Supporting Information

Cytochrome P450-dependent reactive oxygen species (ROS) production contributes to Mn$_3$O$_4$ nanoparticle-caused liver injury

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Evaluation of CYP1A2 activity assays

CYP1A2 activity assays were detected by the formation rate of acetaminophen which is the production of phenacetin. Microsomal proteins were incubated in a mixture (total volume of 0.2 ml) containing 0.1 mol/L PBS buffer (pH 7.4), 12 μL NADPH, and increasing concentrations of phenacetin. Reactions were started by the addition of microsomes, following thermal equilibration at 37°C of incubation mixtures. They were conducted in a shaking water bath at 37°C in aerobic conditions and stopped after 5 min by adding 0.2 ml of ice-cold acetonitrile. Denatured proteins were then removed by centrifugation for 10 min at 12,000 r/min and an aliquot (0.1ml) of the supernatant was analyzed by HPLC with UV detection,

Fig. S1 SEM observation of the synthesized Mn₃O₄ NPs.
Fig. S2 TEM observation of the synthesized Mn$_3$O$_4$ NPs.

Fig. S3 Contents of CYP1A2 activity assays in the livers.
[1] L. Quintieri, P. Palatini, A. Nassi, Flavonoids diosmetin and luteolin inhibit midazolam metabolism by human liver microsomes and recombinant CYP3A4 and CYP3A5 enzymes [J]. *Biochem. Pharmacol.*, 2008, **75**, 1426-37.