**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]:

[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:

[2s]

[3s]

[4s]

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

φw = [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]:

[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]:

[8s]

1. Kulkarni, Ch. V.; Wachter, W.; Iglesias-Salto, G.; Engelskirchenb, S.; Ahualliac, S.Monoolein: a magic lipid? Physical Chemistry Chemical Physics **2011**, 13, 3004–3021, doi:10.1039/c0cp01539c2.
2. Turner, D. C.; Wang, Z.-G.; Gruner, S. M.; Mannock, D. A.; McElhaney, R. N. Structural Study of the Inverted Cubic Phases of di- Dodecyl Alkyl-β-D-Glucopyranosyl-rac-Glycerol. Journal de Physique II **1992**, 2, 2039−2063, doi:10.1051/jp2:1992250.
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].



1. Pontinha, A. D. R.; Jorge, S. M. A.; Diculescu, V. C.; Vivan, M.; Oliveira-Brett, A. M. Antineoplasic Drug Methotrexate Redox Mechanism Using a Glassy Carbon Electrode. Electroanalysis **2012**, 24, 917–923, doi:10.1002/elan.201100558.

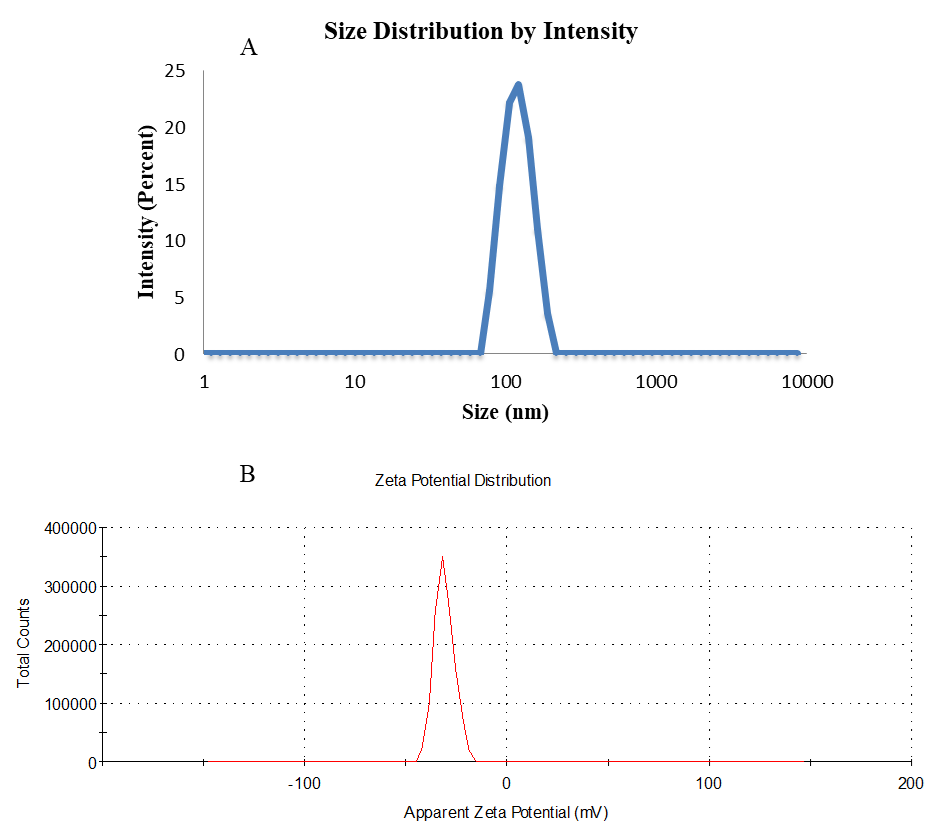
S3 Release profiles of MTX from a cubic phase in pH 7.4 at 25[A] and 37ºC [B].

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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.

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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.

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

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