SUPPORTING INFORMATION

Dual-mode vehicles with simultaneous thermometry and drug release properties based on hollow Y_2O_3:Er,Yb and $Y_2O_2SO_4$:Er,Yb spheres

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Experimental section

Synthesis of materials

Preparation of Y_2O_3:Er,Yb hollow spheres

The synthesis of Y_2O_3:Er,Yb hollow spheres was carried out in 3 steps. First, carbon nanoparticles (CNPs) used as the template were synthesized. For this 4 g glucose was dissolved in 30 mL distilled water. The solution was transferred into a 40 mL Teflon-lined stainless-steel autoclave and heated at 180 °C for 5 h. After cooling down naturally the black powder was collected by centrifugation and washed 2 times with water and once with ethanol. It was left to dry overnight in an oven set at 85 °C. In a second step, the CNPs were used as a template to grown $Y(OH)CO_3$:Er,Yb. For this 0.1 g carbon nanoparticles were dispersed in 25 mL distilled water using an ultrasound bath. Next, 1 mL of 1 M $RE(NO_3)_3 \cdot 6H_2O$ solution (1% Er and 2.5% Yb) and 3 g urea were added to the CNP solution. The solution was heated up to 95 °C for 4 h with continuous stirring. After cooling down to room temperature the product was collected by centrifugation and washed 2 times with water and once with ethanol. In the third step, 0.1 g of the CNPs@$Y(OH)CO_3$:Er,Yb was dispersed in a mixture containing 60 mL ethanol, 80 mL distilled water, 0.2 g cetyltrimethylammonium bromide (CTAB) and 1.2 mL 25% ammonia solution. The suspension was first placed in an ultrasound bath for a few minutes and then left to stir at room temperature for 30 minutes to form a uniform dispersion. Subsequently 0.15 mL tetraethoxysilane (TEOS) was added dropwise to the dispersion under continuous stirring.

The suspension was stirred at room temperature for 6 h and the product was next collected by centrifugation and washed 2 times with water and once with ethanol. The product was dried overnight in an oven at 85 °C. Last, the sample was heat treated in air at 800 °C for 3 h in order to remove the CNPs and CTAB as well as to obtain Y_2O_3:Er,Yb hollow spheres.

Preparation of $Y_2O_2SO_4$:Er,Yb hollow spheres

1 mmol of $RE(NO_3)_3 \cdot 6H_2O$ (2% Er and 18% Yb, 80% Y) was dissolved in 25 mL distilled water and left to stir in a beaker at room temperature. Next, 2 mmol L-cysteine and 0.3 g polyvinylpyrrolidone (PVP) were added to the solution under continuous stirring. After 15 minutes the solution was transferred to a 40 mL Teflon-lined stainless-steel autoclave and heated at 180 °C for 24 h. After cooling down naturally the product was collected by centrifugation and washed twice with distilled water and once with ethanol. The product was dried in an oven at 85 °C overnight to yield the $Y_2O_2SO_4$:Er,Yb precursor material. Next, this material could be further heat treated in air at 850 °C for 2 h to produce $Y_2O_2SO_4$:Er,Yb HT material.

Preparation of $Y_2O_2SO_4$:Er,Yb@Au hollow spheres

50 mg of dried $Y_2O_2SO_4$:Er,Yb precursor or heat treated hollow spheres were suspended in 5 mL of oleylamine (used both as reducing and stabilizing agent). The suspension was stirred and heated to 60 °C for 10 minutes under nitrogen flow. Next, a $HAuCl_4$ solution (6 mg $HAuCl_4$ in 4 mL 2 mL 1-octadocene and 0.5 mL of oleylamine) was injected into the $Y_2O_2SO_4$:Er,Yb suspension. The mixture was kept at 90 °C for 30 minutes with constant stirring. After cooling down to room temperature, the product was collected by centrifugation and washed with ethanol. The product was dried in an oven at 85 °C overnight.

Tests and characterization

Cell toxicity tests: The NHDF cells were seeded in 96-well plates in cell culture media (DMEM with 10% FBS and 1% PenStrep) upon reaching 80-90% confluency at cell concentration of 10,000 cells per well and incubated for 24 hours at 37 °C and 5% CO_2. The following day, the sample powders were suspended in stock solutions of 10 mg/mL in cell culture media and were shaken for 2-3 minutes while vortexing. To break up agglomerates

of particles, particle suspensions were re-dispersed in an ultrasonic bath for 10 minutes. The samples were added to the wells in appropriate concentrations, volumes were equalized (to a total well volume of 180 µL) using cell culture media and incubated for 24 hours at 37 °C and 5% CO_2. After incubation, 20 µL of PrestoBlue™ cell viability reagent was added, and after incubation of 4 hours in the dark, the plates were measured on a TECAN spectrophotometer using 560 nm excitation and 635 nm wavelength emission filters.

Widefield microscopy imaging: For the microscopy experiments, plates were prepared in a similar fashion as described above, instead of adding 20 µL PrestoBlue™ reagent, fluorescent marker Calcein-AM was added to the wells at a concentration of 0.3 µl/well and cells were visualized using a Nikon Ti microscope through a long-pass GFP filter.

STEM, SEM, powder X-ray diffraction, N_2 sorption, TG-DTA: Scanning transmission electron microscopy (STEM) images were taken on a JEOL JEM-2200FS TEM operated at 200 kV. The samples were prepared on a 300-mesh holey carbon copper grid. STEM images were taken with a bright field (BF) or high-angle annular dark field (HAADF) detector. The composition of the sample was determined via energy dispersive X-ray (EDX) spectroscopy in HAADF-STEM mode. Scanning electron microscopy (SEM) measurements were performed using a FEI Quanta 200 FSEM. Powder X-Ray Diffraction (PXRD) patterns were recorded with a Thermo Scientific ARL X'Tra diffractometer, operated at 40 kV and 40 mA using Cu-Kα radiation (λ = 1.5406 Å) from 2θ-angles of 15° to 60°. Nitrogen adsorption–desorption isotherms were measured by using a Micromeritics TriStar 3000 analyzer at –196 °C. The samples were vacuum dried at 120 °C overnight before the measurements. Surface areas were calculated using the Brunauer–Emmett–Teller (BET) method. Thermogravimetry (TG) and differential thermal analysis (DTA) were performed on a Stanton Redcroft 1500 apparatus under air flow, in temperature range from 20 °C to 1000 °C with a heating rate of 10 °C min^{-1}.

Luminescence spectroscopy and thermometry: Luminescence spectra were measured on an Edinburgh FLS920 spectrofluorometer equipped with a Hamamatsu R928P photomultiplier tube used to detect the emission signals in the near UV to visible range. All emission spectra were acquired by excitation with continuous wave (CW) power-tunable (power limit: P_{max} = 400 mW) laser operating at λ_{ex} = 975 nm. Aqueous suspensions of the particles were

measured using a QPOD 2e (Quantum Northwest, USA), which was placed in the spectrometer. Stirring at 600 RPM was employed during the measurements. All emission spectra in the manuscript have been corrected for detector response. All the temperature-dependent data was processed employing the TeSen software: http://www.tesen.ugent.be.

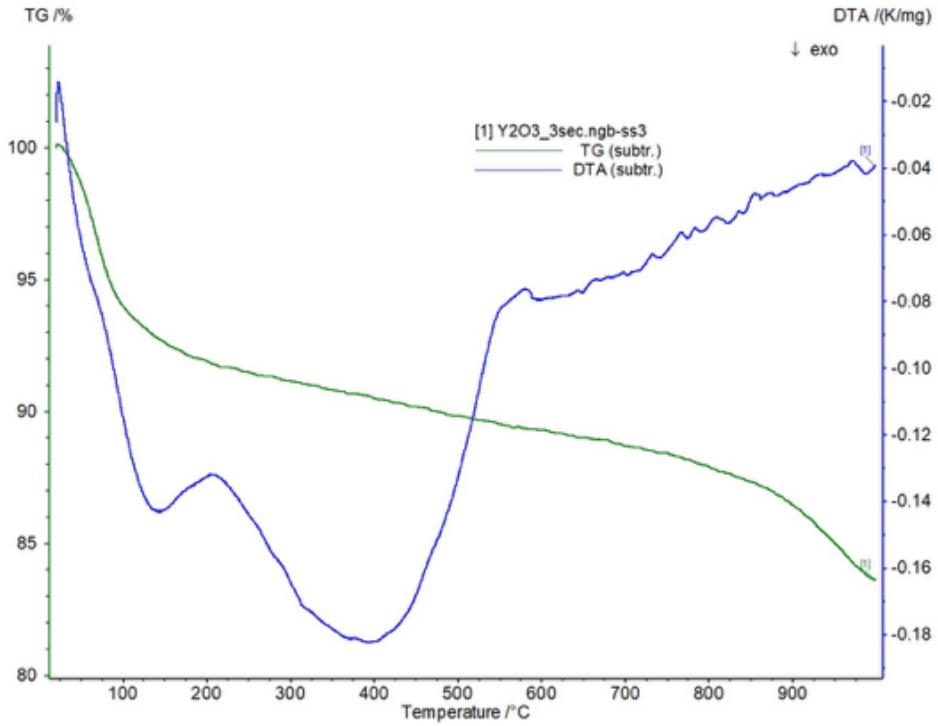

Figure S1. TG-DTA of Y_2O_3:Er,Yb hollow spheres.

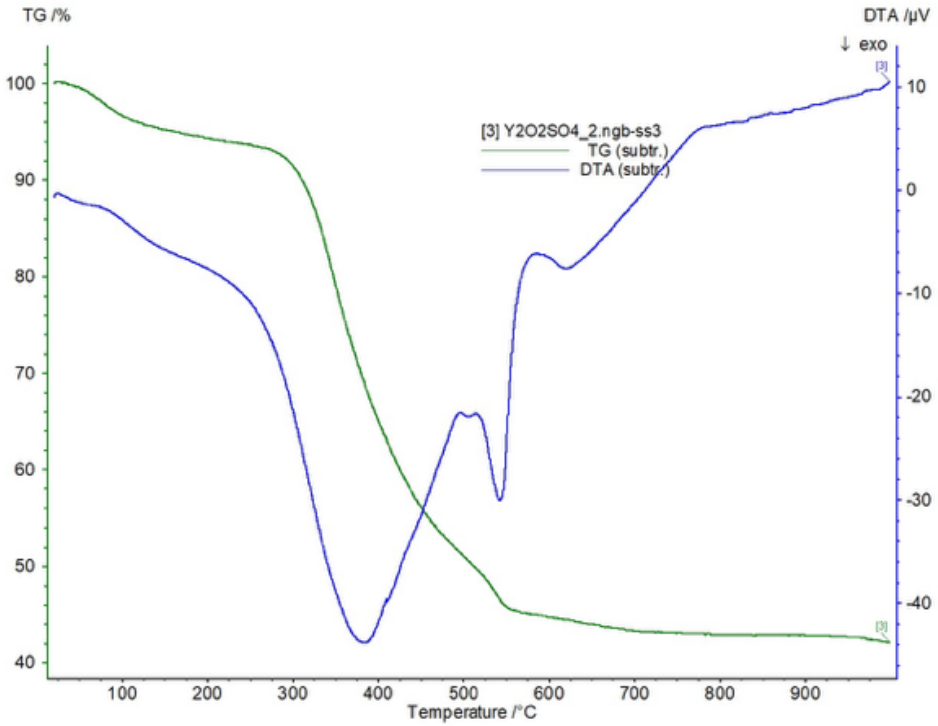

Figure S2. TG-DTA of $Y_2O_2SO_4$ precursor hollow spheres.

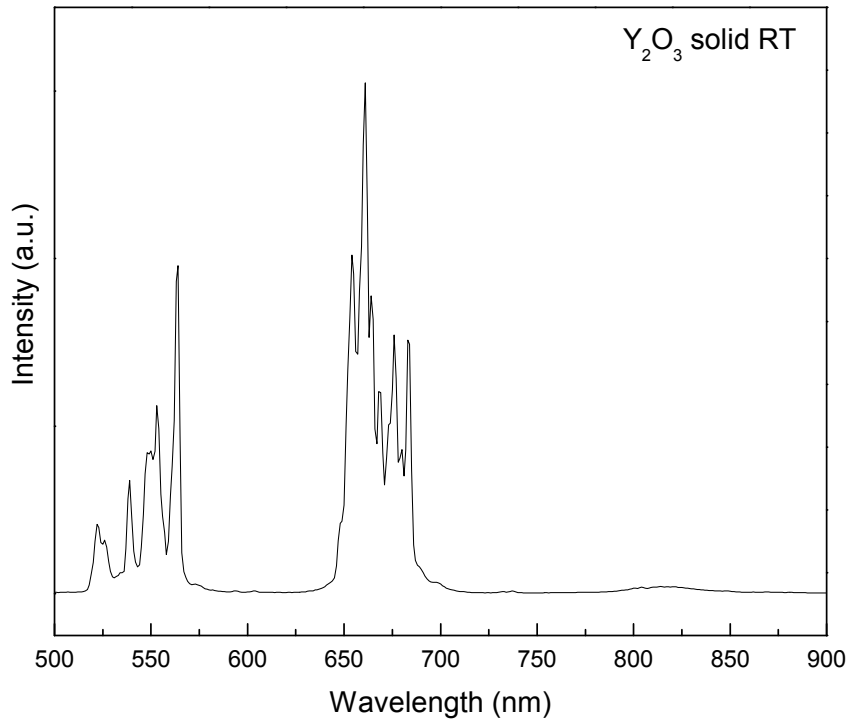

Figure S3. RT emission spectrum of Y_2O_3:Er,Yb hollow spheres measured in solid state.

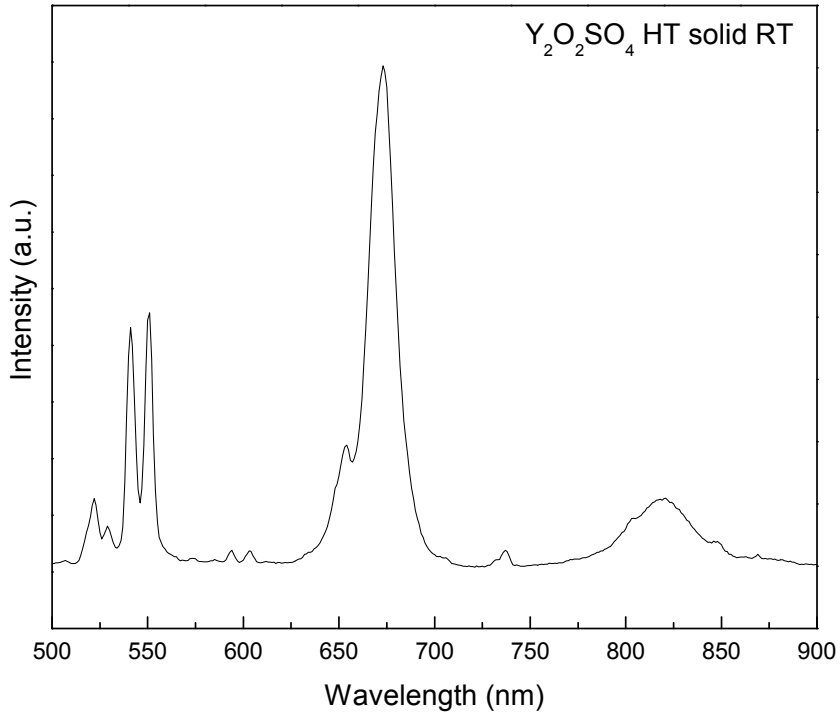

Figure S4. RT emission spectrum of $Y_2O_2SO_4$:Er,Yb precursor hollow spheres measured in solid state.

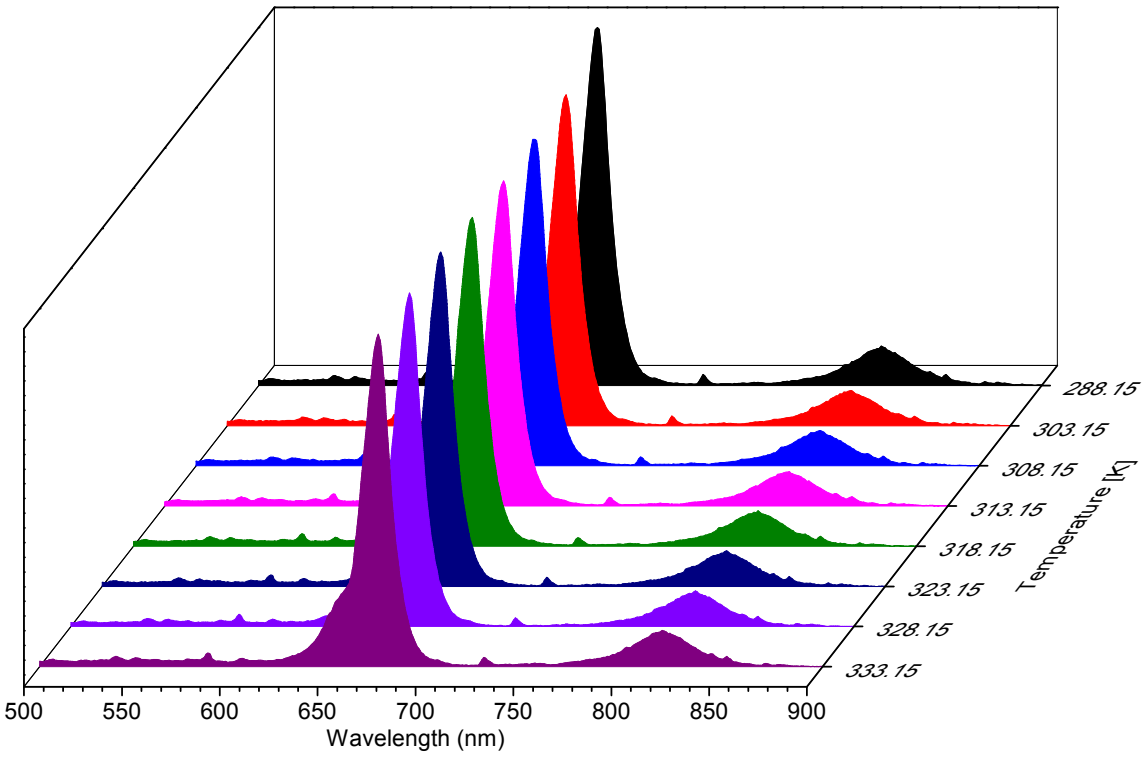

Figure S5. Emission map of $Y_2O_2SO_4$:Er,Yb hollow spheres after heat treatment measured in distilled water at varying temperatures (288.15 – 333.15 K).

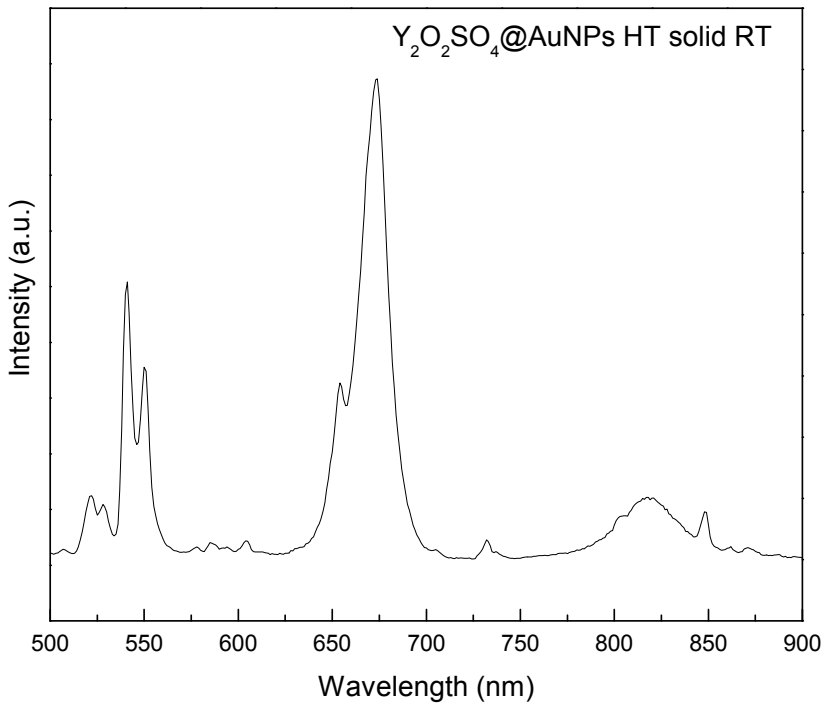

Figure S6. RT emission spectrum of $Y_2O_2SO_4$:Er,Yb@Au precursor hollow spheres measured in solid state.

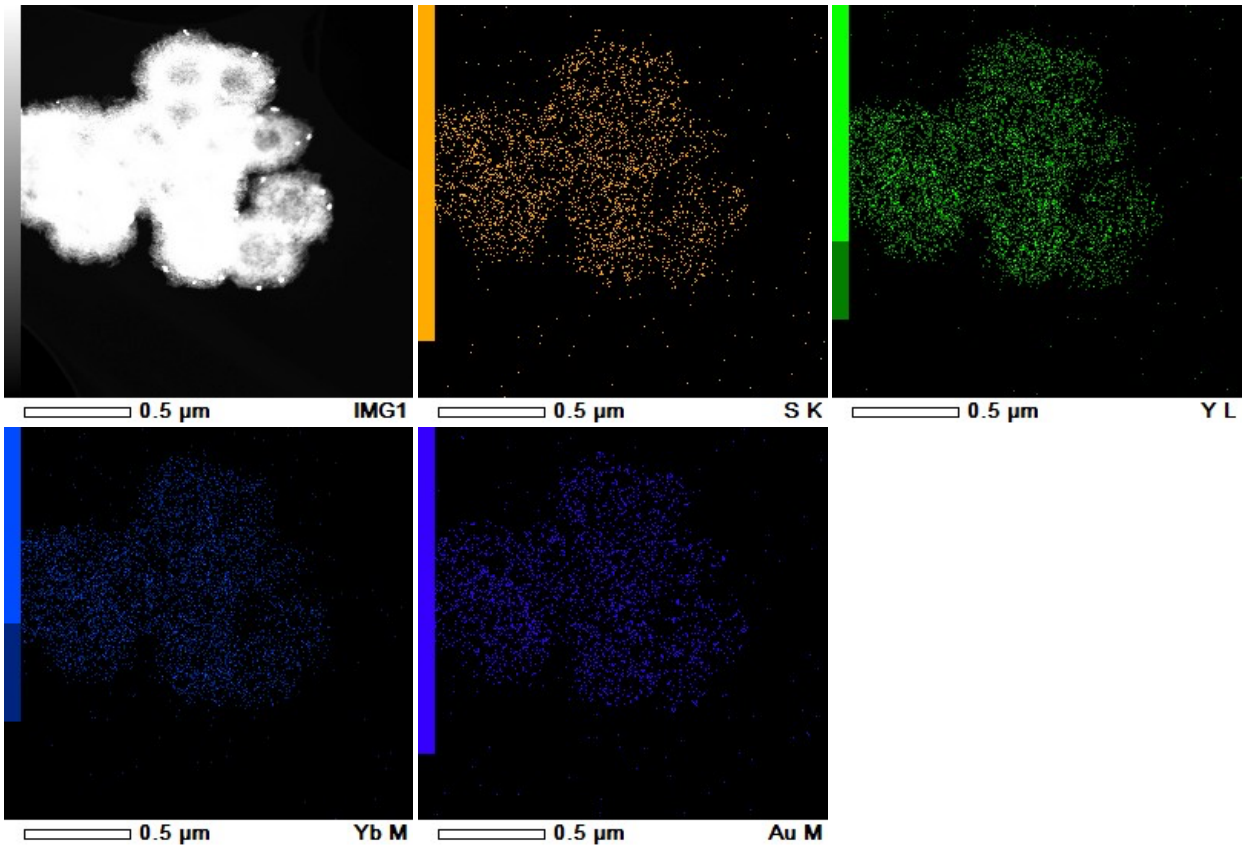

Figure S7. HAADF-STEM with EDX maps of $Y_2O_2SO_4$:Er,Yb@Au precursor hollow spheres. S, Y, Yb, and Au were mapped.

Doxorubicin (DOX) loading and release from Y_2O_3:Er,Yb and $Y_2O_2SO_4$:Er,Yb precursor

DOX·HCl was used for all loading experiments. Loading the rare earth hollow spheres was carried out by dispersing 5 mg of Y_2O_3:Er,Yb or $Y_2O_2SO_4$:Er,Yb in 1 mL phosphate-buffered saline (PBS, pH 7.4) containing 5 mg of DOX. This suspension was left to stir for 24 h, at RT with continuous stirring in the dark. Afterwards the particles were centrifuged at 11000 rpm for 10 minutes. The particles were washed and centrifuged repeatedly until clear supernatant was collected. The supernatant solution was collected for UV-vis analysis to access the concentration of the unloaded DOX using a calibration curve. The obtained Y_2O_3:Er,Yb@DOX or $Y_2O_2SO_4$:Er,Yb@DOX material was dried overnight in an oven at 80 °C. The absorbance was monitored at 480 nm. The amount of DOX loaded in the rare earth hollow spheres was assessed based on the initial mass of DOX and the final mass of DOX detected through UV-vis absorbance analysis in the supernatant.

The drug Loading Capacity (LC%) was calculated using the following formula:

$$LC\% = \frac{mass\ of\ drug\ in\ hollow\ particles}{mass\ of\ DOX\ loaded\ hollow\ particles}\ x\ 100\ \ (eqn\ S1)$$

The drug Encapsulation Efficiency (EE%) was calculated using the following formula:

$$EE\% = \frac{mass\ of\ drug\ in\ hollow\ particles}{mass\ of\ initial\ DOX}\ x\ 100\ \ (eqn\ S2)$$

The DOX drug release was carried out in PBS buffer, at three different pH values: 7.4, 5.5 and 4. In a typical procedure 5 mg of DOX-loaded rare earth hollow sphere particles i.e., Y_2O_3:Er,Yb or $Y_2O_2SO_4$:Er,Yb were dispersed in 0.5 mL PBS buffer. This suspension was poured into a Spectra-Por dialysis bag with a cutoff of 6000-8000 Da (10 mm width and 6.4 mm diameter) and tightly secured with clams on both sides. The dialysis bag was placed horizontally in a vial with 20 mL PBS buffer. The vial was closed and placed on a shaker (Orbital mini shaker, VWR) set at 37 °C. The dialysate containing the released DOX was sampled (3 mL) at appropriate time intervals. The samples were put back to the vial after the UV vis absorbance measurements. The amount of DOX released from the rare earth

hollow sphere particles i.e., Y_2O_3:Er,Yb or $Y_2O_2SO_4$:Er,Yb was measured by monitoring the absorbance of DOX in the dialysate at 480 nm.

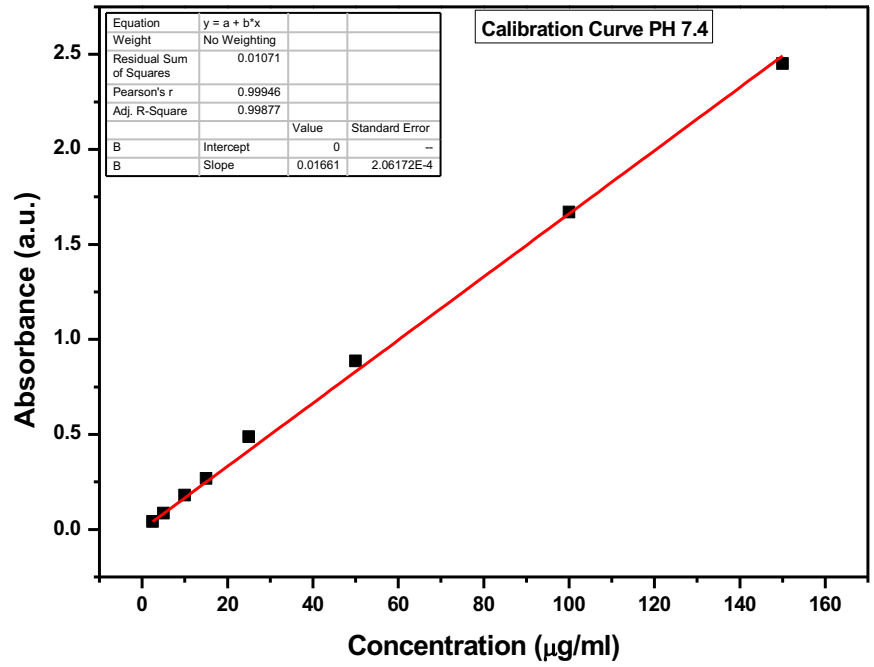

Figure S8. DOX calibration curve for PBS pH 7.4.

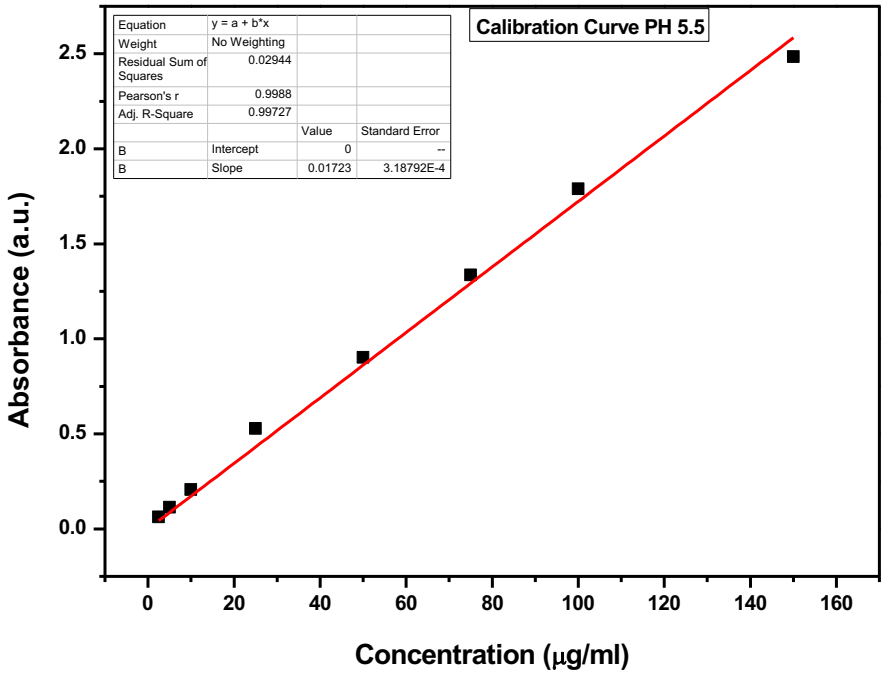

Figure S9. DOX calibration curve for PBS pH 5.5.

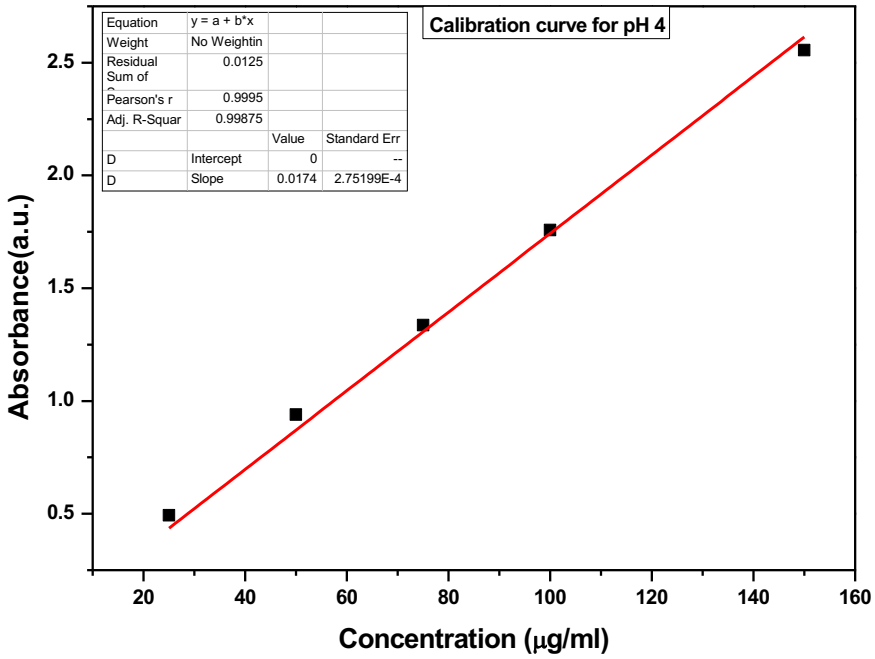

Figure S10. DOX calibration curve for PBS pH 4.

Table S1. Overview of DOX drug loading and release from Y_2O_3:Er,Yb and $Y_2O_2SO_4$:Er,Yb

Host material	%Drug loading capacity	%Encapsulation efficiency	% DOX release within 72 h		
			pH 7.4	pH 5.5	pH 4
Y_2O_3	37.0%	58.6%	9%	16%	22%
$Y_2O_2SO_4$	38.3%	62.0%	6%	12%	26%