

# DFT-calculated Magnetic Parameters of Physiological Copper(II) Complexes with L-asparagine and L-histidine: A Tool for Verification of Predicted Lower-energy Conformers in Aqueous Solution

Jasmina Sabolović,<sup>a</sup> Anne-Marie Kelterer<sup>b</sup> and Michael Ramek<sup>b</sup>

<sup>a</sup> Institute for Medical Research and Occupational Health, Ksaverska cesta 2, HR-10000 Zagreb, Croatia;

<sup>b</sup> Institute of Physical and Theoretical Chemistry, Graz University of Technology, Stremayrgasse 9, A-8010 Graz, Austria  
jasmina.sabolovic@imi.hr

The copper(II) complexes chelated with two amino acids have been isolated from normal human blood serum and reported to be part of an exchangeable serum pool for copper [1,2]. It was shown that a majority of these physiological compounds were Cu<sup>II</sup> complexes with L-histidine (L-His) in the form of electrically neutral bis(L-histidinato)copper(II), and ternary complexes favorably with L-asparagine (L-Asn), L-threonine, and L-glutamine. The experimental studies of these physiological complexes were intensive during the 1970s through the 1980s. However, they did not determine the exact structures of the complexes in solutions. Our recent computational study resolved that missing piece of information for bis(L-asparaginato)copper(II) [Cu(L-Asn)<sub>2</sub>] and (L-histidinato)(L-asparaginato)copper(II) [Cu(L-His)(L-Asn)] by exploring their structural properties and energy landscapes using the density functional theory (DFT) with the B3LYP functional [3]. Systematic conformational analyses in the gas phase and in implicitly modeled aqueous surroundings using a polarizable continuum model located the low-energy conformers, and rationalized the effect of noncovalent interactions on the coordination modes and overall geometries of the complexes.

The predicted lower-energy aqueous structures with various combinations of the in-plane and apical donor atoms are used for DFT calculations of the *g*-factor and hyperfine coupling constants (HFCC) for a quantitative comparison to experimental electron paramagnetic resonance (EPR) data [4-6]. The calculated isotropic *g*<sub>iso</sub> and the most variable *g*<sub>z</sub> component of the **g** tensor, HFCC of the <sup>63</sup>Cu (*A*<sup>Cu</sup>) and <sup>14</sup>N (*A*<sup>N</sup>) centers were compared with their values obtained from the EPR spectra measured in aqueous solutions. The best match between the experimental and calculated magnetic parameters was obtained for the conformers in the coordination modes with the lowest Gibbs free energy values, and an apical oxygen atom (intramolecular or from a water molecule). A smaller *A*<sup>N</sup><sub>iso</sub> is calculated for the *trans* than *cis* conformers, while the B3LYP *A*<sup>Cu</sup><sub>iso</sub> values are very similar for the *trans* and *cis* conformers with the same coordination number. Our EPR interpretation points to the conclusion that in aqueous solution, a water molecule can place itself at the apical Cu<sup>II</sup> position if it is free.

## References

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