

MASTER'S THESIS

Luminescent bioprobes for imaging and inhibition of tumour cells

Xie, Chen

Date of Award:
2017

[Link to publication](#)

General rights

Copyright and intellectual property rights for the publications made accessible in HKBU Scholars are retained by the authors and/or other copyright owners. In addition to the restrictions prescribed by the Copyright Ordinance of Hong Kong, all users and readers must also observe the following terms of use:

- Users may download and print one copy of any publication from HKBU Scholars for the purpose of private study or research
- Users cannot further distribute the material or use it for any profit-making activity or commercial gain
- To share publications in HKBU Scholars with others, users are welcome to freely distribute the permanent URL assigned to the publication

Abstract

On the purpose of designing a novel generation of luminescent bioprobes for imaging and inhibition of tumour cells, a series of lanthanide-ruthenium complexes has been synthesized and characterized by ^1H NMR, ^{13}C NMR, absorption/emission spectroscopy, high-performance liquid chromatography, and mass spectroscopy. Those complexes are qualified to be considered as photo-activatable anticancer prodrugs which consist of a ruthenium (II) complex linked to a lanthanide-based cyclen chelate via a π -conjugated bridge. Comprehensive studies have been performed to evaluate their efficacy as pro-drugs which requires *in cellulo* activity, inhibiting ability, instant monitoring possibility, and safety to normal cells. The resulting complexes are proved to be promising agents for controllable anticancer therapy because the prodrug remains inactive in dark and the release of the active drug is induced by visible light. Drug delivery process can be quantitatively monitored by either the long-lived red europium emission under one- or two-photon excitation or potentially by magnetic resonance imaging signals. Besides of these, the correlation among the drug releasing amount, signaling emission intensity, and mass spectroscopy response, has been proposed for quick and simple quantitative analysis.

Table of Contents

Chapter I Introduction.....	1
1.1 Basics of lanthanides' photophysics	1
1.1.1 Electronic configuration of ions.....	1
1.1.2 Absorption and emission spectra	3
1.1.3 Sensitization of lanthanide luminescence	6
1.1.4 Macrocyclic-based lanthanide ligands.....	8
1.2 Applications of lanthanides in MRI.....	9
1.3 Prodrugs	10
1.3.1 Classification of prodrugs	11
1.3.2 Photo-dissociative prodrugs.....	11
1.3.3 Other examples of photo-dissociated prodrugs.....	13
1.4 Basic requirements for Ln-based prodrugs	15
1.5 Ruthenium complexes as anticancer agents.....	17
Chapter II Tumor-Targeting Photo-responsive anticancer Lanthanide-Ruthenium prodrug.....	19
2.1 Purposes of the research.....	19
2.2 Synthetic scheme	21
2.2.1 Synthesis of RuLnL	21

2.3 Experimental	23
2.3.1 Chemicals and materials	23
2.3.2 Preparation of Compound 2	23
2.3.3 Preparation of Compound 3	24
2.3.4 Preparation of Compound 4	25
2.3.5 Preparation of Compound 7	25
2.3.6 Synthesis of LnL (Ln= Eu or Gd or Dy).....	26
2.3.7 Synthesis of RuLnL (Ln=Eu or Gd or Dy)	27
2.3.8 Photophysical studies.....	27
2.3.9 HPLC characterization and qualitative analysis	27
2.3.10 LC-MS/MS quantitative analysis.....	28
2.3.11 DNA binding assays.....	30
2.3.12 In cellulo studies	31
2.3.13 MTT cell cytotoxicity assays	31
2.3.14 In vitro photoactivation and two-photon in vitro imaging.....	32
2.3.15 Stability test	33
2.3.16 pH effect test	33
2.3.17 Oxygen effect test	34
2.4 Results and discussion	35

2.4.1 Photophysical properties	35
2.4.2 Emission intensity changes of RuEuL under light irradiation	39
2.4.3 Qualitative analysis of dissociation process by HPLC	41
2.4.5 DNA binding and cleavage	43
2.4.6 Quantitative analysis of the drug release	44
2.4.7 Dark/ Light cytotoxicity evaluation	47
2.4.8 In vitro imaging.....	49
2.4.9 Stability of the prodrug and the active drug.....	51
2.4.10 pH effect on the drug release rate	55
2.4.11 Oxygen effects on photodissociation	57
2.5 Proposal of future work	59
2.5.1 Purposes of the proposal	59
2.5.2 Biotin conjugation.....	59
2.5.3 Proposed synthetic route of biotin ligand	61
2.5.4 Proposed structure of RuLnL-Biotin	62
2.6 Conclusions.....	63
List of References	64