

## Sequential release of drugs from Hollow Manganese Ferrate nanocarriers for Breast cancer therapy

**B. N. Prashanth Kumar,<sup>a</sup> Nagaprasad Puvvada,<sup>b,d</sup> Shashi Rajput,<sup>a</sup> Siddik Sarkar,<sup>c</sup> Swadesh K. Das,<sup>c</sup> Luni Emdad,<sup>c</sup> Devanand Sarkar,<sup>c</sup> P. Venkatesan,<sup>a</sup> Ipsita Pal,<sup>a</sup> Goutam Dey,<sup>a</sup> Suraj Konar,<sup>b</sup> Keith R. Brunt,<sup>d</sup> Raj R Rao,<sup>e</sup> Abhijit Mazumdar,<sup>f</sup> Subhas C. Kundu,<sup>g,\*</sup> Amita Pathak,<sup>b,\*\*</sup> Paul B. Fisher,<sup>c</sup> and Mahitosh Mandal,<sup>a,\*\*\*</sup>**

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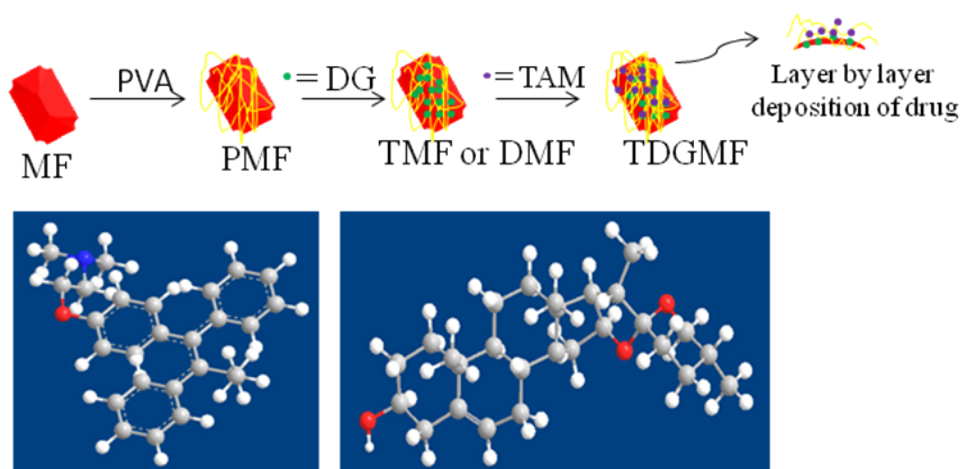
### Tables

Table 1: List of some representative tamoxifen and diosgenin based nanocarriers

Nanoparticles	Morphology	Drugs	Findings	References
Magnetite nanoparticles (Fe <sub>3</sub> O <sub>4</sub> )/ poly(l-lactic acid) composite	Spherical (200 nm)	Tamoxifen	Enhanced cellular uptake and induced cytotoxic effects	[60]
Nanogels Crosslinked by Functional Superparamagnetic Maghemite Nanoparticles	Spherical (80 nm)	Tamoxifen	Thermo responsive mediated drug delivery	[61]
Manganese superoxide dismutase	Spherical (130 nm)	Tamoxifen	Reactive oxygen species induced apoptosis	[62]
Graphene	Multi walled enlogated shapes (50-150 nm)	Tamoxifen	Induced apoptosis	[63]
Cyclodextrin-based nanosponges	Nanosponges (400-600 nm)	Tamoxifen	Oral delivery, Cytotoxic effects	[64]
Diacyllipid-Polymer Micelles	Nanomicells (10 to 40 nm)	Tamoxifen	Drug delivery occurs through enhanced permeability and retention effect	[65]
PEGylated magnetic nanoparticles	Spherical (40 nm)	Tamoxifen	Improved anticancer activity	[66]
Chitosan nanoparticles	Spherical (30-60 nm)	Diosgenin	Drug release studies	[67]
Silica nanoparticles	Spherical (180 nm)	Diosgenin	Extraction of Diosgenin from crude*	[68]
Hollow MnFe <sub>2</sub> O <sub>4</sub> nanocarriers	Octahedron shape (110-220 nm)	Tamoxifen and diosgenin	Increased magnetic saturation along with apoptosis	This study

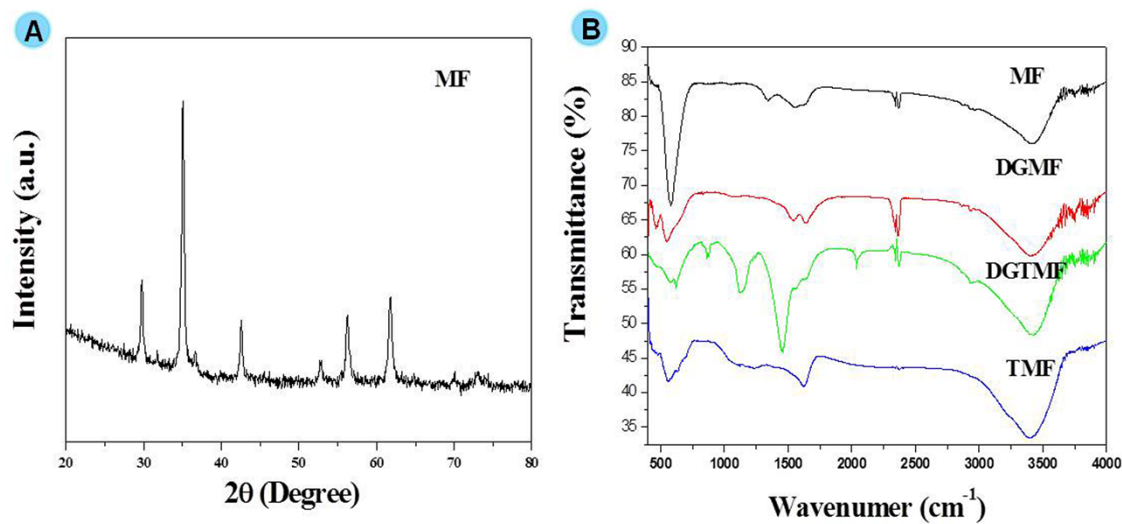
\*Not employed in cancer therapy.

## Synthesis of hollow $\text{MnFe}_2\text{O}_4$ nanocarriers



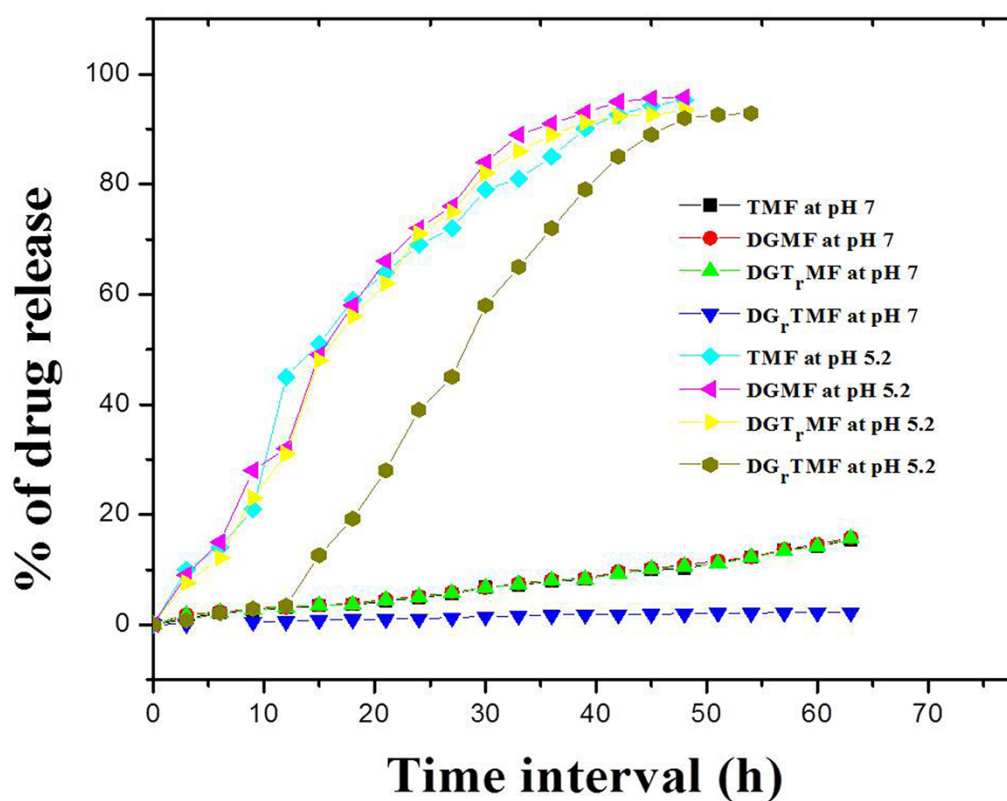
**Scheme1:** Schematic representation for the MF surface coated with PVA followed by encapsulation of TAM or DG or both are deposited by layer by layer and corresponding TAM and DG structures

## XRD and FTIR Analysis



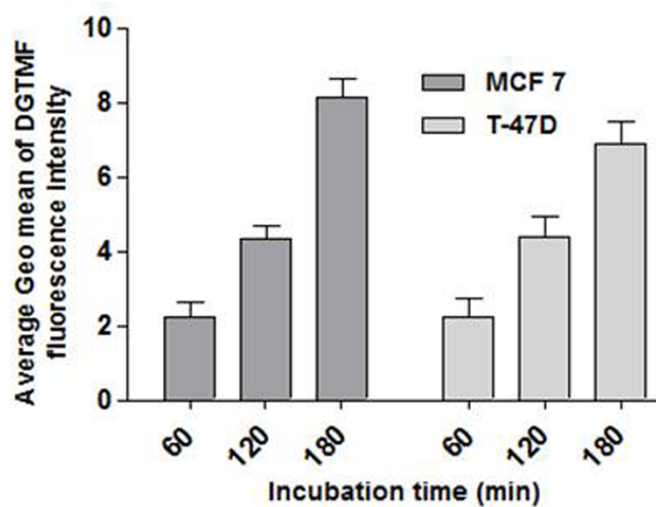
**Figure S1:** (A)XRD Pattern of hollow MF (B) FTIR spectra of MF, DGMF, DGTMF and TMF.

## Drug release studies



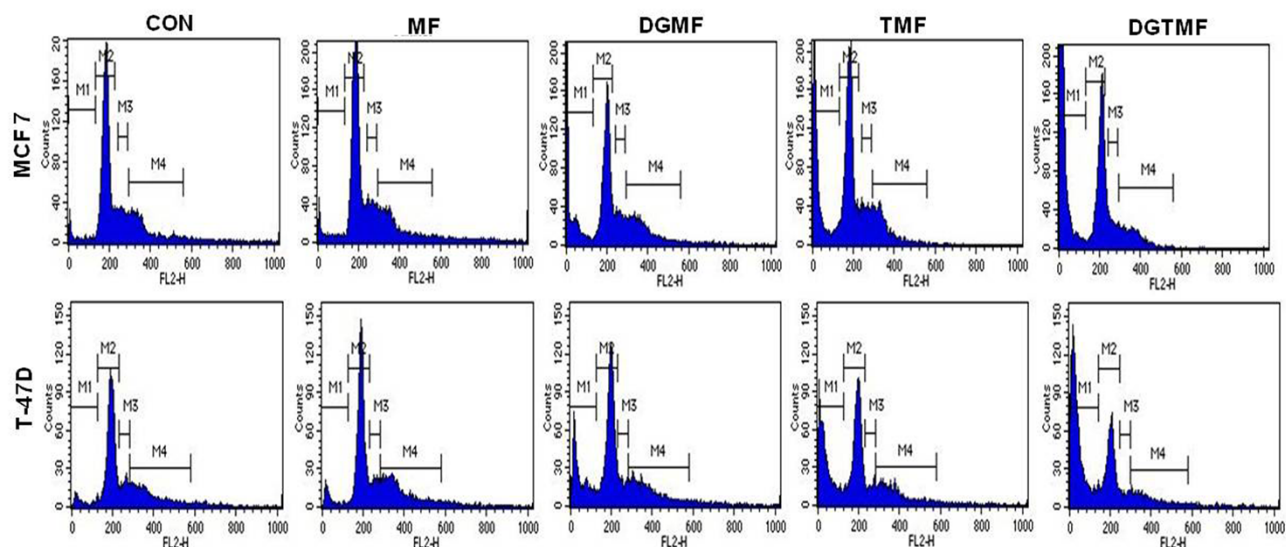
**Figure S2:** Drug release from samples at pH 7 and 5.2 for TMF, DGMF, DGTMF (Where T<sub>r</sub> and DG<sub>r</sub> corresponds to TAM and DG release from DGTMF sample, respectively).

## Cellular uptake of drug loaded nanocarriers

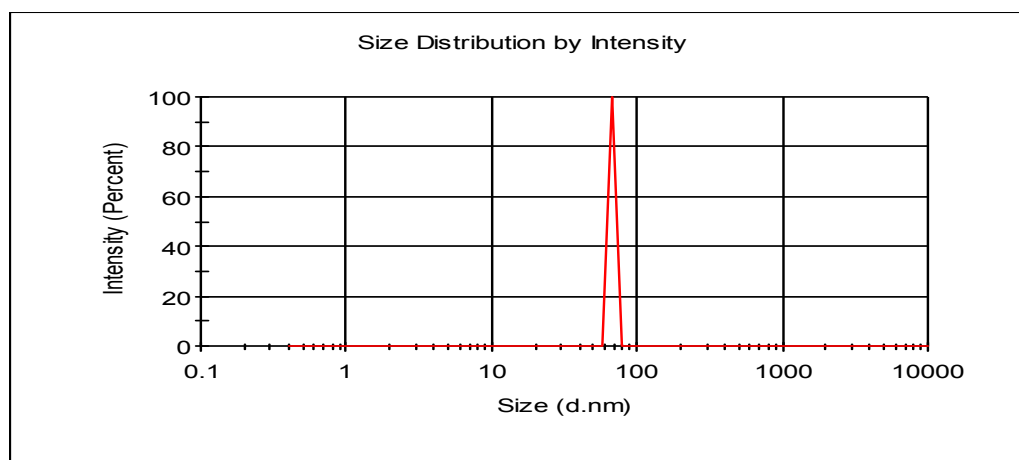


**Figure S3:** Geometric mean analysis of DGTMF cellular uptake through flow cytometry in MCF 7 and T-47D cells. Mean±SD are shown.

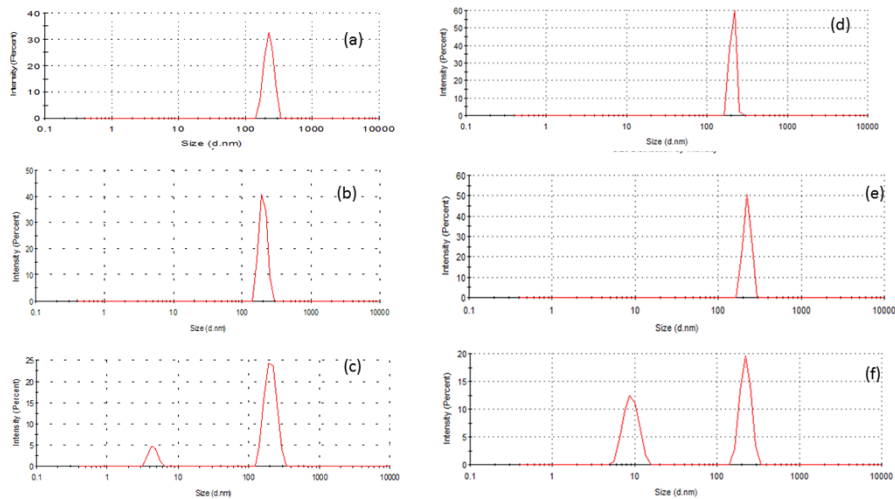
## Cell cycle analysis



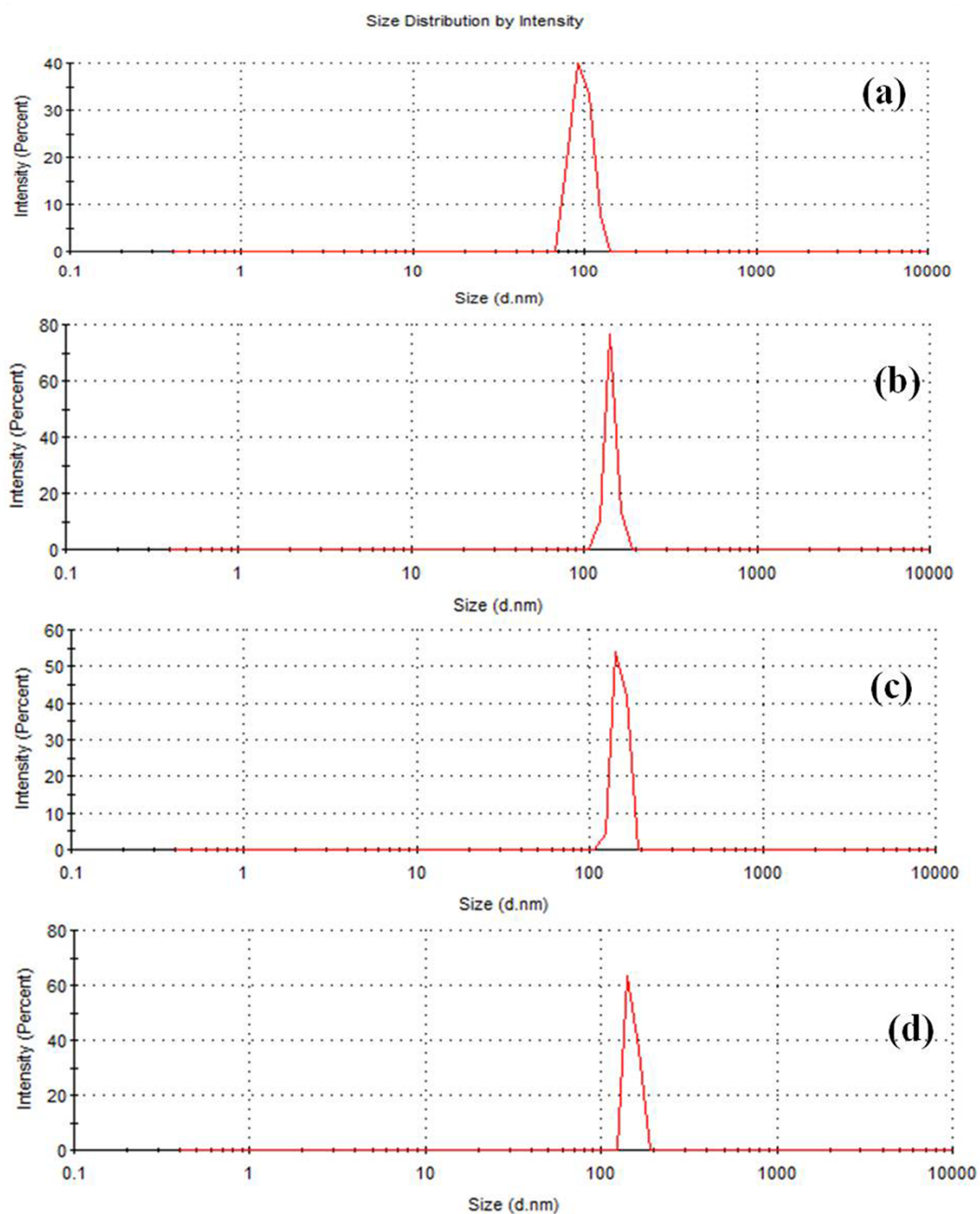
**Figure S4:** Apoptotic activity of different drug loaded nanoparticles on MCF 7 and T-47D cells by flow cytometry phase distribution study



**Figure S5:** DLS measurement of TDGMF sample in cyclohexane (~ 62 nm)



**Figure S6:** DLS measurement of TDGMF sample in flow mode (a-c) and normal mode (e-f). where (a & d) measured in PBS solution, (b and e) cell culture media and (c and f) protein media (less than 10 nm peak in c and f are due to presence of protein molecules).



**Figure S7:** DLS measurement of (a) MF, (b) DGMF, (c) TMF and (d)DGTMF through flow cell method.