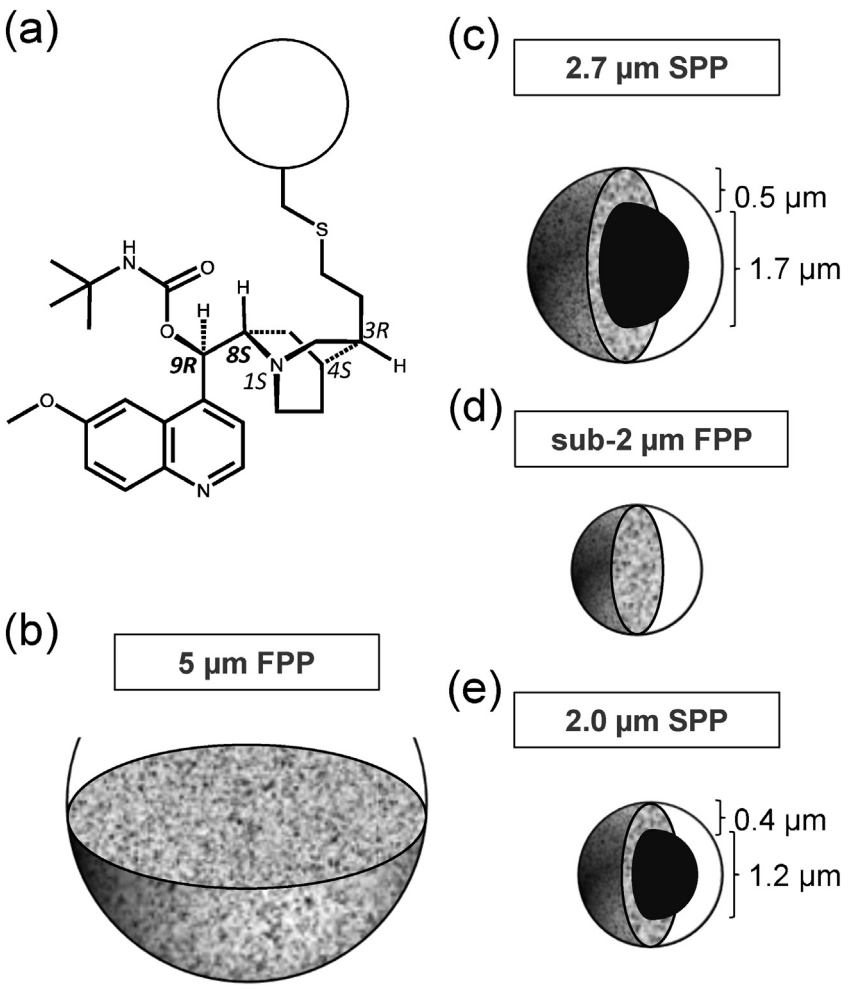

Fig. 1. Surface chemistry of chiral anion-exchange type tBuCQN CSP (a), 5 µm fully porous particle benchmark support (b), 2.7 µm superficially porous particle support with 1.7 µm solid core and 0.5 µm porous shell (c), 1.7 µm fully porous particles (sub-2 µm) (d), and 2.0 µm superficially porous particles with 1.2 µm solid core and 0.4 µm porous shell (e).

Table 1
Summary and characteristics of the tBuCQN CSPs.

particle type	CSP	d_P[1]	pore size[2]	specific surface area	selector coverage[3]	
		[µm]	[Å]	[m^2/g]	[µmol/g]	[µmol/m^2]
FPP	FPP, 5µm, 120Å	4.4	127	325	380	1.17
	FPP, 3µm, 120Å	3.2	125	337	415	1.23
	FPP, 3µm, 200Å	2.9	212	210	232	1.10
	FPP, 1.7µm, 120Å	2.1	135	327	276	0.84
	FPP, 1.7µm, 200Å	2.3	226	201	301	1.50
SPP	SPP, 2.7µm, 90Å	2.7	82	122	170	1.39
	SPP, 2.7µm, 160Å	2.7	156	77	88	1.14
	SPP, 2µm, 160Å	2.0	158	71	110	1.55

[1] Particle size determined by Coulter Counter Method (data from silica supplier).
[2] Pore size determined by B.E.T. (data from silica supplier).
[3] Selector coverage calculation based on nitrogen amount determined by elemental analysis.

chonan carbamates [10] immobilized on 5 or 7 µm fully porous particle (FPP) silica materials paved the way towards the state-of-art in nowadays enantioselective chromatography. Columns packed with 5 µm FPP-based CSPs typically reach around 30,000 theoretical plates per meter. This is quite modest if compared to corresponding RP columns. In spite of ready availability of smaller 3 µm FPP particles since long time such supports were introduced for CSPs only in the 2000s and still not all commercial CSP types have yet been made available on 3 µm FPP support basis. However, recent years have seen some activities to introduce modern particle technologies such as sub-2 µm FPP and sub-3 µm superficially porous particles (SPPs) in the field of chiral separation [11–14] (Fig. 1).

In the mid 1990s, sub-2 µm nonporous silica (NPS) particles became available. They have been evaluated for enantiomer separations as well. Quinine carbamate selectors were immobilized on such 1.5 µm NPS and these particles packed into 33 mm x 4.6 mm ID columns. Fast enantiomer separations within a minute or so,

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