Measuring and modeling adsorption equilibria of non-volatile compounds dissolved in supercritical carbon dioxide on nanoparticles using dynamic methods

Johannes Kern, Monika Johannsen[*]

Institute of Bioprocess and Biosystems Engineering, University of Technology Hamburg, Denickestr. 15, 21071 Hamburg, Germany

A B S T R A C T

Adsorption equilibria of benzoic acid and ibuprofen on AlO(OH) nanoparticles were measured for the first time using a dynamic method, frontal analysis. Possible techniques for creating packed beds of nanoparticles are presented and their suitability for different chromatographic adsorption measurement methods is discussed. Benzoic acid adsorption was measured at 40 °C and 16 MPa on AlO(OH) solid and hollow spheres, ibuprofen adsorption was measured at 40 °C and varying pressures of 10, 15 and 20 MPa on AlO(OH) hollow spheres. A dry packing method was used to create packed beds for the adsorption experiments. The experimental data was modeled with a Peng-Robinson EoS/RAST/BET approach, which shows excellent agreement with the data. The model is discussed as a way to model adsorption in high pressure drop packed beds.

© 2016 Elsevier B.V. All rights reserved.

1. Introduction

Supercritical carbon dioxide is an attractive solvent for many processes that require accurate knowledge of the related adsorption equilibria, e.g. controlled particle deposition (CPD) [1,2] and supercritical fluid chromatography (SFC) [3]. In both processes, small particles are of special interest. In SFC current state-of-the-art is the use of sub 2 μm particles with diameters of about 1.8 μm [4]. In CPD, which can be used for the formation of drug-carrier-systems, particles down to the nanoscale are being investigated [5,6], which show interesting properties for targeted drug delivery and tailored dissolution behavior. In processes with pharmaceutical application, where high standards for residual solvent have to be met, special interest exists in reducing or even avoiding the use of organic solvents, which are used as modifiers for supercritical carbon dioxide.

So far, researchers use static methods to determine the adsorbed amount to nanoparticles, which has the drawbacks that particles have to undergo separate analysis after impregnation, making the method more time consuming [5]. Control of analyte concentration in the supercritical phase is difficult and particles are usually

discarded after one adsorption experiment. Dynamic methods, using a chromatographic system, have multiple advantages: As the particles are fixed within a column it is easy to regenerate the particles in place, either with supercritical carbon dioxide, or, if necessary, with organic solvents that are pumped through the column. This way one column can be used for multiple measurements at different experimental conditions and with different analytes, which is useful in early development stages when only small batches of particles are produced. Furthermore, the analyte concentration can be controlled by mixing a saturated stream with neat carbon dioxide, yielding not only the adsorption at saturation but the whole concentration dependent isotherm. One challenge of dynamic measurements for the determination of adsorption equilibria is the physical inevitability of a pressure drop across the packed bed of adsorbent particles, influencing the experimental results by the resulting density gradient in the fluid [7]. While adsorption equilibria in supercritical carbon dioxide are greatly influenced by pressure, its use also grants a great opportunity when the size of the adsorbent particles is in the nanoscale. Its very low viscosity makes flow through a packed bed possible even with very small particle diameters.

Sometimes, however, it is not possible to avoid large pressure gradients and suitable models have to be found, in order to be able to calculate isobaric data from experiments that were not performed at constant pressure. Thermodynamic models are most promising for this task, as they can be used to consistently describe

the reality of the adsorbed and the bulk phase, also taking into account the solvent, which is often considered inert in many empirical adsorption models.

In this study adsorption experiments have been carried out with benzoic acid and R/S-ibuprofen as model substances for pharmaceutical processes with supercritical carbon dioxide. Benzoic acid was used as a substance with a rather low solubility compared to ibuprofen to investigate the performance of the adsorption apparatus with compounds of different solubilities. The experiments were designed to investigate the adsorption properties of AlO(OH) hollow spheres compared to solid spheres of the same material as well as to measure pressure dependent adsorption isotherms on hollow spheres to show the performance of the dynamic method to retrieve data for the design of industrial adsorption processes.

2. Material and methods

2.1. Particles

2.1.1. AlO(OH) hollow spheres
AlO(OH) hollow spheres with an average diameter of 20–25 nm and a BET surface of 530 m^2/g [6] were provided by Prof. C. Feldmann, KIT, Germany.

2.1.2. AlO(OH) solid spheres
AlO(OH) solid spheres with an average diameter of 10–30 nm and a BET surface of 142.8 m^2/g (provided by manufacturer) were purchased from Sky Spring Nanomaterials, Houston, USA.

2.1.3. AluC Al$_2$O$_3$ solid spheres
Al$_2$O$_3$ nanoparticles "AluC®" with an average diameter of 13 nm and a BET surface of 350 m^2/g (provided by manufacturer) were kindly donated by Evonik, Essen, Germany.

2.2. Chemicals

R/S-Ibuprofen, Ph. Eur., and n-hexane, technical grade, were kindly donated by BASF, Ludwigshafen, Germany. Benzoic acid, 99.5%, was purchased from Bernd Kraft GmbH, Duisburg, Germany. Naphthalene, 98.0%, and 2-propanol, UV/VIS grade, were purchased from Sigma-Aldrich, Munich, Germany. Carbon dioxide, food grade, was purchased from YARA GmbH, Dülmen, Germany.

2.3. Adsorption apparatus

For measuring adsorption equilibria with non-volatile compounds dissolved in supercritical carbon dioxide, an existing apparatus [8] was modified. The apparatus is built up of two coupled chromatographic systems: one containing an adsorption column filled with nanoparticles, one an analytical column, as shown in Fig. 1. Carbon dioxide is condensed and pressurized to up to 30 MPa to fill two thermostated high pressure syringe pumps "A" and "B", which deliver pulsation free and accurate carbon dioxide flow to the adsorption column. The carbon dioxide flow from pump B is led through a saturator which is filled with the analyte and is then mixed with the neat carbon dioxide flow from pump A to allow for a defined analyte concentration. UV/VIS detector 1 is used to detect breakthrough curves from the adsorption column. The adsorption system is operated by setting a constant volumetric flow at the syringe pumps and controlling the column backpressure using a PI-controller actuating a pneumatically driven needle valve downstream of the detector.

A second chromatographic system, equipped with a modifier pump, an analytical column (Kromasil 60 Å, 5 μm, 250 × 4.6 mm) and UV/VIS detector 2, is connected to the adsorption system with a Rheodyne sampling valve, fitted with a 1 μl sample loop, to measure high analyte concentrations that exceed the range of UV/VIS detector 1. It is operated by setting the pressure upstream of the column with a pressure regulator and controlling the carbon dioxide flow with a manual needle valve. Carbon dioxide flow is controlled using a rotameter downstream of the needle valve after separating the modifier.

2.4. Column packing

To prepare a packed bed of nanoparticles with sufficient quality to measure breakthrough curves, different methods for column packing were evaluated. For all packing experiments standard stainless steel HPLC-columns with inner diameter of 4.6 mm, purchased from CS Chromatographie Service GmbH, Langerwehe, Germany, have been used. To ensure there was no loss in particles, the weights of all columns were monitored during the time the experiments were carried out.

2.4.1. "In-situ" method
To retain particles, the column outlet of a 30 × 4.6 mm (bed length × inner diameter) column is closed with a sieve-sandwich filter, which consist of three glass fibre filters with about 0.5 μm pore size that are sandwiched by two stainless steel metal sieves with about 5 μm pore size. The filter assembly is being held in place by the column head.

The column is then filled with a slurry of 2-propanol containing about 3 wt.-% nanoparticles and the column inlet is closed with the same setup. For packing, the column is placed vertically with the outlet facing down into the chromatographic system and pressurized with supercritical carbon dioxide. This way, the organic solvent is pushed out of the column and the particles are filtered against the column outlet to form a thin fixed bed of unknown thickness.

2.4.2. Slurry method
A 10 × 4.6 mm column is packed using a standard slurry packing procedure. The nanoparticles are mixed with the packing solvent and sonicated until homogeneous to form a slurry of about 4 wt.-%. The slurry is prepared with enough particles to fill the column completely plus about 5–10% excess material. For packing, only the column outlet is closed with the sieve-sandwich filter and the column is filled completely with slurry. The column inlet is connected to a reservoir that contains the rest of the slurry. The packing is started by pumping fresh solvent into the reservoir and completed, when a solvent volume equal to the slurry volume plus about 20% was collected at the column outlet. The column is then disconnected from the reservoir, excess particles are gently scraped from the top of the packed bed with a sharp object and the column inlet is closed with sieve-sandwich filters.

2.4.3. Dry packing method
A 10 × 4.6 mm column is filled with dry nanoparticles and supercritical carbon dioxide is pumped through it to compress the particle bed. The column is then reopened and filled with additional particles. This is repeated until there is no visible compression of the packed bed anymore.

Because of the limited availability of the AlO(OH) hollow spheres column packing methods were first tested with AluC particles, which were readily available in larger quantities. Further tests have been performed with AlO(OH) solid spheres where the packing method proved useful for the planned experiments or where the packing method was not applicable to the AluC particles. AlO(OH) hollow spheres where only used to pack one column with the dry packing method. This column was also used for the adsorption equilibria measurements in this study.