



Investigation of mass transfer properties and kinetic performance of high-efficiency columns packed with C₁₈ sub-2µm fully- and superficially porous particles

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List of non-standard abbreviations: EMT = Effective Medium Theory; FPP = fully porous particle; ISEC = inverse size exclusion chromatography; nPSD = narrow particle size distribution; SPP = superficially porous particle; UHPLC = ultra-high performance liquid chromatography

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Abstract

Three columns respectively packed with 2.0 μm superficially porous particles, 1.7 μm fully porous particles and monodisperse 1.9 μm fully porous particles with narrow particle size distribution have been deeply characterized from a kinetic point of view. The 1.9 μm column showed excellent kinetic performance, comparable to that of the superficially porous one. These two columns also exhibit flatter c-branches of the van Deemter curve compared to the 1.7 μm fully porous particles column, resulting in smaller loss of efficiency when they are operated at higher flow rates than the optimal ones. The independent evaluation of each contribution to band broadening has revealed that the difference in kinetic performance comes from the very small eddy dispersion contribution on the 1.9 μm column, surprisingly even lower than that of the superficially porous one. This finding suggests a very good packing of the monodisperse 1.9 μm column. On the other hand, the potential of 1.7 μm fully porous particles is completely broken down by the strong frictional heating effect already arising at relatively low flow rates.

1. Introduction

In the last twenty years, Liquid Chromatography (LC) has been involved in a revolution that has completely changed the perspectives of this analytical technique in terms of efficiency of separation and speed of analysis. Indeed, on the one hand, geometry, size and purity of packing materials have been optimized in order to allow for better performance and faster analysis than those achievable with 2.5-5 μm fully porous particles (FPPs) commonly employed until then. On the other hand, advancement in instrumentation design has allowed to produce modern apparatus with minimized extra-column contribution and suitable to reach very high pressures (UHPLC).

The most effective leap in performance improvement is represented by the decrease of fully porous particle diameter down to sub-2 μm range. Columns packed with these particles are able to produce very narrow peaks with state-of-the-art efficiency easily larger than 300,000 N/m. However, due to their very low permeability, the exploitation of the full advantage of these columns requires modern UHPLC equipments [1–4].

Besides these advancements, particle manufacturers started working also on the morphology of the porous materials in order to develop alternative stationary phases to FPPs. Different types of adsorbents were revamped. It is the case of monoliths, that has started to be increasingly diffused about fifteen years ago after having been used only for niche applications in gas or liquid chromatography for a long time [5]. The advantage of these adsorbents, characterized by a very high bed porosity, is to allow for high speed and low permeability at the same time [6]. However, due to the very reduced surface area, monoliths are in general less retentive than packed beds. The introduction of second-generation superficially porous particles (SPPs), or alternatively called core-shell particles, has undoubtedly marked the advent of the most important alternative to sub-2 μm FPPs [7–

15]. Produced with innovative techniques which allows to obtain particles characterized by very narrow particle size distribution (nPSD), these materials combine the benefit of a high permeability (allowing the use of SPP columns on common HPLC instruments) and very small band broadening [16,17]. As a matter of fact, columns packed with 2.7 μm SPPs provide similar performance to that of sub-2 μm FPPs. The presence of a solid core hinders longitudinal diffusion and reduces mass transfer resistance with respect to FPPs. Moreover, it has been thoroughly demonstrated that also the contribution of eddy dispersion is smaller on these columns, even though the reasons behind this evidence are still under investigation. The roughness of SPPs is the most accredited hypothesis [1, 18], possibly in combination with the nPSD [19–21].

It is worth mentioning that the introduction of SPPs, whose PSD relative standard deviation (RSD) is about 5% or smaller, rekindled the debate about the impact of PSD on column efficiency started at the end of 1960s. In that period, independent studies from different groups evidenced that as long as PSD is smaller than 40% around the mean, efficiency is not altered [22–25]. One decade later, Dewaele and Verzele investigated the effect of PSD by preparing different composition of 3 and 8 μm . Their results confirmed that PSD has no effect on efficiency by running separation at the optimum velocities [26]. Nowadays, the literature regarding this very complex issue is rather contradictory and fragmented [27]. For instance, Cabooter et al. evidenced a quasi-linear correlation between PSD and efficiency [20].

Horváth and coworkers found that the impact of PSD on column efficiency is crucial only for large macromolecules since it mostly affects intraparticle diffusion [28]. From detailed morphological studies based on the simulation of the fluid inside a reconstructed packed bed, Tallarek's group pointed out that when PSD is smaller than 25%, its effect on chromatographic bulk dispersion is negligible, especially if compared to that of the

interstitial bed porosity [29–32]. However, efficiency is greatly influenced by wall effects, which depends on packing procedure and particle properties (including their PSD). Still, studies by Gritti and Guiochon, who prepared columns by mixing 3 and 5 μm particles confirmed the same findings as 40 years ago, that is that there is no effect on plate height as long as PSD is maintained below 40% [33]. This result was also confirmed by Liekens et al., who found only a small decrease of kinetic performance when 3 and 5 μm particles were added for a 25 wt% to a 1.9 μm commercial batch. The deterioration of efficiency become evident when 50 or 75 wt% of larger particles were added [34]. Some of the author of this work recently explored the kinetic performance of two columns packed with sub-2 μm nPSD C18 FPPs with different pore size. Results of that investigation revealed an extremely low eddy dispersion in both cases [35, 36].

In the present work, the kinetic performance of one of three C₁₈ UHPLC columns respectively packed with 1.7 and 1.9 μm FPPs and 2.0 μm SPPs has been investigated. The columns have been fully characterized from a geometrical point of view and their chromatographic performance has been evaluated by using a mixture of benzene derivatives with different retention factors. Each individual contribution to band broadening has been independently calculated by combining van Deemter curve measurements, peak parking experiments and Maxwell's EMT model of diffusion in porous media [37].

2. Theory

Kinetic performance of columns is usually evaluated through the well-known van Deemter equation. The modern expression of this equation involves the use of reduced coordinates which allow to compare columns packed with different particle geometry and

measurements referred to different analytes. The van Deemter equation in reduced coordinates is written as [38]:

$$h = a(v) + \frac{b}{v} + c_s v + h_{heat} \quad (1)$$

where $h = H/d_p$ is the reduced plate height, being H the plate height and d_p the particle diameter. v is the reduced interstitial velocity, defined as:

$$v = \frac{u_e d_p}{D_m} \quad (2)$$

where D_m is the bulk molecular diffusion coefficient and $u_e (= F_v / \pi r_c^2 \varepsilon_e$, being F_v the flow rate, r_c the column radius and ε_e the interstitial porosity) is the interstitial velocity, *i.e.* the velocity of the mobile phase moving around and between particles (but not through them) [39].

Eq. 1 takes into account the contributions of the different mass transfer phenomena that could potentially lead to band broadening during a chromatographic run. In the case of RP-LC separations they are: the eddy dispersion ($a(v)$), the longitudinal diffusion (b/v), the solid-liquid mass transfer resistance across the stationary phase ($c_s v$) and the additional term describing frictional heating (h_{heat}) due to the friction generated by the stream of mobile phase moving along the bed, especially pronounced with columns packed with fine particles.

All these terms can be independently evaluated by coupling simple chromatographic experiments with proper models of diffusion in composite porous media [12, 37, 40–43].

The easiest contribution to be determined is longitudinal diffusion. The b -term describes band broadening in absence of flow, as its contribution is exclusively due to the diffusion of the analyte molecules through the packed bed and the interstitial volume. For this reason, the estimation of this term is usually made through stop-flow measurements (peak parking).

During these experiments, the analyte molecules are injected into the system and when they reach approximately the middle of the column, the flow is suddenly switched off to let them freely diffuse into the packed bed in absence of flow [38, 44–46]. In reduced coordinates, b is given by:

$$b = 2(1 + k_1) \frac{D_{eff}}{D_m} \quad (3)$$

where D_{eff} ($= \Delta\sigma_x^2/2\Delta t_p$, being σ_x^2 the spatial peak variance and t_p the parking time) is the effective diffusion coefficient and k_1 is the zone retention factor, defined as:

$$k_1 = \frac{t_R - t_e}{t_e} \quad (4)$$

where t_R is the retention time and t_e the time spent by the analyte in the interstitial volume.

Under the ergodic hypothesis [47–49], k_1 can also be expressed as:

$$k_1 \equiv \frac{n_{part}}{n_e} = \frac{1 - \varepsilon_e}{\varepsilon_e} [\varepsilon_p + (1 - \varepsilon_p)K_a](1 - \rho^3) \quad (5)$$

where n_{part} and n_e are the number of molecules in the particle volume and in the interstitial volume, respectively, and K_a is the equilibrium constant of the sample between the mobile and the stationary phase. ρ is the ratio between the core radius (r_{core}) and the particle radius (r_p), indeed ρ is 0 for fully porous particles and $\rho = 1$ for non-porous particles. Finally, ε_p is the particle porosity, *i.e.* the fraction of the particle volume occupied by pores [50]:

$$\varepsilon_p \equiv \frac{V_{pores}}{V_{part}} = \frac{\varepsilon_t - \varepsilon_e}{(1 - \varepsilon_e)(1 - \rho^3)} \quad (6)$$

with V_{pores} and V_{part} the pore and the particle volume, respectively, and ε_t ($= V_0/V_{col}$, being V_0 the column void volume) is the total column porosity [51].

Moreover, k_1 is connected to the more often employed phase retention factor, k ($= (t_R - t_0) / t_0$, being t_0 the void time) through the following relationship [11, 52]:

$$k_1 = \frac{(1 + k)\varepsilon_t}{\varepsilon_e} - 1 \quad (7)$$

In order to estimate all the contributions to band broadening, results from peak parking experiments need to be interpreted in the light of a suitable model describing the effective diffusion of analytes in packed beds. Among the many models, the more physically-sound expression of effective diffusion in porous media is given by the Effective Medium Theory (EMT) [52–54]. The Maxwell's expression of EMT has been applied in this work. According to this model, D_{eff} can be described as follows [37]:

$$D_{eff} = \frac{1}{\varepsilon_e(1 + k_1)} \left[\frac{1 + 2(1 - \varepsilon_e)\beta}{1 - (1 - \varepsilon_e)\beta} \right] D_m \quad (8)$$

where β is the polarizability constant, defined as:

$$\beta = \frac{\alpha_{part} - 1}{\alpha_{part} + 2} \quad (9)$$

with $\alpha_{part} = D_p / D_m$ being the ratio between the intra-particle diffusivity, D_p , and the bulk diffusion coefficient, D_m . D_p is correlated to the diffusion coefficient in the porous zone (D_{pz}) through the following equation:

$$D_p = \frac{2K_p D_{pz}}{2 + \rho^3} \quad (10)$$

where K_p is the whole-particle based equilibrium distribution constant. The c_s term in Eq. 1 describes the mass transfer resistance across the particles in the stationary phase. This term, calculated by Kaczmarek [55], is velocity-independent, since there is no flux inside the particles, and it is written as:

$$c_s = \frac{1}{30} \frac{\varepsilon_e}{1 - \varepsilon_e} \left[\frac{k_1}{1 + k_1} \right]^2 \frac{1 + 2\rho + 3\rho^2 - \rho^3 - 5\rho^4}{(1 + \rho + \rho^2)^2} \frac{D_m}{D_p} \quad (11)$$

Finally, the eddy dispersion term, $a(v)$ in Eq. 1, describes the band broadening related to the irregularities of the stream path in the packed bed. It includes trans-channel eddy dispersion, short-range inter-channel eddy dispersion and trans-column eddy dispersion [35]. In achiral systems, $a(v)$ can be determined by subtracting the values of b and c_s (estimated by Eqs. 3 and 11, respectively) from accurately measured h values. By ignoring the impact of frictional heating, this leads to [38, 40]:

$$a(v) = h - \frac{b}{v} - c_s v \quad (12)$$

3. Materials and Method

3.1 Columns and materials

In this work three UHPLC C₁₈ columns with the same dimensions (100 × 3mm, L × I.D.) but packed with particles of different geometry were used. Titan C₁₈ column (FPP-1.9) packed with monodisperse 1.9 μm FPPs, characterized by a narrow particle size distribution with an RSD of about 6% [35], (120 Å pore size, 300 m²/g specific surface area) was generously donated by Supelco Analytical (Merck, USA). Acquity BEH C18 (FPP-1.7) packed with 1.7 μm FPPs (130 Å pore size, 185 m²/g specific surface area) was from Waters (Milford, MA, USA). Finally, Ascentis Express C₁₈ column (SPP-2.0) packed with 2.0 μm SPPs (90 Å pore size, 120 m²/g specific surface area, $\rho = 0.6$) was from Merck/Sigma-Aldrich (Milan, Italy). A 33 × 4.6 mm Micra column (Eprogen, Inc., USA) packed with 1.5 μm non-porous silica particles was purchased by DBA Italia s.r.l. (Italy) and was used in order to estimate bulk molecular diffusion coefficients. Fourteen polystyrene standards from Supelco Sigma-Aldrich (Milan,

Italy) with molecular weights 500; 2000; 2500; 5000; 9000; 17 500; 30 000; 50 000; 156 000; 330 000; 565 000; 1 030 000; 1 570 000; and 2 310 000 were employed for ISEC measurements. Nitrobenzene, benzene, toluene, butylbenzene, acetonitrile and tetrahydrofuran were from SigmaAldrich (St. Louis, MI, USA) and ultra-high quality Milli-Q water was obtained by a Milli-Q water purification system (Millipore).

3.2 Equipment

A Waters Acquity UPLC, controlled by Empower 3 software and equipped with a binary solvent delivery system, an autosampler, a column thermostat, a photodiode array detector with a 500 nL cell, was used for the determination of the van Deemter curves. The equipment was operated under still-air [56, 57] and quasi-adiabatic conditions. The maximum back pressure reachable by the system is 1000 bar. To reduce the extra-column contributions, two 250 × 0.075 mm nano-Viper capillary tubes (Thermo Scientific) were used for the connections of injector-column and column-detector. The extra column peak variance, measured from the injector needle port to the detector cell, was $1.2 \mu\text{L}^2$ (calculated through peak moments) at a flow rate of 1 mL/min. ISEC and peak parking experiments were carried out on an Agilent 1100 Series Capillary LC system equipped with a binary pump system, an autosampler, a column thermostat and a photodiode array detector.

3.3 Inverse Size Exclusion Chromatography

Tetrahydrofuran was used as the mobile phase [58] for Inverse Size Exclusion Chromatography (ISEC) experiments. Injection volume was set at 2 μL , flow rate was 0.2 mL/min and detection wavelength was 254 nm. Retention volumes corrected for the extra-

column contribution were plotted against the cubic root of the molecular weight, M_w . The interstitial volume, V_e , was calculated by extrapolating to $M_w = 0$ the excluded branch of this plot. The thermodynamic void volume, V_0 , was calculated from the elution volume of benzene.

3.4 *van Deemter curve measurements*

Van Deemter curves for nitrobenzene, toluene and butylbenzene were measured at 35°C, with a binary mobile phase made of ACN/water 60:40 %(v/v). The injection volume was set at 0.5 μ L. Retention time (t_R) and column efficiency (N) of eluted peaks were automatically calculated by the Empower software using the method of moments. The detection wavelength was 214 nm; sampling rate was 80 points/s. No correction for extra-column band broadening was necessary due to the very reduced system variance (see before for details).

3.5 *Peak parking experiments*

Peak parking experiments were carried out at 35°C with a mobile phase made of a mixture of ACN/water 60:40 %(v/v). The test compounds were toluene, nitrobenzene and butylbenzene. Parking times were 0; 2; 10; 30 and 40 minutes and the flow rate was 0.2 mL/min. The injection volume was set to 0.5 μ L. Peak parking method was used in order to estimate both effective and molecular diffusion coefficients at 35°C [44, 46, 59]. The spatial peak variance, σ_x^2 , has been calculated through the following equation:

$$\sigma_x^2 = \frac{L^2}{N} \quad (13)$$

where L is the column length and N is the number of theoretical plates. The latter was calculated by using peak width values returned by the software (calculated through the method of moments). Retention times were corrected for the instrument variance (Agilent 1100 was used, see before) and the parking time. D_m values of test compounds in the eluent were estimated by carrying out peak parking experiments on a column packed with non-porous particles (Micra column). For these measurements the flow rate was set to 0.1 mL/min. D_m coefficients were calculated through the following equation:

$$D_m = \frac{D_{eff}}{\gamma_e} \quad (14)$$

Where γ_e is a geometrical parameter, called external obstruction factor [60], that can be easily evaluated by measuring D_{eff} for a molecule whose D_m is known from literature. In this case thiourea in pure water at 25°C was used ($D_m = 1.33 \times 10^{-5}$ cm²/s) [61]. γ_e was found to be 0.68.

4. Results and discussion

Table 1S reports the most relevant physico-chemical characteristics of the columns employed in this work. Information on particle diameter, specific surface area and pore size comes from manufacturers. Columns with the same dimensions and similar particle size were used to eliminate any bias coming from column geometry on column efficiency. In addition, particles are very similar in terms of dimensions and porosity. Porosity values (see Table 1S) have been estimated through ISEC measurements. As it can be observed, ε_e values are close to 0.4 which represents the theoretical limit for well packed columns [62]. As expected, the SPP-2.0 column shows lower values for ε_t and ε_p than FPP columns, due to the presence of the solid core which decreases the volume available for diffusion.

Moreover, SPPs are characterized by a smaller specific surface area with respect to FPPs.

This can be explained by the presence of the solid inner core that reduces the porous zone.

Kinetic performance of the three reversed-phase columns has been evaluated by using three benzene derivatives as probe molecules with increasing affinity for the C₁₈ stationary phases (nitrobenzene < toluene < butylbenzene). As shown in Table 2S, where k_1 values are reported, retention is the smallest on the SPP-2.0 column, as expected. The FPP-1.9 column exhibits the largest retention, in agreement with specific surface area values discussed before. Nevertheless, in this paper the kinetic behavior of the three columns was compared at the same mobile phase composition. The choice of modifying the eluent composition to get similar retention on the different columns was not considered to avoid additional variability in mass transfer through changes in viscosity and molecular diffusion coefficients. In addition, also the stationary phase would change by changing the mobile phase composition. The effects, originated by these modifications, on the kinetic performance of columns can be as important as those given by differences in retention. The other possibility to compare columns at constant retention (with the same mobile phase composition) would be to consider chemically different compounds giving similar k_1 on the different columns. However, this approach has the drawback of neglecting the chemical specificity of molecules.

Van Deemter curves of toluene are reported in Figure 1S (nitrobenzene and butylbenzene follow the same trend). From these plots some features can be evidenced. Firstly, the three columns provide excellent kinetic performance, with reduced plate height below or around 2 and efficiencies even larger than 320 000 N/m for the less retained compounds on FPP-1.9 and SPP-2.0 columns (see Table 3S). By looking deeper into this plot (see the box with a zoom on the minimum of the van Deemter curves), it can be observed that the SPP-2.0

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column provides the best kinetic performance, as expected for packed bed made of SPPs. Surprisingly, even if the FPP-1.9 column is the most retentive, its performance is comparable to the SPP-2.0 one. Indeed, van Deemter curves of the two columns are nearly superimposable, especially at high flow rates. As reported in Table 3S, h_{min} values are only 5-10% larger on the FPP-1.9 with respect to the SPP-2.0, while the minimum of the van Deemter curve is approximately reached at the same v (and hence flow rate, since the two columns are packed with particles of roughly the same diameter and the same experimental conditions between columns are considered). On the opposite, the FPP-1.7 column provides both the lowest efficiency and the smallest optimal reduced velocity, even if it is packed with the finest particles. Another very interesting feature is that the van Deemter curves of the FPP-1.9 and SPP-2.0 are flatter than that of the FPP-1.7, with loss of efficiency of about 5% by increasing the flow rate over the optimal one. This characteristic makes these stationary phases particularly suitable for ultrafast separations, where very high flow rates are employed. On the other hand, this loss is slightly larger for the FPP-1.7 column, reaching 15% for the less retained compound (see Table 3S).

In order to comprehend the reasons behind the experimental features just described, each contribution to band broadening was independently evaluated for the three compounds on the three columns. The b -term has been firstly estimated through peak parking experiments. As reported in Table 4S, the two FPP columns show very similar b -values. Indeed, their van Deemter curves are nearly overlaid at low flow velocities, where longitudinal diffusion is prevailing over the other mass transfer terms. On the other hand, the b -terms are roughly 40% smaller on the SPP-2.0 column, as expected for the presence of the solid core but also for the lower k_1 values. This translates in better efficiency (lower h values) at low flow rates. Solid-liquid mass transfer coefficients, c_s , were estimated through

Eq. 11 by interpreting D_{eff} values from peak parking in the light of Maxwell's EMT model (see Theory section) and they are reported in Table 4S. Overall, c_s terms are remarkably small for all the three columns, indicating that mass transfer kinetics from the stationary to the mobile phase is fast. They are even slightly larger on the SPP-2.0 column, most likely due to its smaller pores with respect to those of FPP columns [35, 63].

Finally, $a(v)$ was calculated by subtracting b/v and $c_s v$ from h (Eq. 12). Fig. 1 shows the different contributions of eddy dispersion on the three columns for toluene (the same curves for nitrobenzene and butylbenzene are reported in Figs. 2S and 3S). From these plots one can easily notice that the values of $a(v)$ of the FPP-1.9 column (red squares) are unexpectedly smaller than those of the SPP-2.0 column (blue triangles) in agreement, however, with Refs. [35, 36]. Small values of eddy dispersion come from efficient packing of columns. As previously mentioned, there are many experimental works reporting on the very small values of eddy dispersion for columns made of SPPs. To the best of our knowledge, on the opposite, this is the first time where a smaller eddy dispersion is observed on a column made of FPPs versus one packed with SPPs of comparable particle size (1.9 μm nPSD FPPs vs. 2.0 μm SPPs).

In light of the consideration that for both particle ensembles the particle size distribution is very narrow (RSD < 5% in both cases), we have a tendency to think that the rheology of particles plays a pivotal role during the packing. 1.9 μm nPSD FPPs are produced by an innovative proprietary synthetic approach that, in addition to generate very similar particles in terms of dimensions, would also lead to a possibly different particle morphology than traditional one. Thus, these different properties would influence the quality of the bed, by reducing its radial heterogeneity during packing (very much as it happens for SPPs). Deeper studies on the morphology of these particles are currently under execution through high-

resolution SEM. Another interesting thing that could be evinced from Fig. 1, 2S and 3S is the more pronounced steepness of the curve of the FPP-1.7 column (green circles) starting from $\nu > 3$ with respect to the others. This behavior is imputable to the presence of frictional heating effects arising already at very low flow rates. This finding is in accordance with previously published data by Gritti and Guiochon [64], demonstrating a very accentuated sensitivity of BEH particles to heat friction. On the other hand, this effect has not been observed for the other two columns.

Finally, it is worth noting that the curves of the FPP-1.7 and SPP-2.0 seem to cross at very low flow rates for all the compounds. A similar finding has been reported also in a recent publication by Desmet's group [65]. However, it is very difficult to explain why this happens since even a small error on the determination of longitudinal diffusion result in significant deviations in the estimated (with subtraction method) eddy dispersion at low flow velocities (especially at $\nu < 2$) [66].

5. Concluding remarks

In this work, the column packed with nPSD 1.9 μm FPPs provided very similar kinetic performance to that of SPP-2.0. The two columns not only exhibited close values of efficiency and optimal reduced velocity, but also very similar flatness of the c-branches of van Deemter curves. This finding allows to operate these columns at higher flow rates over the optimal one without remarkable loss of efficiency. The independent estimation of all the contributions to band broadening has surprisingly revealed that the FPP-1.9 column is characterized by a very good packing. Indeed, the contribution of eddy dispersion of this column is even smaller than that of the SPP-2.0 one, under the same experimental conditions. This is the first time in which a column packed with FPPs exhibits lower values of

a-terms than those of SPPs. Since the two materials are characterized by a very nPSD (with roughly the same RSDs < 5%), we think that rheological properties of the particles might play a fundamental role during the packing process. Indeed, nPSD 1.9 μm FPPs are produced with a novel proprietary synthetic process that, besides producing particles with very similar diameter, would also possibly lead to a different morphology than that of other traditional FPPs. However, an in-depth study on rheological properties of these particles is necessary in order to generalize this concept. Finally, the column packed with the finest particles (FPP-1.7) exhibited the worst kinetic performance due to strong frictional heating already present at relatively low flow rates.

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Conflict of interest statement

The authors declare that they have no conflict of interest.

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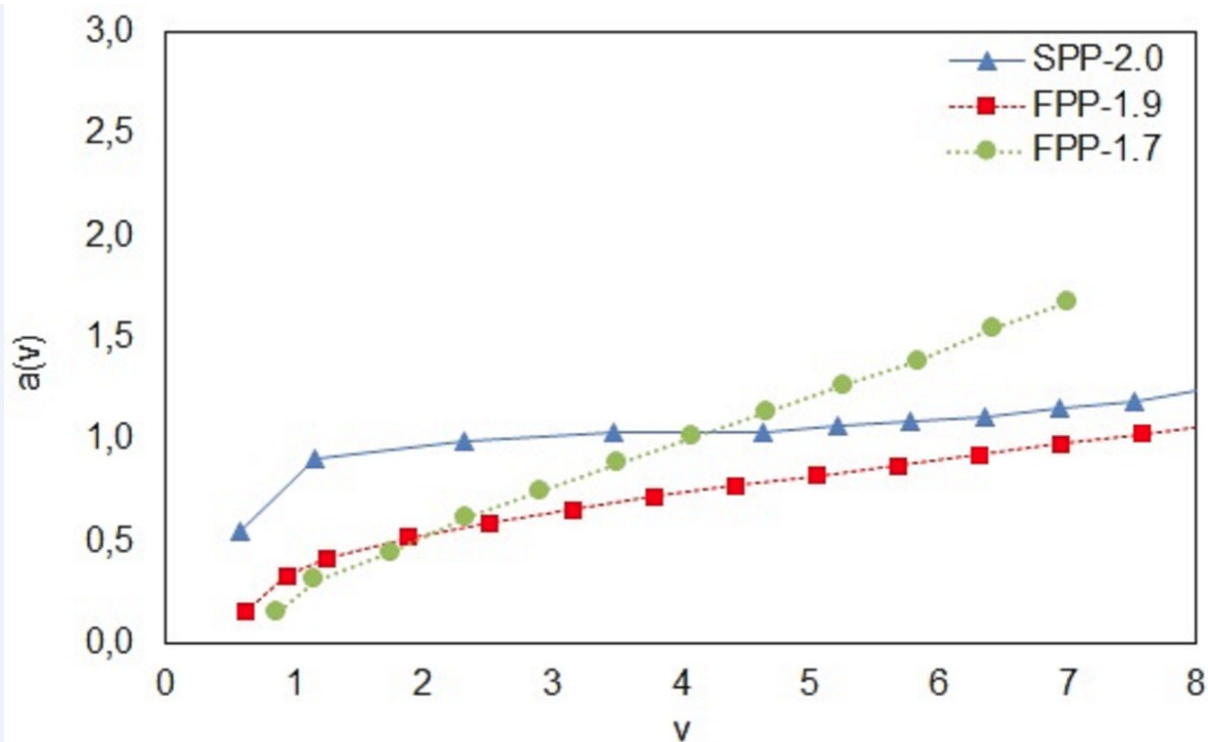
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Figure captions

Fig 1. Contribution of eddy dispersion ($a(v)$) for toluene on SPP-2.0 (blue triangles), FPP-1.9 (red squares), FPP-1.7 (green circles).



Martina Catani received her PhD at the University of Ferrara (Italy) in 2018. She is currently working as a research associate at the same university. In 2019 she spent a period as a post-doctoral research fellow at ETH Zurich (Switzerland).

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