Electronic Supplementary Material (ESI) for Integrative Biology.

Biocompatibility and therapeutic evaluation of magnetic liposomes designed for self-controlled cancer hyperthermia and chemotherapy

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Synthesis of iron oxide and LSMO nanoparticles

Fe_3O_4 nanoparticles were synthesized by co-precipitation method. The black coloured final solution was cooled down to room temperature and particles were allowed to settle down with the help of a magnet. Magnetically separated particles were washed successively with 5% NH_4OH solution, acetone and ultrapure water (resistivity 18.2 MΩ.cm), three times with each solvent followed by an intermediate sonication (20 kHz, 250 W, Vibronics Pvt. Ltd., India) for 5 min between two washing cycles.

$La_{0.75}Sr_{0.25}MnO_3$ was synthesised using the method reported in the literature[14] with little modification. Briefly, La_2O_3, $SrCO_3$ and $MnCO_3$ were separately dissolved in nitric acid and mixed with citric acid and ethylene glycol in ratio of 0.75[La^{3+}]:0.25[Sr^{2+}]:[Mn^{2+}]:1.5[citric acid]:2.25[ethylene glycol] and pH was adjusted to 9 by adding NH_4OH. The mixture was stirred and heated to 80 – 90 ºC to remove water and a pink coloured gel formed. The resulting gel was heated to 250 °C which leads to formation of black dry powder after auto-combustion and the dry powder was calcined at 700 °C and 800 °C for 1 h. Then the calcined powder was ground to fine powder with mortar and pestle. Ground powder was initially washed with ethanol followed by ultrapure water to remove the impurities. Then the magnetic particles were dried in oven.

Characterization of magnetic nanoparticles

Crystallographic structures of iron oxide and LSMO nanoparticles were analysed by Philips X'pert Diffractometer (PAN alytical X'pert, Holland) with a Cu Kα radiation wavelength of 1.54 Å. Mean crystal size of the particles was calculated by using Scherrer's equation. Magnetic properties of Fe_3O_4 as well as LSMO nanoparticles were measured using vibrating sample magnetometer (Lake Shore, Model 7410, USA). For this, dry powder of nanoparticles was placed inside the sample holder and exposed to magnetic field ranging from -20 kOe to 20 kOe. M-H curve were recorded at room temperature. Magnetization values measured in 'memu' were later normalized and expressed in emu/g. In order to

determine Curie temperature (T_c), magnetization vs. temperature measurement was carried out at 100 Oe. T_c value was calculated from derivative of magnetization versus temperature curve. In order to confirm the coating of dextran on the LSMO and the biphasic suspension of LSMO and Fe_3O_4 nanoparticles, FTIR analysis was done using MAGNA-550 FTIR Spectrophotometer (Nicolet Instruments Corporation, USA). For this magnetic fluid was first frozen at -20 °C and then lyophilised. Lyophilised samples were then used to analyse the characteristic FTIR peaks.

Fig. S1

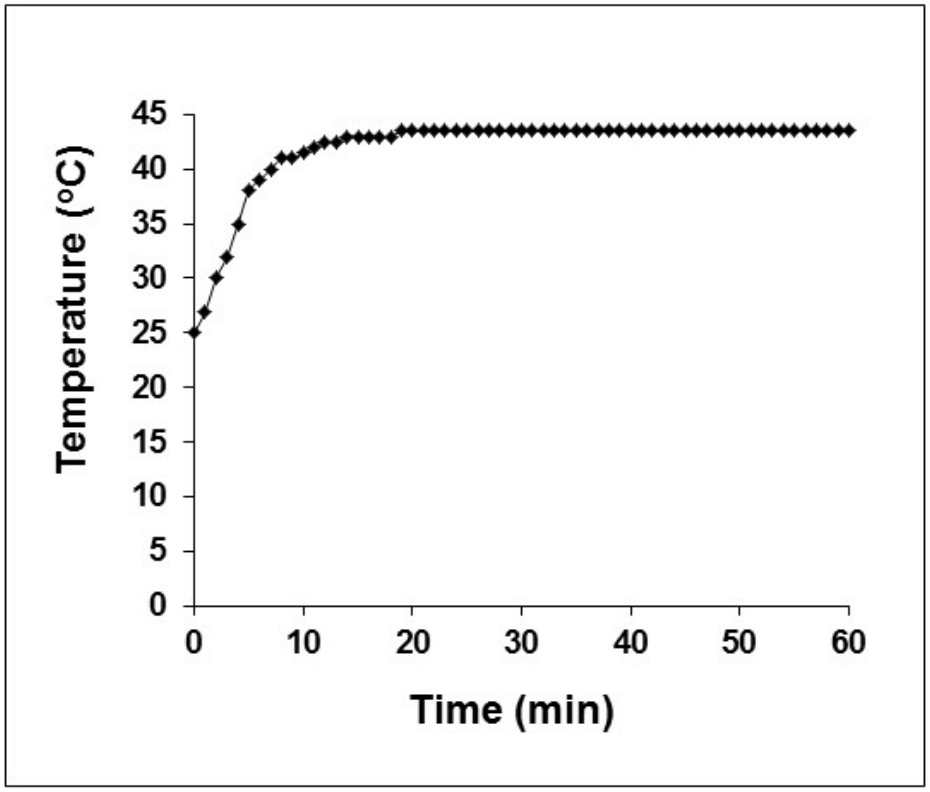

Fig. S1: Temperature profile of magnetic liposomes at field of 27.9 kA/m and 250 kHz frequency

Fig.S2

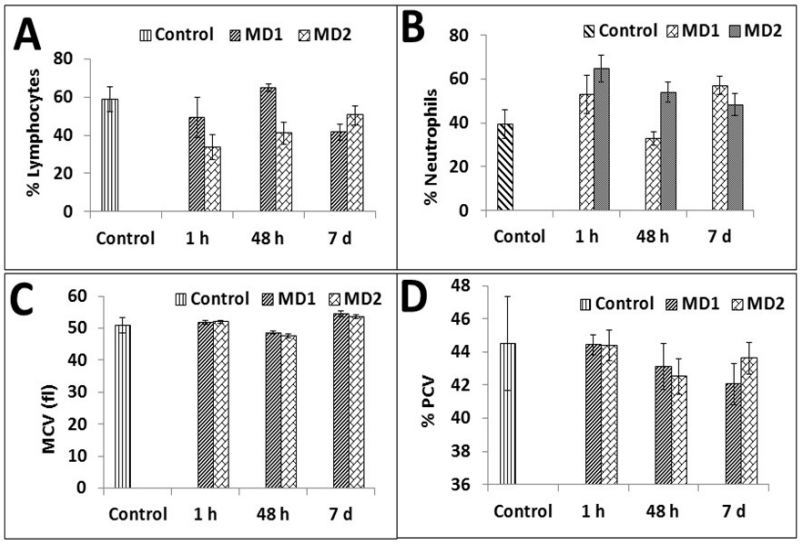

Fig. S2: Variations in blood parameters in mice of experimental groups MD1 and MD2 following intravenous administration of magnetic liposomes containing 1 mg and 2 mg of MNPs respectively; A) Lymphocytes, B) Neutrophils C) MCV, D) PCV (results are expressed as mean ± SD, n = 5, h= hour, d= days).

Fig. S3

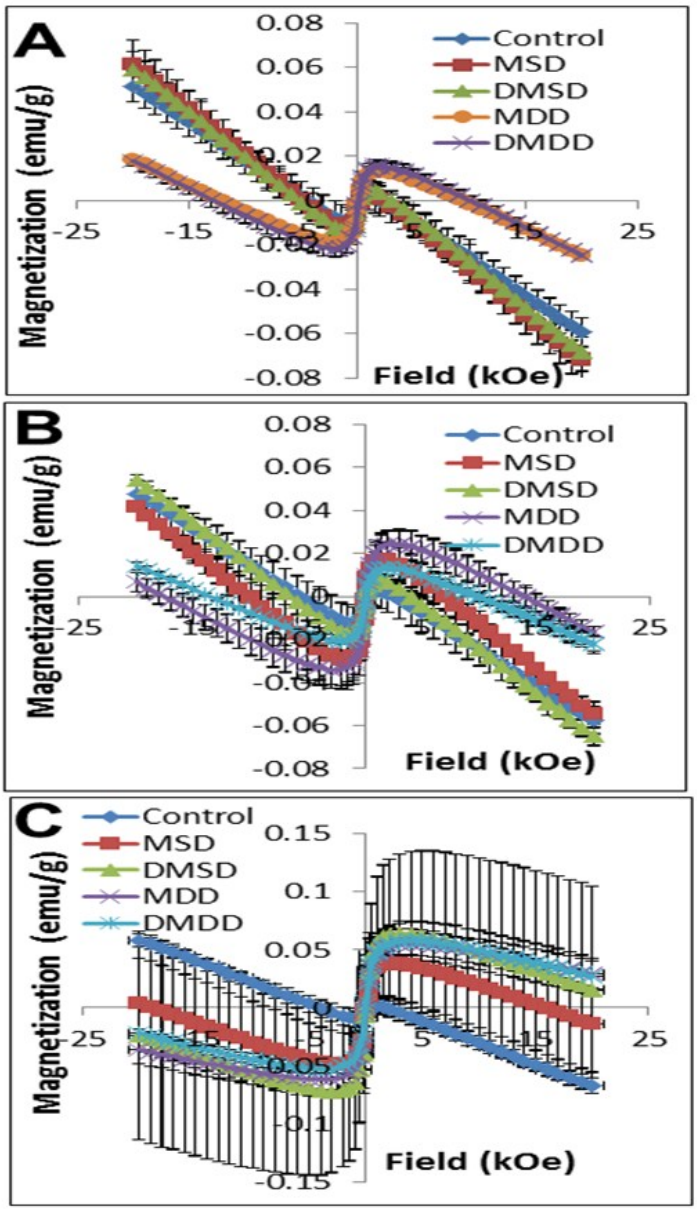

Fig. S3: M -H loops of different organs of mice: A) Liver, B) Spleen, C) Tumour, treated with hyperthermia and combined therapy.