Biocompatible and Stable ZnO Quantum Dots
Generated by Functionalization with Siloxane-core PAMAM Dendrimers

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1. Syntheses and products studies
1.1. Synthesis of siloxane-core PAMAM dendrimers
Six novel dendrons bearing a siloxane group at the focal point have been prepared from 3-aminopropyltrimethoxysilane, methyl acrylate and ethylene diamine (Scheme 1).

**Scheme S1.** Synthetic route to siloxane-core PAMAM dendrimers
The synthesis of siloxane-core PAMAM dendrons was performed according to Tomalia et al.\textsuperscript{1} with slight modifications.

1.1.1. Synthesis of G0.5 dendron
Under nitrogen flow, to a mixture of 3-aminopropyltrimethoxysilane (2 g, 11 mmol) and 20 mL of MeOH was added dropwise at room temperature methyl acrylate (17.2 g, 200 mmol). After 48 h stirring at rt, the solution was heated at 40°C for 30 min. After cooling at rt, MeOH and methyl acrylate were evaporated. The product was obtained as a colorless liquid in 97% yield.

\textsuperscript{1}H NMR (DMSO-d\textsubscript{6}, 200 MHz) : \(\delta = 3.55\) (s, 6H, COOC\(\text{H}_3\)); 3.44 (s, 9H, Si(OCH\(\text{H}_3\))\textsubscript{3}); 2.62 (t, \(J = 6.6\) Hz, 4H, CH\(_2\)CH\(_2\)COOCH\(_3\)); 2.46-2.22 (m, 6H, CH\(_2\)COOCH\(_3\) + SiCH\(_2\)CH\(_2\)N); 1.48-1.27 (m, 2H, SiCH\(_2\)CH\(_2\)CH\(_2\)); 0.50 (t, \(J = 8.1\) Hz, 2H, SiCH\(_2\)).

\textsuperscript{13}C NMR (DMSO-d\textsubscript{6}, 50 MHz) : \(\delta = 172.1, 55.7, 51.1, 49.9, 48.8, 32.0, 19.9, 5.9\).

1.1.2. Synthesis of G1.0 dendron
Under nitrogen flow, to a mixture of ethylenediamine (69.4 g, 1.14 mol) and methanol (17 mL) cooled to 4°C, was added dropwise a 50 weight % solution of dendron G0.5 (4g, 11.4 mmol) in 5 mL MeOH. The mixture was stirred at 4°C for 4 days and then finally heated to 40°C for 30 min. remaining ethylene diamine was removed by azeotroping using a 3/1 toluene/MeOH mixture.

The product was obtained as a pale yellow liquid in 95% yield.

\textsuperscript{1}H NMR (DMSO-d\textsubscript{6}, 200 MHz) : \(\delta = 7.95\) (s broad, 2H, CONH\(_2\)); 3.42 (s, 9H, Si(OCH\(\text{H}_3\))\textsubscript{3}); 3.09-2.88 (td, \(J = J' = 4.6\) Hz, 4H, CONHC\(\text{H}_2\)); 2.72-2.35 (m, 14H, CH\(_2\)NH\(_2\)); 1.51-1.42 (m, 2H, SiCH\(_2\)CH\(_2\)CH\(_2\)); 0.49 (t broad, 2H, SiCH\(_2\)).

\textsuperscript{13}C NMR (DMSO-d\textsubscript{6}, 50 MHz) : \(\delta = 171.8, 55.7, 49.9, 49.5, 42.4, 41.5, 33.3, 19.9, 7.7\).

HRMS (ESI) : \(m/z\) calculated for C\(_{16}\)H\(_{37}\)N\(_5\)O\(_5\)Si [M+H]\textsuperscript{+}, 407.26; found, 407.2.

1.1.3. Synthesis of G1.5 dendron
The synthesis was conducted as described for G0.5 dendron but using 4.9 mmol of the G1 dendron and 39.2 mmol methyl acrylate in 4.5 mL MeOH. The product was obtained as a viscous pale yellow oil in quantitative yield.

\textsuperscript{1}H NMR (DMSO-d\textsubscript{6}, 200 MHz) : \(\delta = 7.63\) (s large, 2H, CONH\(_2\)); 3.55 (s, 12H, COOC\(\text{H}_3\)); 3.41 (s, 9H, Si(OCH\(\text{H}_3\))\textsubscript{3}); 3.21-2.94 (m, 12H, CONHC\(\text{H}_2\)); 2.72-2.05 (m, 38H, CH\(_2\)NH\(_2\)); 1.48-1.34 (m, 2H, SiCH\(_2\)CH\(_2\)CH\(_2\)); 0.49 (t large, 2H, SiCH\(_2\)).

\textsuperscript{13}C NMR (DMSO-d\textsubscript{6}, 50 MHz) : \(\delta = 172.6, 171.4, 54.9, 52.4, 51.3, 49.8, 49.3, 49.0, 48.7, 36.8, 32.1, 20.0, 9.2\).

1.1.4. Synthesis of G2.0 dendron
The synthesis was conducted as described for G1.0 dendron but using 5.1 mmol of the G1.5 dendron and 1.88 mol ethylene diamine in 125 mL MeOH. The product was obtained as a viscous pale yellow oil in a quantitative yield.

\textsuperscript{1}H NMR (DMSO-d\textsubscript{6}, 200 MHz) : \(\delta = 8.01\) (s broad, 2H, CONH\(_2\)); 7.91 (t broad, 2H, CONH\(_2\)); 3.35 (s large, 9H, Si(OCH\(\text{H}_3\))\textsubscript{3}); 3.21-2.94 (m, 12H, CONHC\(\text{H}_2\)); 2.72-2.05 (m, 38H, CH\(_2\)NH\(_2\)); 1.48-1.34 (m, 2H, SiCH\(_2\)CH\(_2\)CH\(_2\)); 0.50 (t broad, 2H, SiCH\(_2\)).

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\textsuperscript{1} D. A. Tomalia, B. Huang, D. R. Swanson, H. M. Brothers II and J. W. Klimash, Tetrahedron 2003, \textbf{59}, 3799.
$^{13}$C NMR (DMSO-d$_6$, 50 MHz): $\delta = 171.7, 171.6, 52.4, 51.1, 50.5, 49.8, 45.1, 42.4, 42.1, 41.5, 34.6, 33.4, 19.8, 10.7.$

HRMS (ESI): $m/z$ calculated for C$_{36}$H$_{77}$N$_{13}$O$_9$Si [M+H]$^+$, 863.57; found, 863.1.

1.1.5. Synthesis of G2.5 dendron

The synthesis was conducted as described for G0.5 dendron but using 2.32 mmol of the G1 dendron and 37.5 mmol methyl acrylate in 4.0 mL MeOH. The product was obtained as a viscous pale yellow oil in a quantitative yield.

$^1$H NMR (DMSO, 200 MHz): $\delta = 7.96$ (t broad, 2H, CON$_2$H); 7.65 (t broad, 4H, CONH); 3.56 (s, 24H, COOC$_3$H$_7$); 3.34 (s, 9H, Si(OCH$_3$)$_3$); 3.23-2.91 (m, 12H, CONHC$_2$H$_2$); 2.83-2.08 (m, 70H); 1.50-1.33 (m, 2H, SiCH$_2$CH$_2$CH$_2$); 0.51 (t broad, 2H, SiC$_2$H$_5$).

$^{13}$C NMR (DMSO, 50 MHz): $\delta = 172.6, 171.3, 55.6, 52.7, 51.4, 51.3, 49.8, 49.7, 49.3, 49.2, 49.0, 48.9, 36.7, 34.6, 33.3, 32.1.$ Signals for Si-CH$_2$ and Si-CH$_2$-CH$_2$ could not be assigned due to their low intensity.

1.1.6. Synthesis of G3 dendron

The synthesis was conducted as described for G1.0 dendron but using 2.58 mmol of the G1.5 dendron and 3.63 mol ethylene diamine in 241 mL MeOH. The product was obtained as a viscous pale yellow oil in a quantitative yield.

$^1$H NMR (DMSO-d$_6$, 200 MHz): $\delta = 8.76$ (t broad, 2H, CON$_2$H); 8.05 (t broad, 2H, CONH); 3.49 (s broad, 9H, Si(OCH$_3$)$_3$); 3.44-2.40 (m, 114H); 1.49-1.33 (m, 2H, SiCH$_2$CH$_2$CH$_2$). Signal for Si-CH$_2$ could not be assigned due to its low intensity.

$^{13}$C NMR (DMSO-d$_6$, 50 MHz): $\delta = 171.6, 171.5, 52.4, 51.1, 50.0, 49.9, 49.8, 49.7, 49.6, 45.0, 44.2, 42.3, 41.4, 37.0, 36.0, 34.4, 33.4, 30.9, 21.1.$ Signal for Si-CH$_2$ could not be assigned due to its low intensity.

HRMS (ESI): $m/z$ calculated for C$_{76}$H$_{157}$N$_{29}$O$_{17}$Si [M+H]$^+$, 1776.21; found, 1776.7.
1.2. Functionalization of oleate-capped ZnO nanoparticles with siloxane-core PAMAM dendrons

1.2.1. Synthesis of oleate-capped ZnO QDs
Zinc acetate (220 mg, 1.2 mmol) was dissolved in hot ethanol (20 mL) under vigorous stirring. Oleic acid (70 mL, 0.22 mmol) is then added and the mixture is heated to reflux. In a separate flask, tetramethylammonium hydroxide (360 mg, 1.99 mmol) is dissolved in refluxing ethanol (5 mL). This solution is then rapidly injected in the flask containing Zn(OAc)$_2$ and oleic acid and the mixture was refluxed for 2 min. The mixture is then diluted with EtOH (50 mL) and cooled down to 0°C with an ice-bath. A white precipitate of ZnO nanoparticles appeared. Particles were centrifugated (15 min at 4000 rpm) with removal of the supernatant. The resulting oleate-capped ZnO QDs were washed several times with ethanol, in which they are insoluble, and finally suspended in toluene (10 mL). Oleate capped ZnO QDs were stored at 4°C in the dark.

1.2.2. Synthesis of ZnO@G1 QDs

Under a nitrogen atmosphere, the oleate-capped ZnO QDs previously prepared were dispersed in 10 mL toluene and treated with 1 mL of a 0.1 M solution of G1 dendron in EtOH. After 5 min stirring at room temperature, 1 mL of a 0.3 M solution of tetramethylammonium hydroxide (TMAH) in EtOH is injected and the temperature was set at 85°C. After 45 min, the solution was allowed to cool and nanoparticles isolated by centrifugation (4000 rpm, 15 min). After removal of the supernatant, ZnO@G1 QDs were washed three times with toluene in which they are insoluble. QDs were then redispersed in water and were further purified by successive precipitation-solubilization rounds using acetone as bad-solvent. After drying for 5 h in vacuo, QDs were redispersed in water for further experiments.
1.2.3. Synthesis of ZnO@G2 QDs

ZnO@G2 nanoparticles were prepared analogously to the reaction above, with the exception that 1 mL of a 0.6 M TMAH solution in EtOH was added to the oleate-capped ZnO QDs and to the G2 dendron.
1.3. Characterization of nanoparticles

Figure S1. Room temperature absorption of ZnO@G1 and ZnO@G2 QDs dispersed in water.
Figure S2. TEM image of water-soluble ZnO@G1 QDs and the corresponding size distribution. The average diameter of QDs (ca. 100 particles counted) is 5.3 nm.
Figure S3. TEM image of water-soluble ZnO@G2 QDs and the corresponding size distribution. The average diameter of QDs (ca. 100 particles counted) is 5.1 nm.
Figure S4. AFM image of water-soluble ZnO@G1 QDs and the corresponding size distribution determined using AFM heights. The average diameter of QDs is 4.9 nm.
Figure S5. AFM image of water-soluble ZnO@G2 QDs and the corresponding size distribution determined using AFM heights. The average diameter of QDs is 4.6 nm.
Figure S6. Zn 2p (a), O 1s (b), Si 2p (c) and N 1s (d) X-ray photoelectron spectra of ZnO@G2 QDs.
Figure S7. AFM image of the ZnO-G3 nanocomposite. The average diameter of QDs is 5.2 nm.
Figure S8. Chemical structure of the G2 dendrimer bearing no siloxane unit at the focal point.
2. Confocal imaging experiments

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(a) \( \lambda \) (580-over nm)

(b) \( \lambda \) (530-560 nm)

Figure S9. Confocal microscopy images of *S. aureus* cells labeled with ZnO@G2 QDs (a) red fluorescence (over 580 nm), and (b) green fluorescence (530-560 nm). The mean surfaces (0.5 ± 0.16 µm²) and the circularity (0.92 ± 0.06) of fluorescent objects determined by laser scanning microscopy are in good accordance with those of *S. aureus* cells. Image width and heigh are equal to 44.6 µm (pixel size 87 nm) and analysed depth = 0.3 µm.