ULST Timisoara

Multidisciplinary Conference on Sustainable Development

15-16 May, 2025

2025 MULTIDISCIPLINARY CONFERENCE ON SUSTAINABLE DEVELOPMENT

ARISTOTLE UNIVERSITY OF THESSALONIKI

LABORATORY OF INORGANIC CHEMISTRY AND ADVANCED MATERIALS

Antioxidant Metal Complexes of Quercetin Derivatives: Synthesis, Characterization, and Therapeutic Potential

Georgia Agathangelou,[1] Sevasti Matsia,[1] Antonios Hatzidimitriou,[2] Athanasios Salifoglou[1]

[1] Laboratory of Inorganic Chemistry and Advanced Materials, School of Chemical Engineering, Aristotle University of Thessaloniki, Thessaloniki 54124, Greece
[2] Laboratory of Inorganic Chemistry, School of Chemistry, Aristotle University of Thessaloniki, Thessaloniki 54124, Greece

E-mail: agathang@cheng.auth.gr

Abstract: Chronic diseases are closely linked to oxidative stress, prompting interest in the use of natural antioxidants, such as quercetin. However, limited bioavailability reduces its therapeutic potential. Sulfonation to form quercetin 5'-sulfonic acid (QSA) improves its stability and solubility. Complexation of QSA with lanthanide metal ions enhances its antioxidant and cytoprotective properties. These binary metal-QSA complexes show promise in *in vitro* biological activity against oxidative stress. This study synthesizes and characterizes such complexes, evaluating their biological potential. The aim is to advance targeted therapies using natural compounds for diseases like cancer.

Introduction

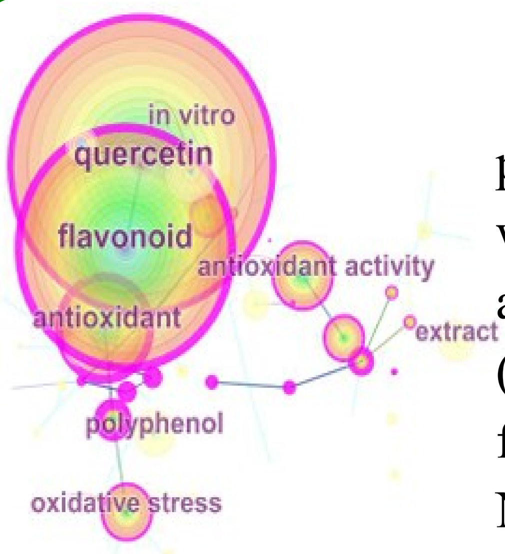


Fig. 1: Co-occurrence map of quercetin[2]

The rising prevalence of chronic diseases, such as cancer, cardiovascular, and neurodegenerative disorders, presents a significant global health challenge. These conditions are often driven by oxidative stress, a phenomenon in which an excess of free radicals overwhelms the body's natural defenses, causing damage to critical cellular structures and contributing to disease development.[1] As a result, natural products with antioxidant properties, such as quercetin (**Fig. 1**), have drawn considerable attention in recent years due to their biological pluripotency. Quercetin, a flavonoid found in various plant-based foods, is known for its strong antioxidant, anti-inflammatory, and anticancer activities.[2] Nevertheless, its clinical application is hindered by poor bioavailability and instability.[3] To address these limitations, attention has turned to the formation of metal ion complexes (**Fig. 2**), especially with lanthanide ions such as lanthanum, cerium, and erbium, which may help enhance quercetin stability and bioactivity. Such complexes offer a promising approach for improving the therapeutic potential of quercetin, effectively counteracting oxidative stress.[4]

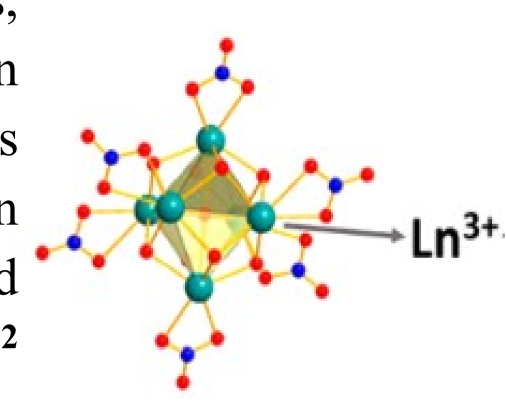
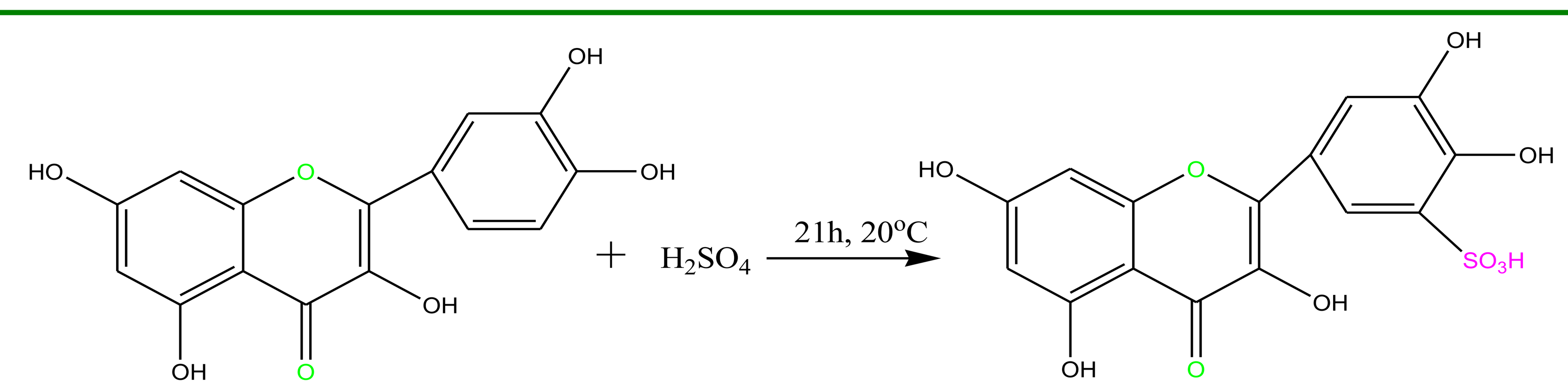


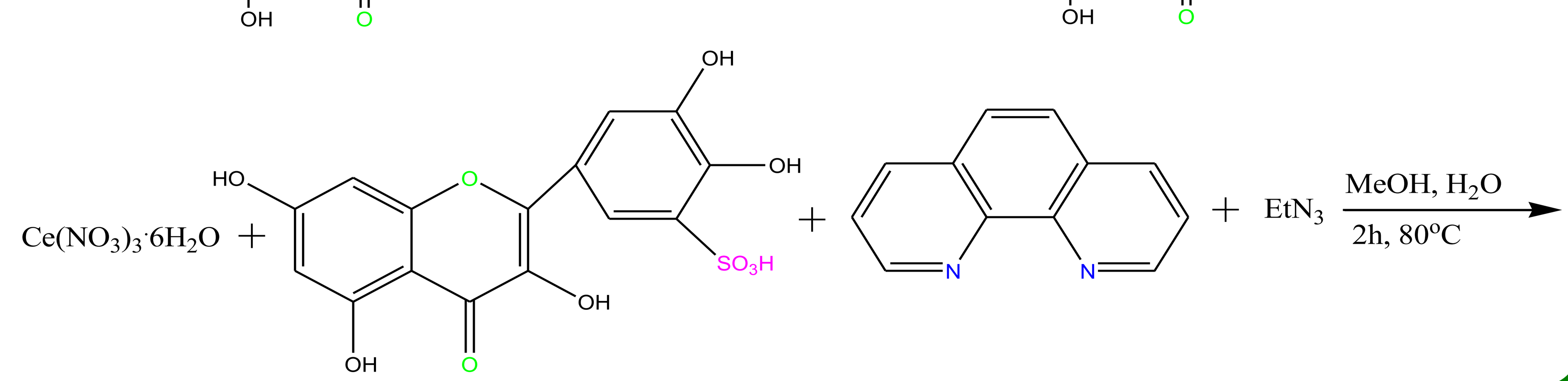
Fig. 2: Chemical lanthanide complex[5]

Materials and methods

1. Materials: Quercetin, H_2SO_4
Reaction techniques: Magnetic stirring with heating at 20 °C for 21 h.
Physicochemical Characterization: Elemental analysis, Fourier Transform Infrared Spectroscopy (FT-IR).



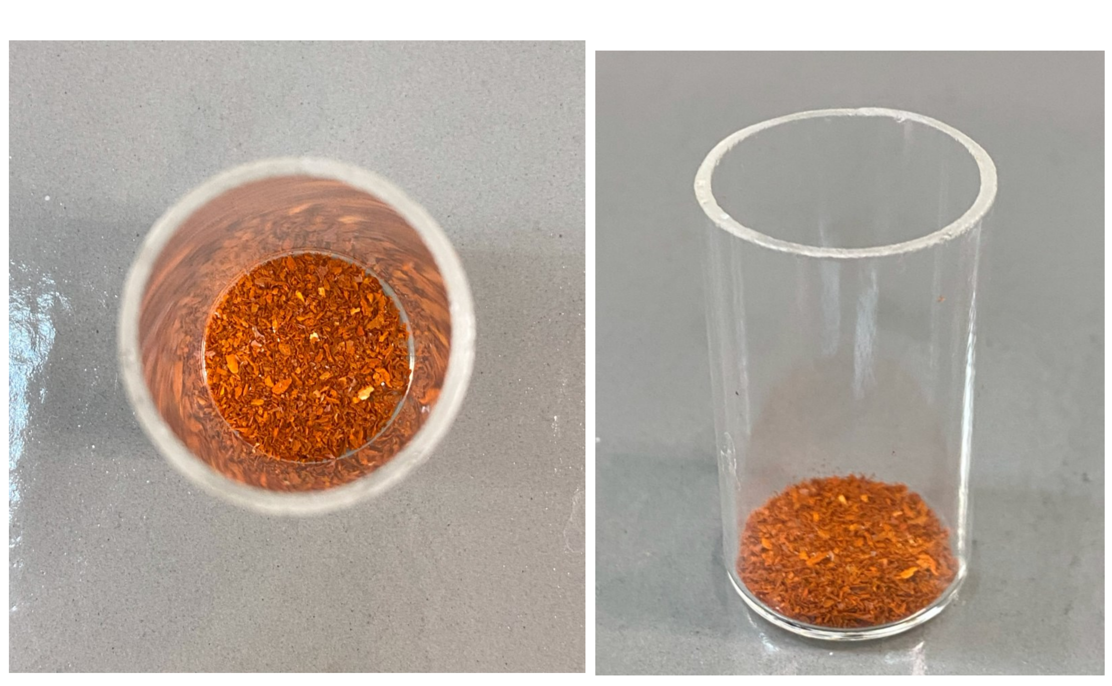
2. Materials: $Ce(NO_3)_3 \cdot 6H_2O$, 5'-sulfonic acid (QSA), 1,10-phenanthroline, triethylamine, methanol, water.
Synthesis techniques: Hydrothermal method, 80 °C and 2 h.
Physicochemical Characterization: Elemental analysis, Fourier Transform Infrared Spectroscopy (FT-IR), UV-Visible, X – Ray crystallography, Luminescence.



Results and discussion

The product of the initial reaction, the identity of which was experimentally confirmed, was subsequently employed in the attempt to synthesize the hybrid ternary Ce(III)-QSA-phenanthroline complex material. Similar experiments were carried out using other lanthanide ions, such as La(III), Nd(III), Sm(III), Er(III), Dy(III) and Eu(III), applying a hydrothermal crystallization method under conditions of 140 °C for 48 h (**Fig. 3**). The investigation into the coordination mechanism of lanthanides with the QSA ligand reveals critical physicochemical factors influencing complex formation, and it is still ongoing. Further experiments are currently being designed, aiming to modify the synthetic conditions and/or employ alternative auxiliary ligands anticipated to facilitate crystallization and isolation of the ternary materials. Physicochemical characterization of the hybrid materials (**Fig. 4**) synthesized so far formulate the profile, thus justifying further use in biological testing pertaining to the etiopathology and theranostics of human diseases.

Fig. 3: 5'-sulfonic acid (QSA)



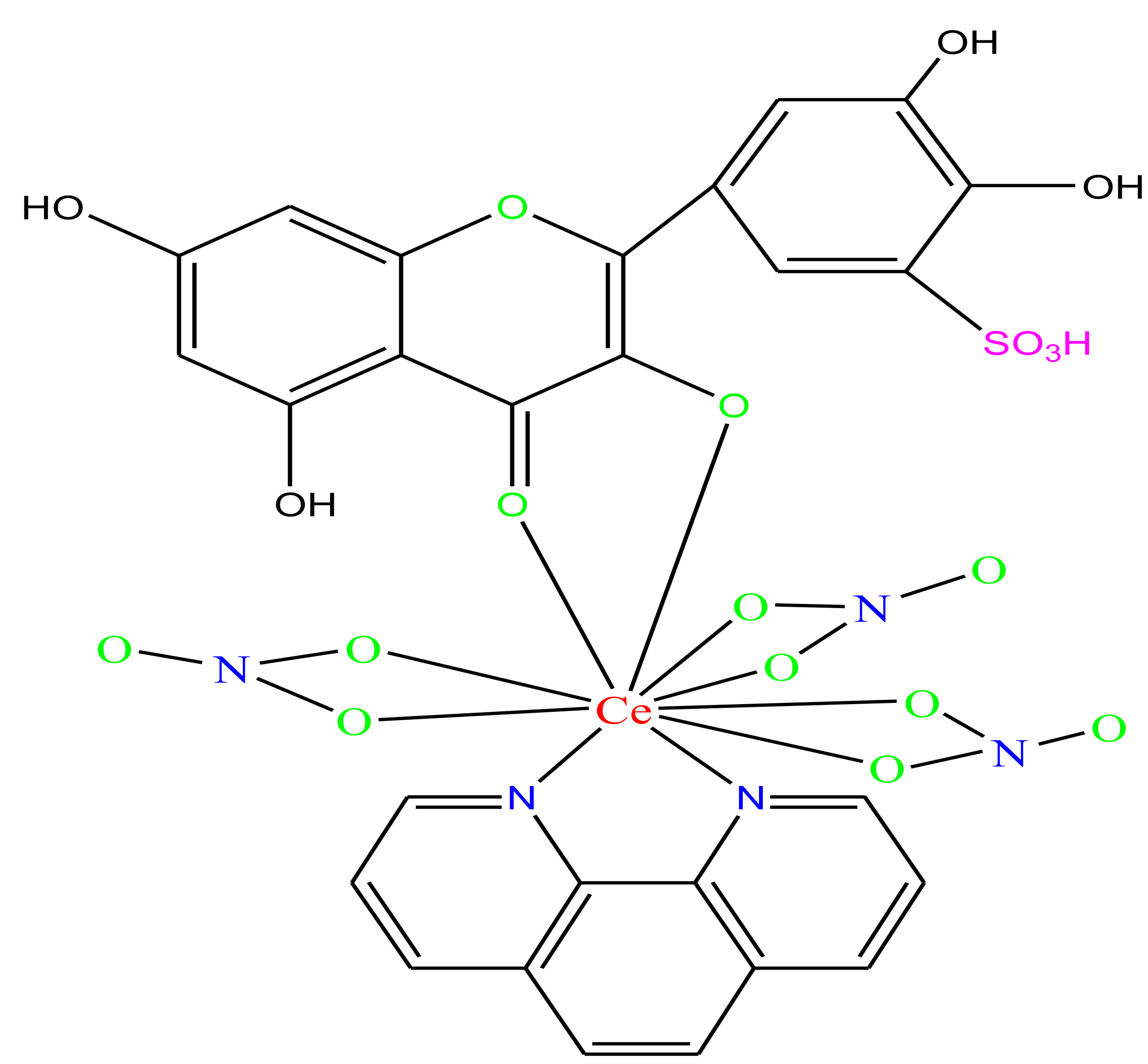


Fig. 4: Ce(III)-QSA-phenanthroline complex

Conclusions

- The QSA ligand was successfully synthesized and structurally verified in the Lab.
- Attempts to form Ce(III)-QSA-phenanthroline complexes under hydrothermal conditions were made and discrete materials were isolated.
- Lanthanide ions (Ln(III) = La, Nd, Sm, Er, Dy, Eu) were used to assemble ternary Ln(III)-QSA-phenanthroline species of biological activity.
- Further optimization of synthetic parameters enabling coordination of Ln(III) with QSA plays an important role in the structural speciation of the hybrid materials, thus justifying further

Literature

[1]. C.M. Spickett, A. Wojton, M. Kopacz, B. Oleksyn, Free Radic. Biol. Med. 33 Suppl. 1 (2002) S209–S210.

[2]. D. Xu, M.-J. Hu, Y.-Q. Wang, Y.-L. Cui, Molecules 24(6) (2019) 1123.

[3]. E. Rodríguez-Arce, M. Saldías, Biomed. Pharmacother. 143 (2021) 112236.

[4]. F.E.A. Magalhães, J.E.T. do Nascimento, S.M. de Morais, D.S. de Lisboa, M. de Oliveira Sousa, Neurotox. Res. 36(4) (2019) 893–903.

[5]. N.C. Martinez-Gomez, H.N. Vu, E. Skovran, Inorganic Chemistry 55(20) (2016) 10083–10089.