Supporting Information

Lipidic Liquid Crystalline Cubic Phases and Magnetocubosomes as Methotrexate Carriers

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S1

Scheme of chemical structure of methotrexate (MTX) and folic acid (FA).

S2

The SAXS measurement, allows to obtain one dimensional function of scattering intensities in function of q - I(q) where q (nm⁻¹) is the length of the scattering vector. The scattering vector is related to the scattering angle—θ—and the wavelength of radiation—λ (in our case it is λCu,Kα = 0.1542 nm) by the relation [1]:

\[ q = \frac{4\pi\sin\theta}{\lambda} \]  

(1)

The q̂ peak values are marked starting with q̂₀ and the ratio q/q̂₀ is calculated. The ratio defines the phase symmetry and Miller indices of the Bragg peak. The lattice parameter a (nm⁻¹) is calculated from the distance between 2 reflection plans d. For cubic phases:

\[ a = d_{hkl}\sqrt{h^2+k^2+l^2} \]  

(2)

\[ d_{hkl} = \frac{2\pi}{q} \]  

(3)

\[ a = \frac{2\pi}{q}\sqrt{h^2+k^2+l^2} \]  

(4)

Size of the water channels was calculated using the lattice parameter and the composition of cubic phases:
\[ \phi_w = \frac{C_w}{C_w + (1 - C_w) \frac{\rho_w}{\rho_l}} \]  
(5)

where \( \phi_w \): water volume fraction, \( C_w \): water weight fraction, \( \rho_w \): density of water = 0.997 g/cm\(^3\), \( \rho_l \): density of lipid, in our case \( \rho_{MO} = 0.942 \) g/cm\(^3\).

Lipid volume fraction was determined from the equation:

\[ \phi_l = 1 - \phi_w \]  
(6)

Lipid chain length \( l \) was determined by solving the following equation [2]:

\[ \phi_{lipid} = 2\delta \left( \frac{l}{a} \right) + \frac{4}{3} \pi \chi \left( \frac{l}{a} \right)^3 \]  
(7)

\( \delta \): ratio of the minimal surface in a unit cell to the quantity (unit cell volume)\(^{2/3}\), \( \chi \): Euler–Poincare’ characteristic, \( a \): lattice parameter of corresponding phase, \( l \): lipid chain length/monolayer thickness.

Radius of water channels - \( r_w \) was obtained by equation [3]:

\[ r_w = \left( \frac{-\delta}{2\pi \chi} \right)^{1/2} a - l \]  
(8)


S3

Scheme of the reduction process of methotrexate [1].


S4

Release profiles of MTX from a cubic phase in pH 7.4 at 25 °C [A] and 37 °C [B].
DPV on GC electrode modified with phases without [A] and with [B] magnetic nanoparticles and the release profiles of MTX from LCPs [C] at pH 7.4 at 25 °C.

The size [A] and zeta potential [B] of magnetocubosomes containing MTX determined with DLS at 25 °C.
Standard calibration curve for methotrexate based on measurement at 303 nm in 0.1 M phosphate buffer, pH 7.4.

Electron cryo-microscopy images of cubosomes [A] and magnetocubosome [B].
Movement of magnetocubosomes in magnetic field.

https://www.youtube.com/watch?v=dY5wi2V3GH4