Multiscale Computational study of 5- Fluorouracil delivery by Zeolite Imidazole Frameworks (ZIFs)

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Zeolitic Imidazolate Frameworks (ZIFs) are considered as potential nanocarriers in biomedical applications such as storage and transportation of drugs, due to their low toxicity, high internal load and controlled release. In this work, the interaction of selected ZIFs with the anticancer drug 5-Fluorouracil (5-FU) is studied, through semi-empirical computational techniques (PM7), Grand Canonical Monte Carlo simulations and also Molecular Dynamics. Our investigation is based on ZIF-8 which is characterized by pH-sensitive controlled drug release [1]. In order to improve the drug interaction with the framework and expand the parent ZIF-8, we replace imidazole with 3-(1H-pyrrol-3-yl)pyridine for each linker. This modified ZIF shows an interaction with 5-FU of 34 kcal/mol, where the parent ZIF-8 has only 12 kcal/mol. Furthermore, Grand Canonical Monte Carlo simulations were employed to determine the loading of 5-FU in both ZIF compounds under different thermodynamic conditions [2], and Molecular Dynamics simulations reveal a detailed comparison between the two ZIF materials.

References

[1] Chun-Yi, S., Chao, Q., Xin-Long, W., Guang-Sheng, Y., Kui-Zhan, S., Ya-Qian, L., Zhong-Min, S., Peng, H., Chun-Gang, W., En-Bo, W. Zeolitic imidazolate framework-8 as efficient pH-sensitive drug delivery vehicle. *Dalton Trans* **2012**, *41*, 6906-6909.

[2] Tylianakis, E.; Froudakis, G. E. Grand Canonical Monte Carlo Method for Gas Adsorption and Separation. *Journal of Computational and Theoretical Nanoscience* **2009**, 6, 335-348.