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Effect of interaction with micellar media on spectral properties of some amphiphilic porphyrins

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Abstract

The use of porphyrinic compounds in the field of theranostic nanomedicine, has increased substantially in the recent years due to their special features such as: long wavelength absorption and emission in the spectral region where the biological tissues absorb, a good photodynamic activity, photostability and low *in vivo* toxicity [1-3]. Despite significant advantages, due to the large π conjugate systems, porpyrins easily form aggregates, which have a significantly lower ability for localization at cellular level and consequently decrease the therapeutic effect. So, before pharmaceutical formulation, it is necessary the study of the spectral and aggregation properties of these compounds in membrane mimetic media, such as micelles, in order to determine the factors that modulate porphyrin–membrane interactions and that may resolve the aforementioned problems [4-6]. The present study included spectral evaluation of some amphiphilic porphyrins in TX-100/water and TX-100/cyclohexane micelles. The obtained results suggests for tested compounds the localization at the interface between the polyethylene oxide chains and the tert-octyl-phenyl etheric residue of the surfactant molecules. Regarding to spectral behavior of the studied porphyrins, the experimental results confirms fact that incorporation in micelles will facilitate a better delivery to the cellular target without determine significant change in their photophysical profile.

Keywords: *amphiphilic porphyrins; micelles; spectroscopy*

Compounds

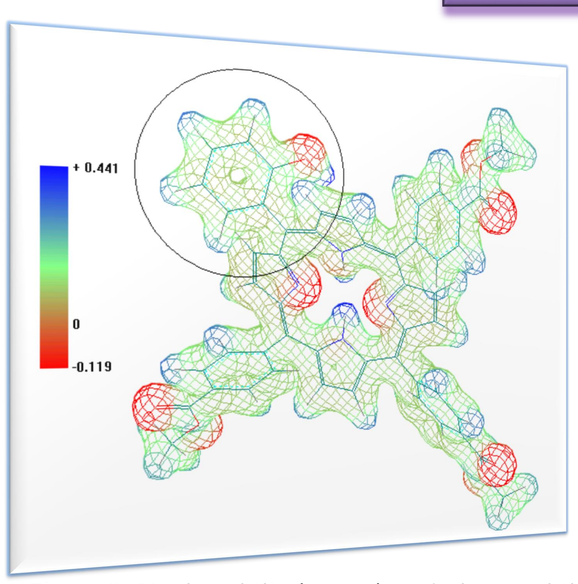
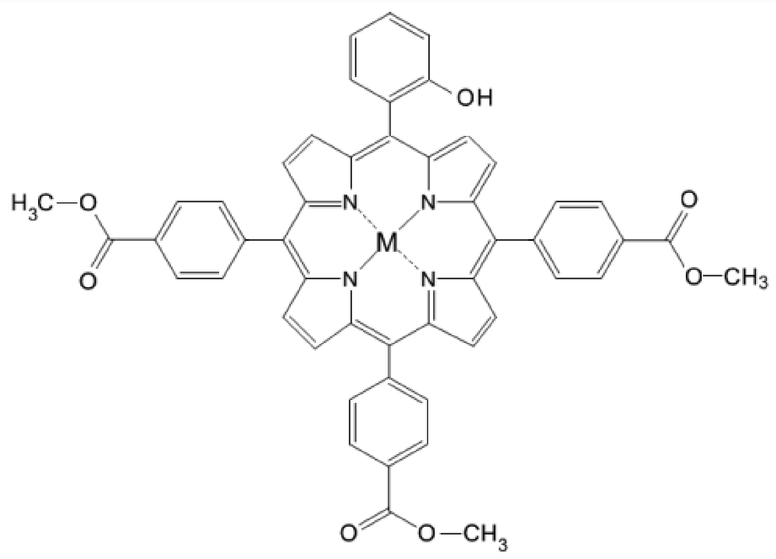
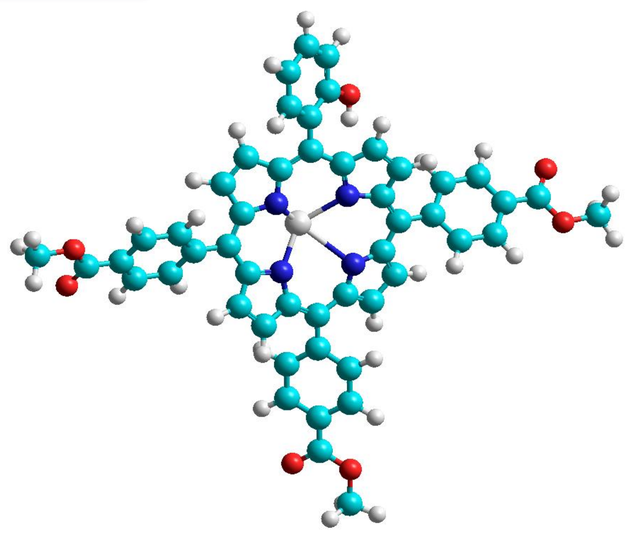


Figure2. Nucleophilic (green) and electrophilic (red)attack susceptible zones underlining the structural asymmetry A3B type



a



b

Figure 1. General structures (a-classic and b-*in silico* optimized) of the amphiphilic porphyrins used in this study [7]
5-(2-hydroxyphenyl)-10,15,20–tris-(4-carboxymethylphenyl)porphyrin, M=2H , (TCMPOHo)
M(II)-5-(2-hydroxyphenyl)-10,15,20–tris(4-carboxymethylphenyl)porphyrin, M=Zn(II), Cu(II), (M(II)TCMPOHo)

Table 1. Theoretic molecular data for studied porphyrins

Porphyrinic compound	Molecular Mass (u.m.a.)	Polarizability (Å³)	Dipole moment (D)	Axis dipole moment (D)		
				X	Y	Z
TCMPOHo	804.86	88.90	3.608	1.71688	-1.9074	-2.48823
CuTCMPOHo	866.39	88.30	3.918	1.55098	-0.45631	3.56904
ZnTCMPOHo	868.21	88.30	2.492	1.73208	-1.73842	0.43367

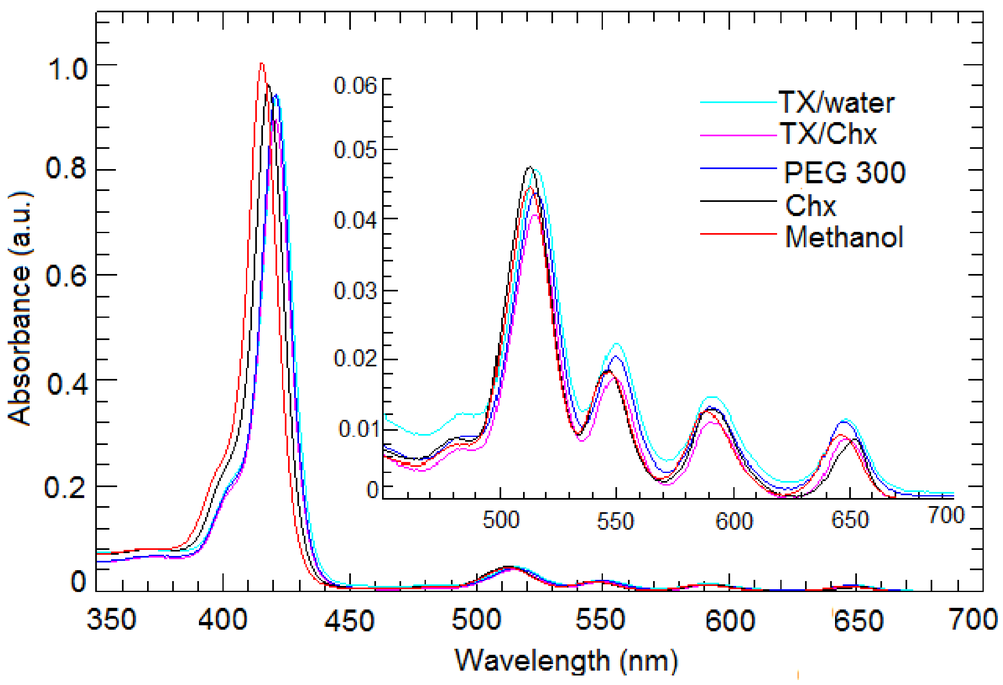


Figure 2. Absorption spectra of $TCMPOH_9$ in different solvents and micellar solutions ($2.5x10^{-6}$M)

Spectral features

Table 2. Absorbtion and emission data of the studied amphiphilic porphyrins in different solvents and micellar media (c=$2.5x10^{-6}$ M)

Solvent	Absorption λmax (nm) [lgε](L mol⁻¹ cm⁻¹)					Emission λmax (nm) [F.I.] (a.u.)
	Soret Band	Qy(1,0)	Qy(0,0)	Qx(1,0)	Qx(0,0)	
5-(2-hydroxyphenyl)-10,15,20–tris-(4-carboxymethylphenyl)porphyrin						
MeOH	415.4 [5.603]	512.5 [4.255]	546.3 [3.860]	588.4 [3.699]	646.6 [3.574]	648.7 [25.5]
Chx	418.0 [5.593]	512.5 [4.279]	546.1 [3.875]	590.7 [3.796]	652.3 [3.544]	650.7 [20.0]
PEG300	420.7 [5.574]	515.4 [3.243]	549.9 [3.916]	590.7 [3.796]	647.3 [3.653]	649.1 [28.5]
TX/water	421.4 [5.577]	515.6 [4.273]	549.9 [3.954]	591.0 [3.778]	648.4 [3.677]	649.7 [15.0]
TX/Chx	420.6 [5.553]	515.0 [4.211]	549.2 [3.845]	590.7 [3.653]	648.3 [3.544]	649.7 [26.0]
Zn(II)-5-(2-hydroxyphenyl)-10,15,20–tris(4-carboxymethylphenyl)porphyrin						
MeOH	423.5 [5.599]		556.6 [4.123]	597.1 [3.537]		604.2 [24.6]
Chx	417.6 [5.596]		546.1 [4.255]	596.9 [3.301]		601.8 [21.0]
PEG300	428.6 [5.615]		558.8 [4.432]	599.3 [4.093]		605.9 [28.5]
TX/water	430.0 [5.549]		559.5 [4.255]	601.0 [4.010]		607,6 [12.7]
TX/Chx	428.9 [5.610]		558.8 [4.339]	599.3 [4.049]		605.4 [25.9]
Cu(II)-5-(2-hydroxyphenyl)-10,15,20–tris(4-carboxymethylphenyl)porphyrin						
MeOH	413.1 [5.670]		538.2 [4.289]			
Chx	414.2 [5.703]		538.1 [4.357]			
PEG300	417.9 [5.495]		539.9 [4.360]			
TX/water	417.9 [5.574]		539.6 [4.357]			
TX/Chx	417.3 [5.673]		539.5 [4.413]			

MeOH=methanol; Chx=cyclohexane; PEG300 = polyethylenegliycol 300; TX/water= 0.24 mM TritonX-100 in water; TX/Chx = 0.66M TritonX-100 in cyclohexane

Conclusions

The study concluded that the spectral properties of the studied compounds have the main characteristics suitable for the next step into the pharmaceutical preformulation. This new A3B type compound, as free-base and metalloporphyrin has good behaviour in the micellar media, PEG 300,methanol and cyclohexane, targeting superior stage in the chain of activation as photosensitizer. It is in silico configured and the general theoretical data obtained matched the real features of the compounds. Moreover, the fluorescence data are similar to other amphiphilic porphyrins, already introduced by us in biological evaluation, as promising candidates in PDT. The steady-state fluorescence emission studies are related to the UV-Vis absorption in what concerns the small differences between the maximum emission peaks in correlation to the chemical structure of the compounds. Also, the porphyrins are at this level evaluated from the polarization point of view, tacking account that the cell membrane is polarized by several similar compounds.

References

1.L.B. Josefsen, R.W. Boyle, *Theranostics*, **2012**, 2, 916–966.
2. M. Ethirajan, Y. Chen, P. Joshi, R.K. Pandey, *Chem. Soc. Rev.*, **2011**, 40, 340–362.
3. P. Rai, S. Mallidi, X. Zheng, R. Rahmanzadeh, Y. Mir, S. Elrington, A. Khurshid, T. Hasan, *Adv. Drug Deliv. Rev*., **2010**, 62, 1094–1124.
4. M. van Elk, B.P. Murphy, T. Eufrásio-da-Silva, D. P. O'Reilly, T. Vermondenf, W. E. Henninkf, G. P. Duffy, E.Ruiz-Hernández, *International Journal of Pharmaceutics*, **2016**, 515, 132–164.
5. M. Cagel, F.C. Tesan, E. Bernabeu, M.J. Salgueiro, M.B. Zubillaga, M.A. Moretton, D. A. Chiappetta, *European Journal of Pharmaceutics and Biopharmaceutics,* **2017**, 113, 211–228.
6. D. Silva Pellosi, I. R. Calori, L. Barcelos de Paula, N. Hioka, F. Quaglia, A. C. Tedesco, *Materials Science and Engineering C,* **2017**, 7, 11–19.
7. L.F.V. Ferreira, D.P.Ferreira, A.S.Oliveira, R.Boscencu, R.Socoteanu, M. Ilie, C. Constantin, M. Neagu, *Dyes and Pigment,* **2012**, 95, 296–303.

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