DISSERTATION INFORMATION

Title: Study on the Complexation of Plumbagin with Cr(III), Ti(IV), Hg(II) and Applications
Major: Chemical Engineering
Major Code: 9520301
Supervisors: Prof. Dr. Le Van Tan and Assoc. Prof. Dr. Tran Nguyen Minh An
Institution: Industrial University of Ho Chi Minh City

1. Dissertation Summary

For the first time, the complexes of plumbagin (PLB) with Ti(IV), Cr(III), and Hg(II) were systematically studied both in solution and in solid state, with a particular focus on their analytical and biological applications. The complexes were formed with molar ratios of Ti:PLB = 1:2, Cr:PLB = 1:3, and Hg:PLB = 1:2 in ethanol–water media. The fluorescence quenching or enhancement mechanisms were elucidated, accompanied by relatively high binding constants ($\log K_{(Ti(PLB)_2)} = 4.60$; $\log K_{(Cr(PLB)_3)} = 4.52$; $\log K_{(Hg(PLB)_2)} = 4.89$). DFT calculations revealed $\Delta E_{HOMO–LUMO}$ values ranging from 2.68–3.02 eV with polarization directed toward the metal ion, consistent with the observed electronic and photophysical properties.

The $Ti(PLB)_2$ complex exhibited strong fluorescence at 605 nm upon excitation at 500 nm, enabling highly sensitive, low-cost quantification of Ti(IV) in sand samples, with results in good agreement with ICP–OES. The $Hg(PLB)_2$ complex was successfully applied for Hg(II) determination by HPLC–DAD, showing a linear calibration range (200–20,000 µg/L, $R^2 = 0.9999$), LOD of 59.5 µg/L, and RSD < 5%. The chromatographic results demonstrated complete separation of PLB and the complex, ensuring analytical accuracy.

Biological evaluations revealed that $Hg(PLB)_2$ exhibited remarkable in vitro activity, including potent α-glucosidase inhibition ($IC_{50} = 40.68 \pm 0.85$ µM), superior to acarbose, and significant cytotoxicity against MCF-7 and HepG2 cancer cell lines ($IC_{50} = 2.39 \pm 0.21$ µM and 1.13 ± 0.13 µM, respectively), outperforming free PLB and ellipticine. In contrast, $Cr(PLB)_3$ showed no notable activity under the same conditions. Molecular docking and 100 ns molecular dynamics simulations with target enzymes (1T8I, 3TOP, 4WCU) indicated stable binding through hydrogen bonds and hydrophobic interactions, with Gibbs free energies ranging from –10.45 to –12.25 kcal/mol.

The interactions of $Cr(PLB)_3$ and $Hg(PLB)_2$ with human serum albumin (HSA) followed a static quenching mechanism at site IIA, inducing secondary structural alterations and perturbations of the Trp214 microenvironment. Strong binding constants ($K_b = 2.5–3.8 \times 10^4$) and FRET distances of ~2.5 nm highlighted their potential for biological binding and drug transport.

Overall, this dissertation provides fundamental insights into the coordination chemistry of PLB with transition metals, supports their application in analytical chemistry, and suggests promising directions for the development of natural product–derived therapeutic agents

2. Novel Contributions of the Dissertation

- For the first time, the complexes of PLB with three metal ions Cr(III), Ti(IV), and Hg(II) in both solution and solid state were synthesized, characterized, and reported.
- The complexation mechanisms of Ti(IV), Cr(III), and Hg(II) with PLB were investigated and discussed based on spectroscopic characteristics.

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- The $Ti(PLB)_2$ complex exhibits fluorescence emission and was applied as a highly sensitive probe for Ti(IV) quantification in real samples. Similarly, the fluorescence quenching behavior of $Cr(PLB)_3$ and $Hg(PLB)_2$ provides the basis for analytical applications using HPLC–DAD.

- In silico studies (molecular docking, molecular dynamics simulations, and ADMET predictions), combined with in vitro experiments, demonstrated that $Hg(PLB)_2$ possesses α-glucosidase inhibitory activity and cytotoxicity against cancer cells, suggesting potential for further biomedical applications.

3. Practical Applications and Future Research Directions

Practical Applications / Potential Applications

- Analytical: The $Ti(PLB)_2$ complex was successfully applied for Ti(IV) quantification via fluorescence (validated with sand samples). The $Hg(PLB)_2$ complex was employed for Hg(II) determination using HPLC–DAD, demonstrating high selectivity and reproducibility.

- Biological: The $Hg(PLB)_2$ complex exhibited in vitro anticancer and antidiabetic activities, consistent with docking and MD simulations, confirming stable binding to HSA and target enzymes.

- Application Prospects: Potential development of fluorescent probes (Ti) and quenching-based probes (Cr, Hg), as well as further studies on drug delivery via HSA.

Issues for Further Research

- More comprehensive evaluation of biological activities (anti-inflammatory, anticancer) on real cell/enzymatic models.

- Detailed molecular simulations of interactions with DNA, albumin, and cancer cell receptors.

- Development of novel PLB derivatives (e.g., methylation, halogenation) to optimize selectivity and fluorescence.

- Exploration of PLB as a sensitive probe for Cr(III) and Hg(II) detection.

- Fabrication of solid-state sensors (thin films, test papers) incorporating PLB complexes for rapid on-site detection using portable fluorescence devices in environmental and biomedical applications.

Supervisors **PhD Candidate**

Prof. Dr. Le Van Tan **Assoc. Prof. Dr. Tran Nguyen Minh An** **Nguyen Van Thoi**

Certification by the Training Institution

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