Retention of urea and caffeine on copper metal organic frameworks (MOFs)

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ABSTRACT

The $[Cu_3(BTC)_2]$ MOF (BTC = 1,3,5-benzenetricarboxylate), also known as HKUST-1 (or MOF-199), is one of the most cited metal-organic framework because it has a large surface area, high pore volume, high chemical stability and also the ability to bind water, among other molecules, by coordinating to the unsaturated Cu(II) sites. In this study we propose two strategies for retention of urea and caffeine in copper metal organic framework ($Cu_3(BTC)_2$). The first one correspond in-situ encapsulation where urea and caffeine are added to copper MOF synthesis precursors and the porous structure is formed around the urea or caffeine molecules. The second one corresponds to post-synthesis encapsulation. Indeed, MOF is obtained by conventional synthesis and activated at 100 °C during 12 h. Finally, urea or caffeine was incorporated into MOF structure by contact solution. Materials were characterized by XDR, FTIR and UV-Vis, to compare both encapsulation methods and identifying the physicochemical properties of MOFs. The results shown in-situ encapsulation of urea and caffeine in $Cu_3(BTC)_2$ produced a guest loading of 25 % and 38 %, respectively. Whereas, post-synthesis method had a guest loading of 30 % and 52 % for urea and caffeine, respectively. All synthesized materials correspond to cubic $Cu_3(BTC)_2$ structure with different red parameters.

Keywords: metal organic frameworks, urea, caffeine, encapsulation, copper MOF.

1 INTRODUCTION

A drug is a chemical substance capable of preventing, controlling, treat, cure or modify undesirable physiological processes [1]. In the last decade, trace pharmaceuticals, at levels ranging from nanograms to micrograms per liter have been reported in the water cycle, including surface water, wastewater, groundwater and less water consumption [2].

Currently drugs are considered contaminants that have a large presence in the environment, especially in water, because people get rid of them by throwing them into the trash or toilet. Additionally, much of ingested drugs are released through urine and reach water bodies, such as antidepressants (diazepam and caffeine), anticonvulsants (carbamazepine), beta-blockers (atenolol, propanolol), regulators of cholesterol (bezafibrate) anti-septic (such as triclosan), antibiotics (penicillin), anti-histamines, analgesics (ibuprofen, diclofenac, naproxen), among others. Especially at the point of discharge of urban sewage, considerable concentrations of those contaminants [3] are presenting.

The advanced and expensive water treatment technology can't eliminate completely all-pharmaceutical products [2]. A recent invention of crystalline material, formed by organic ligands and a metal center, has generated interest because of its various applications including drug retention [4, 5], catalysis [6], guest adsorption (molecular recognition) [7], optical applications [8], sensor technologies [9] and gas storage [10]. These are metal organic frameworks (MOF), they have the ability to store compounds in its porous structure. Both the metal centers as organic ligands can be chosen depending on the field of application, for retention of drugs has been used as metal center iron (Fe) as it is for human consumption [4], however, as proposed for external use, central metallic copper (Cu) was used.

Caffeine is an amphiphilic drug with significant lipolytic activity, becoming a very useful agent mainly in the cosmetic industry. Caffeine molecules have often been used as a model active ingredient, so many formulations of caffeine contained within several different matrices have been studied. These include cyclodextrines , liposomes and niosomes, poly-(epsolon-caprolactone) polymer, PLGA-mPEG copolymers, protein concentrate hydrogel, silica and more recently metal organic frameworks as ZIF-8 [5] or MIL [4].

Drug retention was conducted in two stages, in-situ encapsulation where urea and caffeine are added to copper MOF synthesis and post-synthesis encapsulation. To determine the physicochemical properties of copper MOF we report DRX, IR, and nitrogen adsorption characterization. UV-Vis was used to quantify caffeine and urea encapsulation into copper MOF.

2 EXPERIMENTAL SECTION

2.1 Synthesis

In-situ encapsulation**.** The quantity of 2.0 mmol of benzene-1,3,5-tricarboxylic acid (BTC, 95% purity, Aldrich) was dissolved in 150 mL of distilled water. 50 mL of urea (pharmaceutical standard, Sigma-Aldrich) or caffeine (1,3,7-trimethylxanthine, Reagent Plus, Sigma-Aldrich) solution of 0.1 M was added to the organic solution. Second solution prepared with 3.0 mmol of copper nitrate (99.99% grade, Aldrich) in 40 mL of ethanol anhydrous was gradually added to the organic solution. The synthetic mixture was stirring at room temperature during 12 h. The resulting product was isolated by centrifugation and dried at 323 K for 2 h. Solids and liquids were stored for further characterization. Samples was labeled as Ure-

$Cu_3(BTC)_2$ and Caf- $Cu_3(BTC)_2$ for urea and caffeine retention, respectively.

Post-synthesis encapsulation. $Cu_3(BTC)_2$ MOF was prepared using the reported procedure by Loera-Serna et al. [7] The quantity of 2.38 mmol of 1,3,5-benzenetricarboxylic acid was dissolved in 150 mL of distilled water. Then, a solution containing the quantity of 3.57 mmol of copper nitrate trihydrate and 40 mL of ethanol was added a drip. The synthetic mixture was stirring at room temperature during 12 h. The resulting $Cu_3(BTC)_2$ product was isolated by centrifugation and dried at 323 K for 2 h. Before encapsulation, the $Cu_3(BTC)_2$ was dried overnight at 373 K and 10-3 Torr. The ratio of adsorbent/drug was 0.5g /50 mL of 0.1 M. Samples was labeled as Ure-$Cu_3(BTC)_2$-Post and Caf-$Cu_3(BTC)_2$-Post for urea and caffeine retention, respectively.

2.2 Characterization

The MOFs were characterized by X-ray diffraction (XRD) analysis. A powder diffractometer (Philips X'PERT PRO) coupled to a copper anode X-ray tube was used to identify compounds present in each sample. The FT–IR spectra (4000–650 cm^{-1}) were obtained with a resolution of 2 cm^{-1} on a Bruker Tensor-27 spectrometer, fitted with a DTGS detector. All adsorption measurements were conducted using a BELSORP-max (BELL Japan Inc.) system at -196 ºC. Samples were degassed under dynamic conditions (extra-dry air flow) over 24 h at 100 ºC prior to adsorption measurements. BET specific surface areas were calculated from the N_2 adsorption isotherms. Spectrophotometric analysis was performed using a Shimadzu Pharm Spec UV-VIS spectrometer.

3 RESULTS AND DISCUSION

The X-ray diffraction patterns of urea, caffeine and $Cu_3(BTC)_2$ are show in Figure 1. The diffraction peaks, in $Cu_3(BTC)_2$ correspond to cubic structure of copper metal organic framework, know as HKUST-1 or MOF-199. Peaks was readily indexed as $Cu_3(BTC)_2$ [11], whose average cell parameter is 26.13 Å and crystal size of 292 nm. Diffraction patterns of caffeine and urea present a main peak at 12.3 and 22.5 (2θ).

The Figure 2 compare X-ray diffraction pattern of $Cu_3(BTC)_2$, with patterns of samples prepared by in-situ encapsulation (Caf-$Cu_3(BTC)_2$) and post-synthesis encapsulation (Caf-$Cu_3(BTC)_2$-Post) of caffeine. The diffraction peaks, in all diffractograms, correspond to $Cu_3(BTC)_2$structure.

In sample Caf-$Cu_3(BTC)_2$-Post new peaks at 9.50 y 10.47(2θ) appears, these correspond to new crystalline compound that is not present in any of reference patterns, this provided the same diffraction peaks as Cu(OH)(BTC)(H_2O)]· 2H2O [13]. The background line of Caf- $Cu_3(BTC)_2$-Post X-ray diffraction patterns is not flat; thus, a fraction of the sample is constituted by a noncrystalline compound. The percentage of each compound is estimated from peak areas, assuming that the X-ray absorption coefficient is the same in all copper MOF compounds, the result were 13.72 % of noncrystalline material, 25.73 % of a new crystalline compound and 60.56 % of $Cu_3(BTC)_2$. Note that, if the percentage of crystalline compounds is measured by this way, the percentage of noncrystalline material is determined (amount required to complete 100 %) [12].

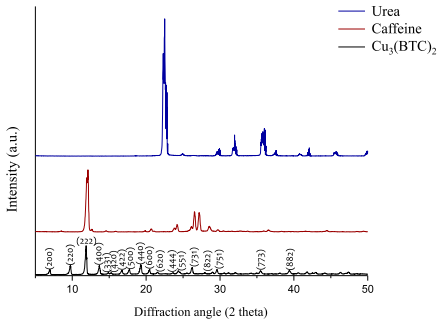

Figure 1. X-ray diffraction patterns of urea, caffeine and $Cu_3(BTC)_22$ synthesized by stirring at room temperature. Numbers above peaks correspond to Miller indexes determined by comparison of $Cu_3(BTC)_2$ [11].

The cell parameter of the cubic structure $Cu_3(BTC)_2$ was found to be 26.13 Å. When caffeine was incorporated to the MOF structure by in-situ encapsulation the cell parameter was 26.14 Å, while the caffeine was incorporated by post-synthesis methodology the cell parameter was 26.13 Å. The differences, ca. 1%, are relevant and beyond experimental error. The crystal size determined by Scherrer equation [13] were 292, 393 and 362 nm for $Cu_3(BTC)_2$, Caf- $Cu_3(BTC)_2$ and Caf- $Cu_3(BTC)_2$-Post, respectively. Main peak of caffeine are not present in both samples, this results can be due to the caffeine incorporation to the MOF structure.

The Figure 3 compare X-ray diffraction pattern of $Cu_3(BTC)_2$, with patterns of samples prepared by in-situ encapsulation, Ure-$Cu_3(BTC)_2$ and post-synthesis encapsulation (Ure-$Cu_3(BTC)_2$-Post) of urea. The diffraction peaks, in Ure- $Cu_3(BTC)_2$ diffractograms, correspond to $Cu_3(BTC)_2$ structure. Main peak of urea are not present in both samples, this results can be due to the urea incorporation to the MOF structure. However, diffraction peaks of Ure-$Cu_3(BTC)_2$-Post correspond to coordination polymer [Cu(OH)(BTC)(H_2O)]· $2H_2O$ structure, reported by Chen et al. [30]. When urea was incorporated to the MOF structure by in-situ encapsulation the cell parameter was 25.97 Å, smaller than cell parameter of $Cu_3(BTC)_2$ (26.13 Å) , urea molecules can be generate higher interactions into the MOF´s cavities, responsible of the decreasing of cell parameter. This interaction can be hydrogen bond as shows in Figure 4. The crystal size determined by Scherrer equation [13] were 292, 394 and

274 nm for $Cu_3(BTC)_2$, Ure-$Cu_3(BTC)_2$ and Ure-$Cu_3(BTC)_2$-Post, respectively.

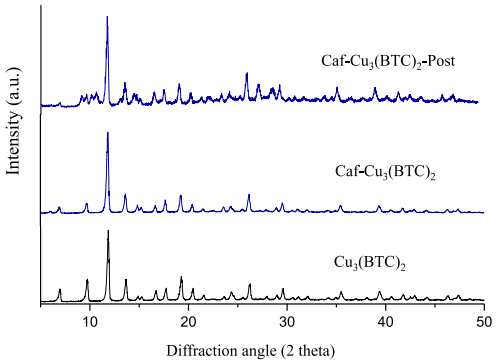

Figure 2. X-ray diffraction patterns of reference sample $Cu_3(BTC)_2$, and copper MOF with caffeine.

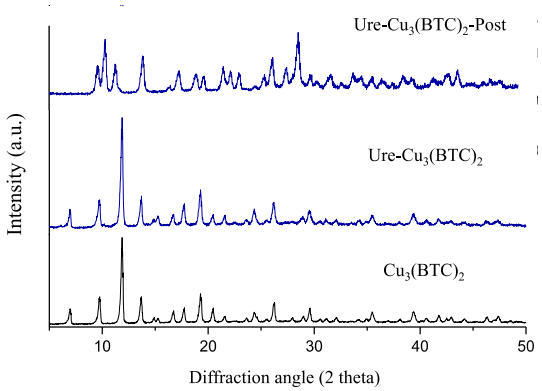

Figure 3. Powder X-ray diffraction patterns of reference sample and copper MOF with urea.

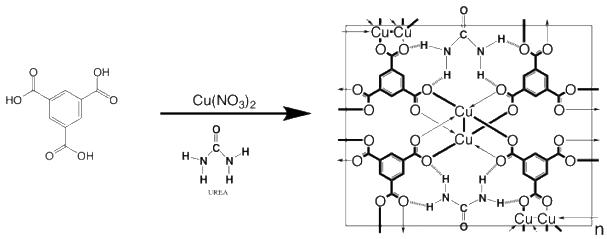

Figure 4. Representation of the adsorption of urea into Cu3(BTC)2 porous.

The FTIR spectra of $Cu_3(BTC)_2$ and caffeine, are compared with MOF sample prepared by in-situ caffeine encapsulation (Caf-$Cu_3(BTC)_2$) and post-synthesis caffeine encapsulation (Caf-$Cu_3(BTC)_2$-Post) in Figure 5. The IR spectrum of $Cu_3(BTC)_2$ clearly evidenced an almost isobidentate behavior of -COO moiety since bands at 1645, 1620, 1570, 1550, 1450 and 1378 cm^{-1} are characteristic of this coordination mode. The latter due to the fact that iso- and aniso-bidentate dicopper (II) carboxylate, type of monomeric clusters are present in the $Cu_3(BTC)_2$ frame [31]. The IR spectrum of caffeine shows a mains band at 1710 and 1652 cm^{-1}, these bands are represented in circles in Figure 5.

The IR spectra of Caf- $Cu_3(BTC)_2$ and Caf- $Cu_3(BTC)_2$-Post is quite the same to that obtained for Cu3(BTC)2. Moreover, $Cu_3(BTC)_2$ bands present in the spectra of the MOF Caf- $Cu_3(BTC)_2$ and Caf- $Cu_3(BTC)_2$-Post, present another set of bands characteristic of caffeine at 1290, 1238 and 1189 cm^{-1}. These results corroborate the incorporation of caffeine to the MOF structure.

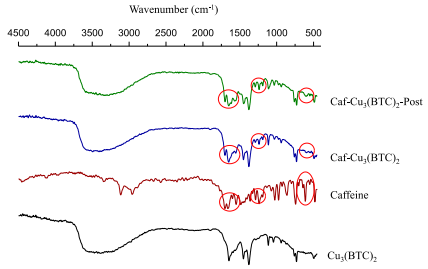

Figure 5. FTIR spectra of references ($Cu_3(BTC)_2$ and caffeine) and copper MOF with caffeine. Circles represent the main differences of IR spectra.

Figure 6 compares spectra of reference samples ($Cu_3(BTC)_2$ and urea) with urea MOF encapsulated during synthesis and post-synthesis, Ure- $Cu_3(BTC)_2$ and Ure-$Cu_3(BTC)_2$-Post, respectively. Bands at 1631, 1590, 1468, 1156 cm-1 are show in urea spectra, attributed to the amides (–CO-NH_2) group according with Spectra Data Base of Organic Compounds (SDBS). The band at 1156 cm-1still appears to the Ure- $Cu_3(BTC)_2$ and Ure-$Cu_3(BTC)_2$-Post samples, due to the urea incorporation to the MOF structure. Intensity bands at 1631, 1590 and 1468 cm-1 have a small intensity and doesn't present in spectra of Ure- $Cu_3(BTC)_2$ and Ure- $Cu_3(BTC)_2$-Post.

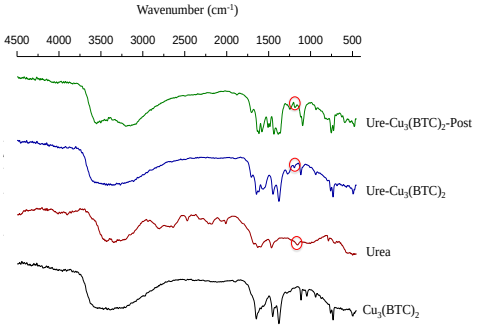

Figure 6. FT–IR spectra of references ($Cu_3(BTC)_2$ and urea) and copper MOF with urea.

Characterization by UV-Vis was conducted in the fluid from the filtrate of the MOF and solutions of the caffeine and urea. Calibration curves and quantification of drug molecules (caffeine and urea) were performed, using the Beer-Lambert Law [16], the concentration of caffeine or urea not retained in the MOF was determined. The results are presented in Table 1. The specific BET and Langmuir surface areas of reference MOF and caffeine and urea encapsulated MOF are presented in Table 2. The

$Cu_3(BTC)_2$ synthesized by stirring at room temperature generate MOF structure with BET and Langmuir specific surface area of 1457.8 and 1752.7 m^2g^{-1}, respectively. Those values are a high area for this type of MOF [7].

Sample	% of caffeine	Sample	% of urea
Caf-$Cu_3(BTC)_2$	38	Ure-$Cu_3(BTC)_2$-Post	25
Caf-$Cu_3(BTC)_2$-Post	52	Ure-$Cu_3(BTC)_2$-Post	30

Table 1. Quantity of caffeine and urea retained, in MOF, determined by VU-Vis.

The specific surface area of caffeine and urea encapsulated sample are smaller than reference sample. These results corroborate the drug molecule encapsulation into the copper MOF porous. The specific BET and Langmuir surface area of Ure- $Cu_3(BTC)_2$-Post could not determined due to the structure. The difference between specific surface area of in-situ samples and pot-synthesis samples can be attributed to the quantity of caffeine and urea, samples prepared by post-synthesis methodology retained 14 % more caffeine and 5 % more urea (UV-Vis results). The specific BET surface area of Caf- $Cu_3(BTC)_2$, Caf- $Cu_3(BTC)_2$-Post and Ure- $Cu_3(BTC)_2$ 40.42, 53.68 and 53.89 % respectively, decreases compare with $Cu_3(BTC)_2$ specific surface area. This result corroborates the caffeine and urea encapsulation into $Cu_3(BTC)_2$ structure.

Sample	$A_{BET}(m^2g^{-1})$	$A_{Langmuir}$ (m^2g^{-1})
$Cu_3(BTC)_2$	1457.8	1752.7
Caf-$Cu_3(BTC)_2$	868.42	1141.8
Caf-$Cu_3(BTC)_2$-Post	675.3	856.9
Ure-$Cu_3(BTC)_2$	672.16	900.51
Ure-$Cu_3(BTC)_2$-Post	a	a

Table 2. Specific BET and Langmuir surface area of MOFs samples. a. Not determined

5 CONCLUSIONS

The preparation method discussed in this work provides copper metal organic framework whit caffeine and urea encapsulates into their pores. Retention was conducted by two different mechanisms; the first retention during synthesis of the MOF (is-situ encapsulation) and the second one retention was in a post-synthesis process. Caffeine has managed to retain 38 % during in-situ encapsulation and 52 % in the post-synthesis encapsulation. Urea retention was 25 % during in-situ encapsulation and 30 % in the post-synthesis encapsulation. Urea retention mechanism by post-synthesis, is considered a possibility for degradation of these solids. Furthermore, urea encapsulation in-situ generate high interaction type H-bond to provide copper MOF with smaller red parameter than the $Cu_3(BTC)_2$. The synthesis encapsulation method can generate caffeine adsorption into the MOF structure with high interaction as in-situ encapsulation or Van der Walss interaction as post-synthesis encapsulation. The most efficient approach to retain caffeine and urea into copper MOF was post-synthesis process.

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