Chemical Engineering Science 107 (2014) 158–164

Contents lists available at ScienceDirect

Chemical Engineering Science

journal homepage: www.elsevier.com/locate/ces

Nanopillar array with multi-scale inter-pillar spacing as chromatography stationary phase support: Theoretical performance evaluation

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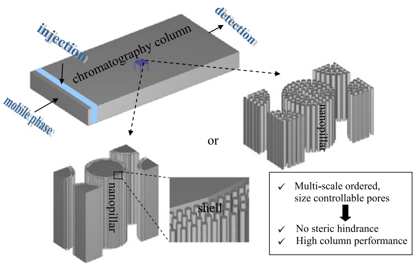
HIGHLIGHTS

- Nanopillar arrays with multiscale inter-pillar spacing as stationary phase support.
- Nanopillar arrays can be used to play the role of porous or core–shell pillars.
- Columns with multiscale, ordered, size controllable pores have better performance.
- Possible velocity slip will improve the column performance.

GRAPHICAL ABSTRACT



ARTICLE INFO

Article history:
Received 25 August 2013
Received in revised form
12 November 2013
Accepted 7 December 2013
Available online 16 December 2013

Keywords:
Nanopillar
Stationary phase
Ordered
Slip
Column performance

ABSTRACT

Nanopillar arrays with nanoscale inter-pillar spacing can be fabricated with increasingly high precision in recent years. We propose to use nanopillar arrays with multi-scale inter-pillar spacing to play the role of porous microstructures in columns for pressure driven liquid chromatography. The pattern of the nanopillar array is adjusted to create special "core–shell" or "totally porous" structures with multi-scale ordered pores. We predict the column performance and the pressure drop of the hypothetical columns by a theoretical model with the aid of the pore scale numerical simulation. The prediction indicates that hypothetical columns have better column performance than that of a real column filled with vertically aligned "core–shell" micropillars with ordered inter-pillar pores but disordered intra-pillar pores. We attribute the better performance of hypothetical columns to the multi-scale ordered, size controllable pores in the special "core–shell" or "totally porous" structures. We also investigate the effect of the velocity slip that may occur at hydrophobic nanopillar surfaces and show that further column performance improvement and flow rate enhancement can be expected.

1. Introduction

Fast development of material science makes it possible to create complex micro/nanostructures with high precision. Controlling the flow pattern of fluid and the transport of solutes or particles or macromolecules in the fluid by micro/nanostructures attracts much attention recently (Amini et al., 2013). Many processes relate to the flow pattern, such as the separation of solutes or particles. Separation usually plays an important role in many areas, such as the biopharmaceuticals, chemistry and chemical engineering. Chromatography is one of the most widely used separation methods. The performance of chromatography columns highly depends on the flow pattern of fluid and the diffusion path of solutes inside columns and thus depends on the structure of the stationary phase support in columns. Hence, it is possible to

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http://dx.doi.org/10.1016/j.ces.2013.12.010

enhance the chromatography column performance by suitably designing the structure of stationary phase supports.

The stationary phase supports of most commercial chromatography columns are particles or monoliths. The inter-particle pores and the inter-skeleton pores are usually randomly distributed. The structure of the stationary phase support is hard to be controlled. In recently years, columns filled with micropillars (De Malsche et al., 2012) or colloidal crystals (Rogers and Wirth, 2013; Wei et al., 2012) in ordered pattern were fabricated. The diameter and the pattern of micropillars and the diameter of colloidal crystals can be adjusted in a range. Theoretical analysis revealed that the ordered microstructure of the stationary phase can be used to realize the high performance separation if the confinement of the column wall is suitably treated (Gzil et al., 2003; Yan and Wang, 2013). An experimental study (De Malsche et al., 2012) on columns filled with vertically aligned, ordered micropillar arrays revealed that the plate number was more than 10^6. Extremely low (submicron) plate height was reported for columns filled with nanoscale silica colloidal crystals (Wei et al., 2012). Although a series of problems remain to be solved, such as the detection, the ordered micropillars and ordered nanoparticles show great potential as the stationary phase support of chromatography columns.

The stationary phase support of chromatography columns is usually totally porous or partially porous to increase the retention capacity. Currently, the method of fabricating chromatography columns filled with totally porous micropillars has not been reported. Various methods (De Malsche et al., 2008; Detobel et al., 2009; Fonverne et al., 2011; Sukas et al., 2013) were reported to create core–shell micropillars. The shell is porous and the pore size is much less than the inter-pillar pores. The column performance depends on the solute band broadening. The solute band broadening in columns filled with core–shell micropillars is contributed from the convection and diffusion in the inter-pillar pores, the diffusion and adsorption in pores of the micropillar's shell and the interfical mass transfer at the interface between the two-scale pores. Reported columns filled with ordered micropillars have ordered inter-pillar pores but disordered pores in the porous shell (De Malsche et al., 2008; Sukas et al., 2013). The ordered inter-pillar pores contribute smaller band broadening than random inter-particle pores. It is straightforward to think about whether there are some methods to decrease the band broadening contributed by diffusion and adsorption in the porous shell of micropillars. Previous research reported that the steric hindrance effect makes the diffusivity of solute molecules inside porous structures be smaller than that in the free bulk fluid (Armatas, 2006; Dechadilok and Deen, 2006; Langford et al., 2006; Wernert et al., 2010). The steric hindrance effect relates to the size of solute molecules and the size of pores. Hence, the pore size distribution in the porous shell of micropillars is an important factor of the column performance. In addition, the effective diffusivity of solutes in stationary phase supports is influenced by the pore connectivity (Armatas, 2006). Therefore, the chromatography column performance may be enhanced if the pore size distribution and the pore connectivity in the porous shell of micropillars can be easily controlled.

Many methods have been developed to fabricate nanopillar arrays with high precision in recent years. Nanopillar arrays with inter-pillar spacing as small as ~15 nm and with the aspect ratio larger than 20 were fabricated by the block copolymer inclusion method and the inductively coupled plasma etch method as reported by Ghoshal et al. (2012). Different values of the inter-pillar spacing and different patterns of nanopillars can be designed and created by the method (Ghoshal et al., 2012). Hence, the fabrication method (Ghoshal et al., 2012) or other ones developed in the near future may be used to design stationary phase support of chromatography columns. A bundle of nanopillars may be used to replace the porous shell or to play the role of a totally porous pillar. The ordered and size controllable features of nanopillar array are expected to provide simpler pore connectivity than currently available porous shell structures and to eliminate the steric hindrance effect.

In this paper, we propose several hypothetical stationary phase supports composed of nanopillar arrays and evaluate the column performance by a volume averaging method model (Yan et al., 2010) with the aid of the pore scale simulation. As a theoretical analysis, we also discuss the effect of velocity slip that may occur at hydrophobic nanopillar surfaces on the flow rate enhancement and the column performance. Since we focus on the theoretical potential of the new chromatography stationary phase support, we don't consider the stationary phase coating uniformity, the material and the physico-chemical properties of the pillar, the flow heterogeneity near the column's wall and the extra-column effect caused by the injection and the detection.

2. Column performance prediction method

The column performance of hypothetical columns is predicted by a volume averaging method model (Yan et al., 2010). The liquid mobile phase is driven by pressure. The support in the column is coated with a thin, uniform stationary phase. The inter-pillar spacing is assumed to be much larger than that of solute molecules, so that the diffusivities of solute in two-scale pores are the same.

The velocity profile in columns is calculated by solving the Stokes equation:

$$\nabla p = \mu \nabla^2 \mathbf{v} \tag{1}$$

Depending on the properties of the fluid and the support's surface, velocity slip may not be neglected, and the slip velocity $\mathbf{v}_{\text{slip}}$ at the support's surface is (Eijkel, 2007)

$$\mathbf{v}_{\text{slip}} = \frac{L_s}{\mu} \boldsymbol{\tau}_{n,t} \tag{2}$$

Considered that the support structure in the hypothetical columns is periodic, the velocity profile is obtained by solving Eq. (1) in a three dimensional unit computational cell with periodic and symmetric boundary conditions at the boundaries of the unit cell. Detailed information of the unit cell will show in the following section.

The plate height of a given column support structure is (Yan et al., 2010)

$$H = \frac{2D_{xx}}{\langle u \rangle} \tag{3}$$

The lumped longitudinal dispersion coefficient D_{xx} as a function of the velocity profile and the retention factor is (Yan et al., 2010)

$$\begin{aligned} D_{xx} = {} & D_m \left[1 + \tfrac{1}{V_m} \textstyle\int_{A_p} n_{\mathrm{L}} f_0 \, dA + \tfrac{k'}{1+k'} \tfrac{1}{V_m} \textstyle\int_{A_p} n_{\mathrm{L}} f_1 \, dA \right] + \tfrac{1}{V_m} \textstyle\int_{V_m} (\langle u \rangle - u) f_0 \, dV \\ & + \frac{k'}{1+k'} \left\{ \frac{1}{V_m} \int_{V_m} (\langle u \rangle - u) f_1 \, dV - \frac{1}{V_m} \int_{V_m} \langle u \rangle f_0 \, dV + \frac{1}{A_p} \int_{A_p} \langle u \rangle f_0 \, dA \right\} \\ & + \left(\frac{k'}{1+k'} \right)^2 \left\{ - \frac{1}{V_m} \int_{V_m} \langle u \rangle f_1 \, dV + \frac{1}{A_p} \int_{A_p} \langle u \rangle f_1 \, dA \right\}. \end{aligned} \tag{4}$$

Detailed information on the closure variables of f_0 and f_1 is shown in the Supplementary material.

The relationship among the average longitudinal velocity $\langle u \rangle$ and the widely used superficial velocity u_s and the interstitial velocity u_i in chromatography related literature is

$$\langle u \rangle = u_s / \varepsilon_t = u_i \times \varepsilon / \varepsilon_t \tag{5}$$