Volume: 14
Year: 2025
ISSN: 2239-2459

ISMEC GROUP SERIES
Symposium Edition: XXXV
https://www.ismecgroup.org/ismec-acta/

ismec 2025

# Acta of the International Symposium on Thermodynamics of Metal Complexes

The **Acta of the International Symposium on Thermodynamics of Metal Complexes 2025** (ISSN: 2239-2459) is published annually online open access by the **ISMEC Group**.

**<u>Editors:</u>**

**Montserrat López-Mesas (President of the ISMEC Group)**

Department of Chemistry (GTS)

Unversitat Autònoma de Barcelona

Facultat de Ciències, 08193 Bellaterra (Cerdanyola del Vallès), SPAIN

montserrat.lopez.mesas@uab.cat

**Alicia Domínguez-Martín (Chair of the Organizing Committee ISMEC 2025)**

Department of Inorganic Chemistry

University of Granada

Campus Cartuja s/n 18071 Granada, SPAIN

adominguez@ugr.es



Acta of the International Symposia on Metal Complexes

ISMEC GROUP SERIES, VOLUME: 14, YEAR: 2025

ISSN: 2239-2459

https://www.ismecgroup.org/ismec-acta/

**International Scientific Committee of ISMEC 2025:**

**Montserrat López-Mesas** — Universitat Autònoma de Barcelona, Spain
President of ISMEC Group

**Natalia Busto** — Universidad de Burgos, Spain
Deputy president of ISMEC Group

**Demetrio Milea** — Università degli Studi di Messina, Italy
Former president of ISMEC Group

**Antonio Bianchi** — Università degli Studi di Firenze, Italy

**Elzbieta Gumienna-Kontecka** — Uniwersytet Wrocławski, Poland

**Enrique García-España** — Universitat de València, Spain
Chair of ISMEC 2022

**Vieri Fusi** — Università di Urbino, Italy
Chair of ISMEC 2023

**Maria Rosa Beccia** — Université Côte d’Azur, France
Chair of ISMEC 2024

**Alicia Domínguez Marín** — University of Granada, Spain
Chair of ISMEC 2025

**Andrea Melchior** — University of Udine, Italy
Chair of ISMEC 2026

## Local Organizing Committee of ISMEC 2025

**Alicia Domínguez Martín**
University of Granada, Spain. Chair of ISMEC 2025

**Juan Niclós-Gutiérrez**
University of Granada, Spain. Co-Chair of ISMEC 2025

**Duane Choquesillo Lazarte**
Consejo Superior de Investigaciones Científicas, Spain

**Ricardo Navarrete Casas**
University of Granada, Spain

**Miguel Ángel Galindo Cuesta**
University of Granada, Spain

**Cristobal Verdugo Escamilla**
Consejo Superior de Investigaciones Científicas, Spain

**Jeannette Carolina Belmont Sánchez**
University of Granada / Consejo Superior de Investigaciones Científicas, Spain

**Estephany Muñoz Hernández**
University of Granada / Consejo Superior de Investigaciones Científicas, Spain

**Francisco Javier Acebedo Martínez**
Consejo Superior de Investigaciones Científicas, Spain

**Joaquín Criado Reyes**
Consejo Superior de Investigaciones Científicas, Spain

# Design and redox properties characterization of metal/tetrabranched peptide adducts as possible superoxide dismutase mimics

Silvia BERTO, [a] Matteo MARAFANTE, [a] Silvia LEVERARO, [b] Maurizio REMELLI, [b] Eugenio GARRIBBA, [c] Riccardo BONSIGNORE, [d] Gianpiero ADAMI, [e] Antonello MERLINO [f], Denise BELLOTTI, [b]

[a] *Department of Chemistry, University of Turin, Via P. Giuria 7, 10125, Turin, Italy*
[b] *Department of Chemical, Pharmaceutical and Agricultural Sciences, University of Ferrara, Via Luigi Borsari 46, 44121, Ferrara, Italy*
[c] *Department of Medicine, Surgery and Pharmacy, University of Sassari, Sassari, Italy*
[d] *Department of Biological, Chemical and Pharmaceutical Sciences and Technologies, University of Palermo, Palermo, Italy*
[e] *Department of Chemical and Pharmaceutical Sciences, University of Trieste, Trieste, Italy*
[f] *Department of Chemical Sciences, University of Napoli Federico II, Napoli, Italy*

*silvia.berto@unito.it*

The alteration in the human physiological redox balance can lead to the increase of reactive oxygen species (ROS), that results in oxidative stress condition, which can cause molecular damage and tissue injury. The protection from ROS naturally occurs by processes mediated by superoxide dismutases (SODs) and catalases (CATs). To reduce oxidative stress damage exogenous SOD and CAT have been used as therapeutic agents [1], although with limited success [2]. Their use is limited by some restrictions, such as low thermal and chemical stability, low adaptation to extreme environments, and expensive preparation and purification processes [3]. To overcome these limitations, investigations have been directed to the design of low molecular-weight antioxidant catalyst. Enzyme mimics (EMs) usually replicate the binding and catalytic activities of natural enzymes, employing: i) metal complexes with comparable catalytic properties, ii) oligopeptides that reproduce the active site structure of naturals enzymes [4]. In this work both strategies were integrated to produce a EMs based on a synthetic tetrabranched structure composed by a scaffold (PWT2 – based on cyclam (1,4,8,11-tetraazacyclotetradecane)) bound to four oligopeptides (Scheme 1) able to bind metal cations [5,6]. The synthesis of the tetrabranched PWT2-peptides has been achieved by binding four identical peptides on the PWT2 scaffold. The final tetrabranched systems is obtained in solution by reacting the maleimide functionalized scaffold PWT2 with the chosen peptides in a classic thiol-Michael reaction at room temperature and in the presence of a weak base, ensuring environmental and economical sustainable synthesis conditions.

P1 – AAHAWGC(S-Methyl)-$NH_2$
P2 – HAWGC(S-Methyl)-$NH_2$
P3 – AAHAWGELLKKLLEELKGC(S-Methyl)-$NH_2$
P4 – HAWGELLKKLLEELKGC(S-Methyl)-$NH_2$

**Scheme 1 -** Peptides synthetized and used to compose the tetrabranched systems.

The redox behaviour of single peptides and/or tetrabranched systems, and their complexes with Cu, Mn, Ni and V(IV)/V(V), have been characterized by means of cyclic voltammetry with the aim to evaluate what chemical system can be considered good candidates to become EMs. In order to simulate the redox behaviour of SOD, in fact, the chemical species redox signals must be between the values -0.37 V and 0.71 V vs Ag/AgCl, with an optimal value at 0.16 V vs Ag/AgCl [7]. The CV measurements conditions were optimized. The main efforts were focused in increasing the sensitivity of the technique and reducing the needed sample volumes. Solid and screen printed electrodes were tested: Glassy Carbon Electrode, (GCE), Gold Electrode, (AuE), Gold Screen Printed Electrode (AuSPE), Carbon Screen Printed Electrode (CSPE), and Multi Wall Carbon Nano Tubes – Carbon Screen Printed Electrode (MWCNT-CSPE). Voltammetric signals were collected on aqueous solutions with: (i) peptide (1.0 mmol $L^{-1}$), (ii) metal cation 1.0 mmol $L^{-1}$ and peptide 1.0 mmol $L^{-1}$; (iii) metal cation and tetrabranched systems 1.0 mmol $L^{-1}$. Tetrabranched systems were tested at different metal-to-ligand ratios. The solutions were prepared in NaCl 0.2 mol $L^{-1}$ at pH 7.3. MOPS (3-(N-morpholino)propanesulfonic acid) was used as pH buffer. Since with the screen-printed electrodes it was possible to work with low amount of solution, they resulted to be particularly suitable to achieve the analytical goal. On the basis of the voltammetric response obtained with CSPE a priority level was assigned to each metal-peptides or tetrabranched system. The voltammetric parameters taken into account to assign the priority are the reversibility of the observed electrochemical process and the potential value related to this process. On the basis of the experimental results the most promising systems are those involving P1 and P3 peptides with copper and manganese, and the tetrabranched system composed with P3 peptide with copper.

Financial support of the National Recovery and Resilience Plan (NRRP), Mission 4 Component 2 Investment 1.1 – NextGenerationEU (grant PRIN PNRR 2022-P2022EMY52; CUP F53D23008960001; project title: “EnzyMime – Biocompatible and sustainable enzyme mimics based on metal complexes with peptide derivatives: synthesis, characterization and potential biological applications”) is gratefully acknowledged.

**References:**

[1] J. M. McCord, M. A. Edeas, *Biomed. Pharmacother.*, **2005**, 59, 139-142.
[2] V. de Benito, M. de Barrio, M.P. de López-Sáez, E. Ordoqui, A. Prieto-García, T. Sainza, M.L. Baeza, *Allergol. Immunopathol.*, **2001**, 29, 272-275.
[3] McCord, J.M. *Dose-Response*, **2008**, 6, 223–238.
[4] E. Kuah, S. Toh, J. Yee, Q. Ma and Z. Gao, *Chem. Eur. J.*, **2016**, 22, 8404 – 8430
[5] M. Perinelli, R. Guerrini, V. Albanese, N. Marchetti, D. Bellotti, S. Gentili, M. Tegoni, M. Remelli, *J. Inorg. Biochem.*, **2020**, 205, 110980-110993.
[6] G. Calo, A. Rizzi, C. Ruzza, F. Ferrari, S. Pacifico, E. C. Gavioli, S. Salvadori and R. Guerrini, *Peptides*, **2018**, 99, 195-204
[7] A. Vincent, J. Rodon Fores, E. Tauziet, E. Quévrain, A. Dancs, A. Conte-Daban, A. Bernard, P. Pelupessy, K. Coulibaly, P. Seksik, C. Hureau, K. Selmeczi, C. Policar, N. Delsuc, *Chem. Commun.*, **2020**, 56, 399—402.