APPLICATION OF CARBON ADSORBENTS IN RENAL FAILURE TREATMENT

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Introduction

Current therapies for the treatment of renal failure, including haemofiltration (HF) and haemodialysis (HD) consist of extracorporeal circuits that remove the blood from the patient's body and pass it through a membrane where the excess water and uraemic toxins are removed.

The main limitation of haemodialysis techniques is the scarce removal of solute in the range of middle to high molecular weight that may cause a progressive accumulation of these molecules with complications in the long term [1]. Moreover haemodialysis requires large amount of dialysate fluid for the removal of uremic metabolites placing a considerable cost burden on the health care provider. The use of adsorbent such as activated carbons may improve efficiency of the extracorporeal techniques either as a material suitable for haemoperfusion or as a method of cleansing and recycling of the patient's ultrafiltrate/dialysate produced during HF or HD.

This study investigates the adsorption efficiency of polymer-based carbon adsorbents with different pore-size distribution produced by MAST Carbon Ltd. (Henley Park, Guildford, Surrey, UK) to remove ibuprofen and the uraemic toxin creatinine from model solutions and from ultrafiltrate obtained from patients with renal failure receiving HF. Ibuprofen was selected for its toxic characteristic associated to renal failure but also as a model for the removal of albumin–bound substances. Ibuprofen is 99% protein bound [2]. The efficiency of the model carbons was compared to that of a commercially available coated activated carbon Adsorba300C.

Results showed that creatinine and ibuprofen could be removed efficiently from both model solutions and ultrafiltrate.

Experimental
1. Adsorbents
Uncoated polymer based granulated activated carbons were obtained from MAST Carbon Ltd. (Guilford, Surrey UK). These activated carbons only differ in their degree of activation burn-off, and their structural characteristics are reported in table (Table 1)

together with the pore size distribution (Figure1). Coated carbon, Adsorba300C, is commercially available (Gambro) and posseses only micropores.

Table 1. Structural characteristics of activated carbons

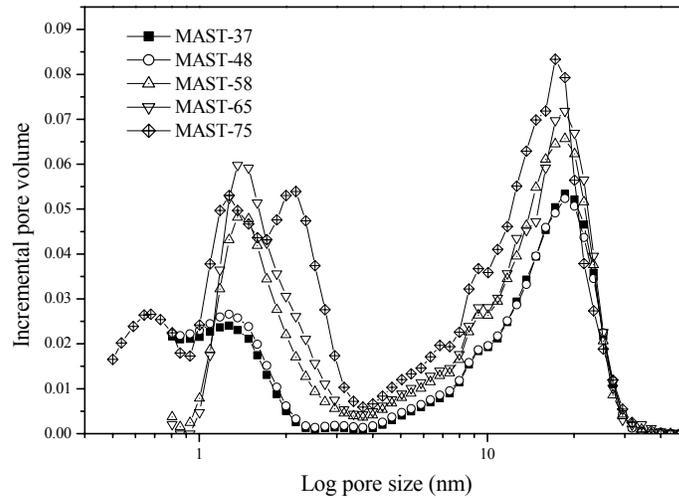| Adsorbent	Activation burn -off	S_{BET} sq.m/g	V_{pore} at P/P$_0$=0.98cc/g
MAST 37%	37%	1147.3	1.15
MAST 48%	48%	1342.0	1.32
MAST 58%	58%	1816.2	1.72
MAST 65%	65%	1838.2	1.73
MAST 75%	75%	2333.2	2.12
Adsorba300C	Coated carbon used as reference material		

Figure 1. MAST carbons pore size distributions with detailed micropores region

2. Batch experiment: adsorption isotherms in protein free solution
Batch experiments were undertaken to test the adsorption capacities of MAST carbons and Adsorba300C for ibuprofen and creatinine in Tyrode buffer.
Samples of carbon (0.03g) were mixed with solutions of ibuprofen (25-2.5mM) or creatinine (0.8-8 mM) in Tyrode buffer (10mL). The slurries were shaken for 24 hours at constant temperature (25°C). The concentration of the adsorbate in the residual solution was analysed by UV-VIS spectrometry (Cary50 spectrometer, Varian) at a wavelength of 263nm for ibuprofen and 234nm for creatinine. The previously established linear Beer-Lambert relationship was used in the concentration analysis. The amount of solute adsorbed by the carbon was determined as follows:

$$q_e = \frac{V(C_o - C_e)}{M} \qquad (1)$$

where q_e is the amount of adsorbate on the carbon at equilibrium, V is the volume of

solution, C_o the initial concentration of adsorbate in the solution, C_e the residual concentration and M the amount of carbon used.

3. Batch experiment adsorption isotherms from protein containing solution

The adsorption of ibuprofen was measured from Tyrode buffer solution containing albumin. Samples of carbon (0.03g) were mixed with solutions of ibuprofen (25 mM – 2.5 mM) in Tyrode buffer in presence of BSA at a constant concentration of 1mg/mL (0.1% w/v). The slurries were shaken for 24 hours and the final solutions were analysed by UV-spectrometry at 263nm using previously described method.

4. Column experiment: adsorption from aqueous solution

Samples of adsorbents (1.5 mL) of MAST-48 were packed in a plastic disposable column with polyethylene septum (d 0.6 cm x h 10 cm) (Merk Ltd). The column was connected to a peristaltic pump and a fraction collector. Ibuprofen (2.6 mM) or creatinine (0.20 mM) solutions in Tyrode buffer were passed through the column with a flow rate of 1 ml/min at room temperature. Fractions were collected every 10 minutes and analysed by UV- visible spectroscopy.

5. Column experiments: adsorption from patient ultrafiltrate

The procedure described in section 4 was used to asses creatinine and ibuprofen removal from ultrafiltrate obtained from patient with acute renal failure receiving continuous haemofiltration.

Creatinine present in ultrafiltrate before and after column was determined using a kinetic assay kit obtained from Alpha Laboratories Ltd. Ibuprofen was spiked in ultrafiltrate 2 hours before use and its concentration in ultrafiltrate was determined by HPLC on a C18 column (150 mm, Jones Chromatography) of 3.5μm particle size. The mobile phase consisted of 40% acetonitrile in ammonium acetate 50 mM (pH 6). The flow rate was maintained at 1.5 ml/min and ibuprofen was monitored at 230 nm.

Results and Discussion

The adsorption isotherms for ibuprofen, expressed as equilibrium concentration against amount of the solute adsorbed per gram of carbon, are reported in Figures 2 and 3. In protein free solutions (Figure 2) the amount of ibuprofen adsorbed increases with the increase of activation burn–off. In protein containing solutions the same trend was shown; the increase in carbon activation results in an increase of ibuprofen adsorption (Figure 3). Moreover the presence of albumin does not appear to affect the amount of ibuprofen adsorbed when compared to the protein free solution suggesting that similar the adsorption may occurs in the micropores. Moreover the coated carbon Adsorba300C showed a high adsorption capacity in protein free solutions (Figure2) but its adsorption capacity decreases significantly in the presence of BSA (Figure 3). The presence of the cellulose coating on Adsoba300C may affect the diffusion of large molecules such as albumin-ibuprofen complex [3] and/or the protein may be adsorbed on the coating reducing the diffusion of ibuprofen into the carbon.
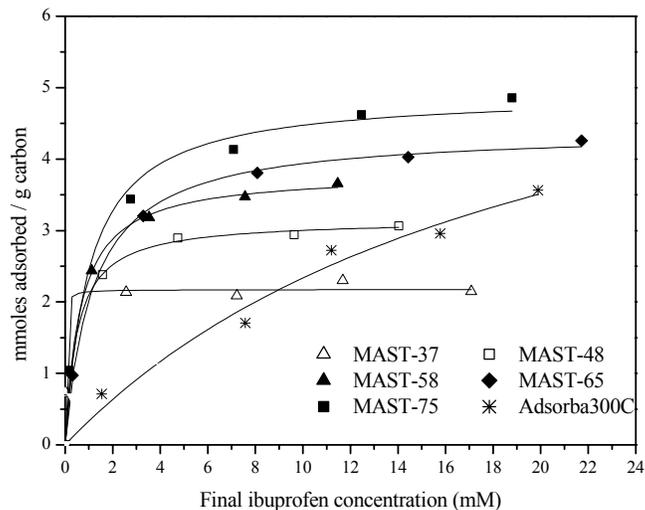
Figure 2. Ibuprofen adsorption isotherms from protein-free solution using different carbons (each point represents a mean of three experiments).
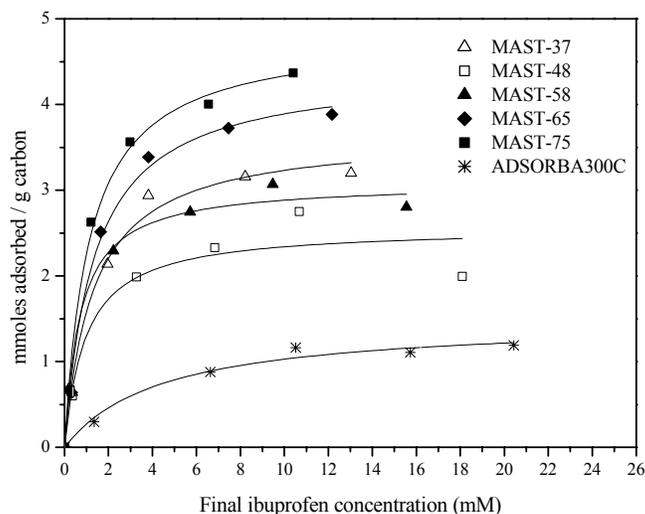

Figure 3. Ibuprofen adsorption isotherms in presence of BSA 1.00 g/dm3 (each point represents a mean of three experiments). Amount of solute adsorbed per g of carbon is plotted against final (equilibrium) concentration.

Creatinine is efficiently adsorbed on MAST carbons (Figure 4), however its adsorption was not related to the MAST activation. The adsorption capacity of creatinine for MAST-48 and MAST-65 are comparable and higher than MAST-37. A large increase in uptake is instead observed for MAST-75. Adsorba300C showed the lowest adsorption capacity for ibuprofen.

Creatinine in a small molecule (Mw: 113.1) and as such is expected to be adsorbed in the micropores of the carbons, however it is clear that an increase of micropores with activation (Figure 1) does not result in an increase in adsorption (Figure 3). This may be due some other mechanism involved in creatinine adsorption rather than physical adsorption
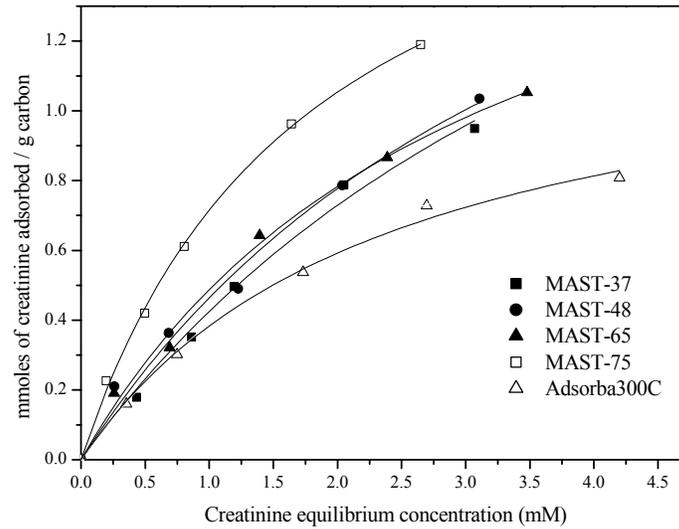

Figure 4. Creatinine adsorption isotherm using different carbons. Amount of solute adsorbed per g of carbon is plotted against final (equilibrium) concentration
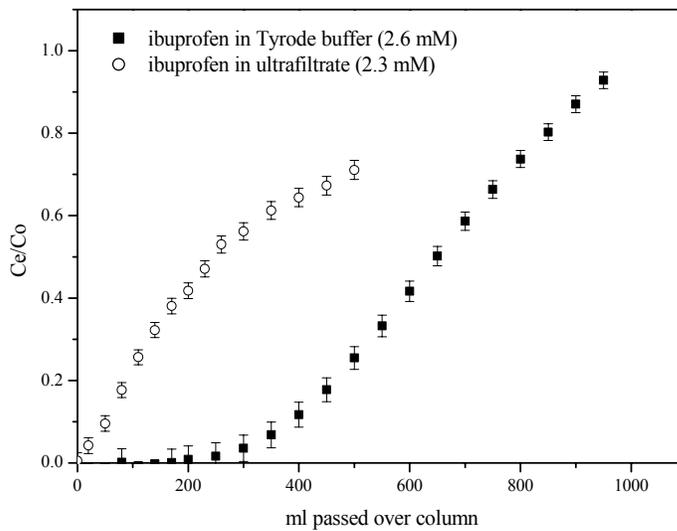

Figure 5. Breakthrough curve of ibuprofen at different concentration on MAST-48
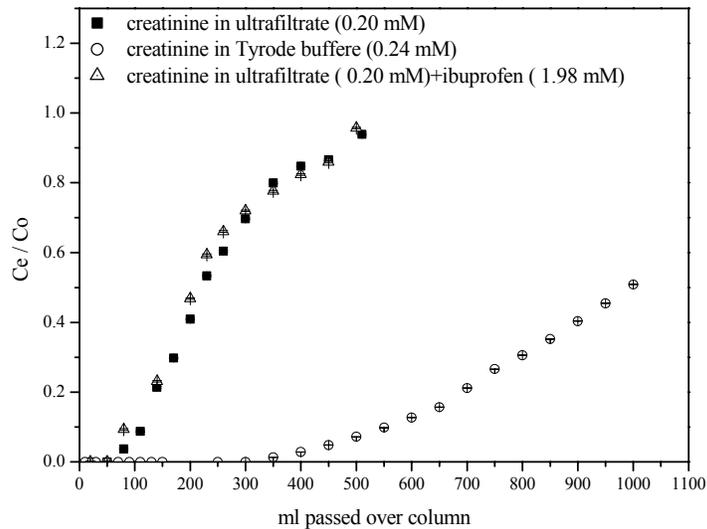
Figure 6. Adsorption of creatinine from ultrafiltrate, in presence of spiked ibuprofen.

From the batch experiments MAST-48 was selected for the column adsorption study. The breakthrough capacity of ibuprofen in ultrafiltrate significantly decreased when compared to adsorption from Tyrode buffer solutions (Figure 5). The same reduction in adsorption was observed for creatinine (Figure 6). This may be due to the fact that ultrafiltrate contains a variety of components that may compete with creatinine and ibuprofen for adsorption onto the carbon. However, as far as creatinine adsorption is concerned the additional presence of ibuprofen in ultrafiltrate does not furthermore decrease its adsorption onto the activated carbon column (Figure 6). This demonstrates that creatinine has a stronger affinity than ibuprofen for the carbon surface when both present in ultrafiltrate.

Conclusions
Activated carbons adsorbents have been shown to have the potential to improve the efficiency of the extracorporeal techniques either as a material suitable for haemoperfusion or as a method of cleansing and recycling of the patient's ultrafiltrate/dialysate produced during HF or HD. Creatinine and ibuprofen, both in the presence or absence of protein, are efficiently removed by MAST carbons and even if the capacity of adsorption for these molecules is reduced when adsorbed from ultrafiltrate they can still offer a good removal of these unwanted toxins.

References
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