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# An advanced thermal decomposition method for the synthesis of novel cobalt-doped core (magnetite) shell (maghemite) iron oxide nanoparticles with ultrahigh heating efficiency for systemic magnetic hyperthermia 

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#### Abstract

Owing to the low heating efficiency of currently available magnetic nanoparticles, it is challenging to reach therapeutic temperatures above $44{ }^{\circ} \mathrm{C}$ in tumors that are generally difficult to access after systemic delivery of nanoparticles at clinical dosage ( $10 \mathrm{mg} \mathrm{kg}^{-1}$ ). In order to solve this problem, we have developed an advanced thermal decomposition method for the synthesis of novel cobalt-doped core (magnetite) - shell (maghemite) iron oxide nanoparticles ( $\mathrm{Co}^{-} \mathrm{Fe}_{3} \mathrm{O}_{4} / \gamma-\mathrm{Fe}_{2} \mathrm{O}_{3}$ ) with an ultrahigh ILP of $48.0 \mathrm{nH} m 2 \mathrm{~kg}^{-1}$. Our in vivo research shows that these nanoparticles containing a cancer-targeting peptide are biocompatible and accumulate well in ovarian cancer grafts after being administered systemically at a concentration of $4 \mathrm{mg} \mathrm{kg}-1$. When exposed to an external AMF ( 420 kHz , $26.9 \mathrm{kA} \mathrm{m}^{-1}$ ), the delivered nanoparticles elevate temperature in both subcutaneous and metastatic cancer tumors to $50^{\circ} \mathrm{C}$. This newly developed synthesis method can be used for the synthesis of both non-doped core-shell nanoparticles and core-shell nanoparticles doped with different metals (e.g., Ni, Co). As a result, this strategy could be extended to the development of novel nanoparticles with even greater heating performance, further advancing systemic magnetic hyperthermia for cancer treatment.


