SPECTROSCOPIC BEHAVIOUR OF PSORALEN DERIVATIVE (5MOP) UPON BINDING TO LIPID VESICLES AND SERUM LIPOPROTEINS

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ABSTRACT

The psoralen derivative, 5-methoxypsoralen (5MOP), binds to human serum low density lipoproteins LDL, with an association constant of 1.4 x 10^5 M^{-1} (1). This binding is accompanied by a large bathochromic shift (60 nm) of the fluorescence spectrum and an increase of the fluorescence quantum yield (Φ_f= 0.005; λ_f^{max}= 450 nm) in LDL with respect to aqueous solution (Φ_f= 0.0016; λ_f^{max}= 510 nm).

Incorporation of 5MOP in LDL induces the fluorescence quenching of the tryptophane residues in this lipoprotein. This observation was attributed to conformational changes of the apoprotein B in the LDL (1). The extreme sensitivity of 5MOP photophysical parameters to the dielectric properties of the solvent was used to emulate the biological environments and therefore to investigate 5MOP photoreactivity.

Key words: Apoprotein B, LDL, lipid vesicles, 5-methoxypsoralen

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RESULTS AND DISCUSSION

Figure 1 shows the excitation (left) and the fluorescence (right) spectra of 5MOP incorporated in different biological environments and in aqueous solution. The fluorescence wavelength maxima, fluorescence quantum yields, fluorescence lifetimes and triplet formation quantum yields of 5MOP in dioxane-water mixtures is correlated with the same photophysical parameters of 5MOP in organized media like micelles, liposomes and lipoproteins, as shown in Table 1.

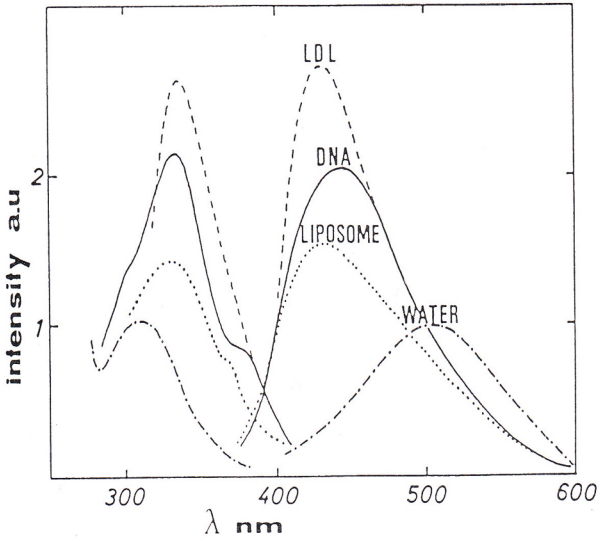

FIGURE 1

-right - Emission spectra at 25°C of 5MOP in lipoproteins, liposomes, DNA and water solutions.
-left - Excitation spectra of the corresponding fluorescence.

The large sensitivity of these parameters to the nature of the medium is due to the solvent influence on the singlet and triplet excited states of 5MOP (Fig. 2). Examination of Fig. 3 shows that the largest fluorescence lifetime and triplet formation quantum yield values and therefore the largest chances of 5MOP to react are found in a narrow polarity range which is centered roughly at 8M of water concentration in dioxane-water mixtures (Fig. 3). From Fig. 3 it is seen that the

TABLE 1

Fluorescence wavelenght maxima (λ_f in nm), fluorescence quantum yields (ϕ_f), fluorescence lifetimes (τ_f in ns) and triplet formation quantum yields (ϕ_T) of 5MOP at 25°C in several media.

SOLVENT	τ_f	λ_f^{max}	ϕ_f	ϕ_T
Dioxane	0.15	440	0.0016	0.090
Dioxane/2.8M H2O	0.67	445	0.0054	0.200
Acetonitrile	0.93	450	0.0100	0.270
DPPC Liposomes	n.d.	450	n.d.	0.270
Dioxane/8M H2O	2.20	450	0.0200	0.350
LDL Lipoproteins	1.09	450	0.0050	0.080
Dioxane/5.5M H2O	1.67	455	0.0125	0.300
SDS Micelles	1.63	480	0.0110	0.060
Dioxane/28M H2O	1.90	485	0.0120	0.060

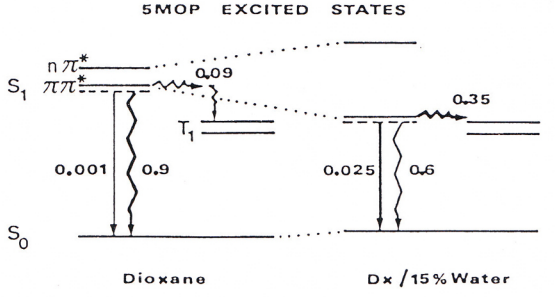

FIGURE 2

Energy levels of the electronic excited states of 5MOP in dioxane and dioxane with 8M of water concentration.

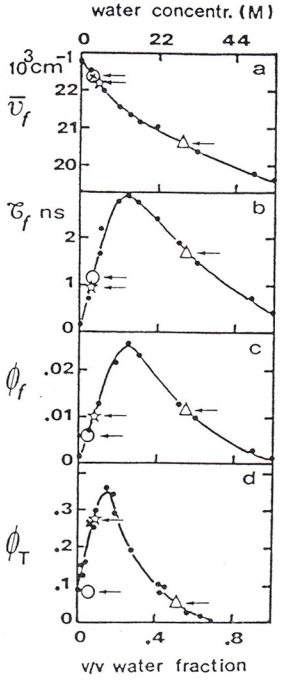

FIGURE 3

Photophysical parameters of 5MOP in dioxane-water mixtures:
$\bar{\nu}_f$: maximum fluorescence wavenumber
τ_f: fluorescence lifetime
ϕ_f: fluorescence quantum yield
ϕ_T: triplet formation quantum yield
Symbols deals with: ◇ 5MOP in 0.01 M SDS micelles; o in acetonitrile; △ in LDL lipoproteins; x in DPPC liposomes.

solubilization environment in human serum lipoproteins, LDL and in liposomes DPPC, falls in this polarity range. These results have interesting photobiological implications because as expected, the triplet formation quantum yield ϕ_T in liposomes is large (0.27), but in contrast, in LDL lipoproteins a much smaller amount of triplet was observed (0.08). This result can be attributed to an efficient triplet reactional process inside the hydrophobic core of this lipoprotein. In conclusion, the anti-psoriatic drug, 5-methoxypsoralen can be easily incorporated in serum lipopro-

teins and plays a role in its clearance via LDL endocytosis in specific cells.

Moreover this lipoprotein environment favours the 5MOP triplet photoreactivity with aminoacid residues during the phototherapy by UVA irradiation.

REFERENCES

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