

Contents

Contents	v
Abbreviations	ix
1. Introduction	1
1.1. General photophysical concepts	1
1.1.1. Electromagnetic radiation	1
1.1.2. Electronic states and excitation of organic molecules	2
1.1.3. Deactivation of the excited states	3
1.1.4. Solvatochromism and micropolarity of biological compounds	5
1.2. Photosensitization	8
1.2.1. Type I process	9
1.2.2. Singlet oxygen and Type II oxidation	10
1.2.3. Type III process	12
1.3. Skin photosensitization: phototoxicity and photoallergy	13
1.3.1. <i>In Vitro</i> phototoxicity assays	14
1.3.2. <i>In Vivo</i> tests	15
1.3.3. Phototherapy: photodynamic therapy	16
1.4. Topical retinoids	17
1.4.1. Adapalene	18
1.4.2. Tazarotene	20
1.5. References	21
2. Abstract	29
2.1. Abstract	29
2.2. Resúmen	31
2.3. Resüm	33

3. Aims	35
4. Environmentally sensitive fluorescence of adapalene	37
4.1 Introduction	37
4.2. Results and discussion	39
4.2.1. UV-vis absorption spectrometry	39
4.2.2. Fluorescence emission	43
4.2.3. Emission properties in the presence of biological components	48
4.3. Conclusion	52
4.4. Experimental part	53
4.4.1. Chemicals	53
4.4.2. Fluorescence emission	53
4.4.3. Molecular modeling	53
4.5. References	54
5. Photosensitizing properties of adapalene	59
5.1 Introduction	59
5.2. Results	60
5.2.1. Phototoxicity assay	61
4.2.2. Fluorescence emission	62
4.2.3. Phosphorescence emission	65
4.2.4. Laser Flash Photolysis	66
4.2.5. Singlet oxygen formation	68
4.2.6. Electron paramagnetic resonance	69
5.3. Discussion	69
5.4. Conclusion	73
5.5. Experimental part	74
5.5.1. Chemicals	74
5.5.2. Fluorescence emission	74
5.5.3. Phosphorescence emission	74

5.6. References	74
6. Mechanistic insights into the photosensitizing properties of the topical retinoid tazarotene	79
6.1 Introduction	79
6.2. Results	80
6.2.1. Singlet excited state properties	80
6.2.2. Triplet excited state properties	82
6.2.3. Interaction with biological components	86
6.2.4. Singlet oxygen formation	88
6.2.5. 3T3 Neutral red uptake phototoxicity test	89
6.3. Conclusion	91
6.4. Experimental part	91
6.4.1. Chemicals	91
6.4.2. Fluorescence emission	92
6.4.3. Phosphorescence emission	92
6.4.4. Steady state photolysis	92
6.5. References	92
7. Instrumentation and general experimental procedures	95
7.1. Chemicals	95
7.2. UV-Vis absorption spectroscopy	95
7.3. Fluorescence emission	96
7.4. Phosphorescence emission	96
7.5. Laser flash photolysis	97
7.5.1. For Chapter 5	97
7.5.2. For Chapter 6	97
7.6. Singlet oxygen emission	99
7.6.1. Time resolved emission, Chapter 5	99
7.6.2. Steady state emission, Chapter 6	99

Contents

7.7. Electron paramagnetic resonance trapping measurements ·····	100
7.8. Irradiation setup ·····	100
7.9. HPLC-MS ·····	100
7.10. Cell culture conditions ·····	101
7.11. <i>In vitro</i> 3T3 neutral red uptake phototoxicity assay ·····	101
7.12. Data analysis and statistics ·····	102
7.13. References ·····	102
8. General conclusions	103
9. Appendix	105
9.1. Appendix Chapter 4 ·····	106
9.2. Appendix Chapter 5 ·····	108
9.3. Appendix Chapter 6 ·····	114
9.4. References ·····	124
9.5. Scientific contributions ·····	125
9.5.1. Publications ·····	125
9.5.2. Congress participations ·····	125