Hybrid, Silica-Coated, Janus-Like Plasmonic-Magnetic Nanoparticles

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ABSTRACT: Hybrid plasmonic-magnetic nanoparticles possess properties that are attractive in bioimaging, targeted drug delivery, in vivo diagnosis, and therapy. The stability and toxicity, however, of such nanoparticles challenge their safe use today. Here, biocompatible, SiO2-coated, Janus-like Ag/Fe2O3 nanoparticles are prepared by one-step, scalable flame aerosol technology. A nanothin SiO2 shell around these multifunctional nanoparticles leaves intact their morphology and magnetic and plasmonic properties but minimizes the release of toxic Ag+ ions from the nanosilver surface and its direct contact with live cells. Furthermore, this silica shell hinders flocculation and allows for easy dispersion of such nanoparticles in aqueous and biological buffer (PBS) solutions without any extra functionalization step. As a result, these hybrid particles exhibited no cytotoxicity during bioimaging and remained stable in suspension with no signs of agglomeration and sedimentation or settling. Their performance as biomarkers was explored by selectively binding them with live tagged Raji and HeLa cells enabling their detection under dark-field illumination. Therefore, these SiO2-coated Ag/Fe2O3 nanoparticles do not exhibit the limiting physical properties of each individual component but retain their desired functionalities facilitating thus, the safe use of such hybrid nanoparticles in bioapplications.

KEYWORDS: silver, iron oxide, silicon dioxide, cancer cell detection, heterodimer

INTRODUCTION

Plasmonic (Au or Ag) nanoparticles are superior markers for cell monitoring in bioimaging, diagnosis and therapy.1 Such nanoparticles can be readily detected and traced by optical techniques such as light scattering,2 dark-field illumination,3 two-photon fluorescence imaging,4 and photon illumination confocal microscopy.5 Alternatives to plasmonic nanoparticles for bioimaging are the commonly used fluorescent organic dyes and semiconducting nanoparticles.6 The former, however, exhibit toxicological properties and must be used with caution, whereas the latter can be toxic in high concentrations7 and their photostability8,9 is limited. Even though plasmonic nanoparticles also induce toxicity,9 they are functionally advantageous over fluorescent organic dyes and semiconducting nanoparticles because they have superior photostability10 and can be used also as photothermal therapeutic agents (e.g., tumor treatment),5 offering an extra functionality in bioapplications.

When plasmonic nanoparticles are combined with another material, e.g., a magnetic component, multifunctional nanostructured materials1 are created, that can be detected and guided by multiple imaging and control techniques. Magnetic resonance imaging (MRI) is an example of a traditional technique, with which magnetic particles can be used as contrast agents11 and for targeted drug delivery by directing them to organs, tissues or tumors using an external magnetic field or for magnetically assisted cell sorting and separation.11 Furthermore, a SiO2 film on the surface of such magnetic nanoparticles facilitates their surface biofunctionalization and minimizes their magnetic interactions13 and flocculation14 or agglomeration.

Composite plasmonic-magnetic nanostructures are typically made by multistep wet methods. Depending on synthesis route, core/shell15 or heterodimer (Janus-like)4 plasmonic-magnetic materials are formed. These “as-prepared” nanoparticles are often hydrophobic requiring a surface modification to stably suspend them in aqueous solutions. Typically, the magnetic material is iron oxide (γ-Fe2O3 or Fe3O4) for its high spontaneous magnetization11 in a superparamagnetic state. Live macrophage cells bound on labeled Ag/Fe2O3 nanoparticles have been imaged and manipulated by an external magnetic field. There are limitations, however, that hinder the use of such materials in bioapplications. First and foremost, their toxicity needs to be addressed before they can be employed.16 Even though Ag has the lowest optical plasmonic losses in the UV–visible spectrum,17 the more expensive Au nanoparticles are preferred for bioimaging because of their lower cytotoxicity.9 The release of toxic Ag+ ions18 when Ag nanoparticles are dispersed in aqueous solutions blocks their safe use in bioapplications. By coating Ag nanoparticles, however, with a nanothin shell, this toxicity can be eliminated while their surface biofunctionalization can be enhanced by hindering also their flocculation that poses another limitation in the use of plasmonic-magnetic
nanomaterials\textsuperscript{11,20} when dispersed in aqueous solutions. Overcoming these particle–particle interactions including magnetic ones requires typically additional surface modification of these particles.\textsuperscript{3}

Here, one-step synthesis of hybrid, silica-coated, plasmonic-magnetic nanomaterials is explored by scalable\textsuperscript{21} flame aerosol technology. The morphology of these composite nanoparticles and the influence of their SiO\textsubscript{2} shell on the release of Ag\textsuperscript{+} ions (Ag leaching) is investigated along with their cytotoxicity against HeLa cells and biocompatibility. The magnetic hysteresis of these nanoparticles is examined and the effect of SiO\textsubscript{2}-coating on their stability in aqueous and phosphate buffer saline (PBS) solutions is explored. The plasmonic properties of these hybrid nanoparticles are investigated and their magnetic guiding is demonstrated. Finally, the feasibility of these multifunctional materials in bioimaging is studied by selectively labeling live Raji and HeLa cells and monitoring them under dark-field illumination.

\section*{EXPERIMENTAL SECTION}

**Hybrid SiO\textsubscript{2}-Coated Ag/Fe\textsubscript{2}O\textsubscript{3} Nanoparticle Synthesis.** Silica-coated Ag/Fe\textsubscript{2}O\textsubscript{3} particles were made in one-step with an enclosed flame aerosol reactor, described in detail elsewhere.\textsuperscript{12} In brief, the composite core Ag/Fe\textsubscript{2}O\textsubscript{3} nanoparticles were made by flame spray pyrolysis (FSP) of precursor solutions containing iron(III) acetylatedionate (Sigma Aldrich, purity ≥97\%) and silver acetate (Sigma Aldrich, purity ≥99\%) dissolved in 2-ethylhexanoic acid and acetonitrile (both Sigma Aldrich, purity ≥99\%) and dispersed by 5 L/min O\textsubscript{2} (all gases Pan Gas, purity >99\%) forming a spray (pressure drop = 1.5 bar at the nozzle tip) that was ignited by a ring-shaped, premixed methane/oxygen flame (1.5/3.2 L/min) and sheathed by 40 L/min O\textsubscript{2}. The Fe precursor concentration was kept constant at 0.5 M, while corresponding amounts of silver acetate were added to reach the nominal Ag wt\%, which was defined as \( x = \frac{m_{Ag}}{(m_{Ag} + m_{Fe2O3})} \), and labeled as \( x\text{Ag/Fe}_{2}\text{O}_{3} \).

The freshly formed composite \( x\text{Ag/Fe}_{2}\text{O}_{3} \) particles were coated in-flight by swirl injection of hexamethyldisiloxane (HMDSO, Sigma Aldrich, purity ≥99\%) vapor with 15 L/min nitrogen (PanGas, purity >99\%) at room temperature through a metallic ring with 16 equivalent openings. The ring was placed on top of a 20 cm long quartz glass tube followed by another 30 cm long such tube. The HMDSO vapor was supplied by bubbling nitrogen through approximately 350 mL liquid HMDSO in a 500 mL glass flask. The SiO\textsubscript{2} amount was kept constant in the product particles and was calculated at saturation conditions\textsuperscript{22} (bubbler temperature 10 °C and 0.5 L/min N\textsubscript{2}) corresponding to 23 wt\% for pure Fe\textsubscript{2}O\textsubscript{3} core particles\textsuperscript{13} (SiO\textsubscript{2} wt\% = \( m_{SiO2}/(m_{SiO2} + m_{Fe2O3}) \)). Silica-coated pure core Ag or Fe\textsubscript{2}O\textsubscript{3} particles were made at identical conditions in the absence, however, of the corresponding precursor (Fe or Ag precursor, respectively).

**Particle Characterization.** High-resolution transmission electron microscopy (HRTEM) and scanning transmission electron microscopy (STEM) was performed on a Tecnai F30 (FEI; field emission gun, operated at 300 kV). The STEM images were recorded with a high-angle annular dark field (HAADF) detector revealing the Ag nanoparticles with bright Z contrast. Product particles were dispersed in ethanol and monitored them under dark-field illumination.

The release of Ag\textsuperscript{+} ions was measured by monitoring the Ag\textsuperscript{+} ion concentration of aqueous suspensions containing the composite particles.\textsuperscript{23} Particles were dispersed by ultrasonication (Sonics vibra-cell, 5 min at 75\% amplitude with a pulse configuration on/off of 0.2s/0.2s) in deionized water (Milli-Q) and their Ag\textsuperscript{+} ion concentration was monitored with an ion selective electrode and an ion meter (Metrohm, 867 module).\textsuperscript{18} The measurements were calibrated using silver containing aqueous solution (silver standard, Aldrich) with a calibration slope of 59.3 mV/log [Ag\textsuperscript{+}]. Diffusive gradients in thin film (DGT) measurements were performed and the Ag concentration was measured with an ICP-MS.\textsuperscript{18} The optical properties of the composite particles were measured with UV/vis spectroscopy (Cary Varian 500) of their aqueous suspensions. Particles were dispersed in deionized water and in phosphate PBS solution by ultrasonication (Sonics vibra cell, 5 min, power 50\%, pulse on/off 0.2 s/0.2 s). Size distributions of particles in aqueous and PBS solutions and \( \zeta \)-potential measurements of aqueous suspensions\textsuperscript{24} were obtained by dynamic light scattering (DLS, Zetavizer, Malvern Instruments). Magnetic measurements were made on a Princeton Measurements Corporation vibrating sample magnetometer (VSM).

**Biocompatibility of the Hybrid Biomarkers.** The cytotoxicity of uncoated and SiO\textsubscript{2}-coated 35Ag/Fe\textsubscript{2}O\textsubscript{3} nanoparticles was investigated with the human cell line HeLa. The cell viability was monitored by using the LIVE/DEAD fixable dead cell stain kit (Invitrogen) and flow cytometry (~5000 cells counted).\textsuperscript{25} Suspensions of nanoparticles in PBS were prepared by ultrasonication as above and added on HeLa cells (2 × 10\textsuperscript{5} cells at a volume ratio of 1:1). The following three incubation conditions were examined: with composite Ag/Fe\textsubscript{2}O\textsubscript{3} particle concentration of 5 mg/L (Ag concentration of 1.45 mg/L) (i) at 4 °C for 1 h (identical to the conditions during particle binding with cells for bioimaging) and at Ag concentrations of 5, 2.5, 1.25, and 0.625 mg/L incubated at 37 °C for (ii) 1 and (iii) 24 h. As a negative control to assess viability, pure PBS was added instead of the particle suspension. Staurorospin (20 \( \mu \)M, Sigma) was used as a positive control. This drug induces strong cytotoxicity and consequently apoptosis, leading to cell death. Error bars correspond to the standard deviation of three measurements.

**Bioimaging.** For bioimaging, 5 mg/L SiO\textsubscript{2}-coated 35Ag/Fe\textsubscript{2}O\textsubscript{3} nanoparticles were dispersed by ultrasonication as above in sterile PBS. Purified mouse monoclonal antibody against hDC-SIGN (MAB1621, R&D Systems) was reconstituted in water with a concentration 1 mg/mL. One-hundred microliters of this antibody-containing solution were added in 5 mL of the particle suspension for surface biofunctionalization. After its incubation for 1 h at room temperature, the biofunctionalized particles were washed with PBS three times. HeLa and Raji cells expressing or not the protein hDC-SIGN were washed three times with PBS. The biofunctionalized particles were added to cells (2 × 10\textsuperscript{5} and 5 × 10\textsuperscript{5} cells for HeLa and Raji cells, respectively) in a 1:1 ratio (v/v) reaching a final volume of 2 mL and then incubated for 1 h at 4 °C. As controls, cells which do not express hDC-SIGN were incubated\textsuperscript{26} at 4 °C in the presence or absence of biofunctionalized particles. The optical detection was performed with a microscope equipped with a dark-field condenser (Olympus MM) and a black-and-white CCD camera. The biofunctionalization was verified by monitoring the shift of the plasmon absorption band of the nanosilver\textsuperscript{14} with a UV/vis spectrometer (Varian Cary 500).

\section*{RESULTS AND DISCUSSION}

**Morphology.** Uncoated and SiO\textsubscript{2}-coated \( x\text{Ag/Fe}_{2}\text{O}_{3} \) nanoparticles were made with varying Ag-content \( x \) (wt \%). Figure 1a shows a STEM image of uncoated 50Ag/Fe\textsubscript{2}O\textsubscript{3}. There are Ag nanoparticles (bright spots) attached onto Fe\textsubscript{2}O\textsubscript{3} particles (gray) forming dumbbell- or Janus-like particles. Figure 1b shows a TEM image of SiO\textsubscript{2}-coated 10Ag/Fe\textsubscript{2}O\textsubscript{3} nanoparticles where Ag particles (dark spots) are attached on the Fe\textsubscript{2}O\textsubscript{3} particles (gray)
as in Figure 1a, but there is an amorphous (light gray) SiO₂ shell or film encapsulating the core Ag/Fe₂O₃ particles. Figure 1c shows this more clearly with an image of a SiO₂-coated 35Ag/Fe₂O₃ nanoparticle at higher magnification. The iron oxide and the silver particles are completely coated by a smooth, amorphous SiO₂ shell or film of a couple nm thickness.¹³ All STEM and TEM images indicate that there is no significant trace of individual or separate Ag or Fe₂O₃ particles, a prerequisite for their bioapplication. The average crystal size of the γ-Fe₂O₃ is approximately 15 nm and independent of the presence of Ag or SiO₂, even though there is a small presence of α-Fe₂O₃ within the samples.¹³ The α-Fe₂O₃ content was slightly increased at Ag-content x = 50 wt %. This could be attributed to the higher combustion enthalpy of the employed precursor solutions for the largest Ag-content, and thus higher temperatures within the enclosed flame aerosol reactor.¹³ The average Ag crystal size increases with increasing Ag-content²³ (from ~10 nm for the 20Ag/Fe₂O₃ to ~20 nm for the 50Ag/Fe₂O₃) and was also rather independent from the presence of the SiO₂ shell.

**Magnetic and Plasmonic performance.** Figure 2a shows the magnetization of all SiO₂-coated particles normalized to their Fe₂O₃ mass at various Ag-contents x at room temperature. All particles show some hysteresis, which indicates that are magnetically blocked during the measurement. The coercive force, however, is very low (inset of Figure 2a) while the SiO₂-coating does not influence¹³ their magnetic properties. The highest magnetization (Ms = 39.4–46.1 emu/g) of the lower Ag-content particles (x = 6–35 wt %) is similar to pure Fe₂O₃ core (38.4 emu/g). These Ms values are lower than that of bulk γ-Fe₂O₃ (63.6 emu/g),²⁷ as smaller crystallites¹³ are employed here that contain²⁷ α-Fe₂O₃.

Figure 3a shows the UV/vis absorbance of the SiO₂-coated hybrid particles for x = 10 (purple), 20 (yellow) 35 (green) and 50 wt % (blue) here in aqueous suspensions before (B = 0, solid lines) and after application (B > 0, broken lines) of an external magnetic field by a permanent Ni–Cu–Ni magnet (inset). At B = 0 for the 10Ag/Fe₂O₃ (purple line) the Ag-content is rather low and the Ag-metal plasmon absorption band is not distinguishable as the spectrum is dominated by the Fe₂O₃ absorption. However, for an increasing Ag-content x > 10 wt % the Ag plasmon band clearly emerges²⁰ at ~400 nm. This indicates that the optical properties of Ag nanoparticles are not influenced²⁰ by the presence of Fe₂O₃ nor SiO₂. At B > 0, however, all absorption spectra (from Fe₂O₃ and Ag) disappeared completely and the suspension is transparent, since all particles have been attracted to the cuvette bottom (Figure 3a, inset) by the magnet. This further verifies that there are no individual Ag nanoparticles present in the as-prepared sample, but only composite Ag/Fe₂O₃.
remained dispersed in solution (Figure 3b, inset, B > 0) exhibiting the characteristic yellowish color that is attributed to that nanosilver size\textsuperscript{14} and concentration.

**Stability in Aqueous Suspensions and Buffer Solutions.** When multifunctional (hybrid) nanoparticles are employed in bioimaging, they have to be stable in solution. Figure 4 shows the hydrodynamic size distributions of the SiO\textsubscript{2}-coated (a) and uncoated (b) 35Ag/Fe\textsubscript{2}O\textsubscript{3} particles in water (solid lines) and in PBS (broken lines) immediately after their dispersion (t = 0 h). The SiO\textsubscript{2}-coated particles (a) have quite a low degree of agglomeration in both water and PBS (d\textsubscript{h} = 50–500 nm). The uncoated samples (b), however, have a bimodal distribution and much larger agglomerate diameters (500–7000 nm), reaching the limit of the particle size measurement. That is attributed to the absence of SiO\textsubscript{2} which acts as an antiflocculation agent,\textsuperscript{14} as the SiO\textsubscript{2}-coated particles are stable when dispersed in water and PBS (Figure 4c). In contrast, the formation of the larger agglomerates of uncoated particles results in their sedimentation within both aqueous and PBS suspensions (after 2 h) as seen in Figure 4d.

This stability is especially desired for bioapplications otherwise the resulting agglomerates (flocs) would be similarly sized to the target biological systems (e.g., Raji or HeLa cells) prohibiting their use for cell imaging. Additionally, these silica-coated particles are hydrophilic\textsuperscript{22} as-prepared and therefore readily dispersible without requiring an extra functionalization step. The exhibited stability of the SiO\textsubscript{2}-coated hybrid nanoparticles is further verified by \(\zeta\)-potential measurements in water. For all Ag-contents \((x = 0–50 \text{ wt%})\) the \(\zeta\)-potential of the SiO\textsubscript{2}-coated particles varies from \(-42\) to \(-48 mV\), in agreement with other SiO\textsubscript{2}-coated nanoparticles made by flame\textsuperscript{20} or wet chemistry.\textsuperscript{26} For the uncoated Ag/Fe\textsubscript{2}O\textsubscript{3} particles, the \(\zeta\)-potential lies from \(-0.5\) to \(-5.0\ mV\), also in agreement with those of wet-made Fe\textsubscript{2}O\textsubscript{3} or Ag\textsuperscript{31} nanoparticles.

**Biocompatibility of SiO\textsubscript{2}-Coated Hybrid Plasmonic-Magnetic Biomarkers.** To evaluate the effect of the SiO\textsubscript{2} shell or film on the core Ag/Fe\textsubscript{2}O\textsubscript{3} particles on the Ag\textsuperscript{+} ion release (leaching), the Ag\textsuperscript{+} ion concentration, [Ag\textsuperscript{+}] (Figure 5a), was monitored in aqueous suspensions of silica-coated and uncoated Ag/Fe\textsubscript{2}O\textsubscript{3} by ion selective electrode (ISE, open symbols)\textsuperscript{23} and diffusive gradients in thin film (DGT, filled symbols)\textsuperscript{18} measurements. Figure 5a shows this [Ag\textsuperscript{+}] as a function of Ag-content \(x\) (in the \(x\text{Ag/Fe}_{2}O_{3}\) particles) for the uncoated (triangles) and SiO\textsubscript{2}-coated (circles) particles, for an equal Ag mass concentration of 50 mg/L. The [Ag\textsuperscript{+}] was attained immediately upon dispersion and was constant over a period of, at least, 24 h.\textsuperscript{25} The value obtained when deionized water was measured by ISE are also shown (gray broken line). There was a good agreement between ISE and DGT for the uncoated 35Ag/Fe\textsubscript{2}O\textsubscript{3}: the silver mass dissolved as silver ions was 7 ± 1.7% by ISE and 8.6 ± 0.5% by DGT. For the SiO\textsubscript{2}-coated there was a small difference, the mass dissolved as silver ions for lower Ag-content \(x\text{Ag/Fe}_{2}O_{3}\) nanoparticles\textsuperscript{23} that contain smaller Ag nanoparticles. As the Ag-content \(x\) increases, Ag nanoparticles grow bigger releasing less Ag\textsuperscript{+} ions\textsuperscript{25} from their surface. Silica-coated \(x\text{Ag/Fe}_{2}O_{3}\) release much less [Ag\textsuperscript{+}] especially for the fine Ag nanoparticles \((d_{h} < 20 \text{ nm at } x = 6–50 \text{ wt%})\). As the Ag-content \(x\) increases, a minimal Ag\textsuperscript{+} ion release for \(x = 50 \text{ wt%}\) occurs, which is comparable to the SiO\textsubscript{2}-coated Ag/Fe\textsubscript{2}O\textsubscript{3} nanoparticles. Nevertheless, the uncoated 50Ag/Fe\textsubscript{2}O\textsubscript{3} particles
have the lowest magnetization and poor stability in aqueous suspensions (Figure 4d). For the lower Ag content $x$ (6–35 wt %), however, the inert silica shell minimizes nanosilver leaching significantly, but not completely. Few Janus-like particles have been partially coated by incomplete mixing of HMDSO vapor with the core Ag/Fe$_2$O$_3$ nanoparticles.

To assess the cytotoxicity and biocompatibility of these particles as biomarkers, we incubated them for 24 h at 37 °C with HeLa cells. Figure 5b shows the fraction of dead HeLa cells for different biomarker particle concentrations (5, 2.5, 1.25, and 0.625 mg/L Ag), as well as for the positive and negative controls. In the absence of toxic agents (negative control), there is no significant fraction of apoptotic cells (only the standard, $\sim 10\%$). The SiO$_2$-coated hybrid biomarkers did not induce any toxicity for this incubation period (24 h), further indicating their biocompatibility with HeLa cells. The toxicity evaluation of the uncoated plasmonic-magnetic nanoparticles was not possible, as these particles formed large agglomerates and settled quite fast (Figure 4d), thus not giving reliable toxicity results. This emphasizes the limitations of toxicological tests of agglomerated nanoparticles, as their sedimentation inhibits their correct evaluation. It should be noted that for incubation conditions of 1 h at 4 and 37 °C with the SiO$_2$-coated Ag/Fe$_2$O$_3$ nanoparticles, similar results were obtained and no apoptotic cells were detected (not shown).

**Bioimaging.** The potential of these multifunctional nanoparticles as biomarkers is explored by selectively binding them on tagged living cells. So the surface of SiO$_2$-coated 35Ag/Fe$_2$O$_3$ nanoparticles was labeled (biofunctionalized) with an antibody against the human form of DC-SIGN (hDC-SIGN). Figure 6a shows a shift $\Delta\lambda \approx 10$ nm of the Ag metal normalized plasmon absorption band of these particles after antibody adsorption on their surface. The higher refractive index of the antibody over that of PBS causes a red shift of the Ag plasmon absorption band. This shift remains even after washing the nanoparticles with PBS, excluding thus the effect of medium change.

Figure 6b shows a dark-field image of Raji cells that do not express hDC-SIGN on their surface (untagged Raji cells) in the absence of labeled particles. The characteristic scattering from the cell membrane as well as from intracellular components can be barely observed. With the exception of very few residual scatterings, probably originating from unwashed labeled particles, identical results were obtained when such cells were incubated with labeled particles (Figure 6c). This suggests that

![Figure 4](image-url)
the SiO₂-coated 35Ag/Fe₂O₃ particles labeled with the antibody against hDC-SIGN do not unspecifically bind to the cell surface.

In contrast, when Raji cells, that express hDC-SIGN on their surface (tagged cells), are incubated with the labeled particles, it can be seen that the surface of the cells is completely covered by the present hybrid particles (Figure 6d) that strongly scatter light and appear very bright (Ag) under dark-field-illumination. This indicates that by labeling the surface of these nanoparticles with an antibody, they can specifically bind to cells that express the corresponding ligand biomolecule. Additionally, the magnetic manipulation of such cells was possible in the presence of an external magnetic field (permanent magnet, not shown).

These biofunctionalized biomarkers were also used with human HeLa cells that also express the hDC-SIGN. Similarly to the Raji cells, untagged HeLa cells show limited scattering (Figure 6e). When, however, cells that express on their surface the hDC-SIGN are incubated with particles labeled with antibodies against DC-SIGN (Figure 6f), there is a strong scattering originating from the plasmonic silver, and enabling their detailed imaging and fast detection.

**CONCLUSIONS**

Hybrid, Janus- or dumbbell-like Ag/Fe₂O₃ nanoparticles are made and coated with a nanothin SiO₂ shell or film by one-step, scalable flame aerosol technology. These “as-prepared” nanoparticles were dispersible in aqueous and buffer solutions without any surface treatment. The plasmon absorption band of Ag appeared clearly for an increasing Ag content and size, and the near superparamagnetic Fe₂O₃ component allowed for the
magnetic manipulation of the Ag/Fe₂O₃ nanoparticles in aqueous suspensions. The SiO₂ coating reduced drastically the release of Ag⁺ ions when nanoparticles were dispersed in aqueous suspensions, essentially “curing” their cytotoxicity and enabling them as biocompatible multifunctional probes for bioimaging. Their agglomeration (floculation) in aqueous suspensions was minimized by SiO₂ coating, in contrast to uncoated Ag/Fe₂O₃ particles which flocculated and settled within few hours.

The potential of these superior hybrid plasmonic-magnetic nanoparticles as bioprobes was explored by successfully labeling their surface and specifically binding them on the membrane of tagged Raji and HeLa cells. Their detection under dark-field illumination was achieved. The hybrid nanocomposite SiO₂-coated Ag/Fe₂O₃ particles prevented the individual limitations of Fe₂O₃ (poor particle stability in suspensions) and of Ag (toxicity) nanoparticles, while retaining the desired magnetic properties of Fe₂O₃, the inert surface of SiO₂ and the plasmonic optical properties of Ag at the nanoscale.

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