Supporting Information

Antineoplastic Busulfan encapsulated in Metal Organic Framework nanocarrier: first *in vivo* results

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Materials and methods

MIL100 and MIL100-Bu nanoparticles preparation and characterization was performed as descrived elsewhere[1,2].

Animal studies

Animal experiments were conducted according to the Guide for the Care and Use of Laboratory Animals published by the US National Institutes of Health (8th edition, 2011). All experimental procedures were reviewed and approved by the Animal Experimentation Ethics Committee of the Faculty of Pharmacy of Paris-Sud 11 University, France. In total, 18 female Wistar rats (210±10 g) were randomly divided in three different groups receiving a unique intravenous dose of the above-mentioned treatments. In all groups, treatments were suspended in glucose 10 % up to a total volume of 0.5 mL and administered via the jugular vein. For the intravenous administration anesthesia was induced by Isoflurane inhalation. Then, an incision was performed near the chest to access the jugular vein and intravenous administration was done using a 25 G needle. Chest was closed using surgical staples. After receiving the treatment animals were kept in metabolic cages to collect both urine and feces. To study the PK profile, 400 µL of blood was extracted at different time points (5, 15 and 30 min., and 1, 3 and 8 h). Also, 24 h after treatment animals were sacrificed, blood was extracted and organs (liver, spleen, lungs and kidneys) collected to analyze the trimesate content.
Immediately after extraction, blood was centrifuged at 3,600 rpm for 10 min. and then the supernatant was collected and 5 units/mL of heparin added. Urine was also centrifuged (14,500 rpm, 10 min) and 100 µL of sulfuric acid 0.1 M was added to the supernatant. Besides, organs were fixed in 4 % formaldehyde. In all cases, samples were stored at -20 °C until analyzed. The HPLC method followed to quantify the trimesate concentration in the organ samples has been described elsewhere[3]. Extraction in serum was performed as follows. Serum (50 µL) was mixed with 1 mL of PBS 1 M and 2 mL of methanol to cause protein precipitation. After incubating for 45 min, liquid phase was harvested by centrifugation and evaporated at 90 °C overnight. Prior to HPLC 50 µL injection, 600 µL of the mobile phase (50 % PBS pH 2.5 and 50 %MeOH) were added and sample was filtered (0.15 µm). HPLC processing method was the same than for the organ samples. Finally, already described GC-MS method to quantify Bu was followed.

References

1 P. Horcajada, T. Chalati, C. Serre, B. Gillet, C. Sebrie, T. Baati, J. F. Eubank, D. Heurtaux, P. Clayette, C. Kreuz, J.-S. Chang, Y. K. Hwang, V. Marsaud, P.-N. Bories, L. Cynober, S. Gil, G. Férey, P. Couvreur and R. Gref, *Nat. Mater.*, 2010, **9**, 172–8.

2 M.G. Chiper, P. Horcajada, G. Maurin, L.L. Lesueur , A. Seck , A. Paci, P. Couvreur, C. Serre, R. Gref. *Unpublished*, 2015.

3 T. Baati, P. Horcajada, R. Gref, P. Couvreur and C. Serre, *J. Chromatogr. B Anal. Technol. Biomed. Life Sci.*, 2011, **879**, 2311–2314.