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Effects of structure on the performance of latex nanoparticles as a pseudostationary phase in electrokinetic chromatography

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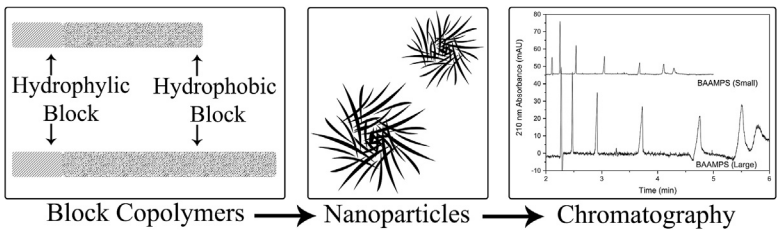
HIGHLIGHTS

- RAFT controlled polymerization is used to generate several amphiphilic nanoparticles.
- Nanoparticles with systematic variations in structure and chemistry are generated.
- Nanoparticles evaluated as pseudostationary phases in electrokinetic chromatography.
- Nanoparticle structure affects chromatographic selectivity and performance.
- Anomalous dispersion and band broadening is reported and discussed.

GRAPHICAL ABSTRACT



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ABSTRACT

The fundamental relationships between the structure and chemistry of latex nanoparticles synthesized by reversible addition fragmentation chain transfer (RAFT) controlled living polymerization and their subsequent performance as pseudostationary phases (PSP) are reported in this paper. RAFT enables the rational optimization of latex nanoparticle pseudostationary phases and control of the behavior of the PSP. Nanoparticles comprised of amphiphilic diblock copolymers of 2-acrylamido-2-methylpropane sulfonic acid-derived ionic/hydrophilic blocks and butyl- ethyl- or methyl-acrylate-derived hydrophobic blocks were synthesized in two sizes. The mobility, methylene selectivity, and efficiency of each of the six pseudostationary phases are reported, as well as the relationship between monomer quantity and NP size. Linear solvation energy relationships are reported and compared to SDS micelles and previous nanoparticle pseudostationary phases. The solvation characteristics and selectivity of nanoparticle pseudostationary phases is shown to be affected primarily by the structure of the hydrophobic copolymer block. Butyl acrylate nanoparticles 17 nm in diameter are found to provide the best overall separation performance with over 500 thousand theoretical plates generated in 6 min separations.

Abbreviations: AMPS, 2-acrylamido- 2-methyl-1-propane sulfonic acid; BAAA, Butyl Acrylate/ Acrylic Acid; BAAMPS, Butyl Acrylate/ 2-acrylamido- 2-methyl-1-propane sulfonic acid; EAAMPS, Ethyl Acrylate/ 2-acrylamido- 2-methyl-1-propane sulfonic acid; MAAMPS, Methyl Acrylate/ 2-acrylamido- 2-methyl-1-propane sulfonic acid; mCTA, macro chain transfer agent; LSER, inear solvation energy relationship; NP, nanoparticle; PSP, pseudostationary phase; RAFT, radical addition-fragmentation chain transfer.

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1. Introduction

Since the introduction of electrokinetic chromatography (EKC) over 30 years ago [1], the field has seen significant development and refinement of available methods, techniques, and hardware [2]. Extensive research has been conducted on the pseudostationary phase (PSP) materials that effect EKC separations, leading to unique separation selectivity, broader applicability, and improved compatibility with mass spectrometric (MS) detection.

Sodium dodecyl sulfate (SDS) micelles have been utilized as a PSP since the introduction of EKC, and remain the most widely utilized PSP. Micellar SDS has many positive attributes that recommend its use as a PSP. These include that SDS: 1) is available in high purity, 2) provides consistent EKC performance, 3) has good electrophoretic mobility as a PSP, and 4) has had its EKC performance extensively researched and modeled.

There are various EKC applications, however, for which SDS and other micellar PSPs are not suitable. First, the separation of extremely hydrophobic analytes requires significant organic modifier in the background electrolyte (BGE), which cannot be used with micellar PSPs. Organic modifiers dramatically reduce the stability of micelles and increase the critical micelle concentration (CMC) of micellar PSPs [3–5]. Second, the speed of separations may be hindered with use of micellar PSPs. Micellar EKC solutions contain free surfactant that does not contribute to the separation but does contribute to typically high conductivity. This conductivity limits the electrical potential that may be applied before Joule heating begins to degrade efficiency [6], curtailing the speed of separations. Third, the micellar surfactants complicate the interfacing of EKC with electrospray ionization (ESI) and mass spectrometric (MS) detection due to ionization suppression [7] and high background signal. Attempts to employ micellar PSPs with MS detection require complex techniques such as partial filling [8–12], where only part of the capillary is filled with PSP to prevent elution of the PSPs alongside the analytes. However, perhaps the greatest limitation of micellar PSPs is that they provide limited opportunity to optimize selectivity of the PSP to the chromatographic task.

Many methods to address these innate limitations of micellar PSPs have been reported including: 1) polymerization of the micelle core to produce molecular micelles, addressing the limitation of stability in organically modified BGEs [13–15] and ionization suppression in ESI-MS [16], 2) random copolymer PSPs that provide access to alternate PSP selectivities via monomer selection [17–19], and 3) functionalization of the ionic shell of the micelle, or particle, to improve mobility and provide greater selectivity, including enantiomeric selectivity [20–23]. These advances individually mitigated many of the limitations of micellar PSPs, but no one PSP had emerged that combined all of the desired PSP properties in a single material.

In the early 2000s, latex nanoparticles (NP) were first reported as PSPs and early work illustrated their potential as a PSP, including compatibility with ESI-MS [24–27]. With the introduction of controlled living polymerization methods, which provided synthetic control over NP chemistry and architecture, the potential for a single material that could simultaneously fulfill all the various requirements of a PSP was realized.

Several authors have previously reported the synthesis of polymeric latex NPs from amphiphilic di-block polymers by employing recent advances in Reversible Addition Fragmentation Chain Transfer (RAFT) living polymerization techniques [28–30]. The di-block copolymers are thought to aggregate to form NPs with a hydrophilic/ionic shell surrounding a hydrophobic core.

We have recently demonstrated that these NPs provide PSP performance at or above that of SDS, while simultaneously providing the ability to control selectivity via monomer selection [31–33]. Incorporating stronger acid moieties in the hydrophilic block polymer provides high PSP mobility. The hydrophobic core of the NP demonstrated the potential to be “tuned” to provide the desired selectivity [33]. These latex NP PSPs have demonstrated compatibility with ESI-MS detection [32], organic modifiers [32], and are active over a wide pH range [33]. We have also evaluated cationic forms of these NPs and demonstrated good performance is provided regardless of whether they are cationic or anionic [34].

In this work, we take advantage of the unprecedented control over the size and chemistry of latex NPs afforded by the RAFT polymerization technique to synthesize latex NPs with systematic variation in structure. From the performance of an ensemble of these NP PSPs, we report for the first time fundamental investigations into the relationships between latex NP core chemistry and size, and the resulting EKC performance and selectivity of the NP PSP. Latex NPs with hydrophobic cores consisting of butyl-, ethyl-, and methyl-acrylate provide three degrees of core hydrophobicity. Each of these three core chemistries of NP was synthesized in small (average 15 nm) and large (average 126 nm) diameters. The ionic shells of the NPs are formed from 2-Acrylamido-2-methylpropane sulfonic acid (AMPS) monomer, which provides excellent electrophoretic mobility even at low pH [33]. The composition of the NP also provides the naming convention: NPs with a poly(butyl acrylate) core and poly(AMPS) shell are referred to as BAAMPS. Methyl and ethyl acrylate NPs are referred to as MAAMPS and EAAMPS respectively.

2. Materials and methods

2.1. Synthesis

Synthesis utilized 2-acrylamido-2-methylpropane sulfonic acid (AMPS) (Aldrich, 99%), 4,4′-azobis(4-cyanovaleric acid) (V-501, Aldrich, ≥98.0%), butyl acrylate (Aldrich, 99%), ethyl acrylate (Aldrich, 99%), 1-butanethiol (Aldrich, 99%), carbon disulfide (Aldrich, 99.9%), 2-bromopropionic acid (Aldrich, 99%), hexane (EMD, HPLC Grade), sodium hydroxide (EMD, GR ACS), and 2000 MWCO Spectra/Por regenerated cellulose dialysis membrane. All water used in syntheses was distilled and deionized 18 MΩ water (Barnstead D8991). Compounds were characterized utilizing a 400 MHz Bruker NMR, and a Malvern Zetasizer Nano ZS dynamic light scattering (DLS) utilizing the supplied method for latex NP sizing. For DLS analysis, latex NP suspensions were diluted in 10 mM Tris buffer at pH 7.2 to replicate EKC solvent conditions.

2.1.1. Chain transfer agent (CTA)

RAFT polymerization requires an amphiphilic chain transfer agent (CTA) to control polymerization and generate living polymers. 2-{((butylsulfanyl)-carbonothioyl)sulfanyl}propanoic acid (CTA) was synthesized by the Ferguson procedure [28] as previously reported [33]. 3.6 g (40 mM) butylthiol, 6.4 g of 25% w/v NaOH, and 2.0 mL of acetone were stirred for 30 min. 2.7 mL (45 mM) carbon disulfide was added and stirred for 30 min before the solution was cooled with an ice bath to maintained the temperature at less than 30 °C while 6.3 g (41 mM) 2-bromopropionic acid was added followed by 6.6 g of 25% w/v NaOH. The ice bath was removed and the reaction was stirred overnight. All base was neutralized with 10 M HCl and the CTA was purified by extracting into hexane and evaporated to dryness in vacuo. Powdery, bright yellow CTA was recovered at 90.3% yield. Synthesis of the CTA is confirmed by proton NMR with chemical shifts that match literature values [28].

2.1.2. Macro chain transfer agent (mCTA)

Latex NPs are generated through the synthesis of A-B block

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