Nanoparticles made of amphiphilic biotransesterified cyclodextrins: ultrastructure and thermal behavior

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1. INTRODUCTION

One major challenge of nanomedicine is to design nanocarriers that deliver active compounds to a target site, at a sufficient concentration and without premature degradation, in order to maximize the efficiency of the substance while limiting secondary effects. Nowadays, the use of colloidal vectors of bioactive molecules is a well-tried approach [1]. In this context, we have developed colloidal nanovectors based on cyclodextrin (CD) amphiphilic derivatives [2-4]. After nanoprecipitation, most derivatives formed structured nano-objects. The knowledge of the morphology and ultrastructure of these nanovectors is crucial to optimize their formulation and lyoavailability. In addition, we have recently shown that these systems may provide an interesting alternative for injectable use of artemisinin, a well-known antimalarial lipophilic drug [5].

2. RESULTS

2.1 Experimental section

βCDs were acylated on their secondary face using thermolysin to catalyze the transesterification. After dissolution in acetone, a series of βCD-C_n (n = 6 to 14) derivatives were nanoprecipitated in water [4]. The resulting nanoparticles were observed by cryo-TEM with a Philips CM200 'Cryo' microscope operating at 80 kV. Small-angle X-ray scattering (SAXS) patterns were collected from concentrated suspensions at the BM02 beamline at ESRF (Grenoble, France). The thermal evolution of the systems was monitored by recording SAXS patterns of suspensions in sealed glass tubes every 10°C from 25 to 130°C. After cooling, the suspensions were observed by cryo-TEM as well.

2.2 Morphology and ultrastructure of the particles after nanoprecipitation

The SAXS patterns of freshly prepared suspensions revealed periodic structures in the particles when the grafted alkyl chains contained at least 8 carbon atoms. In most cases, 3 to 5 diffraction rings were observed whose distribution was consistent with a hexagonal structure when the degree of substitution (DS) of the parent derivative was higher than 5 (Fig. 1a,d). βCD-C_n (n = 8, 10 and 12) particles had a barrel-like morphology, exhibiting two different sets of longitudinal lattice fringes depending on their orientation in the embedding ice film (Fig. 1b). For the smallest particles, axial projections of the hexagonal lattice were sometimes observed. βCD-C_{14} particles had tortuous shapes and a multidomain structure. Lattice images showed longitudinal and axial projections of the hexagonal structure (Fig. 1e). The particles obtained from βCD-C_{10} (Fig. 1g,h) and βCD-C_{14} derivatives with a DS lower than 5 were spherical, exhibiting a multilamellar structure with concentric bilayers of amphiphilic CDs [6].

2.3 Morphology and ultrastructure of hydrothermally-treated nanoparticles

Upon heating to 130°C, the repeating distance of the multilamellar systems slightly increased but no structural transition was observed (Fig. 1i). The hexagonal structure of the βCD-C_8 system disappeared at 95°C, a lamellar organization forming upon cooling. Hexagonal-to-hexagonal transitions were detected at 80-100°C in βCD-C_n systems with n = 10, 12 and 14. Upon cooling, βCD-C_{10} particles were converted to multilamellar nanospheres (Fig. 1c). βCD-C_{12} particles became spherical too but no clear structure was recognized. βD-C_{14} particles exhibited a bulkier prismatic morphology and were constituted of a hexagonal packing of hollow hoops (Fig. 1f).

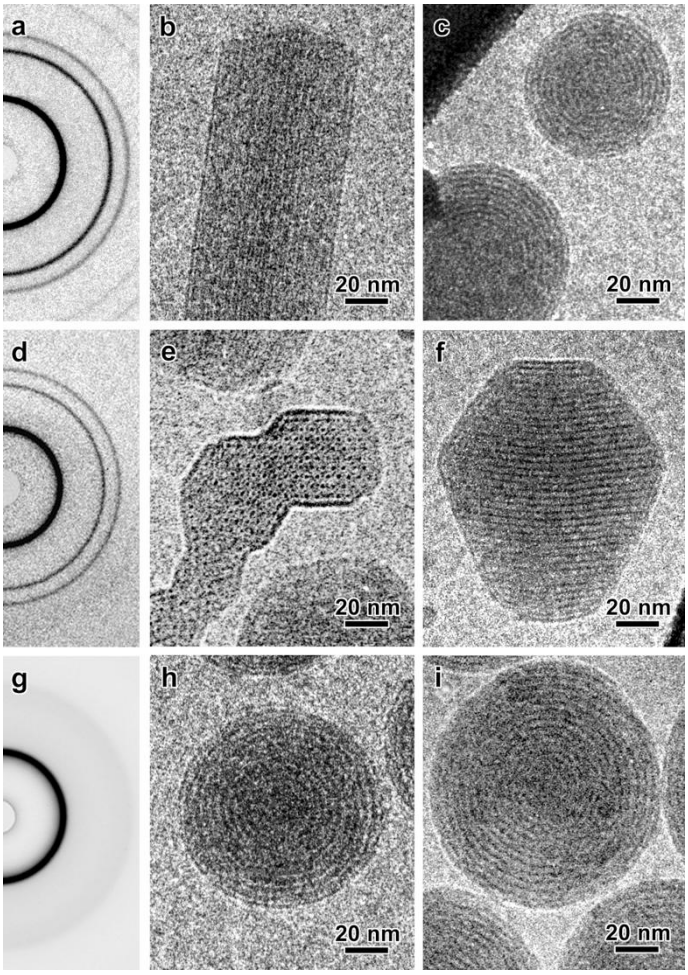

Figure 1. SAXS patterns (a,d,g) and cryo-TEM images of nanoparticles prepared from βCD amphiphilic derivatives: βCD-C_{10} with DS 7 (a-c), βCD-C_{14} with DS 7 (d-f) and βCD-C_{10} with DS 4 (g-i). a, b, d, e, g and h correspond to the systems nanoprecipitated at room temperature while in c, f and i, the suspensions have been heated at 130°C.

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