Electronic Supplementary Material (ESI) for New Journal of Chemistry. This journal is © The Royal Society of Chemistry and the Centre National de la Recherche Scientifique 2020

## **Supporting Information**

## Bi-Functional Nature of Nanoceria: Pro-Drug and Drug-carrier potentiality towards receptor mediated targeting of doxorubicin

Madhura A. Damle<sup>a,b</sup>, Varsha G. Shetty<sup>c</sup>, Alok P. Jakhade<sup>a</sup>, Ruchika Kaul-Ghanekar<sup>c</sup>, Rajeev

C. Chikate<sup>a\*</sup>

<sup>a</sup>Nanoscience Group, Department of Chemistry, Post-graduate & Research Center, MES Abasaheb Garware College, Karve Road, Pune-411004, India.

<sup>b</sup>Department of Biotechnology, MES Abasaheb Garware College, Karve Road, Pune-411004, India.

<sup>c</sup>Cell and Translational Research Laboratory, Interactive Research School for Health Affairs (IRSHA), Bharati Vidyapeeth University Medical College Campus, Dhankawadi, Pune, Maharashtra, India

\*Corresponding author: email: rajuchikate29@gmail.com, rajeev.chikate@mesagc.org

Fax: +91-20-25438165; Tel: +91-20-41038216

## **List of Figures**

Figure S1: Figure S1: UV spectra of CeO<sub>2</sub> nanoconjugates
Figure S2: TEM images of (a) CeO<sub>2</sub> NPs, (b) PEG-CeO<sub>2</sub> NPs (Inset SAED)
Figure S3: The % stability of the nanoconjugates over a period of 48 h.
Figure S4: DLS (a, c & e) and Zeta Potential (b, d & f) for CeO<sub>2</sub>-DOX (a, b), CeO<sub>2</sub>-(DOX-FA) (c, d) and CeO<sub>2</sub> – PEG-(DOX-FA) (e, f).
Figure S5: Redox potentials of uncoated CeO<sub>2</sub> NPs (a, b) and PEGylated NPs (c, d) at pH 4.4 and 9.2 respectively.
Figure S6: DNA binding assay for (a) uncoated and (b) PEG-CeO<sub>2</sub> NPs
Figure S7: Cell viability of 293T Cells on treatment with (a) CeO<sub>2</sub> NPs ; (b) PEG-CeO<sub>2</sub> NPs
Figure S8: Cell viability studies on MCF-7 cells after exposure to PEG, FA and DMSO at different concentration (0.25-2 μg/mL)
Figure S9: Monochromal images of MCF-7 cells by confocal microscopy on treatment with CeO<sub>2</sub> NPs and its nanoconjugates, a: Control cells, b: DOX, c: CeO<sub>2</sub>, d: PEG-

CeO<sub>2</sub>, e: CeO<sub>2</sub>-DOX, f: CeO<sub>2</sub> –(DOX-FA), g & h: PEG-CeO<sub>2</sub>-(DOX-FA)

Table T1: IC<sub>50</sub> values for the DOX loaded CeO<sub>2</sub> nanoconjugates

Total No. of Figures – 7

Total No. of Tables – 1

Figure S1: UV spectra of CeO<sub>2</sub> nanoconjugates



Figure S2: TEM images of (a) CeO<sub>2</sub> NPs and (b) PEG-CeO<sub>2</sub> NPs. (Inset SAED)



Figure S3: The % stability of the nanoconjugates over a period of 48 h.



**Figure S4:** DLS (a, c & e) and Zeta Potential (b, d & f) for  $CeO_2$ -DOX (a, b),  $CeO_2$ -(DOX-FA) (c, d) and  $CeO_2$ - PEG-(DOX-FA) (e, f).





**Figure S5:** Redox potentials of uncoated CeO<sub>2</sub> NPs (a, b) and PEGylated NPs (c, d) at pH 4.4 and 9.2 respectively.

Figure S6: DNA binding assay for uncoated (a) and PEG CeO<sub>2</sub> NPs (b)



Figure S7: Cell viability of 293T Cells on treatment with (a) CeO<sub>2</sub> NPs and (b) PEG-CeO<sub>2</sub> NPs



Figure S8: Cell viability studies on MCF-7 cells after exposure to PEG, FA and DMSO at different concentration (0.25-2  $\mu$ g/mL)



**Figure S9:** Monochromal images of MCF-7 cells by confocal microscopy on treatment with CeO<sub>2</sub> NPs and its nanoconjugates, a: Control cells, b: DOX, c: CeO<sub>2</sub>, d: PEG-CeO<sub>2</sub>, e: CeO<sub>2</sub>-DOX, f: CeO<sub>2</sub> –(DOX-FA), g & h: PEG-CeO<sub>2</sub>-(DOX-FA)



Sr. No.	Compound	DOX loading (wt.%)	IC50 (µg/mL)	Ref.
1	CaCO <sub>3</sub> .DOX	19.3	1.83	1
2	DOX-DNA@CaP	12.4	0.68	2
3	Chitosan-CuO-DOX	15. 97	30.0	3
4	Chitosan-SiO <sub>2</sub> -Fe <sub>3</sub> O <sub>4</sub> -DOX	19.81	1.5	4
5	Au-GA-DOX	9.1	0.15	5
6	Ti-MIL 125-DOX	25	5.62	6
7	CeO <sub>2</sub> -DOX	12	3.54	
8	CeO <sub>2</sub> -(DOX-FA)	5.9	3.28	Present work
9	CeO <sub>2</sub> -PEG-(DOX-FA)	2.3	3.09	

Table T1: IC<sub>50</sub> values of DOX-conjugated metal-based nanocarriers against MCF-7

- A. Hamidu, A. Mokrish, R. Mansor, I.S.A. Razak, A. Danmaigoro, A.Z. Jaji and Z.A. Bakar, Modified methods of nanoparticles synthesis in pH-sensitive nano-carriers production for doxorubicin delivery on MCF-7 breast cancer cell line, *Inter. J. Nanomedicine*, 2019, 14, 3615.
- J. Liu, L. Li, R. Zhang and Z.P. Xu, Development of CaP nanocomposites as photothermal actuators for doxorubicin delivery to enhance breast cancer treatment, J. Mater. Sci. Technol., 2020 (accepted manuscript), DOI.org/10.1016/j.jmst.2020.02.029.
- N.B. Varukattu, R. Vivek, C. Rejeeth, R. Thangam, T. Ponraj, A. Sharma and S. Kannan, Nanostructured pH-responsive biocompatible chitosan coated copper oxide nanoparticles: A polymeric smart intracellular delivery system for doxorubicin in breast cancer cells, *Arabian J. Chem.*, 2020, 13, 2276.
- 4. M. Rahimi, K.D. Safa, E. Alizadeh and R. Salehi, Dendritic chitosan as a magnetic and biocompatible nanocarrier for the simultaneous delivery of doxorubicin and methotrexate to MCF-7 cell line, *New J. Chem.*, 2017,**41**, 3177.
- W.I. El-Ghareb, M.M. Swidan, I.T. Ibrahim, A.A. ElBary, M.I. Tadros and T.M. Sakr, 99mTc-Doxorubicin-loaded gallic acid-gold nanoparticles (99mTc-DOX-loaded GA-Au NPs) as a multifunctional theranostic agent, *Inter.J.Pharmaceutics*, 2020 (accepted manuscript), : DOI.org/10.1016/j.ijpharm.2020.119514
- J.L. Song, Z.Q. Huang, J. Mao, W.J. Chen, B. Wang, F.W. Yang, S.H. Liu, H.J. Zhang, L.P. Qiu, J.H. Chen, A facile synthesis of uniform hollow MIL-125 titanium-based nanoplatform for endosomal escape and intracellular drug delivery, *Chem. Eng. J.*, 2020, **396**, 125246.