**Supporting Information**

**Hybrid delivery systems for methotrexate - lipidic liquid crystalline cubic phases and cubosomes with magnetic nanoparticles**

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S1

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]:

$q=\frac{4πsinθ}{λ}$ [1s]

The qi peak values are marked starting with q0 and the ratio qi/q0 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:

$a=d\_{hkl}\sqrt{h^{2}+k^{2}+l^{2}}$ [2s]

$d\_{hkl}=\frac{2π}{q}$ [3s]

$a=\frac{2π}{q}\sqrt{h^{2}+k^{2}+l^{2}}$ [4s]

Size of the water channels was calculated using the lattice parameter and the composition of cubic phases:

φw = $\frac{Cw}{Cw+\left(1-Cw\right)\frac{ρw}{ρl}}$ [5s]

where φw - water volume fraction, Cw - water weight fraction, ρw - density of water = 0.997 g/cm3, ρl - density of lipid, in our case ρMO = 0.942 g/cm3.

Lipid volume fraction was determined from the equation:

φl = 1- φw [6s]

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

$φlipid=2δ\left(\frac{l}{a}\right)+\frac{4}{3}πχ\left(\frac{l}{a}\right)^{3}$ [7s]

δ - ratio of the minimal surface in a unit cell to the quantity (unit cell volume)2/3,χ - Euler–Poincare´ characteristic, *a* - lattice parameter of corresponding phase, *l* - lipid chain length/monolayer thickness.

Radius of water channels - *rw* was obtained by equation [3]:

$r\_{w}=\left(\frac{-δ}{2πχ}\right)^{{1}/{2}}a-l$ [8s]

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3. 3. Anderson, D. M.; Gruner, S. M.; Leibler, S. Geometrical Aspects of the Frustration in the Cubic Phases of Lyotropic Liquid Crystals. Proceedings of the National Academy of Sciences of the United States of America **1988**, 85, 5364−5368, www.jstor.org/stable/32152.

S2 Scheme of the reduction process of methotrexate [1].



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S3 Release profiles of MTX from a cubic phase in pH 7.4 at 25[A] and 37ºC [B].



S4 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 25ºC.



S5 The size [A] and zeta potential [B] of magnetocubosomes containing MTX determined with DLS at 25ºC.



S6 Standard calibration curve for methotrexate based on measurement at 303 nm in 0.1 M phosphate buffer, pH 7.4.



S7 Electron cryo-microscopy images of cubosomes [A] and magnetocubosome [B].

