Equilibrium and Kinetics of Vancomycin Adsorption on Polymeric Adsorbent

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Isolation step of vancomycin, a glycopeptide antibiotic, is usually done from fermentation broth filtrate, while its adsorption directly from the whole broth could rationalize the process. The equilibrium and kinetics of vancomycin adsorption from broth supernatant, diluted and whole broth on polymeric adsorbent was studied in this work. Experimental equilibrium data was correlated with Sips, Langmuir, Freundlich, and linear adsorption isotherms. Agreement between measured and regressed data for the first three mentioned models did not vary much and was relatively high. The maximum adsorbed amount for supernatant was higher than for fermentation broths because mycelium particles blocked adsorbent surface. Liquid film mass transfer studies showed that external mass transfer resistance could have been neglected. Diffusion of vancomycin inside adsorbent particles was acknowledged using a nonstructural, homogenous surface diffusion and bidisperse pore models. Model simulations indicated that kinetics of the process could be improved by using smaller adsorbent particles. © 2011 American Institute of Chemical Engineers *AIChE J,* 58: 99–106, 2012
Keywords: vancomycin, adsorption, equilibrium, kinetics, model

Introduction

Biotechnological processes for producing active pharmaceutical ingredients generally consist of several stages such as the removal of solids (recovery), isolation of product, purification, and polishing.[1] In many cases, it is possible to combine the first two stages, recovery and isolation. If solvent extraction is the method of choice to isolate the compound, a whole broth extraction can be applied. In case of an adsorption, the process can be carried out in a fluidized (expanded) bed, which allows biomass to pass unhindered through the bed of adsorbent particles therefore eliminating the need for biomass removal before adsorption.

Adsorption is a surface phenomenon, where compounds from gas or liquid phase are concentrated on the surface of solid adsorbent particles. As a unit operation, it is widely used in isolation and purification processes in the chemical industries including biotechnology and environmental technology. It is a dynamic process, where the rate of adsorption is controlled by mass transfer processes outside and inside of adsorbent particles. The maximum quantity of a certain compound adsorbed per unit mass is determined by the equilibrium. Equilibrium data are represented in the form of adsorption isotherms, which can be described by a number

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Table 1. Physical Properties of Amberlite XAD 16N Polymeric Adsorbent

Physical Property	Value
Matrix	Macroreticular aliphatic crosslinked polymer
Physical form	White translucent beads
Density	1015−1025 kg m^{-3}
Particle size	
Harmonic mean size	0.56–0.71 mm
Uniformity coefficient	≤2.0
Fines content	<0.350 mm (maximum 2.0%)
Coarse content	>1.18 mm (maximum 2.0%)
Specific surface area	≥800 m^2 g^{-1}
Porosity	≥0.55

of models of which the Langmuir and the Freundlich isotherm models are the most known.[2]

Adsorption kinetics and equilibrium may essentially be studied in two ways using nonstructural models, which may either be empirical[3] or are based on the law of mass action,[4,5] or, on the other hand, structural models,[6–10] such as those encompassing uniform adsorbent particle size,[6,7,9,10] particle size distribution,[8] or even the bimodal distribution of pores within the adsorbent particles.[10] The nonstructural models may be quite efficient in describing the experimental data;[3–5] however, they have less predictable behavior in cases when a structural characteristic such as particle size, surface area, porosity, or distribution of the mentioned properties is concerned. Therefore, structural models seem to have more extrapolative characteristics not necessarily lacking in general model fit. Nevertheless, they are more rigorous to solve, often requiring the use of numerical tools.

Published literature describing adsorption kinetics and equilibrium of active pharmaceutical ingredients and modeling of adsorption processes of the latter are scarce. Among others, Fonseca and Cabral[11] described in situ recovery of penicillin acylase. Recovery of vitamin B12 on nonionic polymeric adsorbents was described by Ramos et al.[12] and recovery of cephalosporin C on polymeric adsorbent by Mishra et al.[13] Modeling of adsorption of a bacterial lipase was presented in the work of Millitzer et al.[14]

Vancomycin is a glycopeptide antibiotic used in the prophylaxis and treatment of bacterial infections. It is a product of fermentation, synthesized by the bacteria *Amycolatopsis Orientalis*. In the vancomycin downstream process, biomass is removed first by the means of a cross flow microfiltration and subsequently vancomycin is adsorbed from permeate onto an appropriate adsorbent resin in a packed bed column. Removal of biomass by means of crossflow microfiltration is an expensive operation and therefore an expanded bed adsorption (EBA) could be applied as a more economical solution.

The intention of the work was to experimentally determine the kinetics and equilibrium data for adsorption of vancomycin from whole broth, diluted broth, and broth supernatant on polymeric adsorbent resin to evaluate the impact of biomass concentration on the efficiency of the adsorption process. Data collected can be used further in modeling vancomycin adsorption dynamics in a packed or an EBA processes.

Experimental

Preparation of fermentation broth and supernatant media

Fresh whole fermentation broth (FB) collected immediately after the end of fermentation, was used to prepare diluted media and supernatant. Distilled water was used for dilution obtaining media with 50% (by vol.) and 20% (by vol.) broths. Broth supernatant was produced by centrifuging the broth in a laboratory centrifuge (Megafuge 1.0R, Heraeus, Germany) at 4000–6000 rpm for 10–15 min.

Adsorbent and adsorbent pretreatment

Amberlite XAD16N (Rohm and Haas, Philadelphia, PA), a nonionic, hydrophobic, crosslinked polymeric adsorbent resin was used in this study. Properties are summarized in the Table 1. Fresh adsorbent, before use, was washed with distilled water to remove imbibed salts. Washing efficiency was checked by measuring conductivity of washing liquors.

High-pressure liquid chromatography analysis

The concentration of vancomycin in samples was determined by means of high-pressure liquid chromatography (HPLC). A HP 1200 HPLC system (Agilent Technologies, Palo Alto, CA), with a degasser, gradient pump, auto-sampler, column thermostat, and ultraviolet detector was used. A HPLC column was Zorbax SB-Aq, 50 × 4.6 mm^2, 1.8 μm (Agilent Technologies, Palo Alto, CA). A gradient was applied for chromatographic separation. The mobile phase A was 5 mM phosphate buffer of pH 2.6 and the mobile phase B was 100% (by vol.) acetonitrile. The gradient was the following: 0 min, 5% (by vol.) B; 3.85 min, 10.5% (by vol.) B; 5 min, 80% (by vol.) B; 6.5 min, 80% (by vol.) B; 7.5 min 5% (by vol.) B. The flow rate of the mobile phase was 1.0 mL min^{-1} and the temperature of the column 45°C. Vancomycin was detected at 240 nm. The retention time was 4.1 min.

Adsorption equilibrium and kinetics experiments

To determine adsorption isotherms, different amounts (0.2–4.0 g) of adsorbent were weighed into 13 flasks of 25 mL each. A liquid medium of 20 mL (supernatant, diluted, or whole broth) was added into each flask. Flasks were vigorously shaken on the laboratory shaker KS 501 Digital (IKA, Germany) for 24 h at room temperature (23 ± 1°C). Samples of liquid were transferred from the flask into Eppendorf micro test tubes and centrifuged at 13,400 rpm for 10 min (MiniSpin®, Eppendorf, Germany) to separate adsorbent particles and biomass from the liquid. Supernatant (the liquid above adsorbent particles and biomass sediment obtained after centrifugation) was filtered over a 0.22-μm polyethersulfone (PES) syringe filter (TPP AG, Switzerland) and analyzed by means of HPLC to determine the concentration level of the remaining vancomycin in the liquid phase. The amount of adsorbed vancomycin was calculated from a mass balance.

To determine adsorption kinetics, 4 g of adsorbent resin was weighed into 15 flasks of 25 mL each. A liquid medium (supernatant, diluted, or whole broth) of 20 mL was added into each flask. Flasks were shaken at various rotational speeds on a laboratory shaker KS 501 Digital (IKA, Germany) at room temperature (23 ± 1°C). At every predefined

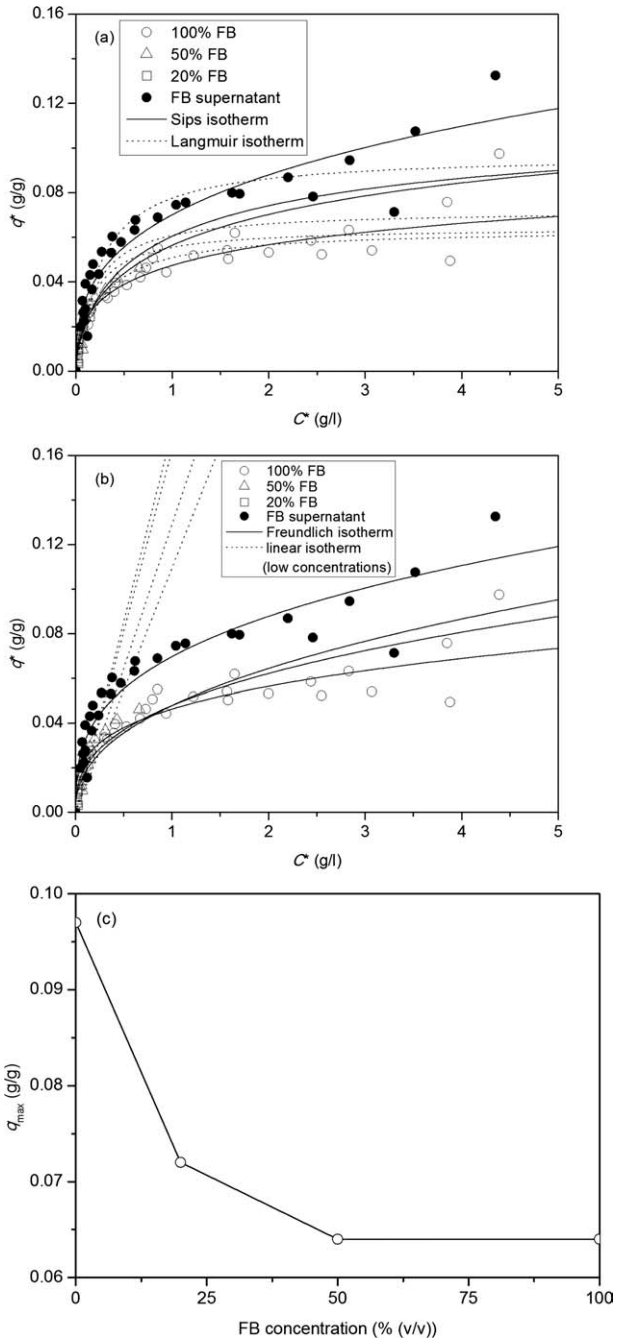

Figure 1. Equilibrium data for the adsorption of vancomycin on polymeric adsorbent during batch experiments (a and b).

Symbols represent measured data; lines represent model data. Maximum adsorbed concentration, q_{max}, as a function of fermentation broth (FB) concentration (c).

time interval one flask was removed from the shaker for the chemical analysis of vancomycin, which was done as already described above.

Scanning electron microscopy

The morphologies of the cut surfaces of the neat and used adsorbents were determined by scanning electron microscopy (SEM) (JSM-7600F Scanning Electron Microscope, Jeol Ltd., Japan) at 10 kV. The samples were fixed onto sample holder using a conductive component, sputtered with gold, and painted on one side with conductive paste.

Results and Discussion

Adsorption equilibrium and estimation of adsorption isotherm model parameters

Figure 1 shows experimental equilibrium data for adsorption of vancomycin from media with different biomass concentration in terms of the equilibrium adsorbed mass of vancomycin per adsorbent mass (q^*, g g^{-1}) vs. the equilibrium vancomycin concentration in liquid phase (C^*, g L^{-1}). All isotherms exhibit the same shape, having a linear part in the low concentration range and then a plateau, as the resin becomes saturated. A pronounced data scatter at higher equilibrium liquid concentrations is attributed to sensitivity of the mass balance calculation, i.e., the amount of the adsorbed compound per mass unit of adsorbent. Within the high concentration range, already a small experimental error is observed, e.g., analytical error <5% has a pronounced impact on calculated values.

Experimental data was fitted with Sips (Eq. 1), Langmuir (Eq. 2), Freundlich (Eq. 3), and linear (Eq. 4) adsorption isotherm models. Corresponding model curves are shown in Figure 1. Estimated model parameters are summarized in the Table 2.

$$q^* = \frac{q_{\max} C^{*n}}{K_D + C^{*n}} \tag{1}$$

$$q^* = \frac{q_{\max} C^*}{K_D + C^*} \tag{2}$$

$$q^* = q_{\max} C^{*n} \tag{3}$$

$$q^* = K_{ads} C^* \tag{4}$$

As expected the Sips isotherm provides the best agreement between measured and regressed data. This may be explained by three estimated parameters, which define the equation of

Table 2. Adsorption Equilibrium Parameters

	Fermentation Broth Concentration (%, by vol.)			
Parameters	100	50	20	Supernatant
Sips isotherm				
q_{max} (g g^{-1})	0.129	0.150	0.120	0.912
n (/)	0.430	0.548	0.674	0.358
K_D (g^n/L^n)	1.73	1.65	0.98	12.01
R^2 (/)	0.873	0.929	0.713	0.905
Langmuir isotherm				
q_{max} (g g^{-1})	0.064	0.064	0.072	0.097
K_D (g L^{-1})	0.25	0.16	0.19	0.25
R^2 (/)	0.872	0.911	0.707	0.904
Freundlich isotherm				
q_{max} (L^n/g^n)	0.046	0.048	0.048	0.070
n (/)	0.286	0.375	0.427	0.333
R^2 (/)	0.834	0.901	0.707	0.904
Linear isotherm				
K_{ads} (L g^{-1})	0.110	0.123	0.162	0.171
R^2 (/)	0.580	0.383	0.412	0.509

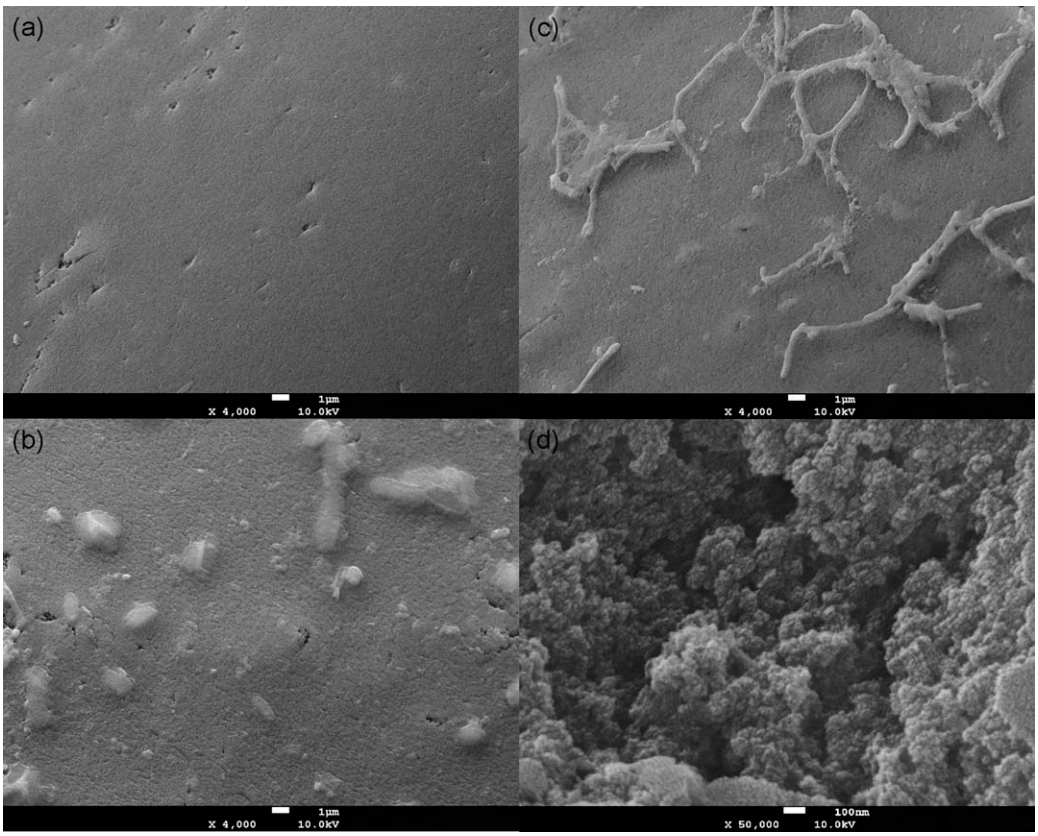

Figure 2. SEM images of polymeric adsorbent surface: clean surface of neat adsorbent (a), surface fouled by suspended particles after the adsorption from the fermentation broth supernatant (b), surface fouled by suspended particles (mainly biomass) after the adsorption from the whole broth (c), and magnified surface of neat adsorbent showing the pore structure (pore diameter of approximately 20–30 nm) (d).

this isotherm, whereas the Langmuir and Freundlich isotherms include only two parameters. Furthermore, the Langmuir and Freundlich isotherms correspond similarly with the measured data, as may be observed from R^2 values in Table 2, which were not considerably lower than in the case when the Sips isotherm was used. Thus, the adsorption equilibrium may be satisfactorily described by the physical mechanism underlying Langmuir equation nonetheless, the overall curve fit is better in the case of the Sips equation. The linear isotherm was fitted solely for low concentrations (<0.5 g L^{-1}).

The measured data scatter at the higher equilibrium liquid concentrations (C^*) worsened the overall agreement between the measured and regressed data over the complete C^* range. A noticeable data scatter only occurs at the equilibrium liquid concentrations >2 g L^{-1} (Figure 1). If only lower C^* were used in the regression analyses, the discrepancies (in terms of R^2) would have been considerably lower.

As shown in Figure 1, equilibrium adsorbed concentration, q^*, at the same equilibrium liquid concentration, C^*, increases with decreasing fermentation broth concentration, its value being the greatest for the fermentation broth supernatant. As all media used contained the same dissolved species, probable reason for lower adsorption efficiency is not competitive adsorption of dissolved species but rather fouling of adsorbent surface with suspended solids (biomass, fermentation medium residues, etc.). This means that less pore internal surface is available for adsorption because of mechanical blockage of pore openings. Influence of biomass concentration on maximum amount of vancomycin adsorbed is for Langmuir type of isotherm illustrated in the Figure 1 as a plot of q_{max} vs. biomass concentration. Langmuir type of isotherm was chosen, because of physical meaning of q_{max} constant. Figure 2 shows SEM images of adsorbent resin surface, i.e., unused adsorbent surface (a), surface fouled with suspended particles present in the broth supernatant (b), and surface fouled with suspended particles present in whole fermentation broth (c).

Determination of the role of liquid mass transfer resistance around adsorbent particles

Subsequently, the role of liquid mass transfer resistance around adsorbent particles had to be determined to be able to study the kinetics of adsorption of the active ingredient from either fermentation broth or its supernatant individually within the examined range of rotational speeds. Figure 3 shows that the vancomycin concentration decreases within certain experimental error due to its adsorption onto polymeric adsorbent. This decrease stays practically the same, regardless of the rotational speed. Interestingly, there does not seem to be a noticeable mass transfer resistance even at extremely low rotational speed (50 min^{-1}). The initial concentration (C_0) does not influence much mass transfer around

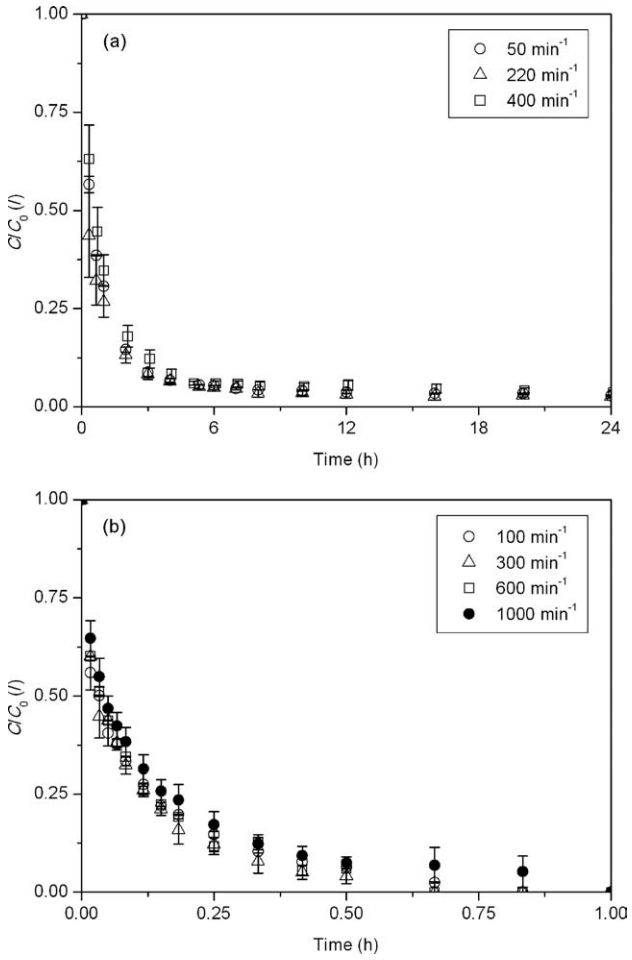

Figure 3. Active ingredient concentration profile [100% (by vol.) fermentation broth (FB) (a) and fermentation broth (FB) supernatant (b)] for the adsorption of vancomycin on polymeric adsorbent during batch experiments at three different rotational speeds.

particles [vancomycin concentrations are low enough (<7 g L^{-1}) not to influence liquid properties and hydrodynamic conditions, nonetheless biomass concentration, i.e., fermentation broth concentration affects the latter]; moreover, the mass transfer around particles seems to be more or less absent as presented in Figure 3.

Adsorption kinetics

Diffusion of vancomycin inside the particle is described by considering three various possible situations: the reversible second order/first order kinetics (RSFK) model, the homogenous surface diffusion model (HSDM), and the bidisperse pore model (BPM).

The differential mass balance in an element of the batch volume for vancomycin concentration may be due to the absence of mass transfer resistance around adsorbent particles expressed by the following equation (ε represents the batch void volume and ρ represents the solid density):

$$\frac{\partial C}{\partial t} = -\frac{1-\varepsilon}{\varepsilon}\rho\frac{\partial \bar{q}}{\partial t} \tag{5}$$

The initial condition (IC) is given as follows:

$$t = 0 \rightarrow C = C_0 \tag{6}$$

RSFK model. The differential mass balance in the solid phase is represented according to the following mathematical kinetic model (RSFK):

$$\frac{\partial \bar{q}}{\partial t} = k_1 C(q_{\max} - \bar{q}) - k_2\bar{q} \tag{7}$$

where k_1 and k_2 are intrinsic kinetic constants, C is the vancomycin concentration in the solution (initial vancomycin concentration is C_0), $\overline{q}$ is the antibiotic concentration adsorbed on the polymer, and $q_{\max}$ is the maximum adsorption capacity of the resin. The IC was given as follows:

$$t = 0 \rightarrow \bar{q} = 0 \tag{8}$$

Homogenous surface diffusion model. The HSDM is based on the assumption that the transport of species is determined either by external mass transfer in the liquid phase if the latter is not negligible, or by external equilibrium between the liquid and solid phase and by intraparticle diffusion resistance in the form of surface diffusion within the adsorbent particle. Assuming homogeneous spherical adsorbent particles and a concentration-independent diffusivity (this assumption was relaxed by Yang et al.[15] without offering any particular advantage in model fit), the intraparticle transport and solute uptake is described by the following equation:[15]

$$\frac{\partial q}{\partial t} = \frac{D_l}{r^2}\frac{\partial}{\partial r}\left(r^2\frac{\partial q}{\partial r}\right) \tag{9}$$

where q is the solute loading in the adsorbent phase (kg kg^{-1}), D_l is the intraparticle diffusion coefficient (m^2 s^{-1}), and r is the radial distance (m) measured from the center. The boundary condition (BC) and IC are the following:

$$t = 0 \rightarrow q = 0 \tag{10}$$

$$r = 0 \rightarrow \frac{\partial q}{\partial r} = 0 \tag{11}$$

$$r = R_p \rightarrow q = q^* \tag{12}$$

At the external surface of the particle ($r = R_p$), instantaneous equilibrium is assumed between the organic molecule concentrations in the liquid and solid phases, which are coupled using the Sips isotherm, as obtained from the adsorption equilibrium experiments (see discussion above).

$$q* = \frac{q_{\max}C^n}{K_D + C^n} \tag{13}$$

The average solute concentration in the adsorbent particle is defined as:

$$\bar{q} = \frac{3}{R_p^3}\int_0^{R_p} qr^2 dr \tag{14}$$

Table 3. Adsorption Kinetics Parameters Determined Using Sips Isotherm

	Fermentation Broth Concentration (%, by vol.)			
Parameters	100	50	20	Supernatant
RSFK Model				
k_1 (10^{-2} L g^{-1} h^{-1})	5.8	9.2	16.0	40.0
k_2 (10^{-2} h^{-1})	6.6	10.3	7.8	1.9
R^2 (/)	0.978	0.992	0.990	0.941
HSDM Model				
D_l (10^{-14} m^2 s^{-1})	2.94	1.69	0.95	3.78
R^2 (/)	0.987	0.999	0.994	0.947
BPM Model				
D_l (10^{-11} m^2 s^{-1})	2.53	0.96	1.63	2.84
D_μ (10^{-17} m^2 s^{-1})	0.47	2.95	1.50	1.46
R^2 (/)	0.976	0.995	0.993	0.923

Bidisperse pore model. The BPM assumes that the adsorbent particle is an agglomerate of a number of equal size microparticles. A porous intergel region forms in between the microparticles. Before the organic molecule adsorbs inside the microparticle, it must be transported from the particle surface through the intergel region to the surface of the microparticles. In the intergel porous region, transport is described by the following equation:[16]

$$\frac{\partial C_m}{\partial t} = -\frac{1-\varepsilon_m}{\varepsilon_m}\rho\frac{\partial \bar{q}_\mu}{\partial t} + \frac{D_l}{r^2}\frac{\partial}{\partial r}\left(r^2\frac{\partial C_m}{\partial r}\right) \tag{15}$$

The BC and IC are the following:

$$t = 0 \rightarrow C_m = 0 \tag{16}$$

$$r = 0 \rightarrow \frac{\partial C_m}{\partial r} = 0 \tag{17}$$

$$r = R_p \rightarrow C_m = C \tag{18}$$

C_m is the solute concentration in the intergel porous region (kg m^{-3}), $\bar{q}_\mu$ is the volume-averaged solute concentration in the solid phase (microparticles, kg kg^{-1}; see Eq. 24 below). R_p is the particle external radius (m). D_l is the intergel porous region diffusivity (m^2 s^{-1}), given by $(\varepsilon_m/\Gamma)D_b$ with ε_m being the void fraction in the porous region, Γ, the tortuosity, and D_b, molecular diffusivity.

Transport and adsorption in the microparticles are described by following:

$$\frac{\partial q_\mu}{\partial t} = \frac{D_\mu}{r_\mu^2}\frac{\partial}{\partial r_\mu}\left(r_\mu^2\frac{\partial q_\mu}{\partial r_\mu}\right) \tag{19}$$

with the BC and IC being

$$t = 0 \rightarrow q_\mu = 0 \tag{20}$$

$$r_\mu = 0 \rightarrow \frac{\partial q_\mu}{\partial r_\mu} = 0 \tag{21}$$

$$r_\mu = R_\mu \rightarrow q_\mu = \frac{q_{max}C_m^n}{K_D + C_m^n} \tag{22}$$

q_μ is the solute concentration (kg kg^{-1}) in the microparticle, D_μ is the microparticle diffusivity (m^2 s^{-1}), and R_μ is the microparticle radius (m). Equation 22 is the Sips isotherm, which has been shown experimentally to describe vancomycin adsorption in the macroreticular crosslinked poly(divinylbenzene) adsorbent (see above). The average concentration throughout the adsorbent particle is defined as follows:

$$\bar{q} = \frac{3}{\rho R_p^3}\int_0^{R_p} r^2\left(\rho\bar{q}_\mu + \frac{\varepsilon_m}{1-\varepsilon_m}C_m\right)dr \tag{23}$$

where $\overline{q}_\mu$ is given by the equation:

$$\bar{q}_\mu = \frac{3}{R_\mu^3}\int_0^{R_\mu} q_\mu r_\mu^2 dr_\mu \tag{24}$$

The results in Tables 3 and 4 show that all three models describe the intraparticle adsorption for fermentation broth well, as the coefficients of determination are in the range $R^2 =$ 0.97–0.99. It is interesting that the coefficient for supernatant is worse; it is in the range $R^2 = 0.92$–0.94. We assume that this is because of the analytical experimental error at low concentrations of active ingredient at higher adsorption rates. Concentration profiles for the adsorption of vancomycin on polymeric adsorbent during batch experiments are presented in Figures 4–6. Results include the measured data and RSFK, BPM, and HSDM model data using the Sips isotherm and the Langmuir isotherm to describe equilibrium. The rate of vancomycin disappearance from the bulk solution is higher in the case of supernatant. This is somehow inversely proportional to the fermentation broth concentration. The initial concentration (C_0) does influence kinetics models through the IC (Eq. 6); nonetheless this influence on the adsorption process itself is not predominant as may be seen from Figures 4–6. C_0 is the same for 100% FB and 100% supernatant (6.8 g L^{-1}), whereas C_0 is lower for both 20 and 50% FB. Nevertheless, these two curves lie in between 100% FB and 100% supernatant (Figures 4–6), which may only lead to the conclusion that the adsorption process kinetics are mainly affected by FB concentration and not as much by vancomycin initial concentration. Generally, the concentration of vancomycin on the particle surface and inside the particle, as well as its adsorption rate, is proportional to the adsorption capacity. In the case of fermentation broth, the adsorbent

Table 4. Adsorption Kinetics Parameters Determined Using Langmuir Isotherm

	Fermentation Broth Concentration (%, by vol.)			
Parameters	100	50	20	Supernatant
RSFK Model				
k_1 (10^{-2} L g^{-1} h^{-1})	12.9	22.4	26.9	39.5
k_2 (10^{-2} h^{-1})	5.0	9.3	7.5	25.4
R^2 (/)	0.982	0.993	0.991	0.944
HSDM Model				
D_l (10^{-14} m^2 s^{-1})	3.08	1.83	0.80	3.96
R^2 (/)	0.983	0.992	0.993	0.924
BPM Model				
D_l (10^{-11} m^2 s^{-1})	2.52	0.96	1.49	2.83
D_μ (10^{-17} m^2 s^{-1})	0.43	2.93	1.33	1.46
R^2 (/)	0.975	0.994	0.993	0.913

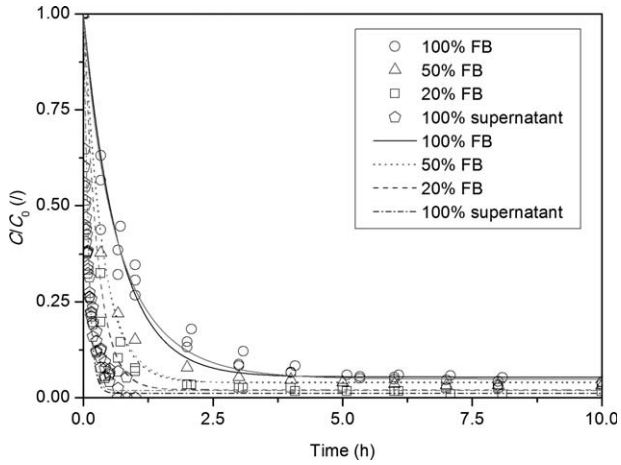

Figure 4. Active ingredient concentration profile for the adsorption of vancomycin on polymeric adsorbent during batch experiments.

Symbols represent measured data; lines represent RSFK model data using Sips isotherm (black lines) and Langmuir isotherm (grey lines) to describe equilibrium.

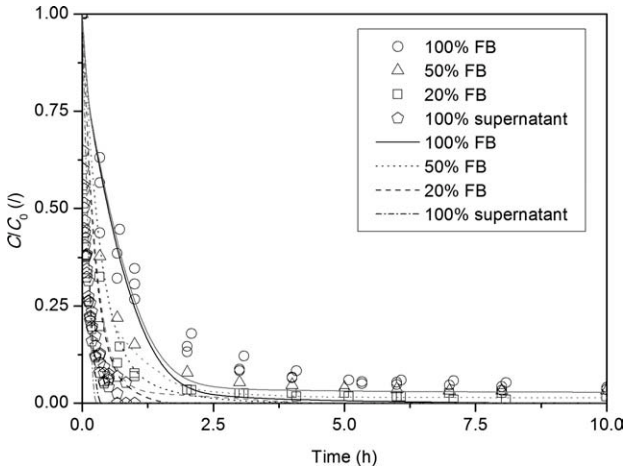

Figure 6. Active ingredient concentration profile for the adsorption of vancomycin on polymeric adsorbent during batch experiments.

Symbols represent measured data; lines represent BPM model data using Sips isotherm (black lines) and Langmuir isotherm (grey lines) to describe equilibrium.

surface is fouled with biomass particles that lower adsorption capacity (Figure 1). Higher capacity means faster adsorption on the particle. Following this, slower liquid–solid mass transfer of vancomycin within adsorbent particles occurs in the case of fermentation broth with lower adsorption capacity of these particles. This is because of the lower concentration gradient from the bulk liquid in pores to the adsorbent surface, compared with adsorption from the pure supernatant, where the adsorption capacity of the adsorbent particles is the highest.

The comparison of the external and internal mass transfer resistance shows that the adsorption of vancomycin inside the particle controls the global adsorption kinetics of the process. At given molecular diffusivity and the actual adsorption rate, the global rate of the adsorption can be increased by reducing the particle size.[10] The effect of the particle size on the global adsorption rate is shown in Figure 7. Here, the experimental data of the batch experiment regressed with a corresponding model (HDSM). These are compared with the predicted results of the same model, but for larger and smaller particles. In all cases, the external mass transfer resistance was neglected. The results show that $C/C_0 = 0.1$ is obtained experimentally in approximately 3.0 h, whereas for three-times smaller particles the same value would be obtained in <30 min. The process would be substantially longer for three-times larger particles. Therefore, the kinetics of adsorption could be greatly improved by using smaller adsorbent particles, such as XAD1600N (Rohm and Haas; $2R_p = 400$ μm). These smaller particles can grant higher adsorption rates although they consist of similar polymer matrix as the polymeric resin used in this study.

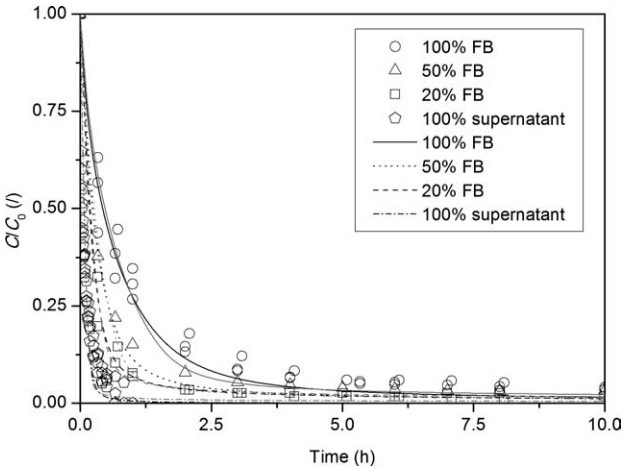

Figure 5. Active ingredient concentration profile for the adsorption of vancomycin on polymeric adsorbent during batch experiments.

Symbols represent measured data; lines represent HSDM model data using Sips isotherm (black lines) and Langmuir isotherm (grey lines) to describe equilibrium.

Conclusions

The equilibrium data for adsorption of vancomycin on polymeric adsorbent can be described with Sips, Langmuir, and Freundlich isotherm models with very similar coefficients of determination (R^2). The highest adsorption capacity was obtained with pure supernatant. The mycelium particles in the fermentation broth block the adsorbent surface and consequently decrease the adsorption capacity. Furthermore, equilibrium adsorption capacity depends on the mass of suspended adsorbent particles in a batch of a given liquid broth or supernatant volume. That is for the lowest equilibrium C^* values, the largest amount of adsorbent is applied to a given liquid volume, and therefore the highest extent of adsorption occurs (equilibrium adsorption capacity), thus the remaining equilibrium C^* in the liquid phase is the lowest. This blocking might be a significant problem for anyone looking to improve the economics of the adsorption process from the whole broth to avoid microfiltration.

The film mass transfer resistance has no effect on the rate of the adsorption, whereas the intraparticle diffusion significantly affects the adsorption process. It was studied by using

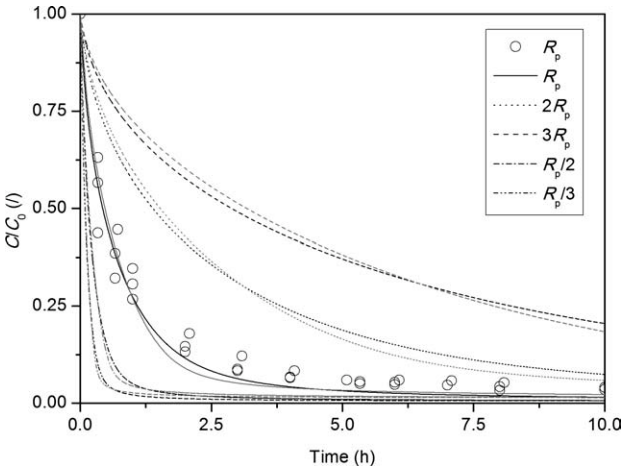

Figure 7. Active ingredient concentration profile for the adsorption of vancomycin on polymeric adsorbent from 100% (by vol.) fermentation broth (FB) during batch experiments at five different adsorbent particle sizes.

Symbols represent measured data; lines represent HSDM model data using Sips isotherm (black lines) and Langmuir isotherm (grey lines) to describe equilibrium.

the RSFK model, the HSDM, and the BPM. The HSDM gave the best agreement.

Intraparticle diffusion slows down the adsorption of vancomycin with the particles of particular size investigated here. However, process kinetics could be improved by using smaller particles, which is shown by model calculations.

The classical chemical engineering approach—separate study of equilibrium and process kinetics—gave a better insight into the overall process of adsorption of vancomycin on industrial scale. The results incite further research of the examined phenomena and hopefully a successful improvement of the industrial application will ensue.

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