

**Experimental electron density of Zn-aspirinate complex: the subtlety of a 3d<sup>10</sup> metal bonding to a drug-ligand.** Spasojevic-de Biré<sup>1</sup>, A.; Kremenovic<sup>1</sup>, A.; Bouhmaida<sup>2</sup>, N.; Morgant<sup>3</sup>, G.; Ghermani<sup>4</sup>, N.E.; [spaso@spms.ecp.fr](mailto:spaso@spms.ecp.fr) <sup>1</sup>Ecole Centrale Paris, SPMS UMR CNRS 8580 1, Grande Voie des Vignes, 92295 Châtenay-Malabry cedex, France. <sup>2</sup>LSM, Université Cadi Ayyad, Faculté des Sciences Semlalia, Boulevard Prince Moulay Abdallah, BP 2390, 40000 Marrakech, Morocco. <sup>3</sup>Laboratoire de Cristallographie Bio-inorganique, Faculté de Pharmacie 5, Rue Jean-Baptiste Clément, 92296 Châtenay-Malabry cedex, France. <sup>4</sup>LPP UMR CNRS 8612, Faculté de Pharmacie 5, Rue Jean-Baptiste Clément, 92296 Châtenay-Malabry cedex, France.

The design of metal-drug complexes is of a particular interest in the pharmacological researches. Metal combinations with pharmaceutical agents are known to improve the drug activity and to decrease the toxicity. The metal itself can be pharmacologically active (Cu) or can even regulate enzyme metabolism (Zn, Mg). Non-steroidal anti-inflammatory drugs (NSAID's), like aspirine derivatives, have a large spectrum in the therapy of common infections. NSAID's are also known to produce *in vivo* serious gastro-intestinal complications when the drug molecules are used alone. Therefore, the bonding interaction between the metal and the drug-ligand is an essential step in the understanding of further predictive biochemical enzyme inhibitions. In this study, the electron density distribution of Zn-aspirinate complex ( $\text{Zn}[\text{C}_9\text{O}_5\text{H}_9]\text{H}_2\text{O}]_2$ ) is derived from multipole refinements (Hansen-Coppens model) of accurate 100 K diffraction data (up to  $\sin\theta/\lambda = 1.15 \text{ \AA}^{-1}$ ). 81909 equivalent reflections were collected on a Siemens CCD diffractometer (MoK $\alpha$  radiation). The data processing yields an internal factor  $R_{\text{int}} = 4,07\%$  and 5082 unique data ( $I > 3\sigma(I)$ ) which are used in the refinements. The title compound crystallizes in monoclinic C2/c centrosymmetric space group. The crystal structure exhibits a monodentate aspirinate ligand ( $\text{Zn-O}(\text{acid group}) = 1.996(1) \text{ \AA}$ ,  $\text{Zn-O}(\text{H}_2\text{O}) = 2.019(1) \text{ \AA}$ ). Zn atom is tetrahedrally coordinated to two water molecules and to two oxygen atoms of two drug-ligands. The experimentally electron density obtained in the Zn-O bonds is discussed with respect to a hypothetical metal orbital hybridization (3d, 4s). The electrostatic potential is also calculated from the atomic multipole populations.