



## Supporting Information

for

### **The preparation temperature influences the physicochemical nature and activity of nanoceria**

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## Additional experimental data

**Table S1:** Physicochemical properties of NM-212 and the solvothermally synthesized nanoceria.

| Metric  | NM-212  |              | Solvothermal synthesis-produced |           |
|---|---|--------------|---------------------------------|-----------|
|   | Value   | Reference    | Value                           | Reference |
| Mean primary particle Feret diameter by SEM               | 28 nm   | [1]          |                                 |           |
| Primary particle size, by TEM                             | <10 to >100 nm  | [2]          |                                 |           |
| Mean primary particle size                                | 40 nm   | [3,4]        |                                 |           |
| Mean primary particle diameter, Feret, and area           | 22 nm, 29 nm, 484 nm <sup>2</sup>                                     | This article | 4.2 nm                          | [5-7]     |
| BET surface area  | 27 m <sup>2</sup> /g  | [1-4,8-10]   |                                 |           |
| Hydrodynamic diameter (and polydispersity index) in water | 207 nm (0.196)  | [9]          | 11 nm                           | [6,7]     |
| Hydrodynamic size (and mean polydispersity) in water      | 213 nm (0.255)  | [2]          |                                 |           |
| Equivalent spherical diameter in water                    | 135 nm  | [2]          |                                 |           |
| Agglomerate diameter                                      | 3000–150,000 nm   | [3]          |                                 |           |
| Agglomerate density                                       | 2 g/m <sup>3</sup>  | [3]          |                                 |           |
| Dispersion stability (half-life) in water                 | 2676 min  | [2]          |                                 |           |
| Crystallite phase/planes                                  | Crystalline, cerianite like, irregular, roughly globular, ceria-cubic | [2,3,9]      | Face-centered cubic fluorite    | [6,7]     |
| Shape   | Polyhedral  | [2]          | Hexagonal                       | [7]       |
| Shape   | Mixed spheroidal and platelets  | [10]         |                                 |           |
| Shape   | Cubic or triangular   | This article |                                 |           |
| Purity  | >99.5%  | [10]         |                                 |           |
| TGA-induced weight loss                                   | 0.7%  | [3]          | 15%                             | [7]       |
| TGA-induced weight loss                                   | 1.3%  | This article |                                 |           |
| Surface chemistry (3-10 nm depth)                         | C 79.9%, O 17.7%  | [3,4]        |                                 |           |
| Surface chemistry (0-12 nm depth), by XPS (PROSPEcT)      | C 75.2%, O 22.9%, Ce 2%   | [2]          |                                 |           |

|   |   |              |  |       |
|---|---|--------------|--|-------|
| Surface chemistry (0-10 nm depth) XPS   | C 31.9%,<br>O 42.1%,<br>Ce 25.7%                        | [2]          |  |       |
| Surface chemistry pelleted, XPS (JRC)   | C 19.5%,<br>O 66.9%,<br>Ce 13.6%                        | [2]          |  |       |
| Surface chemistry, FTIR   | Peaks at 1630,<br>1420, and 1320<br>cm <sup>-1</sup>    | This article |  |       |
| Elemental mapping (EDS)   | Majority Ce and O, with small % C and Na                | This article |  |       |
| Particle coating  |   |              | Citrate (monolayer)  | [7]   |
| Zeta potential in water   | 42 mV at pH 7, positive over entire physiological range | [3,9]        |  |       |
| Zeta potential in water   | 33 mV   | [2]          |  |       |
| Zeta potential  | 15 mV at pH 7   | [4]          | -40 mV at pH 7   | [7]   |
| Zeta potential  | 42 mV at pH 7   | [3]          |  |       |
| IEP   | above pH 10 (always cationic)                           | [3]          | pH 1.41  | [7]   |
| Hydrophobicity (water contact angle)  | 60  | [4]          |  |       |
| Oxidation state (within the XPS-accessible surface layer)                         | Ce <sup>3+</sup> 14%                                    | [3,9]        | Core primarily Ce <sup>4+</sup> , surface predominantly Ce <sup>3+</sup> | [5-7] |
| Oxidation state   | Ce <sup>3+</sup> 6.9%, Ce <sup>4+</sup> 93.1%           | [2]          |  |       |
| Oxidation state (particle edge)   | ca. 90% Ce <sup>4+</sup>                                | This article |  |       |
| Oxidation state (particle center)   | ca. 90% Ce <sup>4+</sup>                                | This article |  |       |
| Surface reactivity, as photon efficiency  | 1.3 x 10 <sup>-2</sup>                                  | [3,9]        |  |       |
| TEM image of dry powder   | Figure 1B   | [1]          | Figure 1-1   | [7]   |
|   |   |              | Figure 1   | [6]   |
| SEM image of dry powder   | Figure 1E   | [1]          |  |       |
| HRTEM/STEM image of primary crystallite, primary particles, and their agglomerate |   |              | Figure 1   | [5]   |
| TEM image of primary particles  | Figure 1  | [9]          |  |       |
| TEM image of primary particles  | Figures 17 & 18 show irregular,                         | [2]          |  |       |

|  |                           |              |  |  |
|--|---------------------------|--------------|--|--|
|  | non-homogeneous particles |              |  |  |
| TEM image of primary particles   | Figure 1                  | This article |  |  |
| SEM image of dry powder  | Figure 2b                 | [3]          |  |  |
| SEM image of dry powder  | Figure 1b                 | [9]          |  |  |
| SEM image of dry powder  | Figure 2                  | [2]          |  |  |
| TEM image before and after 7-day incubation in phagolysosomal simulant fluid       | Figure 4d                 | [10]         |  |  |
| TEM image after 28-day incubation in phagolysosomal simulant fluid                 | Figure 3b                 | [3]          |  |  |
| SEM image after 28-day incubation in phagolysosomal simulant fluid                 | Figure 2c                 | [9]          |  |  |
| Selected area diffraction after 28-day incubation in phagolysosomal simulant fluid | Figure 3b                 | [3]          |  |  |

**Table S2:** Reports of nanoceria solubility.

| Dissolution                | Solubilizing media/conditions  | Physicochemical identity (average primary particle size in nm), ((average hydrodynamic size in nm))                            | Reference |
|----------------------------|--|--|-----------|
| No significant dissolution | 72 h at 37 °C in pH 7.0 physiological saline                                   | (7), ((13)), specific surface area 87 m <sup>2</sup> /g  | [11]      |
| No significant dissolution | 72 h at 37 °C in pH 4.5 artificial phagolysosomal fluid                        |  |           |
| 1.3%, 1.8%, 0.8%, and 0.9% | 24 h in pH 7.8 DMEM + 10% FBS  | (7), BET 63 m <sup>2</sup> /g; (7), BET 44 m <sup>2</sup> /g; (7), BET 38 m <sup>2</sup> /g; and (7), BET 63 m <sup>2</sup> /g | [12]      |
| 3% and 0.08%               | 28 d in pH 4 or 7 artificial soil solution                                     | (8 to 9)   | [13]      |
| 2.3%, 0.3%, and 0.06%      | 28 d in pH 4, 7, or 9, 0.1 M NaCl  | (8 to 9), ((130 at pH 4.5; >1000 at pH 7, and 300 at pH 9))  |           |
| No significant dissolution | 24 h at room temperature in pH 7.4 artificial interstitial fluid               | (4), ((132)), surface area 66 m <sup>2</sup> /g; and (10), ((88)), surface area 24 m <sup>2</sup> /g                           | [14]      |
| 0.2% and 0.3%              | 24 h at room temperature in pH 5.5 artificial lysosomal fluid                  |  |           |
| Extremely poor             | Water at neutral pH  | (45) (NM-211); (28), <b>(NM-212)</b> ; and (615), (NM-213)   | [1]       |
| No dissolution             | 24 h in DMEM-FBS   | (14), specific surface area 84 m <sup>2</sup> /g   | [15]      |
| <0.001%                    | 24 h at 25 °C in water   | (10 to 200), ((>10,000)), specific surface area 33 m <sup>2</sup> /g   | [16]      |
| <0.001%                    | 24 h at 25 °C in DMEM + 10% fetal calf serum                                   |  |           |
| Extremely small solubility | At 37 °C in DMEM + 10% FBS   | (8), ((669 in PBS and 191 in DMEM + 10% FBS)); (20), ((35 in PBS and 61 in DMEM + 10% FBS))                                    | [17]      |
| Insignificant              | Exposure to artificial daylight, initially at pH 8.5 and at pH 6.2 after 112 d | (4)  | [18]      |
| <0.001%, 0.002%            | 28 d in water  | NM-211 and <b>NM-212</b>   | [3,9]     |
| <0.001%, <0.001%           | 28 d in DMEM + fetal calf serum  |  |           |
| <0.001%, <0.001%           | 28 d in phagolysosomal simulant fluid  |  |           |
| <0.001%                    | 28 d in PBS  |  |           |

|   |  |  |      |
|---|--|--|------|
| <0.001%   | 7 and 28 d in fasted state simulated intestinal fluid  | <b>NM-212</b>  |      |
| 0.02%   | 1 and 28 d in 0.1 N HCl  |  |      |
| 5%, 8%, and 18% in 1- and 50 mM ascorbate and 10 mM glutathione   | CeO <sub>2</sub> -coated mesoporous silica 3 d with 1, 5, 10, or 50 mM ascorbate or 1, 5, or 10 mM glutathione     | (4)  | [19] |
| Greater for smaller ENMs, at pH 4 than 6, and in presence of gum arabic and absence of KH <sub>2</sub> PO <sub>4</sub>                                  | 7 d in 20% Hoagland solution at pH 4 or 6, and added gum arabic or phosphate deletion                              | (8.9), ((140)), BET 233 g/m <sup>2</sup> ; (22.8), ((129)), BET 22.4 g/m <sup>2</sup> ; (63.9) ((1182)) BET 4.9 g/m <sup>2</sup> | [20] |
| No dissolution  | 21 d in DI water, fish medium (pH 7.3), daphnia medium (pH 7.9), or seawater (pH 8.8)                              | NM-211, <b>NM-212</b> , and NM-213   | [2]  |
| <0.0025% for NM-211, NM-212, 0.3% for NM-213  | 72 h at 24 °C in pH 6.5 synthetic soft water   |  |      |
| Solubility constant ( <i>K<sub>sp</sub></i> )   | 0.13   |  | [21] |
| Dissolution rate: 0.0576 and 0.0741 mmol·kg <sup>-1</sup> ·h <sup>-1</sup>  | 120 h in pH 1.65 in 0.01 mM NaNO <sub>3</sub>  | Uncapped (32) and (78), BET surface area 40 and 11.5 m <sup>2</sup> /g   | [22] |
| Dissolution rate: 0.0362 and 0.0209 mmol·kg <sup>-1</sup> ·h <sup>-1</sup>  | 120 h in pH 1.65 in 0.01 mM NaNO <sub>3</sub> and 0.1 mM phosphate   |  |      |
| Dissolution rate: 0.0168 and 0.0177 mmol·kg <sup>-1</sup> ·h <sup>-1</sup>  | 120 h in pH 4.5 in 0.01 mM NaNO <sub>3</sub> and 0.2 M Na acetate  |  |      |
| Dissolution rate: 0.0057 and 0.0084 mmol·kg <sup>-1</sup> ·h <sup>-1</sup>  | 120 h in pH 4.5 in 0.01 mM NaNO <sub>3</sub> , 0.2 M Na acetate, and 0.1 mM phosphate                              |  |      |
| No detectable dissolution   | 120 h in pH 7.5  |  |      |
| No detectable dissolution   | 120 h in pH 12.4   |  |      |
| 0.4% in water, + PO <sub>4</sub> 0%, 14% in citric and ascorbic acids, + PO <sub>4</sub> 0.3%, 3.7% in citric acid and catechol, + PO <sub>4</sub> 1.9% | 21 d in pH 5.5 with 1 mM citric and ascorbic acid or citric acid and catechol, and KH <sub>2</sub> PO <sub>4</sub> | (25), ((123 in water, 1235 in organic solution, and 1485 in organic solution and phosphate))                                     | [23] |
| 0% lung, ~0.2% intestinal, ~0.2% gastric IVC method, 5.5% gastric SBRC method   | 24 h at 37 °C in simulated lung (pH 4.5 and 7.3), 4 h intestinal, and 2 h gastric (pH 1.8 IVG and 1.5 SBRC) fluids |  | [24] |

|  |  |  |        |
|--|--|--|--------|
| <3%  | 7 d at 37 °C in pH 4.55 phagolysosomal simulant fluid  | NM-211, <b>NM-212</b>  | [10]   |
| Extremely low solubility   | 30 m in MES buffer at pH 4.5, 5.5, 6.5, or 7.5   | (18), ((542 in water and 250 in DMEM)), zeta 22 mV in water and -15 mV in DMEM | [25]   |
| No detectable dissolution  | 96 h in water  | (24), ((~ 3000 in water))  | [26]   |
| 1.1% and 0.19%   | 7 d at 37 °C in pH 4.55 phagolysosomal simulant fluid  | NM-211, <b>NM-212</b>  | [27]   |
| 0.06 ng/cm <sup>2</sup> /h   | Lysosomal dissolution rate   |  | [4]    |
| 0.3% in medium, no increase with 0.01 M HCl or 1 mM citric acid, 0.9% in ascorbic acid, 44% in ascorbic and citric acids | 3 h in pH 7.1 Luria-Bertani medium, with 0.01 M HCl (not pH 7.1), 1 mM ascorbic and/or 1 mM citric acid  | (8 x 168 rods)   | [28]   |
| Dissolution half-life 58,200 h   | 28 weeks in pH ~ 6 iso-osmotic water   | <b>Solvothermal synthesis-produced nanocereria of this report</b>              | [5,29] |
|  | 28 weeks in pH ~ 4.5 iso-osmotic water   |  |        |
| Carboxylic acid-dependent dissolution half-life 800 to 3150 h  | 28 to 30 weeks at 37 °C in pH 4.5 iso-osmotic 110 mM acetic, adipic, citric, glutaric, DL-3-hydroxybutyric, lactic, DL-malic, pimelic, succinic acid, or tricarballylic acid |  |        |
| Dissolution half-life 7490 h   | 28 weeks in 20 mM pH 4.5 iso-osmotic ammonium  |  |        |
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