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. In this context, we have developed colloidal nanovectors based on cyclodextrin (CD) amphiphilic derivatives. 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 [Gèze et al., Mater. Sci. Eng. C29 (2009), 458]. The resulting nanoparticles were observed by transmission electron microscopy (TEM) after negative staining and by cryo-TEM. 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.

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 (Figs. 1a,d). βCD-C_8 (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 (Figs. 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.

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. βCD-C_14 particles exhibited a bulkier prismatic morphology and were constituted of hexagonally-packed hollow hoops (Fig. 1f).

Acknowledgement: The authors gratefully acknowledge funding from Agence Nationale de la Recherche, ESRF and Institut de Chimie Moléculaire de Grenoble.
Fig. 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 8 (d-f) and βCD-C_{18} with DS 4 (g-i). a, b, c, 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.