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SYNTHESIS AND CHARACTERIZATION OF SMART FLUORESCENT POLYMERS FOR BIOMEDICAL APPLICATIONS

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Consiglio Nazionale delle Ricerche

Introduction:

In the last 15 years, the smart materials have aroused considerable interest in the field of biomedicine and in particular in **drug delivery**. It is a process of administration of a pharmacologically active compound that is dissolved, trapped or encapsulated in nanometric sized polymeric carriers (Figure 1). [1] The drug delivery system must have important characteristics including biodegradability, biocompatibility, stability and above all they must not release toxic substances into the body. [2]

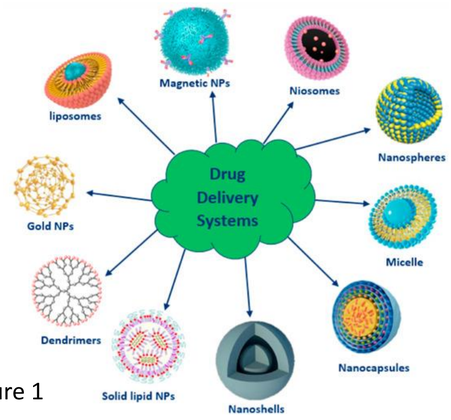


Figure 1

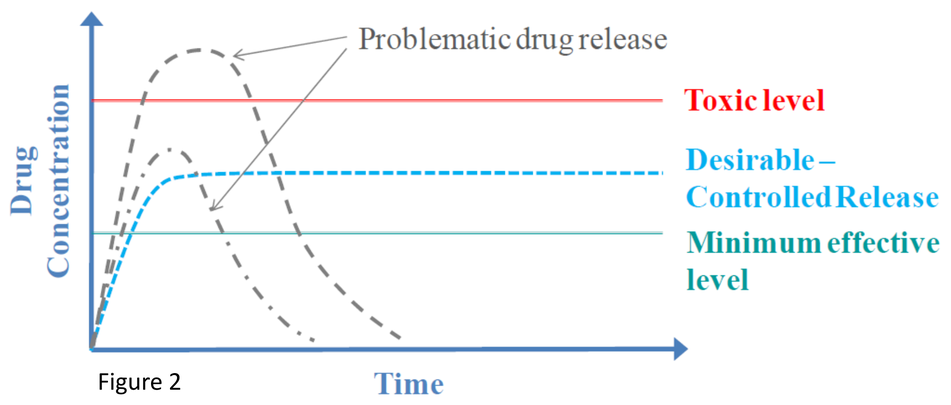
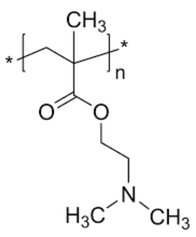


Figure 2

The central goal of drug delivery is to maximize therapeutic activity while minimizing side effects and to maintain the concentration of the drug in the therapeutic band for the set time (Figure 2). [3]

Smart polymers are in the vanguard of drug administration technology since they show an active response to small signs and changes in the surrounding environment, which translates into significant changes in their microstructure and in their physical and chemical properties. In particular the smart polymers most used in drug delivery are divided into two main categories: temperature-sensitive polymers and pH-sensitive polymers. [4]



Thermo-responsive and pH responsive smart polymer

PDMAEMA
(Poly N,N'-dimethylaminoethyl methacrylate)

Due to the high toxicity, it is used only as a carrier of anticancer drugs and being a polybasic polymer, it swells and releases the drug as the pH decreases (Figure 3). [5]

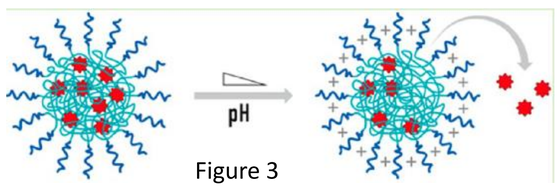


Figure 3

Although PDMAEMA is cytotoxic, its cytotoxicity is lowered if it is copolymerized with a non-cytotoxic hydrophobic segment. Furthermore, this segment can also act as a fluorescent probe chemically binding to a carrier, which allows to follow the path of the drug in human body.

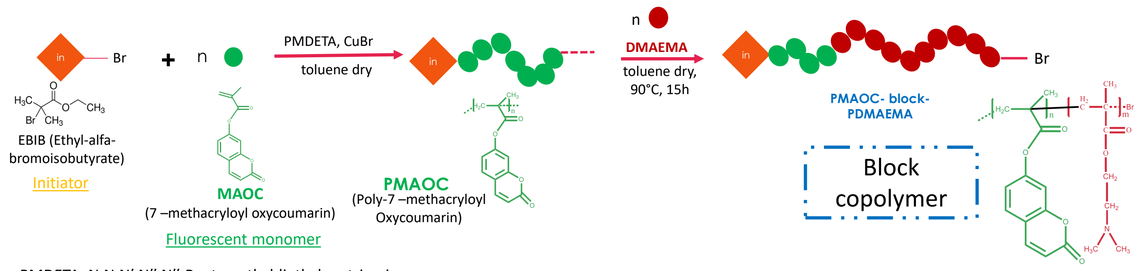
drug + carrier + Fluorescent probe

Antitumoral agent — PDMAEMA

New drug delivery system

Results:

Sequential polymerization by ATRP



PMDETA: N,N,N',N'',N''-Pentamethyldiethylenetriamine

Copolymerization conditions

EBIB	CuBr	PMDETA	MAOC	DMAEMA
1	3,5	3,5	40	400
1	2	2	10	100
1	2	2	20	200

MICROSTRUCTURAL CHARACTERIZATION

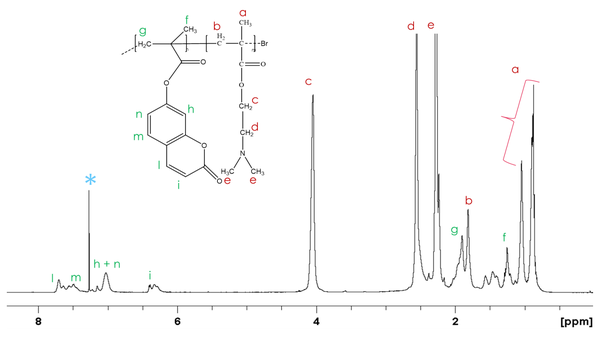


Figure 4: ^{1}H-NMR spectrum of PMAOC – block - PDMAEMA (600 MHz; $CDCl_3$; RT)

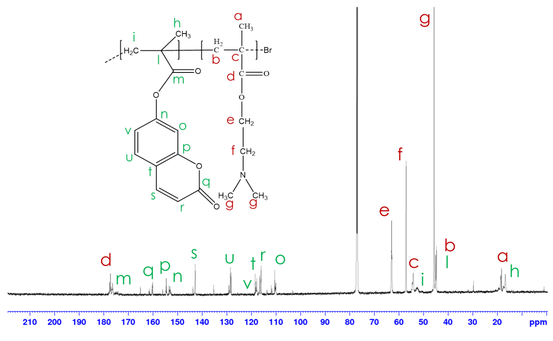


Figure 5: ^{13}C-NMR spectrum of PMAOC – block - PDMAEMA (600 MHz; $CDCl_3$; RT)

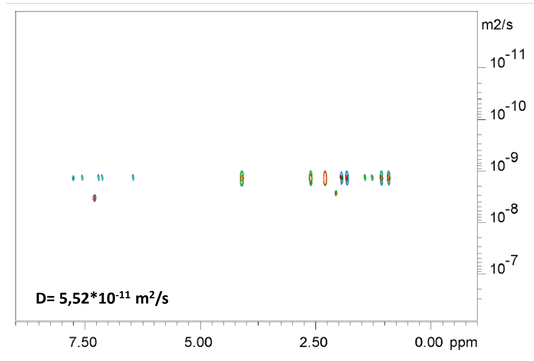


Figure 6: 2D-NMR DOSY spectrum of PMAOC – block - PDMAEMA (600 MHz; $CDCl_3$; RT)

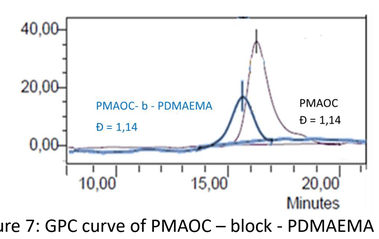


Figure 7: GPC curve of PMAOC – block - PDMAEMA in $CHCl_3$, RT

Dosy and GPC analysis confirm that the block copolymers are obtained.

PHYSICO-CHEMICAL CHARACTERIZATION

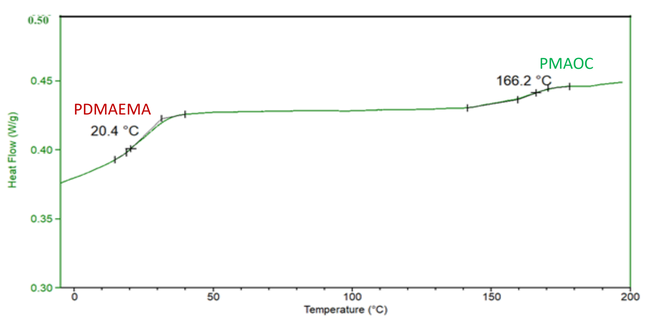


Figure 8: DSC curve of PMAOC – block – PDMAEMA, 10°C/min, N_2

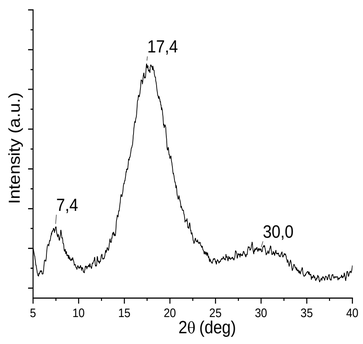


Figure 9: x-ray spectrum of PMAOC – block – PDMAEMA, 10°C/min, N_2

Thermogravimetric curve (DSC) show two different glass transitions relative to the PMAOC block and the PDMAEMA block.

The x-ray spectrum suggests the amorphous nature of the copolymers.

OPTICAL CHARACTERIZATION

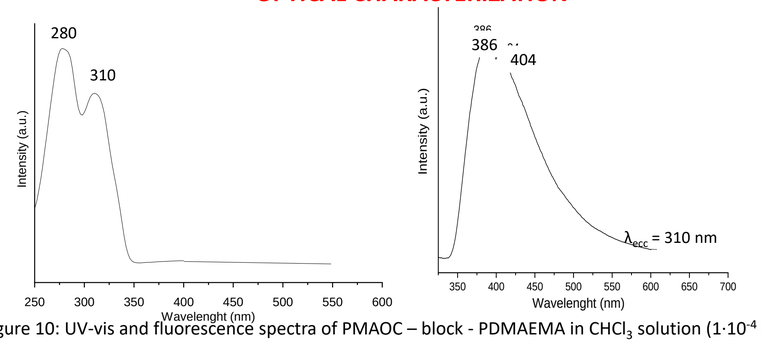


Figure 10: UV-vis and fluorescence spectra of PMAOC – block - PDMAEMA in $CHCl_3$ solution ($1\cdot10^{-4}$ M)

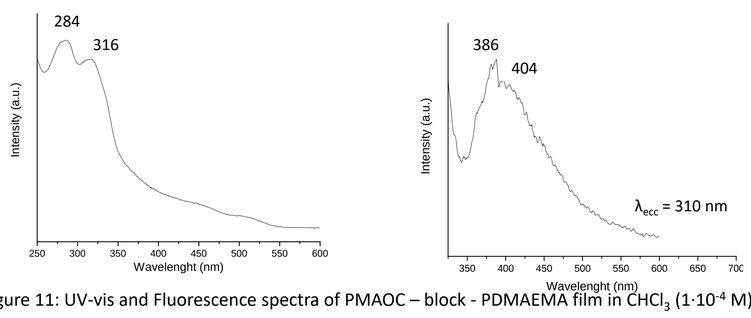


Figure 11: UV-vis and Fluorescence spectra of PMAOC – block - PDMAEMA film in $CHCl_3$ ($1\cdot10^{-4}$ M)

The UV and Fluorescence analysis performed on the solution and the film of copolymers show the typical bands expected for the coumarin group.

Conclusions:

- ✓ A potential drug delivery system consisting of coumarin as a probe and PDMAEMA as a carrier was synthesized via ATRP.
- ✓ The block copolymer are obtained by varying the molar ratio between fluorescent monomer and initiator of 10 to 1, 20 to 1 and 40 to 1 to have a different length of the fluorescent block chain.
- ✓ GPC analysis, Dosy 2D NMR and DSC analysis confirm that the block copolymer is obtained.
- ✓ UV and Fluorescence analysis confirm the copolymerization with a fluorescent monomer because they show the typical bands of coumarin.

WORK IN PROGRESS

To investigate the possibility of copolymers to generate micelles and possibly evaluate their critical micellar concentration (CMC) to incorporate the anticancer drug and study its release.

References:

1. Baudis, S.; Behl, M.; Lendlein, A., Smart Polymers for Biomedical Applications, Macromol. Chem. Phys., 2014; **issue:** 2399−2402
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4. Almeida, H., et al.; *Journal of Applied Pharmaceutical Science;* **2012;** 2, 01-10
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