

Synthesis of Cu and Co complexes of bosentan and study of solubility at different pHs

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ABSTRACT

The low solubility and dissolution rate of active pharmaceutical ingredients (API) are an important limitation for oral transport and absorption, therefore they have a low bioavailability. For this reason, research has emerged in the pharmaceutical industry to modify an API to improve some of its properties through so-called "essential metals". Metallic drug complexes can modify the important physicochemical properties of the API, as well as its stability, solubility and rate of dissolution. It has been shown that the active principles used to regulate blood pressure form stable complexes with metal, increasing their therapeutic effect. This study focuses on the synthesis and characterization of copper and cobalt complexes of bosentan (Figure 1), an API indicated as a controller of pulmonary arterial hypertension. In the Cambridge Structural Database, there is a report of Zn complex with this active ingredient. The copper complex shows better solubility at pH 3 and 7 compared to the API and the cobalt complex, while cobalt complex has an improvement in its solubility at pH 8.

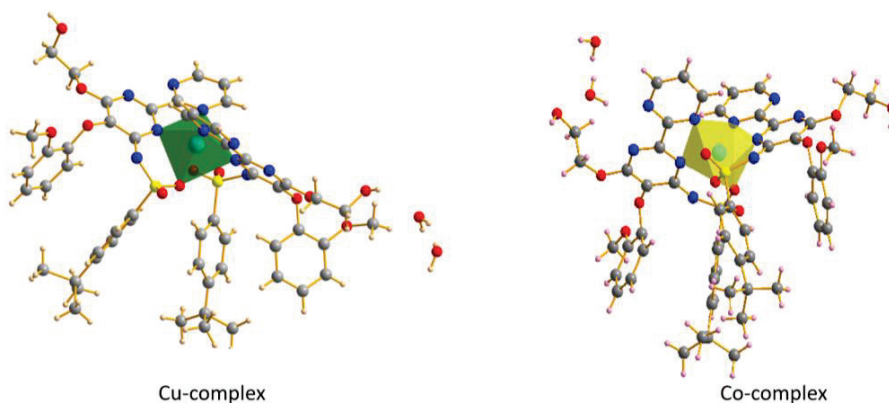


Figure 1. Complex $M-(\text{Bosentan})_2$ ($M= \text{Cu}, \text{Co}$).

References

Khandar, A. A., Mirzaei-Kalar, Z., White, J. M., Hosseini-Yazdi, S. A., Kebriaeezadeh, A., Jouyban, A. (2017). *Journal of Molecular Liquids*, 234, 64–72