Polymethine dyes incorporated in emissive PLGA and Albumin Nanoparticles

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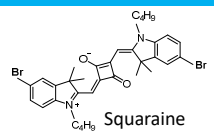
Introduction

❑ Strong absorbance on NIR region and excellent photochemical properties of polymethine dyes make them excellent probes in theragnostic applications. However, the improvement of physicochemical properties in the physiological conditions needs to be addressed. In this context, the incorporation of these dyes inside nanoparticles (NPs) is extremely important to control their photochemical and photophysical properties in aqueous media [1][2].

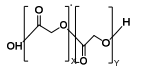
❑ Recently, **Albumin NPs** garnered interest as carriers to encapsulate hydrophobic drugs, thanks to their high biodegradability, biocompatibility and easier production procedures [3].

❑ Poly(lactide-co-glycolide) (**PLGA) NPs** has attracted considerable attention due to their excellent physicochemical properties, FDA and EMA approval as Drug Delivery Systems (DDS), versatile formulations and methods to incapsulate several both hydrophilic or hydrophobic molecules [4].

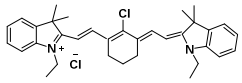
Objective: design of albumin and PLGA NPs for the incorporation of polymethine dyes known for the Photodynamic (PDT) activity, specifically cyanines and squaraines [1] [2], to enhance their physicochemical properties in aqueous media.



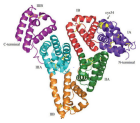
Squaraine



PLGA



Cyanine



Albumin

Material and methods

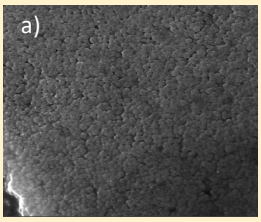
Human Serum Albumin (HSA) NPs

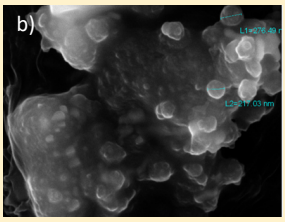
Desolvation technique followed by addition of glutaraldehyde crosslinking agent were used for HSA NPs preparation, by modifying the procedures reported in the literature [3].

✓ Human serum albumin (HSA)

✓ Desolving agent; ethanol

Results





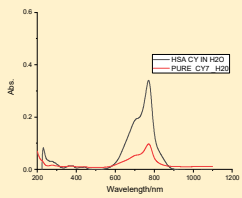
FE_SEM image a) Empty HSA NPs b) HSA_CY7 NPs

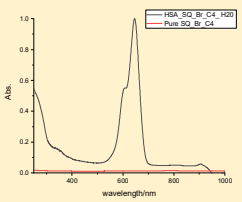
DLS and FE_SEM results of empty and dye loaded HSA NPs

	HSA empty (Glu.)	HSA empty (EDC)	HSA_CY7 NPs DLS	HSA_SQ_Br_C4 NPs FE_SEM
Size	250	168	325	178
PDI	0.2	0.18	0.44	-
Zeta potential	-25	-23	-20	-

Solvatochromism of dye loaded HSA

Solvent	CY_7	HSA_CY_7	SQ_Br_c4	HSA_SQ_Br_c4
MeOH	778	776.5	636	637
EtOH	780	781	640	639
DMSO	792	790	652	650
Acetone	780	780	643	640
H_2O	770	771	Not soluble	645





a) HSA_CY7 NPs in H_2O b)HSA_SQ_Br_C4 NPs in H_2O

Material and methods

Poly(lactide-co-glycolide) (PLGA) NPs

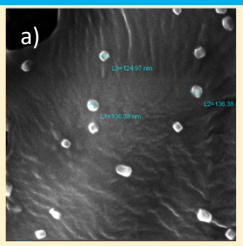
Nanoprecipitation with probe sonication for empty and dye loaded polymeric PLGA NPs according to the pervious reported method [5]

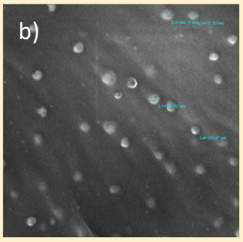
✓ Ratio of PLA / PGA; 50:50

✓ Acetone

✓ Stabilizing agent; Pluronic (F_127)

Results





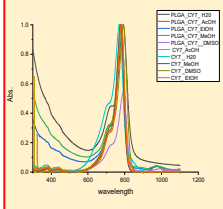
FE_SEM image a) Empty PLGA NPs b) PLGA_SQ_Br_C4 NPs

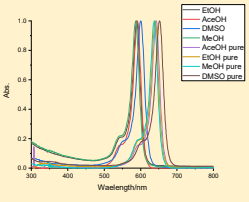
DLS and FE_SEM results of empty and dye loaded PLGA NPs

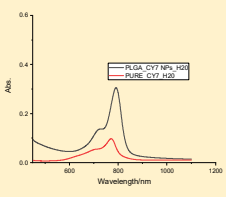
	PLGA empty	PLGA _ CY7	PLGA_SQ_Br_C4 FE_SEM
Size	234	419	109
PDI	0.25	0.35	-
Zeta potential	-20	-1	-

Solvatochromism of dye loaded PLGA

Solvent	SQ_Br_C4	PLGA_SQ Br_C4 NPs	CY7	PLGA_CY7 NPs
Acetone	642	592	779	781
MeOH	637	586	777	776
EtOH	639	588	780	781
H_2O	-	645	770	776
DMSO	652	600	792	791







a) PLGA_CY7 NPs b) PLGA_SQ_Br_C4 NPs c) PLGA_CY7 NPs in H_2O

Conclusions

✓ Empty HSA NPs showed smaller size, PDI and are less stable using EDC compared to glutaraldehyde.

✓ Empty PLGA NPs with a ratio of PLA to PGA 50:50 and Pluronic as stabilizing agent showed smaller size and PDI compared to PVA as stabilizing agent.

✓ The encapsulation of cyanine and squaraine dyes in the HSA and PLGA NPs are confirmed by the presence of hypsochromic shifts in the salvatochromism analysis.

✓ The water solubility of cyanine and squaraine encapsulated in HSA was enhanced. In case of PLGA NPs, only the cyanine showed higher solubility. Unexpectedly, for squaraine dye the solubility has not been enhanced. Actually, this study is still in progress.

Reference

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[2] L. Serpe et al., Eur. J. Med. *Chem., vol. 113, pp. 187–197, 2016, doi: 10.1016/j.ejmech.2016.02.035. [3] B. Von Storp et al., vol. 2048, 2012.*

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[5] M. M. El-hammadi, Á. V Delgado, C. Melguizo, J. C. Prados, and J. L. Arias, Int. J. Pharm., vol. 516, no. 1–2, pp. 61– 70, 2017.