

“SULFAMERS”-BASED POLYMERIC VESICLES FOR DRUG DELIVERY APPLICATIONS

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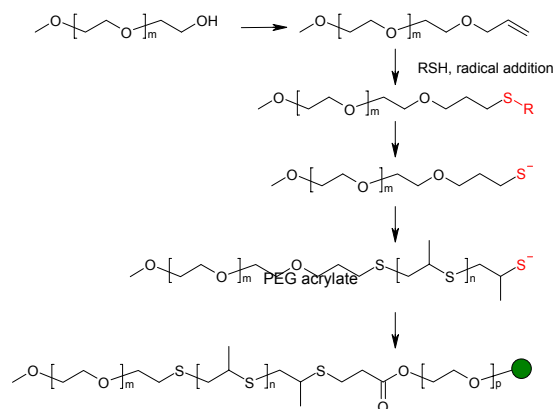
INTRODUCTION: The growing interest devoted to amphiphilic polymers and to their self-assembling in aqueous environment, brought to extensive investigations for the block copolymers of the Pluronic series, and in more recent years to poly(ethylene)-*bl*-poly(ethylene glycol) (PEG)¹, poly(styrene)-*bl*-PEG² and some others. In most cases the phase behaviour in water showed high complexity and a variety of structures were detected. Indeed only in a few literature examples amphiphilic synthetic polymers were shown to form vesicles³, and they are generally demanding in synthesis, difficult to functionalise with bioactive molecules and/or degradable groups and present only AB or ABA structures.

In this communication we report on a new method for the synthesis of amphiphilic polymers that can be used for the preparation of AB, ABA, ABA' (A' chemically analogous, but physically different than A), ABC, ABCBA and other structures, where B is the hydrophobic part and A, A' and C the hydrophilic ones. Those block copolymers were able to form vesicles in water in a wide range of concentrations.

METHODS: The synthetic path is based on the anionic ring-opening polymerisation of episulfides, initiated by a thiolate group. The initiator is generated in situ from a PEG chain containing a protected thiol (a thio- or dithioester), avoiding the use of free thiols and thus the problems arising from disulfide formation.

The living anionic process produces a polysulfide chain with a reactive thiolate end, which was used to couple the polymer with an acrylate-terminated PEG through Michael-type addition. The mild character of the end-capping reaction allows the insertion of sensitive biological groups, e.g. peptides.

RESULTS: In water environment these structures have been proved by Freeze-Fracture TEM to form lamellar phases and, upon dilution and extrusion, unilamellar vesicles having a diameter of 100-200 nm. Preliminary encapsulation studies were performed using a dye (crystal violet). In the picture is shown a Freeze-Fracture TEM image of



Scheme 1: One-pot reaction scheme of ABA' "Sulfamer"

the vesicle suspension that retained the colour after dialysis.

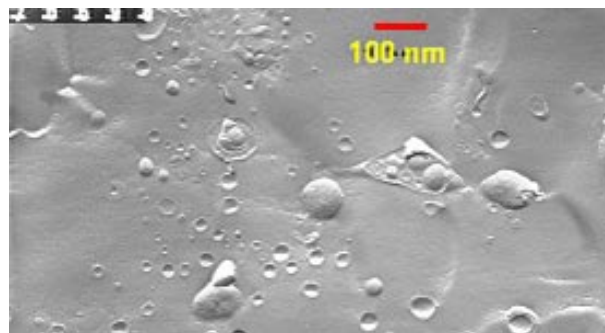


Fig.1 FF-TEM picture on the CV-EO₁₆PS₂₅EO₈ vesicles suspension.

DISCUSSION & CONCLUSIONS: We believe that vesicles based on those block copolymers are ideal candidates for controlled and targeted drug delivery systems. Their stability over much longer time, when compared to phospholipid vesicles is an additional advantage allowing the study of their biostability *in vitro* and *in vivo*.

REFERENCES: (1) Won, Y.-Y., Davis, H.T., Bates, F.S. *Science* **1999**, 283, 960-963. (2) Eisenberg, A., Yu, K *Macromolecules* **1998**, 31, 3509. (3) Nardin, C., Hirt, T., Leukel, J., Meier, W. *Langmuir* **2000**, 16, 1035-1041.