Tuning the nanostructure and surface charge of phytantriol-based cubosomes using choline based ionic liquids

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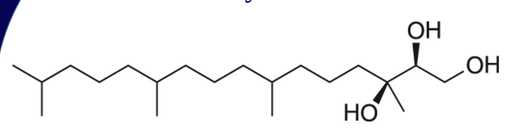
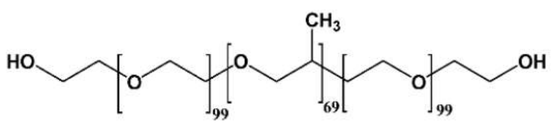
The interest in lyotropic liquid crystalline nanoparticles (LCNPs) as drug delivery vesicles continues to grow owing to their unique structural features. Controlling the structure of these particles by rational design to suit specific applications is paramount. Ionic liquids (ILs) are designer solvents, of which some are known to support the self-assembly of amphiphiles, and can be used as designer solvents for LCNPs. We examined the internal nanostructures of phytantriol (PHY) based LCNPs doped with 12 choline containing ILs, at 5 PHY-IL mole ratios. Our results show the formation of cubosomes with two crystallographic space groups, Pn3m and Im3m. The internal nanostructures of the PHY nanoparticles depend on the anion group of the IL and the IL concentration. Moreover, particles containing PHY and ILs having the basic amino acids (arginine, histidine, and lysine) as anions precursors displayed a positive surface charge when prepared in acetate and citrate buffers.

Experimental design

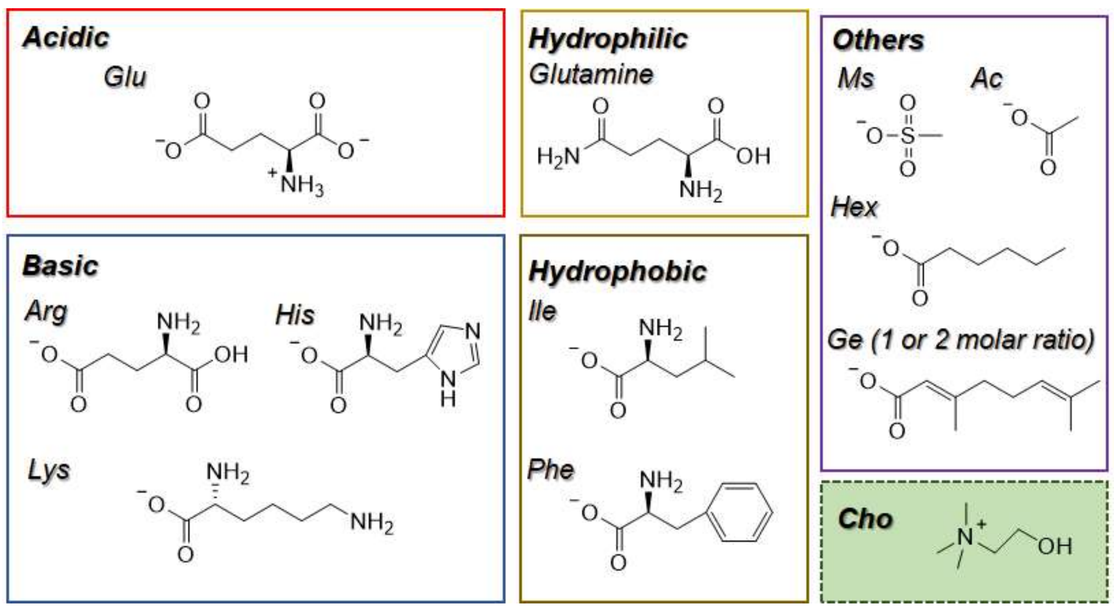
Phytantriol



Pluronic F127



Chemical structures of the precursors of the cations and anions used in the ionic liquid's synthesis.

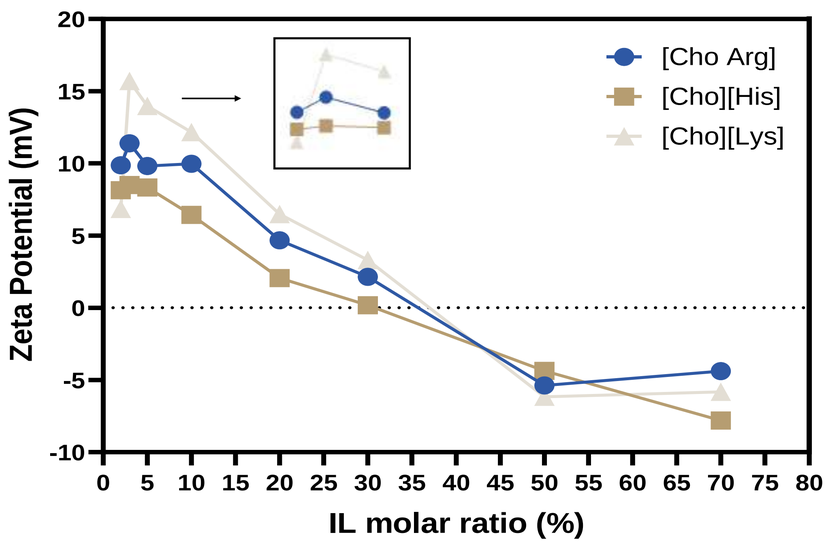


Techniques used:

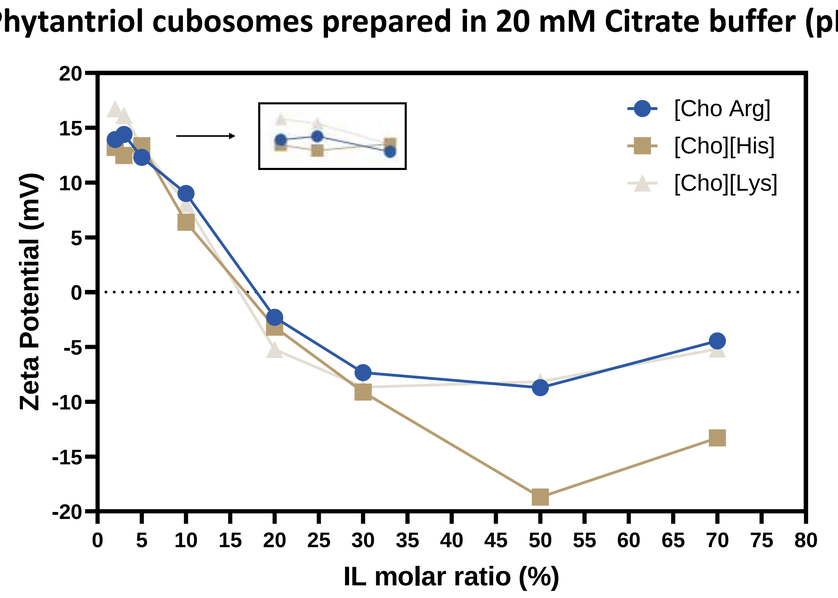
- Dynamic light scattering (DLS)
- High throughput synchrotron small angle X ray scattering (SAXS)

Zeta potential

Phytantriol cubosomes prepared in 20 mM Acetate buffer (pH 4)

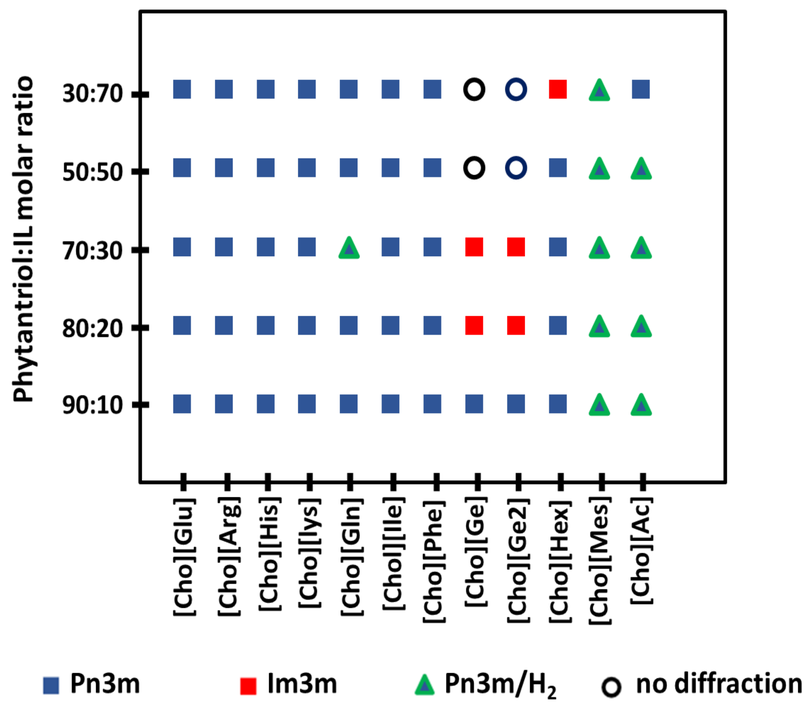


Phytantriol cubosomes prepared in 20 mM Citrate buffer (pH 2.5)

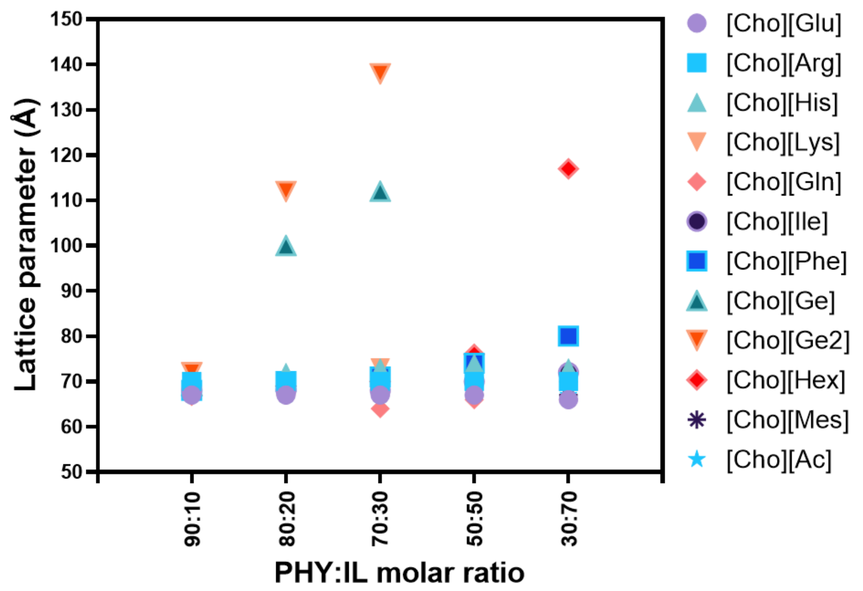


Zeta potential of PHY-based cubosomes containing ionic liquids composed of the basic amino acids arginine, histidine, and lysine as anion precursors, prepared in 20 mM Acetate buffer (pH4) and 20 mM Citrate buffer (pH 2.5). Particles with a positive surface charge were obtained in samples prepared in both buffer at low ILs concentrations.

Mesophase and lattice parameter



Partial phase diagrams of PHY LCNPs doped with 12 choline based ionic liquids at 5 PHY:IL molar ratio. Cubosomes with the Pn3m crystallographic space group were mostly obtained. Cubosomes with the Im3m crystallographic space group, as well as a mixture of cubosomes and hexosomes were also obtained in some samples.



Lattice parameters of the particles in all samples. Cubosomes with the Pn3m crystallographic space group had lattice parameters between 67 and 78 Å. Cubosomes with the Im3m crystallographic space group had lattice parameters between 100 and 140 Å.

Conclusion

- Most ILs maintained the cubic phase with the Pn3m crystallographic space group, with changes occurring in the lattice parameters of the particles.
- The nanostructure of the particles depends on the identity of the anions, and the ILs concentration.
- Positive particles were obtained in particles composed of ILs with the basic amino acids as anion's precursors, reflecting the potential of using ILs as a substitute for cationic lipids.

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