Cisplatin encapsulation generates morphologically different multicompartments in the internal nanostructures of nonlamellar liquid-crystalline self-assemblies

ABSTRACT

Cisplatin (cis-diamminedichloroplatinum(II)) is among the most potent cytotoxic agents used in cancer chemotherapy. The encapsulation of cisplatin in lipid-based drug carriers has been challenging owing to its low solubility in both aqueous and lipid phases. Here, we investigated cisplatin encapsulation in nonlamellar liquid-crystalline (LC) nanodispersions formed from a ternary mixture of phytantriol (PHYT), vitamin E (Vit E), and an anionic phospholipid [either phosphatidylglycerol (DSPG) or phosphatidylserine (DPPS)]. We show an increase in cisplatin encapsulation efficiency (EE) in nanodispersions containing 1.5–4 wt % phospholipid. The EE was highest in DPPS-containing nanodispersions (53–98%) compared to DSPG-containing counterparts (25–40%) under similar experimental conditions. Through structural and morphological characterizations involving synchrotron small-angle X-ray scattering and cryogenic transmission electron microscopy, we further show that varying the phospholipid content of cisplatin-free nanodispersions triggers an internal phase transition from a neat hexagonal (H2) phase to a biphasic phase (internal H2 phase coexisting with the lamellar (Lα) phase). However, cisplatin encapsulation in both DPPS- and DSPG-containing nanodispersions generates the coexistence of morphologically different multicompartments in the internal nanostructures comprising vesicles as a core, enveloped by an inverted-type surface bicontinuous cubic Im3m (primitive, QIIP) phase or H2 phase. We discuss the biophysical basis of these drug-induced morphological alterations and provide insights into the potential development of inverted-type LC nanodispersions for cisplatin delivery.