

# Synthesis and characterization of a Cu(II) and a Ni(II) complex with a curcumin derivative. Study of their interaction with CT-DNA and BSA.

A. Ravanou, D. Kassianos, C. Methenitis\*,

Laboratory of Inorganic Chemistry, Department of Chemistry, National and Kapodistrian University of Athens, Panepistimiopolis Zografou, 15771 Athens, Greece

e-mail: [anastrvn@chem.uoa.gr](mailto:anastrvn@chem.uoa.gr), [methenitis@chem.uoa.gr](mailto:methenitis@chem.uoa.gr)

Curcumin, a polyphenolic pigment of the rhizome of turmeric or *Curcuma longa* L., has received considerable attention because of its bioactive effects, pharmaceutical, biotechnological and medicinal applications [1, 2]. Despite all these facts, the utility of curcumin is limited by its low bioavailability and chemical stability [2]. Structural modifications have been implemented in curcumin to overcome these obstacles and enhance its overall anticancer activity. These modifications are aimed to increase bioavailability and stability and elevate selective toxicity against cancer cells [1, 3]. Among them, the synthesis of metal complexes of curcumin derivatives have been found to exhibit better pharmacological properties and photo induced anticancer activity against different types of cancers [4]. In our work, the Copper (II) and Ni (II) complexes with a curcumin derivative were synthesized and characterized. Also the interaction with CT-DNA and BSA were investigated. Characterization of both the ligand and the complexes was carried out using the following spectroscopic techniques: mass spectroscopy (MS), nuclear magnetic resonance (NMR), fluorescence, infrared (IR) and ultraviolet-visible (UV-Vis) spectroscopy. Then, the interaction of these compounds with CT-DNA and BSA was studied by means of cyclic dichroism (CD), ultraviolet-visible (UV-Vis) spectroscopy, fluorescence, and viscometry. The results of this study showed the ability of both the ligand and the complex to interact with DNA and BSA. Based on the structure of the ligand and the experimental data in the JOB method, we have the formation of a Cu(II):curc stoichiometry complex = 1:1 and a Ni(II):curc stoichiometry complex = 1:1 as well as a Ni(II):curc stoichiometry complex = 2:1. From spectrophotometric titration the binding constants  $K_b$  of the complexes with CT-DNA were found to be in the range of  $10^5$ - $10^6$   $M^{-1}$ . From the competitive activity studies with Ethidium Bromide, the complexes were found to act competitively. The cyclic dichroism spectra showed an intense ICD effect and the interaction of the complexes with DNA causes a conversion of the B structure of DNA to A. The hydrodynamic method of viscometry confirms the interaction by intercalation for ratios up to about 0.2. The complexes interact with BSA with a binding constant value of  $10^5$   $M^{-1}$ , within the range of  $10^4$ - $10^6$ , so that the protein is a good transporter of the drug.

## References

1. P. Anand et al. / *Cancer Letters* 267 (2008) 133–164.
2. Sharifi-Rad J et al, *Front. Pharmacol.* 11 (2020): article 01021.
3. M. Sumi, N.T. Nevaditha, B. Kumari. *Inorganica Chimica Acta* 549 (2023) 121397.
4. S. Banerjee, A.R. Chakravarty. *Acc. Chem. Res.* 48 (2015) 2075–2083