Synthesis and characterization of Pt(II) and Pd(II) complexes with the amino acid mimosine.

Carlos M. Manzano*, Pedro P. Corbi.

Abstract
Platinum(II) complexes with amino acids and their analogs of palladium(II) have been studied for years given their potential as antitumor drugs. The present work focus on the synthesis and characterization of new Pt(II) and Pd(II) complexes with the amino acid L-mimosine, a non-essential amino acid, which is able to block cell proliferation in vivo and inhibit tumor growth. The complexes were characterized by elemental and thermogravimetric analyses, infrared and solid state NMR spectroscopic measurements. The proposed molecular compositions for the compounds are PtCl2(C8H10N2O4) 1.5 H2O and PdCl2(C8H10N2O4) 1.0 H2O.

Key words: Mimosine, metal complexes, NMR.

Introduction
Platinum(II) complexes, like carboplatin and oxaliplatin, were developed as a less toxic alternative to cisplatin. They are often used against many different tumors, such as testicular, ovarian, head, neck and bladder cancers.[1] Lately, Pd(II) complexes have been considered in the medicinal chemistry, even though they are kinetically more reactive than the Pt(II) analogs.[2] On the other hand, the Pd(II) complexes are usually more soluble and can have higher antitumor activity than cisplatin.[3] Mimosine is an L-amino acid found in leaves and seeds of Leucaena glauca and Mimos a pudica. This amino acid shows many cytotoxic characteristics such as folate metabolism inhibition [4], apoptosis induction [5], blocking of cell proliferation in vivo and inhibition of tumor growth.[6] The goal of this project is to synthesize and characterize new Pt(II) and Pd(II) complexes with mimosine.

Results and Discussion
The complexes of Pt(II) and Pd(II) with mimosine (PtMMO and PdMMO) were synthesized by similar procedures. Mimosine (0.48 mmol) was solubilized in aqueous acidic solution (pH=4.0) and K2PtCl4 or K2PdCl4 (0.48 mmol) were added. The precipitation of a yellow solid was observed after 20 hours of stirring for PtMMO and after 2 hours for the PdMMO. The obtained solids were filtrated, washed with cold water and ethyl ether, and dried over P2O5. The yields were 44.6% for the PtMMO and 57.5% for PdMMO.

For [PtCl2(C8H10N2O4)]·1.5H2O: anal. Calcd. (%): C, 19.56; H, 2.67; N, 5.70. Found (%): C, 20.48; H, 2.77; N, 5.73. IR spectroscopy: ν(C=O) 1655 cm⁻¹ (shifted 35 cm⁻¹ from the free ligand) and ν(Pt–N) 563 cm⁻¹.


IR spectroscopy: ν(C=O) 1653 cm⁻¹ (shifted 37 cm⁻¹ from the free ligand) and ν(Pd–N) 559 cm⁻¹.

NMR spectroscopic characterization was performed in the solid state as the complexes were insoluble or unstable in all the solvents tested. The 13C NMR CP/MAS experiment showed the shift on the carbon atom of the carbonyl group of the ligand from 171 ppm to 188 ppm for PtMMO and 185 ppm for PdMMO. Image 1 presents the 15N solid state NMR for the complexes in comparison to the free ligand (MMO-HCl), proving the coordination of the NH2 group.

Conclusions
Two complexes of Pt(II) and Pd(II) with L-mimosine were synthesized and characterized. A square planar structure is proposed for these complexes, in which the mimosine molecule is coordinated to the metals by the nitrogen of the amino group and the oxygen of the carboxylic group.

Acknowledgement
This work was supported by grants from FAPESP (2012/08230-2) and CNPq (442123/2014-0). Carlos Marrone Manzano is grateful to CNPq-PICB for financial support.

References
1. Boulkas, T.; Vougiouka, M. Oncology Reports. 2004, 11, 559-595