

Fluorescence studies of potential antitumoral 6-heteroarylthieno[3,2-*b*]pyridines in solution and in nanoliposomes

Photobiology, biophysics and skin photochemistry

M. Solange D. Carvalho,^{a,b} Elisabete M. S. Castanheira,^a Andreia D. S. Oliveira,^a Ricardo C. Calhella,^b Maria João R. P. Queiroz^b

^aCentre of Physics (CFUM) and ^bCentre of Chemistry (CQ/UM), University of Minho, Campus de Gualtar, 4710-057 Braga, Portugal; msolangeddc@gmail.com

Thienopyridine derivatives have been shown interesting biological activities. New fluorescent 6-heteroarylthieno[3,2-*b*]pyridines (Figure 1), recently synthesized by us, have shown interesting inhibitory growth activity on three human tumor cell lines, MCF-7 (breast adenocarcinoma), NCI-H460 (non-small cell lung cancer) and A375-C5 (melanoma) [1].

In this work, the fluorescence properties of compounds **1-4** were studied in solution and in liposomes of different compositions. Compounds **1-4** present very reasonable fluorescence quantum yields in different solvents ($0.05 \leq \Phi_F \leq 0.50$), but are not fluorescent in alcohols and water.

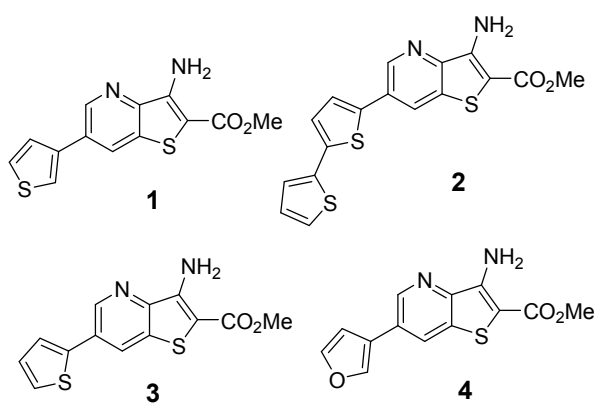


Figure 1. Structure of the compounds **1-4**.

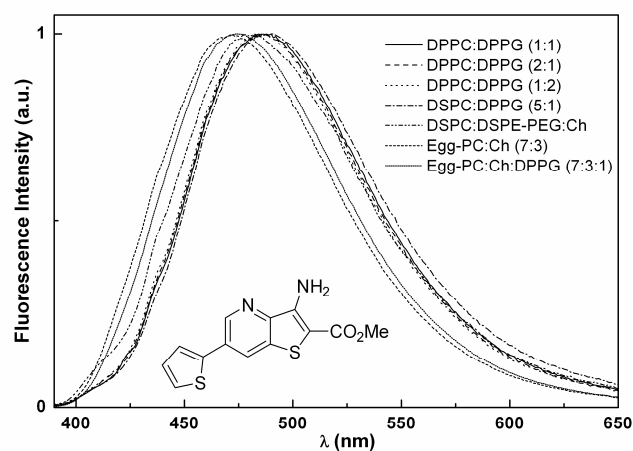


Figure 2. Normalized fluorescence spectra of **3** in nanoliposomes.

Nanosized liposomes (diameter ≤ 120 nm, measured by DLS) with incorporated compounds were prepared using egg yolk phosphatidylcholine (Egg-PC), dipalmitoyl phosphatidylcholine (DPPC), distearoyl phosphatidylcholine (DSPC), dipalmitoyl phosphatidylglycerol (DPPG), with or without cholesterol (Ch) and distearoyl phosphatidylethanolamine-(PEG)2000 (DSPE-PEG).

The four compounds exhibit reasonable fluorescence emission when incorporated in liposomes (example of compound **3** is presented in Figure 2). Fluorescence anisotropy measurements indicate that compounds **1-4** can be transported in the hydrophobic region of the lipid bilayer. The liposomal formulation Egg-PC:Ch:DPPG (7:3:1) is the one with smaller size and lowest polydispersity. These results may be important for future drug delivery applications of these potential antitumoral compounds using nanoliposomes as drug carriers.

Acknowledgements: FCT, QREN and FEDER for financial support to CFUM [PEst-C/FIS/UI0607/2011 (F-COMP-01-0124-FEDER-022711)] and CQ/UM [PEst-C/QUI/UI0686/2011 (FCOMP-01-0124-FEDER-022716)] and to the research project PTDC/QUI/81238/2006 (FCOMP-01-0124-FEDER-007467). M.S.D. Carvalho thanks her PhD grant (SFRH/BD/47052/2008) to FCT, POPH-QREN, FSE.

References:

[1] M.-J.R.P. Queiroz, R.C. Calhella, L.A. Vale-Silva, E. Pinto, R.T. Lima, M.H. Vasconcelos, *Eur. J. Med. Chem.*, 45 (2010) 5628.