Contribution (Poster)

Fluorescence studies of new potential antitumoral di(hetero)arylethers derivatives of a thieno[3,2-*b*]pyridine encapsulated in nanoliposomes

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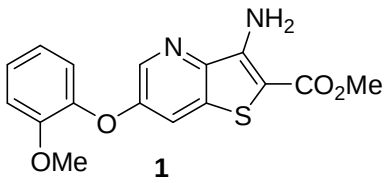
Nanoliposomes are new technological developments for the encapsulation and delivery of bioactive agents. Because of their biocompatibility and biodegradability, along with their size, nanoliposomes have potential applications in a vast range of fields, including nanotherapy. Nanoliposomes are able to enhance the performance of bioactive agents by improving their bioavailability, *in vitro* and *in vivo* stability, as well as preventing their unwanted interactions with other molecules [1].

Nanoliposomes may contain, in addition to phospholipids, other molecules such as cholesterol (Ch) which is an important component of most natural membranes. The incorporation of Ch can increase stability by modulating the fluidity of the lipid bilayer preventing crystallization of the phospholipid acyl chains and providing steric hindrance to their movement. Further advances in liposome research found that polyethylene glycol (PEG), which is inert in the body, allows longer circulatory life of the drug delivery system [2].

In this work, new potential antitumoral di(hetero)arylethers derivatives of a thieno[3,2-*b*]pyridine, **1** and **2**, synthesized by us, have been encapsulated in different nanoliposome formulations, composed of egg-yolk phosphatidylcholine (Egg-PC), dipalmitoyl phosphatidylcholine (DPPC), dioleoyl phosphatidylcholine (DOPC), dimyristoyl phosphatidylglycerol (DMPG), distearoyl phosphatidylcholine (DSPC), with or without Ch and distearoyl phosphatidylethanolamine-(polyethylene glycol)2000 (DSPE-PEG).



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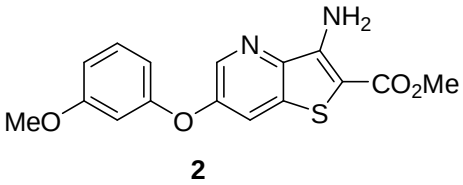

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Compounds **1** and **2** were evaluated for the *in vitro* cell growth inhibition on three human tumor cell lines, breast adenocarcinoma (MCF-7), non-small cell lung cancer (NCI-H460) and a melanoma cell line (A375-C5), after a continuous exposure of 48 h, exhibiting very low GI_{50} values (μM) in the three tumor cell lines (Table 1).

Table 1. Values of compounds **1** and **2** concentration needed for 50% of cell growth inhibition (GI_{50}).

	GI_{50} (μM)		
	MCF-7	**NCI-H460**	**A375-C5**
1	1.4 ± 0.1	1.4 ± 0.2	1.1 ± 0.1
2	2.5 ± 0.1	2.5 ± 0.3	2.3 ± 0.1

Doxorubicin was used as control: GI_{50} MCF-7 = 43.3 ± 2.6 nM; NCI-H460 = 130.2 ± 10.1 nM; A375-C5 = 35.6 ± 1.6 nM.

Nanoliposomes were prepared by injection of an ethanolic solution of the different lipid mixtures in aqueous media under vigorous stirring, above the melting transition temperature of the lipids, followed by six extrusion cycles through 100 nm polycarbonate membranes. Dynamic light scattering (DLS) measurements indicated that the nanoliposomes with the incorporated compound are generally monodisperse and with diameters between 70 nm and 120 nm.

Compounds **1** and **2** exhibit fluorescence in non-polar media, while no emission is observed in protic solvents (like ethanol, methanol and water). The two compounds show significant emission when incorporated in nanoliposomes (Figure 1) and fluorescence anisotropy values are generally high. This behavior indicates that both compounds can be transported in the hydrophobic region of the lipid bilayer. These results may be important for future drug delivery applications of the new potential antitumoral di(hetero)arylethertheinopyridines, using nanoliposomes as drug carriers.

Acknowledgements

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References

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[2] Y. Malam, M. Loizidou, A. M. Seifalian, Trends in Pharmacol. Sci. **30** (2009) 592.

Figures

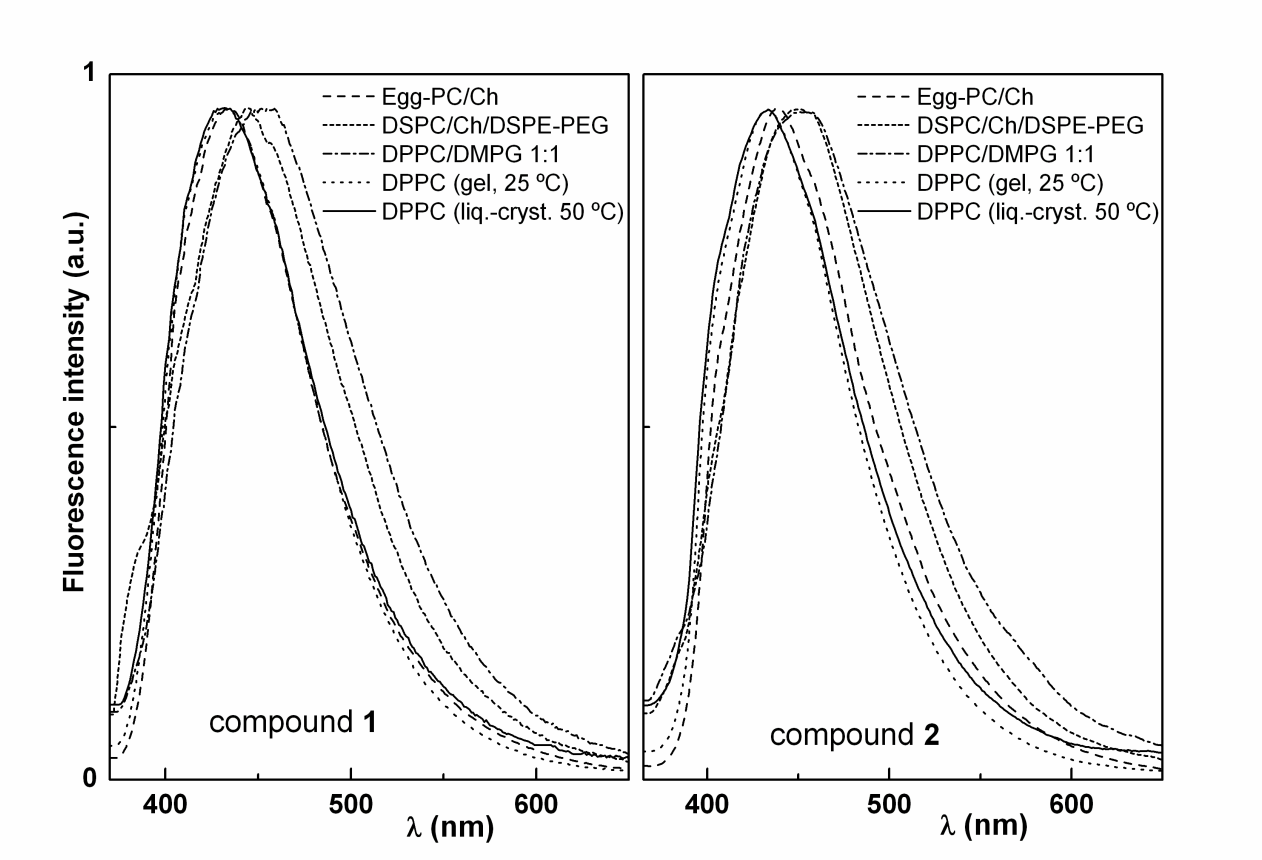

*Figure 1. Normalized fluorescence spectra of compounds **1** and **2** in several nanoliposome formulations.*