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

Photobiology, biophysics and skin photochemistry

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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.

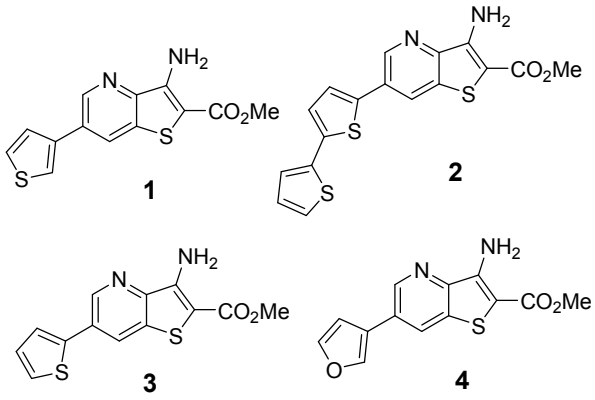

Figure 1. Structure of the compounds **1-4**.

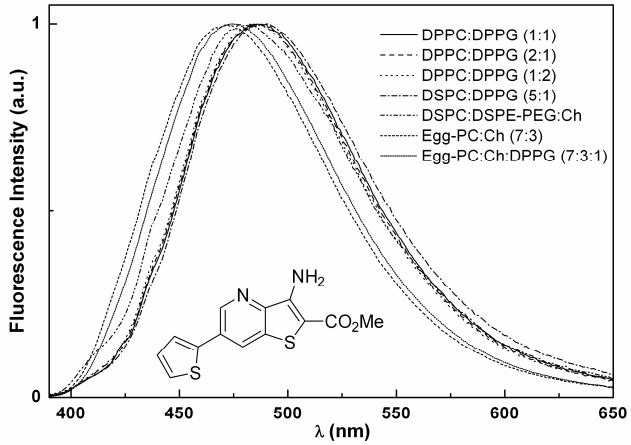

Figure 2. Normalized fluorescence spectra of **3** in nanoliposomes.

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.

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References:

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