Synthesis Of Fluorescent Heteroaromatic Compounds Using Dehydroamino Acids As Building Blocks, Studies Of DNA And Biomembranes Interactions. Evaluation Of Antiproliferative Effects On Tumor Cell Lines

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Background: The synthesis of new anticancer agents is an important goal. Aims: 1) To synthesize new fluorescent compounds, a 3-(dibenzothien-4-yl)indole (**1**), a 3-(benzothien-3-yl)benzothieno[2,3-*b*]pyrrole (**2**) and a 3-(benzothien-2-yl)benzothieno[3,2-*b*]pyrrole (**3**). 2) To study their interaction with DNA and liposomes. 3) To evaluate their effects in tumor cell lines.
Methods:. Absorption and fluorescence spectroscopies were used to study their photophysical properties in different solvents and their interactions with salmon sperm ds-DNA including fluorescence quenching experiments with iodide ion. Their interaction with liposomes of dipalmitoyl phosphatidylcoline (DPPC) prepared by injection, was studied by fluorescence. The antiproliferative effects on tumor cell lines of breast adenocarcinoma (MCF-7), glioblastoma (SF-268) and non-small cell lung cancer (NCI-H460) were evaluated after a continuous exposure of 48h, using the protein-binding dye sulforhodamine B. Results represents means ± SEM of 3 exp. performed in duplicate.
Results: Compounds **1**-**3** were synthesized in good yields. In the fluorescence spectra a red shift in the λ_{em} (nm) is observed from apolar to polar solvents. In the fluorescence spectra using increasing [DNA]/[compound] ratios an increase in the emission intensity is observed. The fraction of molecules accessible to iodide ion was very low. In DPPC liposomes (25 ^{o}C) the emission spectra are very similar to the ones in cyclohexane. The results of the antiproliferative effects are shown below.

Compound	GI_{50} (μM)		
	MCF-7	SF-268	NCI-H460
1	11.00±0.60	17.0±1.20	12.70±1.50
2	7.88±0.08	7.85±1.26	14.13±1.73
3	19.10±11.50	38.70±8.90	3.90±0.30

Conclusions: 1) The preferred mode of binding with DNA is the intercalation. 3) Their location in liposomes of DPPC is the hydrophobic region. 4) A good to high inhibitory effect on the growth of the tested cell lines was observed. Compound **3** shows a high specificity for the NCI-H460 cell line.
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