β-Carboline alkaloids: photosensitizing properties and biotechnological application

Photochemistry and Molecular Photobiology Research Group

Biotechnology,
Organic Chemistry,
Physical Chemistry,
Photochemistry and Photobiology,
Natural Products,
Microbiology.

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Research Interests:

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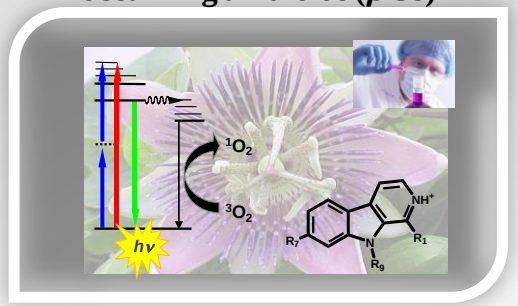
Photochemistry of naturally occurring alkaloids (βCs)



Research lines

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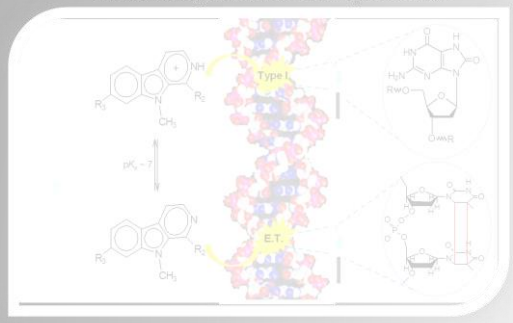

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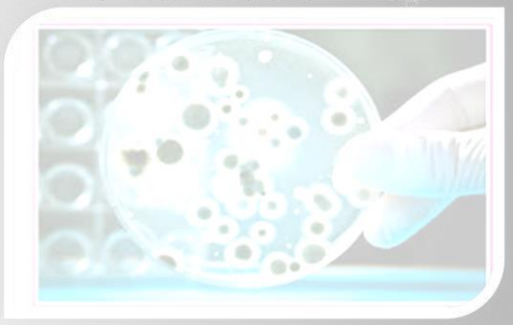

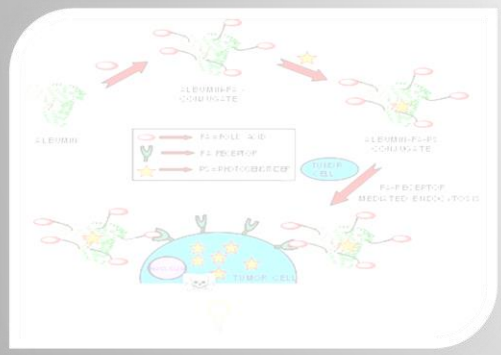

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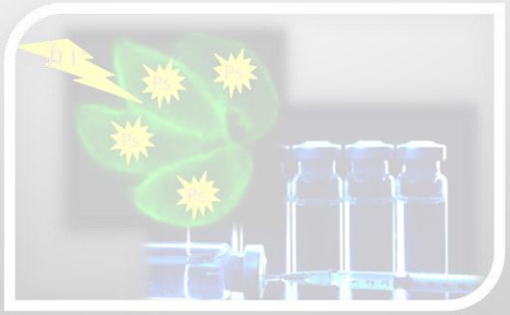

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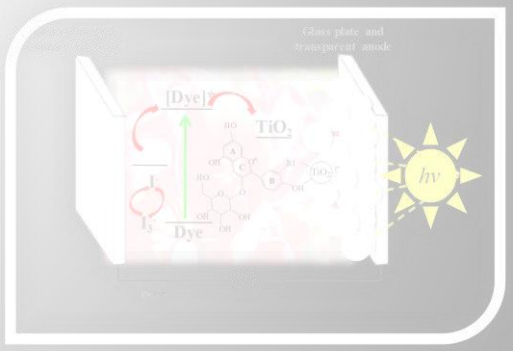
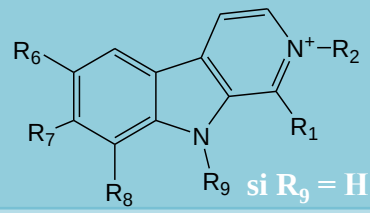


Natural dyes for dye sensitized solar cells (DSSC)

β-carbolines (βCs)

✓ Family of alkaloids derived from *9H*-pyrido-[3,4-*b*] indole o norharmane (nHo)

Full aromatic βCs



si R_2 = H → pK_{a1} ~ 7-8

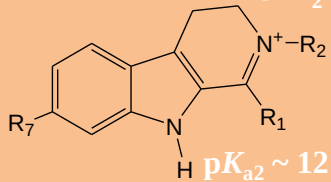
si R_9 = H → pK_{a2} ~ 12-14

Compound (short name)	R_1	R_2	R_6	R_7	R_8	R_9
***nor*Harmane (nHo)**	-H	-H	-H	-H	-H	-H
2-methyl-*nor*Harmane or *Nor*melinonine F (2-Me-nHo)	-H	$-CH_3$	-H	-H	-H	-H
Harmane (Ho)	$-CH_3$	-H	-H	-H	-H	-H
2-methyl-harmane or Melinonine F (2-Me-Ho)	$-CH_3$	$-CH_3$	-H	-H	-H	-H
Harmine (Ha)	$-CH_3$	-H	-H	$-OCH_3$	-H	-H
Harmol	$-CH_3$	-H	-H	-OH	-H	-H
7-Chloro-9-methyl-*nor*Harmane (o bauerine A)	-H	-H	-H	-Cl	-H	$-CH_3$
7,8-diChloro-1-hydroxy-9-methyl-*nor*Harmane (o bauerine C)	-OH	-H	-H	-Cl	-Cl	$-CH_3$

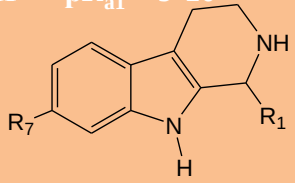
Although they are widespread in nature, the main biological role of βCs is still unknown and the molecular bases of the mechanisms involved in such processes are poorly understood.

Dihydro-βCs Tetrahydro-βCs

si R_2 = H → pK_{a1} ~ 9-10

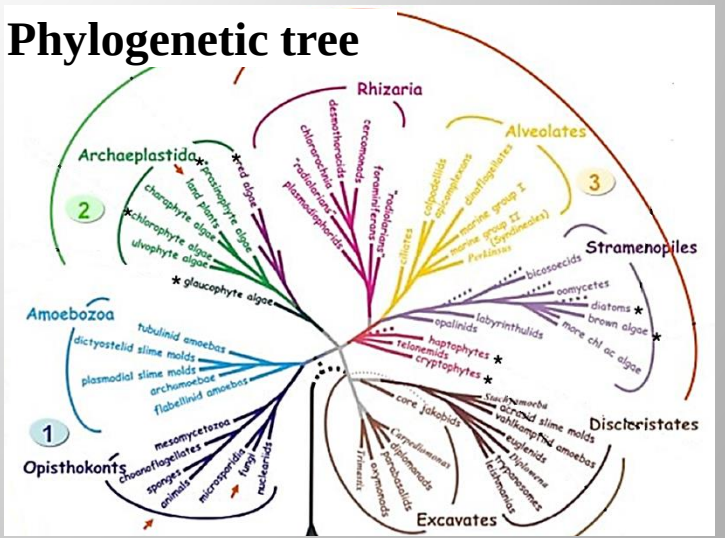


pK_{a2} ~ 12



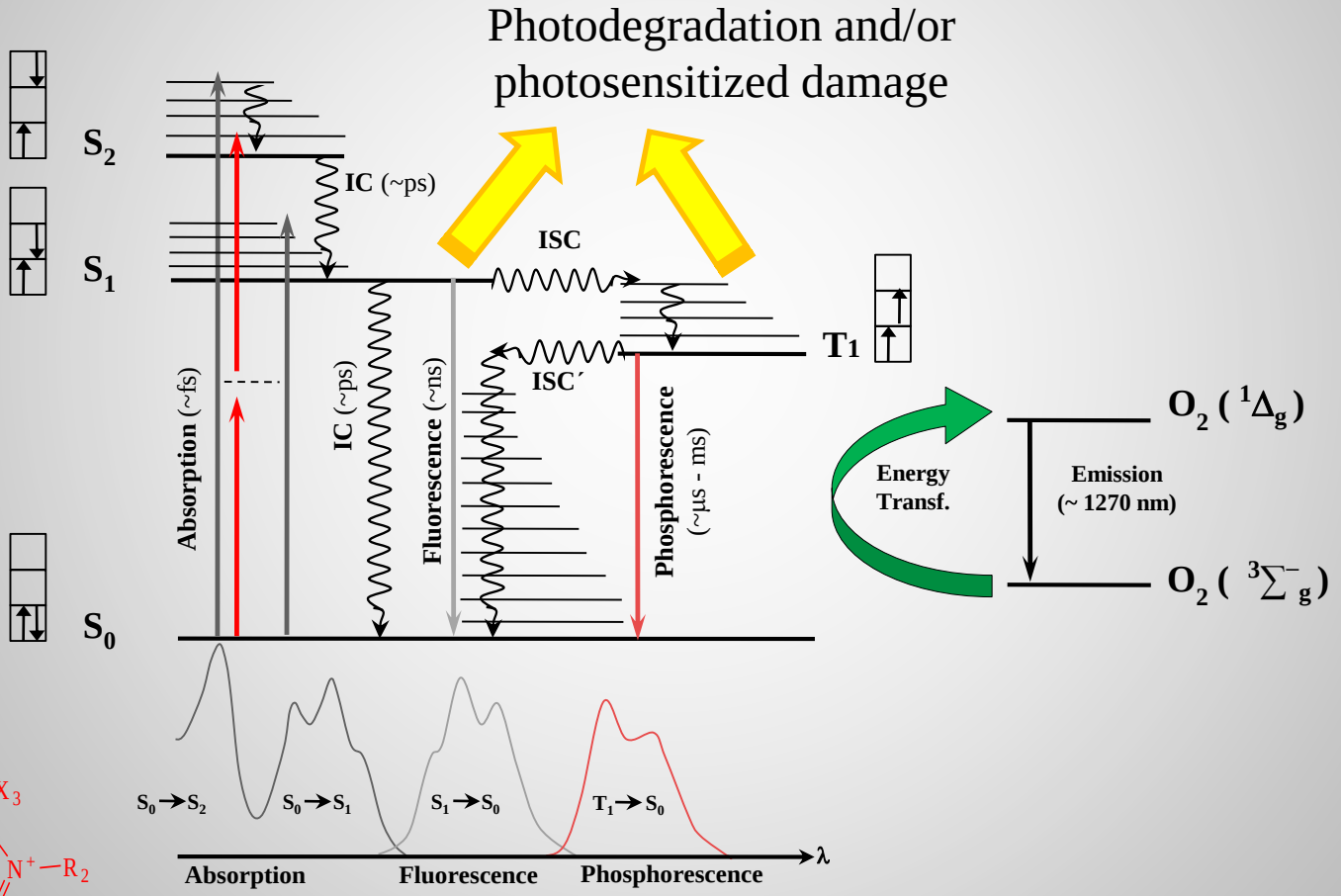
Compound (short name)	R_1	R_2	R_7	R_9
Harmaline (d-hHa)	$-CH_3$	-H	$-OCH_3$	-H
Tetrahydroharmine (t-hHa)	$-CH_3$	-H	$-OCH_3$	-H
Harmalol	$-CH_3$	-H	-OH	-H
2-methyl-harmalane (*2*-Me-Hlano)	$-CH_3$	$-CH_3$	-H	-H

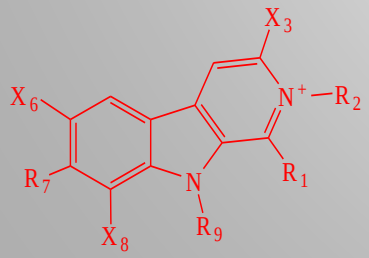
Phylogenetic tree



Objectives

- Study of the **photophysical** and **photochemical** properties of βCs.
- Evaluation of their **photosensitizing properties** on biomolecules.





$$\Phi_F + \Phi_R + \Phi_{IC} + \Phi_{ISC}\,(\Phi_P\,,\,\Phi_\Delta) = 1$$

Photochemistry of βCs in aqueous solution

Conclusions

- ✓ βCs are quite photostable ($\Phi_R \sim 10^{-3}$).
- ✓ In different tropical plants, subject to high doses of sunlight, βCs could act as endogenous protective agents, avoiding UVB- and UVA-induced damaging.
- ✓ Fluorescence emission represents the main deactivation pathway of photoexcited βCs ($\Phi_F \sim 0.50 - 0.90$)

Physiological roles that deserve to be further investigated:

- Accessory pigments (UVA) for light-harvesting**.**
- Fluorescent-induced pollinators attraction.

- ✓ The quite high k_T values observed ($\sim 10^7$-10^8) make some βCs good candidates to act as antioxidant in living systems subject to photo-induced oxidative stress.
- ✓ βCs show a quite low efficiency of ROS production (Φ_{H2O2}, $\Phi_{OH}^{\bullet} \sim 10^{-3}$ and $\Phi_{\Delta} \sim 0.08$ -0.20)

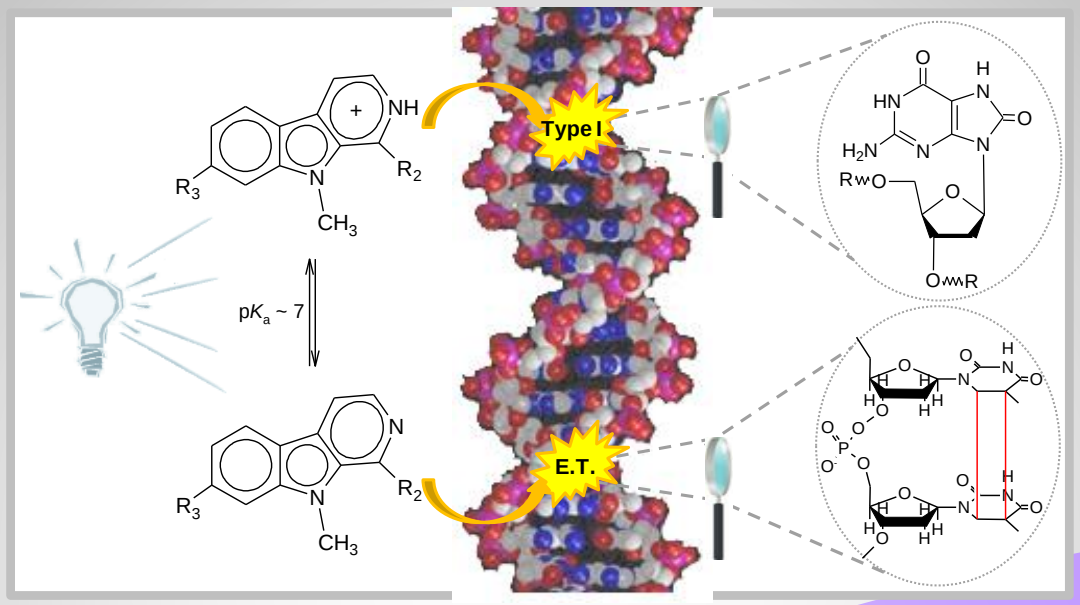
Physiological roles that deserve to be further investigated:

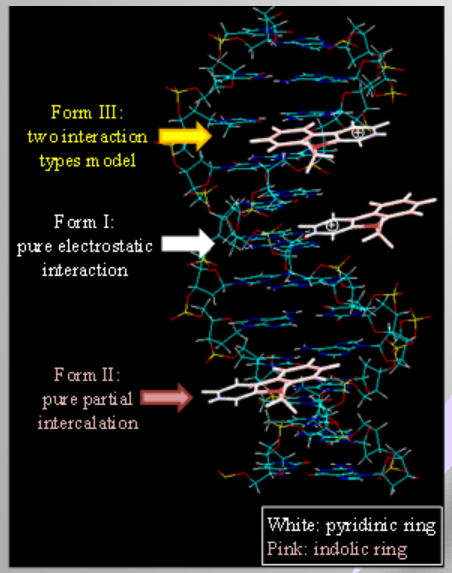
- Defence response does not seems to be important
- βCs can act in photo-triggered intracellular signalling (*via* ROS and pH).

Mercader *et. al.*, *J. Molec. Graph. Mod.*, **2009**, 28, 12–19
Gonzalez *et. al.*, *J. Phys. Chem. A,* **2009**, 113, 6648–6656
Gonzalez *et. al.*, *Photochem. Photobiol. Sci*., **2009**, 8, 1139–1149
Cabrerizo *et. al.*, *Chem. Phys. Chem*, **2010**, 11, 796–798
Alomar *et. al.*, *J. Photochem. Photobiol. B: Biol*, **2014**, 136, 26–28
Hršak *et. al.*, *Phys. Chem. Chem. Phys.*, **2015**, 17, 12090-12099
Rasse-Suriani *et. al.*, *Phys. Chem. Chem. Phys.*, **2016**, 18, 886-900
Rasse-Suriani *et. al.*, *Photochem. Photobiol.* **2017**

Photosensitization of cell-free DNA by βCs

Results





Interaction

Kinetics

Damage profile

Mechanisms

Toxicity and mutagenicity

Gonzalez *et. al.*, *Org. Biomol. Chem.*, **2010**, 8, 2543–2552
Gonzalez *et. al.*, *Org. Biomol. Chem.*, **2012**, 10, 1807–1819
Vignoni *et. al.*, *Org. Biomol. Chem.*, **2013**, 11, 5300–5309
Vignoni *et. al.*, *J. Photochem. Photobiol. B: Biol*, **2014**, 132, 66-71
Yañuk *et. al.*, *Phys. Chem. Chem. Phys.*, **2015**, 17, 12462-12465

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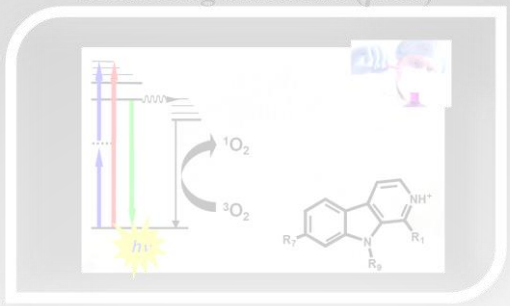

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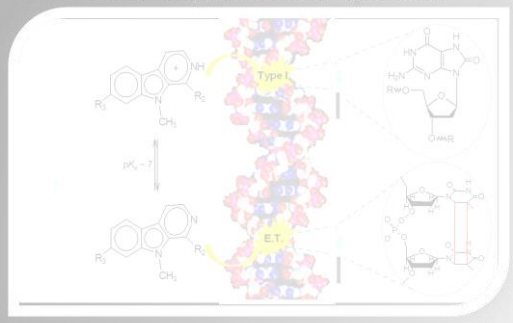

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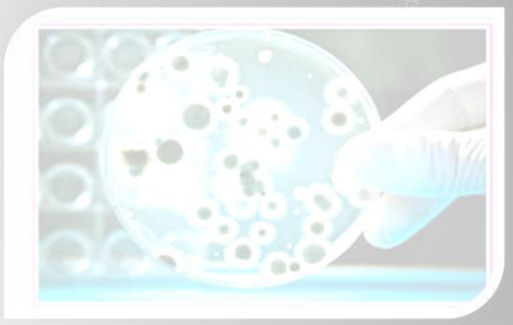

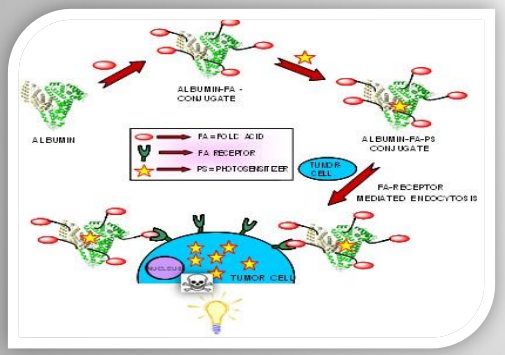

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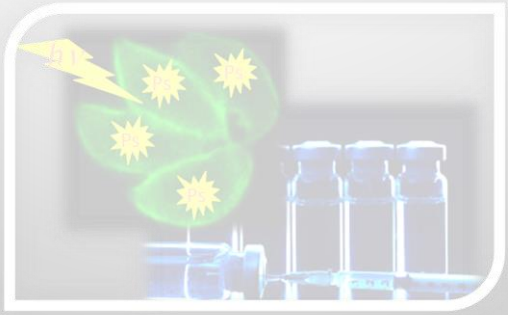

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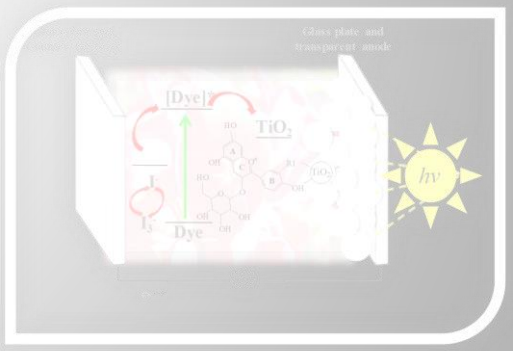

Natural dyes for dye sensitized solar cells (DSSC)

Photodynamic therapy (PDT)

Introduction

PDT makes use of light (UV, visible and/or IR) **to activate a** complementary photosensitive molecule (**photosensitizer**, Ps). These activated molecules (Ps*) **then confer therapeutic effects** at the target treatment site.

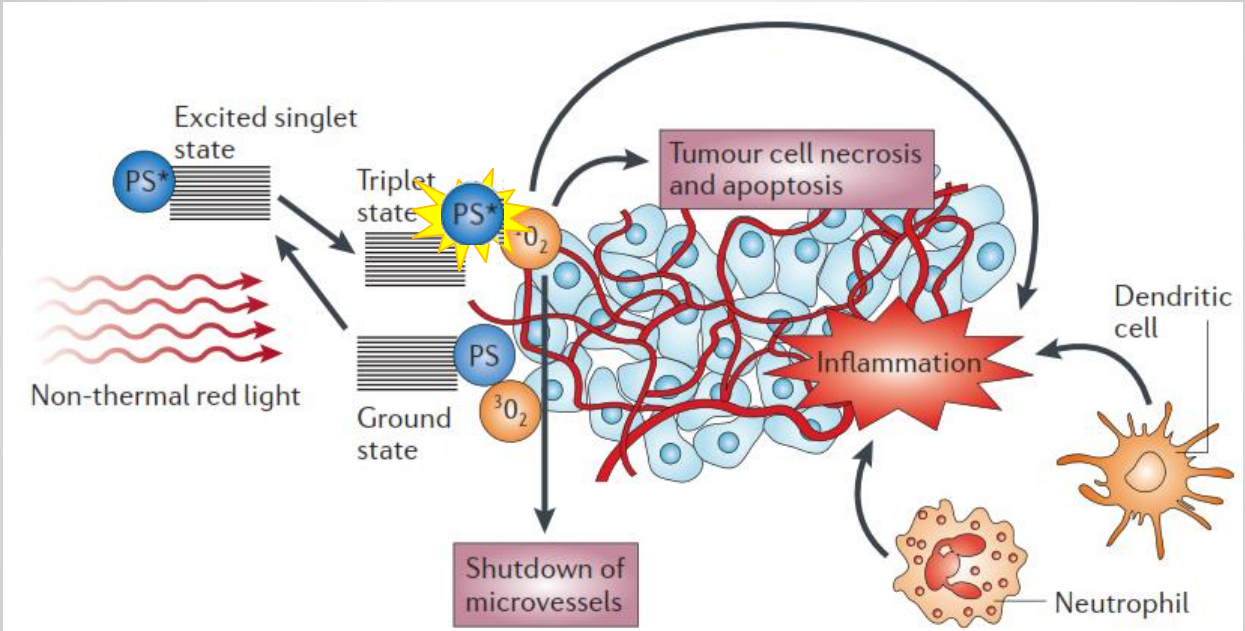

Figure 1 | **The mechanism of action on tumours in photodynamic therapy.** The photosensitizer (PS) absorbs light and an electron moves to the first short-lived excited singlet state. This is followed by intersystem crossing, in which the excited electron changes its spin and produces a longer-lived triplet state. The PS triplet transfers energy to ground-state triplet oxygen, which produces reactive singlet oxygen ($^1O_2$). $^1O_2$ can directly kill tumour cells by the induction of necrosis and/or apoptosis, can cause destruction of tumour vasculature and produces an acute inflammatory response that attracts leukocytes such as dendritic cells and neutrophils.

Castano *et al. Nature Reviews Cancer*, ***2006***, 6, 535–545

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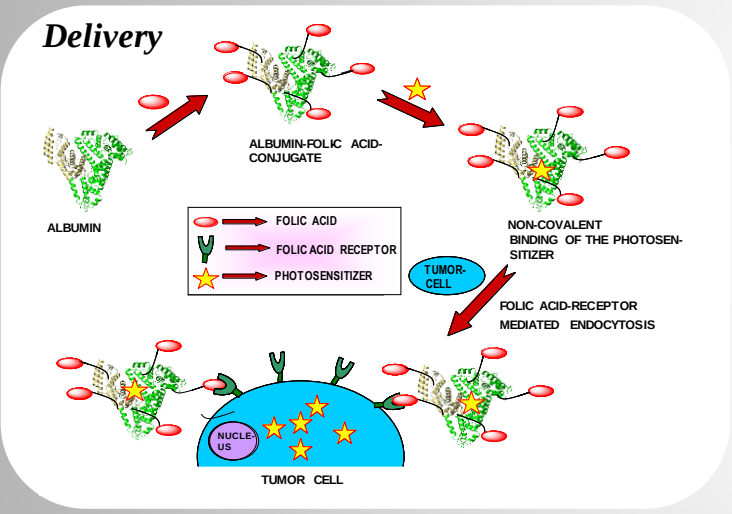
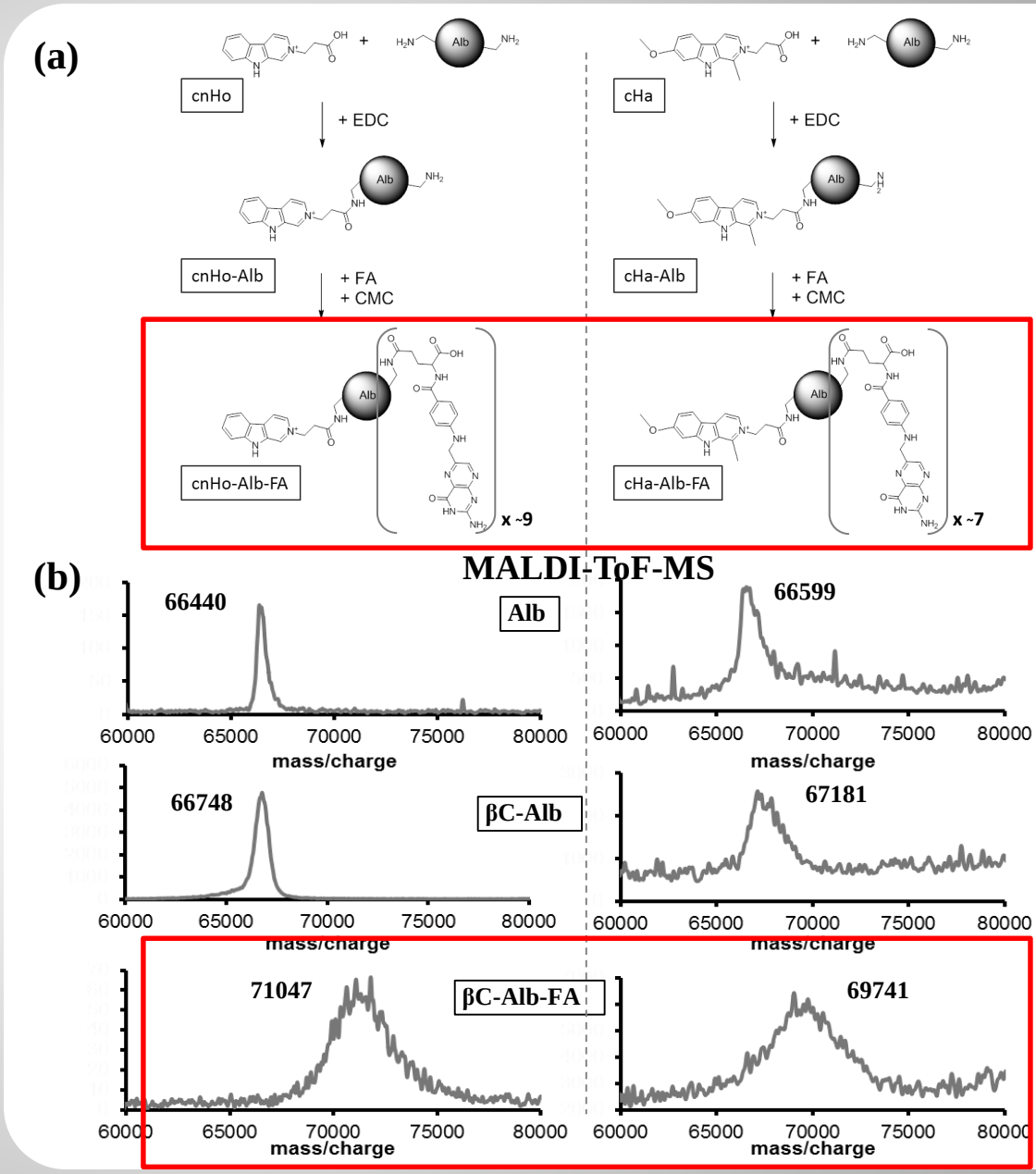
Synthesis and characterization of βC-Albumin-Folate conjugates

Results





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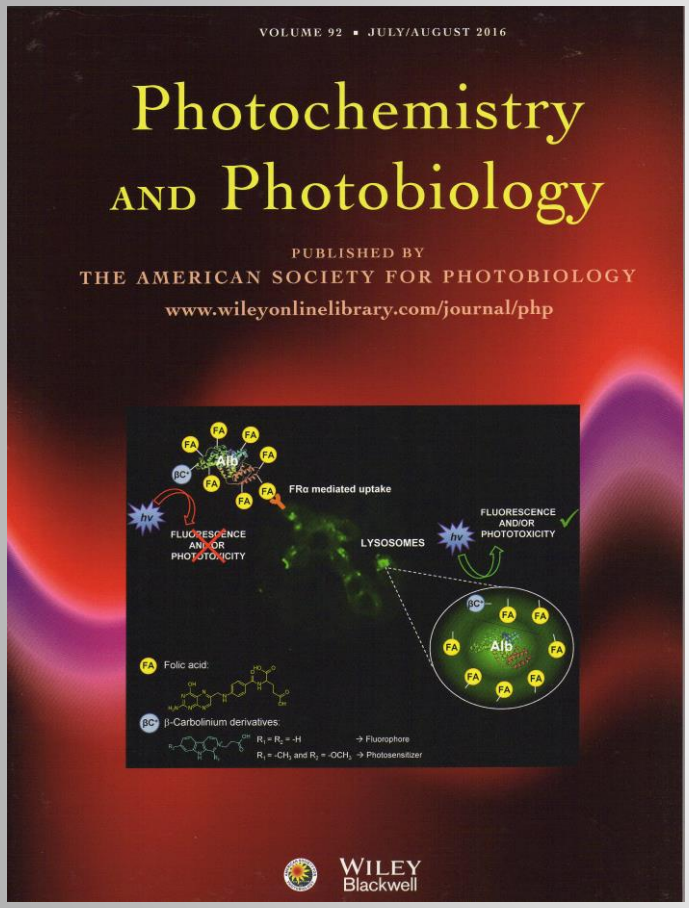

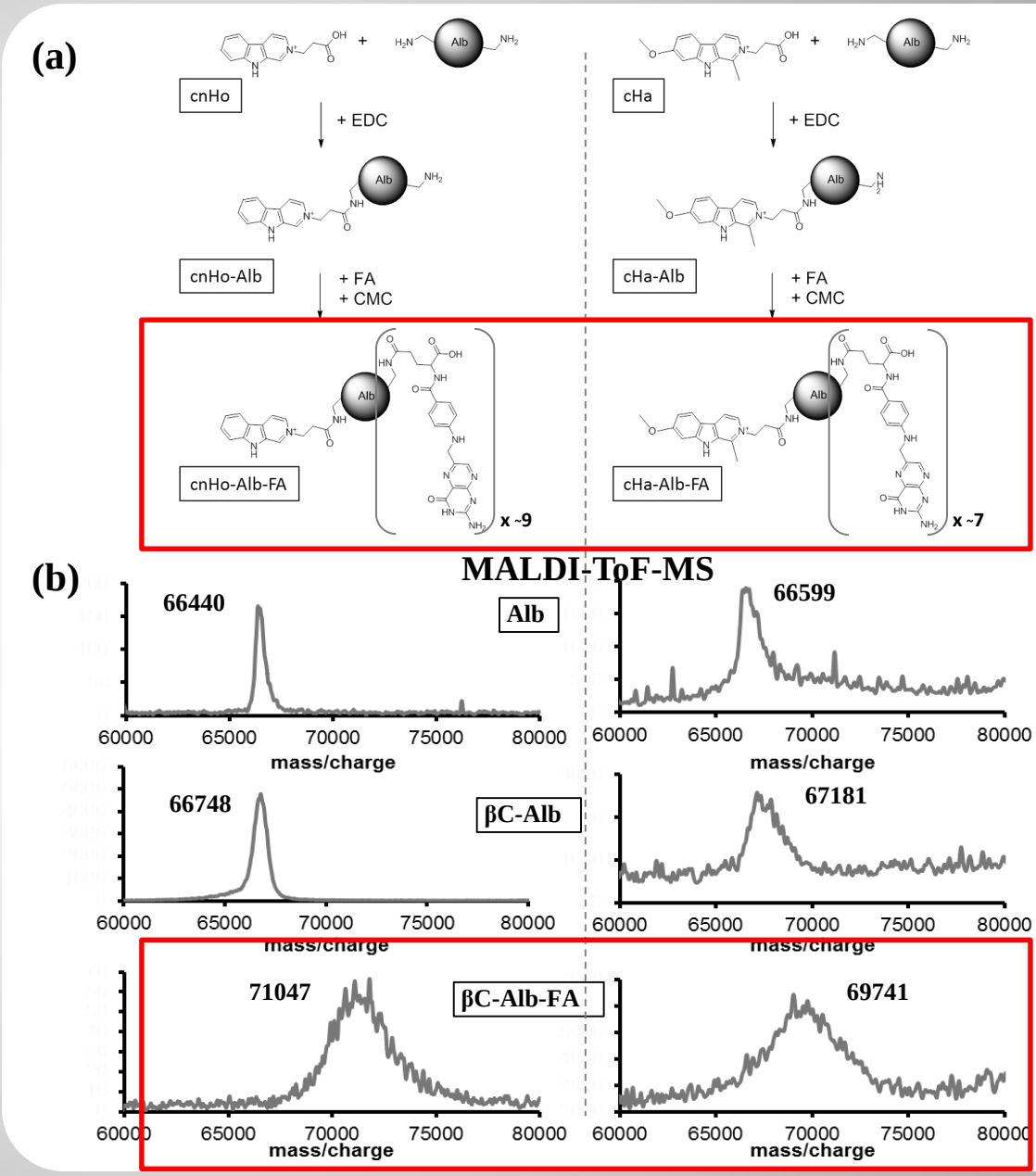

•K. Butzbach, F. A. O. Rasse-Suriani, M. M. Gonzalez, F. M. Cabrerizo and Bernd Epe. *Photochem. Photobiol.*, **2016**, 92, 611-619.

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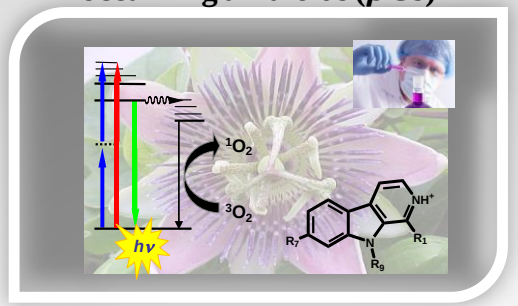

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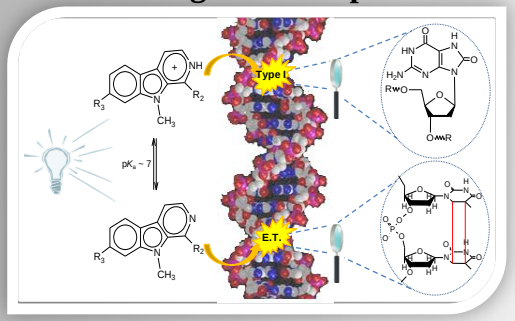

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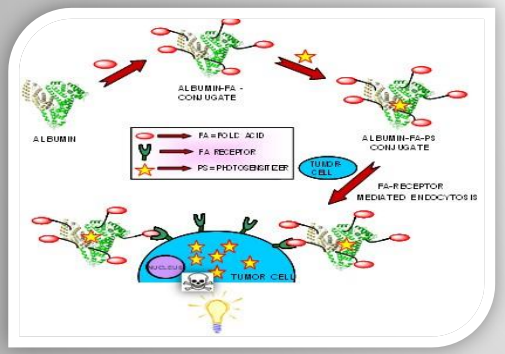

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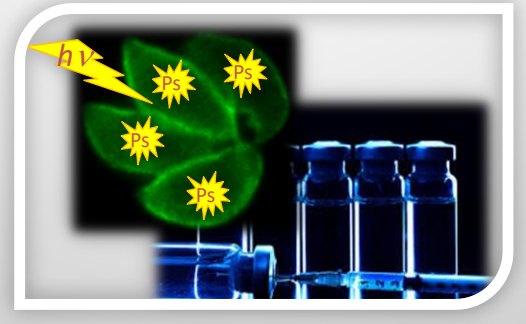

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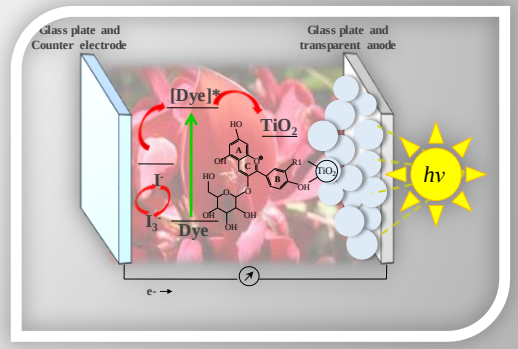

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