

In situ reduction of Ag on magnetic nanoparticles with gallic acid: effect of the synthesis parameters on morphology

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1 ***In situ* reduction of Ag on magnetic nanoparticles with gallic acid: effect of the**
2 **synthesis parameters on morphology**

3
4 **Abstract**

5 Fe₃O₄—Ag composite nanoparticles (NPs) were prepared by a new *in situ* reduction of
6 Ag on the surface of Fe₃O₄ NPs using gallic acid as reducing agent in different NPs/gallic
7 acid ratio. The obtained NPs were characterized by Field-Emission Scanning/Scanning
8 Transmission Electron Microscopy and Fourier-transform infrared spectroscopy in order
9 to evaluate their crystal structure, their morphology, the effective functionalization and
10 the presence of Ag. Different morphologies were obtained: polydispersed aggregates,
11 nanoflower-like and nanodumbbell nanocomposites, depending on the synthesis
12 conditions. Well-defined Fe₃O₄-Ag nanodumbbells were obtained in aqueous media, with
13 NPs/gallic acid ratio of 10:1. It was also assessed that silica shell is not a key issue to
14 optimize the morphology of Ag NPs nucleated on the Fe₃O₄ core.

15
16 **Structured Abstract**

17 **Aim:** Synthesis of Fe₃O₄—Ag composite nanoparticles by a new *in situ* reduction of Ag
18 NPs on the surface of Fe₃O₄ NPs using gallic acid as reducing agent.

19 **Materials & Methods:** The influence of process parameters on NPs morphology and
20 functionalization was evaluated by means Field-Emission Scanning/Scanning
21 Transmission Electron Microscopy and Fourier-transform infrared spectroscopy.

22 **Results and Conclusions:** The synthesis conditions affect the morphology of the
23 obtained nanoparticles, evidencing the formation of polydispersed aggregates,
24 nanoflower-like or nanodumbbell nanocomposites. In particular, well-defined

25 nanodumbbells were obtained in aqueous media, with NPs/gallic acid ratio of 10:1; while
26 the presence of a silica shell did not improve the morphology of Ag NPs nucleated on the
27 Fe₃O₄ core.

28

29 **Lay abstract:**

30 Nanoparticles (NPs) are extensively investigated in the biomedical field for the diagnosis
31 and the treatment of tumors. The aim of this work is to develop a simple and green method
32 to produce composite nanoparticles, formed by iron oxides (magnetic) and silver NPs.

33 Magnetic NPs can be moved using an external magnetic field and localized in the tumor;
34 silver NPs can generate useful heat to kill tumor cells when exposed to light and possess
35 antibacterial properties. The performed study showed that by varying the process
36 parameters (e.g. amount of reagents, presence of coatings on the particles ...), it is possible
37 to obtain multifunctional NPs with different shapes and sizes, potentially useful for the
38 treatment of tumors.

39

40 **Keywords**

41 Magnetic nanoparticles, silver nanoparticles, *in situ* reduction, gallic acid.

42

43 **Introduction**

44 Magnetic nanoparticles (MNPs) are one of main objects of study in the current literature
45 concerning nanotechnology [1, 2]. MNPs are often suggested in biomedical applications
46 as drug carriers due to their ability, when exposed to an external magnetic field, to be
47 moved purposely to a target site in the human body. Most of the MNPs described in
48 literature are composed of iron oxide (mainly Fe₃O₄ or γ-Fe₂O₃) often used as magnetic

49 cores enclosed into an organic or inorganic shell (such as silica, gold, fatty acid, citric
50 acid and others) [3-5]. Iron oxide MNPs are among the most appropriate nanoplatforms
51 for biomedical applications due to their chemical stability, superparamagnetism,
52 biocompatibility, easiness of synthesis and since they can be further functionalized with
53 molecules of particular interest, such as anticancer drug or specific bioactive molecules
54 [3-5]. Iron oxide MNPs are used as contrast agents in magnetic resonance imaging
55 (MRI), drug delivery systems [6, 7] and deeply investigated for applications in the field
56 of cancer treatment by hyperthermia [2, 8, 9].

57 The decoration of the magnetic core with ultra-small metal nanoparticles can further
58 enhance the variety of potential applications of this versatile category of nanoplatform in
59 biomedical field, merging the magnetic properties of the core with the peculiar properties
60 of metal nanoparticles [10, 11].

61 For example, silver nanoparticles are of great interest because they exhibit peculiar
62 functionalities, such as, among others, antimicrobial, antiviral, optical and catalytic
63 properties [12-15]. Their chemical stability, biocompatibility and long-term efficacy
64 toward a broad bacterial spectrum make them suitable in many biomedical applications
65 as targeted tool for *in situ* infection treatment [16].

66 Besides the well-known antimicrobial activity [14, 17, 18], silver nanoparticles are of
67 great interest in the field of surface-enhanced Raman spectroscopy [19] and photothermal
68 cancer therapy [20]. Silver nanoparticles exhibit strong absorption band at about 400 nm.
69 The position of the absorption band can vary depending on the size and shape of silver
70 nanoparticles.

71 Magnetic iron oxide nanoparticles and silver nanoparticles can be combined into
72 nanocomposite platforms implementing the above mentioned properties [6]. For example,

73 the decoration of Fe₃O₄ nanoparticles with Ag nanoparticles gives rise to enhanced optical
74 responses [21]. Moreover, the combination of magnetic (Fe₃O₄) and antibacterial (Ag)
75 properties, can be exploited for the magnetic targeting and removal of antimicrobial
76 agent.

77 Since magnetic nanoparticles are very sensitive to agglomeration, many methods have
78 been investigated in literature to impart electrostatic or steric repulsion, such as the
79 coating with organic (e.g. surfactants, polymers) or inorganic materials (e.g. silica, metal
80 oxides, metals) [22, 23]. Moreover, MNPs have been decorated with noble metals NPs,
81 especially Au NPs, by using different approaches [24]. One of the proposed methods to
82 decorate MNPs with metallic NPs is to cover the magnetic NPs with a silica layer, which
83 can be easily functionalized and acts as intermediate layer between the magnetic core and
84 the metallic NPs [25]. Noble metal NPs can be also directly attached to the magnetic core
85 using silanes or coupling and reducing agents such as NaBH₄, hydroxylamine, plant
86 extracts, or by the metal NPs adsorption on magnetic NPs surface [11, 24, 26-30].

87 In the present work we report a new method to prepare Fe₃O₄—Ag composite
88 nanoparticles by *in situ* reduction of Ag on a magnetic core of Fe₃O₄, focusing the
89 attention on the effect of process parameters (synthesis media and functionalization steps)
90 on the nanoparticles nucleation and morphology. In particular, Gallic Acid (GA) has been
91 used for the first time, on the basis of authors knowledge, as *in situ* reducing agent for Ag
92 nanoparticles directly on Fe₃O₄ NPs' surface. GA has been chosen for its above
93 mentioned double action, as well as for its intrinsic anti-inflammatory and anti-tumor
94 action, and for its potential sustainability, due to the possibility to be extracted from
95 vegetal wastes coming from the food production chains [31]. The obtained composite
96 NPs, due to both the magnetic properties of Fe₃O₄ and the optical/antibacterial properties

97 of Ag NPs, can be a useful tool for targeting bacterial infection as well as for treating
98 tumor and associated complications.

99

100 **2. Experimental**

101 Each experimental step is described in the following paragraphs. All reactants were
102 purchased from Sigma Aldrich[®]/Merck.

103

104 **2.1 Synthesis of CA stabilized MNPs**

105 The synthesis of Fe₃O₄ NPs (Magnetite-based - M NPs) was carried out by co-
106 precipitation [32-34]. As reported also in [10, 11], M NPs were synthesized by mixing
107 aqueous solution of Fe²⁺ and Fe³⁺ salts in alkaline conditions for ammonium hydroxide
108 NH₄OH (Merck, 25% aqueous solution) [5]. Two solutions 0.1 M of ferrous chloride
109 FeCl₂ · 4 H₂O and ferric chloride FeCl₃ · 6H₂O (Sigma Aldrich, > 99%) were prepared
110 separately by dissolving the required quantities of FeCl₂ · 4H₂O and FeCl₃ · 6H₂O in 100
111 ml of bi-distilled water, magnetically stirred in two distinct beakers. The pH was around
112 3 for the ferrous chloride solution, and around 2 for the ferric chloride solution. After the
113 complete dissolution of the salts, 50 ml of 0.1M FeCl₃ · 6H₂O and 37.5 ml of the 0.1M
114 FeCl₂ · 4H₂O were mixed in a beaker, reaching a pH value around 1.7.

115 The pH was then adjusted to about 10 by adding NH₄OH dropwise to the iron salts
116 solution, under continuous mechanical stirring: the mixture turned to black, due to the
117 formation of a suspension of iron oxide NPs (M NPs).

118 The as obtained suspension was then sonicated for 20 minutes and washed in bi-distilled
119 water, using a magnet to induce sedimentation. The as obtained M NPs were finally re-
120 suspended in 100 ml of bi-distilled water reaching a pH between 7-8.

121 Aiming to improve the MNPs suspension stability, the synthesis was followed by the M
122 NPs stabilization with Citric Acid (CA) [32, 33]. 120 ml of a 0.05 M of CA (Sigma
123 Aldrich, > 99.5%) solution were added to the M NPs, previously separated by
124 sedimentation, adjusting the pH to a value of 5.2 by adding dropwise a concentrated
125 NH₄OH solution. The new suspension was then heated to 80 °C and stirred (150 rpm) for
126 90 minutes. The duration of the heating step was optimized in order to promote the CA
127 adsorption on the M NPs while minimizing the magnetite decomposition to maghemite.
128 Finally, the CA-capped MNPs were rinsed by means of an ultrafiltration device (Solvent
129 Resistant Stirred Cells - Merck Millipore)(4 steps in 50 ml of bi-distilled water at pH =
130 10.2) and suspended in 120 ml of bi-distilled water, adjusting the pH of the final water
131 suspension to 10.2 with diluted ammonia.

132

133 **2.2 Silica coating on MNPs**

134 A part of CA-capped MNPs was coated with a silica shell following the Stöber method
135 [34] by suspending them in a mixture of Tetraethyl orthosilicate (TEOS) as silica
136 precursor, ethanol and water (ethanol:water volume ratio of 4:1), under stirring in orbital
137 shaker at 37 °C and 150 rpm for 3 hours. Approximately 0.002 ml of TEOS for each mg
138 of magnetic nanoparticles was used. Then, the obtained MS NPs were double-washed
139 with bi-distilled water using an ultrafiltration device and re-dispersed in water.

140

141 **2.3 Functionalization with aminopropyltriethoxysilane (APTES)**

142 To enhance the interaction between Ag NPs and magnetic NPs, terminal -NH₂ groups
143 were introduced on the surface of both M NPs (route A) and MS NPs (route B) by means
144 of functionalization with APTES (> 98%, Merck).

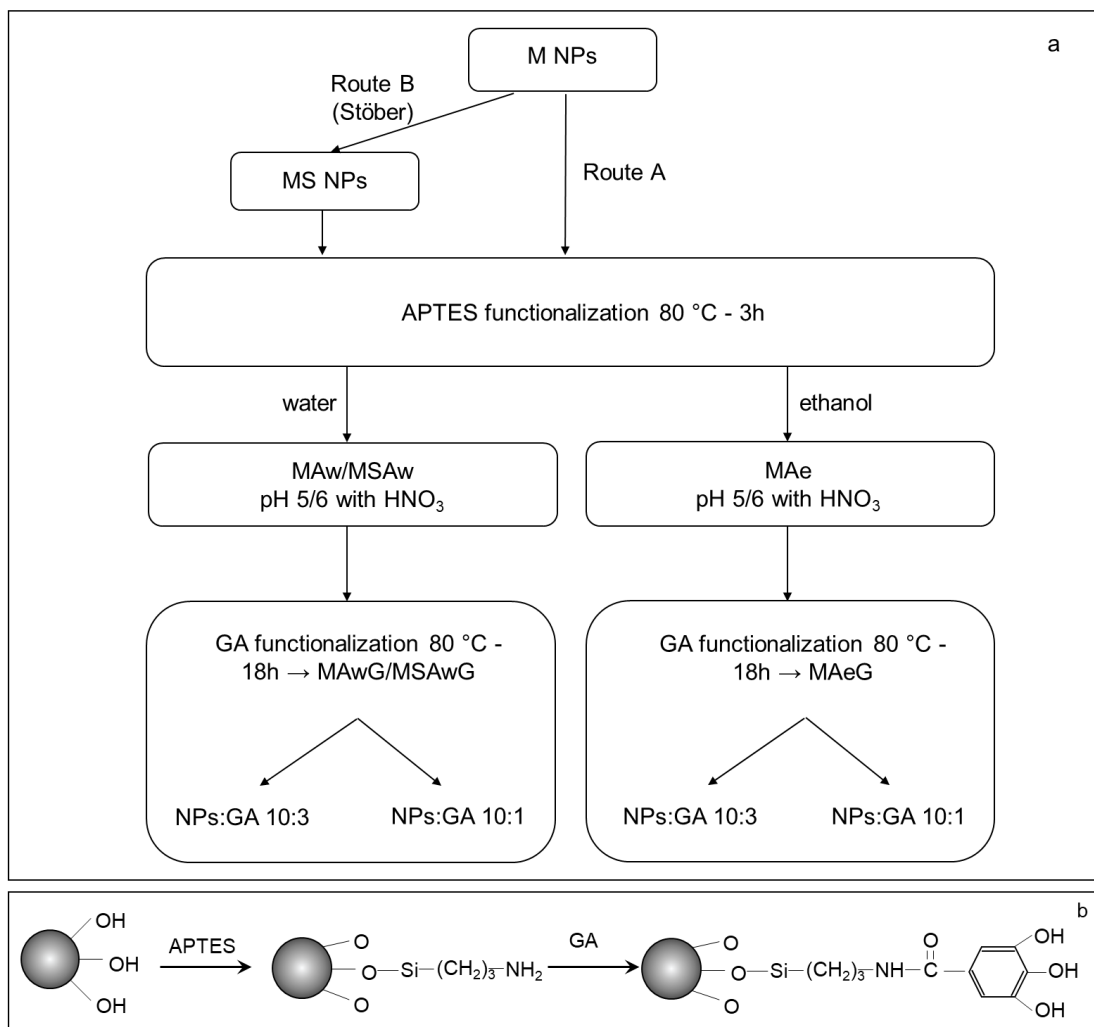
145 The functionalization with APTES on the M NPs was performed including a final step of
146 washing and re-suspension in two different media (ethylic alcohol or water) in order to
147 verify the role of the medium on GA grafting and, in turn, on the nucleation of Ag NPs.
148 MS NPs were resuspended only in water.
149 For this step, 3 ml of each magnetic NPs suspension were diluted in 50 ml of absolute
150 ethanol (anhydrous, >99.9%, Carlo Erba Reagents) and sonicated for 3 minutes. 10 μ l of
151 APTES were then added to the resulting colloidal suspensions. The obtained suspensions
152 were then heated at 80 °C under mechanical stirring for three hours. The stirring time has
153 been prolonged respect to the conventional synthesis reported in literature, to enhance the
154 APTES grafting and assure a uniform presence of terminal amine group on the magnetic
155 nanoparticles surface, as reported in previous works [10, 11, 35]. Subsequently, the
156 mixtures were cooled at room temperature, the nanoparticles were magnetically separated
157 and centrifuged (7500 rpm /20 minutes) for three times, washed in distilled water and re-
158 suspended in water or ethanol (M NPs) or only in water (MS NPs) up to a volume of 50
159 ml. To induce positive charge at the surface of the APTES-coated nanoparticles, a diluted
160 HNO₃ solution (0.05 ml of 6 M HNO₃ with 20 ml of water) was added drop by drop until
161 reaching a pH value \approx 5-6, and stirred for 10 minutes.

162

163 **2.4 Functionalization with GA**

164 Gallic acid (GA) was added to both ethanol and water-based M NPs suspensions using
165 two different NPs/GA weight ratio (10:3 and 10:1) [37] and to water-based MS NPs
166 suspension using a NPs/GA weight ratio of 10:1. The mixtures were stirred for 18 h at 80
167 °C, at the end of the treatment the NPs dispersed in ethanol were washed and centrifuged

168 three times with ethanol and re-suspended in ethanol; the same procedure was adopted
 169 for NPs dispersed in water, using bi-distilled water as washing and dispersion medium.
 170 Figure 1 resumes the steps of the functionalization process.



171

172 **Figure 1:** functionalization process (a) and scheme (b) of MAwG and MAeG synthesis.

173

174 2.5 Synthesis of Fe₃O₄—Ag composite nanoparticles

175 The reduction of Ag NPs was performed both for ethanol and water dispersed M NPs and
 176 MS NPs, using a AgNO₃/GA weight ratio of 1.7. AgNO₃ was dissolved in water and
 177 mixed with the NPs suspension at 37 °C for 15 minutes at 150 rpm; the pH of the mixture
 178 was adjusted to about 11 using NH₄OH. At the end of the synthesis the mixture was

179 washed with bi-distilled water, NPs were magnetically separated and re-dispersed in bi-
 180 distilled water for further analysis.

181 Table 1 reports the acronyms of the obtained NPs and resume their synthesis steps.

	Magnetite	Silica shell	Synthesis in water (w) or ethanol (e)	APTES	Gallic acid (GA)	Silver
M	✓					
MAw	✓		w	✓		
MAe	✓		e	✓		
MAwG	✓		w	✓	✓	
MAeG	✓		e	✓	✓	
MAwGAg	✓		w	✓	✓	✓
MAeGAg	✓		e	✓	✓	✓
MS	✓	✓				
MSAw	✓	✓	w	✓		
MSAwG	✓	✓	w	✓	✓	
MSAwGAg	✓	✓	w	✓	✓	✓

182

183 **Table 1:** acronyms and resume of NPs synthesis steps.

184

185 **2.6 Characterization**

186 The structural characterization of M NPs was carried out by means of wide-angle (2θ
 187 within 10-70°) X-ray diffraction analysis (XRD – X’Pert Philips diffractometer) using
 188 the Bragg Brentano camera geometry and CuKα incident radiation. The identification of

189 crystalline phases was performed by using X'Pert HighScore program equipped with
190 PCPDFWIN database.

191 To evaluate the effective functionalization with APTES and GA, all NPs before the *in*
192 *situ* reduction of silver were analyzed by means of Fourier-transform infrared
193 spectroscopy (FTIR Tensor 27, Bruker Optics S.p.A, Ettlingen, Germany) from 4500 to
194 300 cm⁻¹ and with 2 cm⁻¹ resolution. OPUS software (v. 6.5, Bruker S.p.A) was used for
195 instrumental control and spectral acquisition.

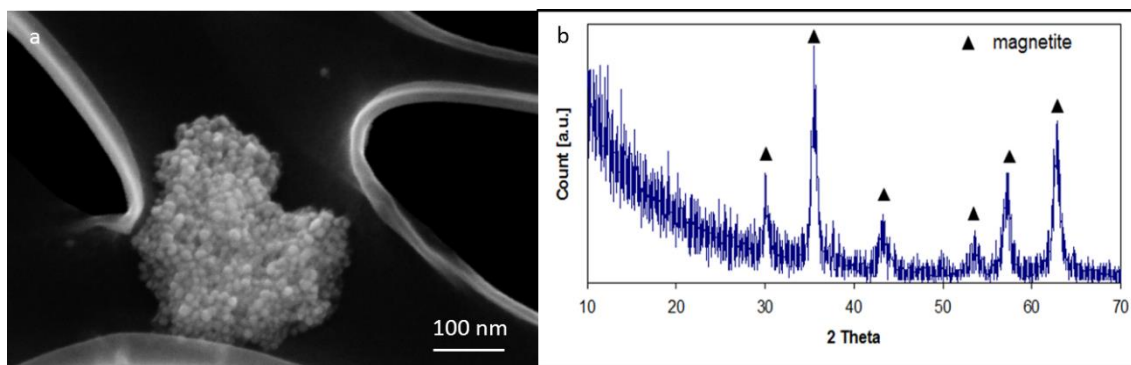
196 In order to investigate the NPs functionalization after each synthesis step, the formation
197 of Ag NPs and their dimension and distribution, all nanoparticles were characterized in
198 terms of morphology and composition by means of FESEM (Field-Emission Scanning
199 Electron Microscope - SUPRATM 40, Zeiss, Germany) and STEM (Scanning
200 Transmission Electron Microscopy - Merlin Gemini Zeiss, Germany), equipped with
201 Energy Dispersive Spectroscopy (EDS). For STEM observation a drop of each NPs
202 suspension was placed on a copper grid with carbon film (SPI Supplies® Brand Lacey
203 Carbon Coated 200 Mesh Copper Grids – JEOL S.p.A.). STEM analyses were carried out
204 using different detectors and signals (secondary and backscattered electrons, the Bright
205 Field - BF and Dark Field – DF) in order to better distinguish the metallic NPs.

206

207 **3. Results**

208 **3.1 Route A**

209 Morphological (FESEM) and phase (XRD) analyses of M NPs (Figure 2) revealed the
210 presence of NPs with spherical morphology and a diameter of about 5-20 nm. The XRD
211 pattern reports the presence of only magnetite/maghemite phase, in accordance with the
212 synthesis performed in air.



213

214 **Figure 2:** CA stabilized M NPs: a) morphological evaluation (FESEM), b) XRD
 215 analysis

216

217 Table 2 reports the peaks and bands identified by FTIR analysis of M NPs (stabilized with
 218 CA), MAw, MAwG, MAe and MAeG. Figure 3 shows as example the curves obtained
 219 for M, MAw and MAwG NPs/GA 10:3. As it can be noticed, M NPs spectrum shows the
 220 presence of Fe-O bond between 500-600 cm^{-1} typical of iron-oxide NPs [38], the
 221 asymmetric stretching of C-O from the COOH group of CA at 1310 cm^{-1} , the large peak
 222 between 1400 cm^{-1} and 1660 cm^{-1} can be assigned both to COO-Fe bonding (in literature
 223 1431 cm^{-1}) and to the shift of peak characteristic of symmetric vibration of C=O due to
 224 the CA interaction with magnetite; moreover a band at about 1700 cm^{-1} , relative to the
 225 C=O stretching vibration from the free COOH group of CA, is still visible. In the curve a
 226 band between 2600-2950 cm^{-1} ascribable to CH_2 stretching and a barely resolvable band
 227 at about 3300 cm^{-1} due to OH stretching are also observable [38-40]. The MAw NPs
 228 spectrum shows a shoulder at 850-950 cm^{-1} ascribable to the stretch of Si-OH symmetric
 229 vibration or Si-O-Fe bond, and two bands around 960 and 1000-1150 cm^{-1} belonging to
 230 the stretching of Si-O and Si-O-Si groups. The peaks at about 1330 and 1620 cm^{-1}
 231 relative to C-N and NH stretching vibrations respectively, the band between 2920-2850
 232 cm^{-1} ascribable to the stretching and vibration of C-H and the bands at 3445 and 1640 cm^{-1}

233 ¹, attributable to the N–H stretching vibration and NH₂ bending mode of free NH₂ groups
 234 [41-43], are hardly attributable due to the overlapping with CA peaks.

235 The functionalization with GA introduces three peaks between 1600-1200 cm⁻¹ ascribable
 236 to the C=C bond, a small peak at about 1700 cm⁻¹ relative to the C=O stretch of carboxylic
 237 group and a band centered at about 3400 cm⁻¹ relative to OH groups of GA [44, 45].

238 FTIR spectra of M, MAe and MAeG (obtained peaks reported in table 2) evidence a band
 239 between 400 and 500 cm⁻¹ ascribable to Fe-O bond and the peak at 1310 cm⁻¹ due to the
 240 asymmetric stretching of -CO from the COOH group, the peak probably due to both the
 241 COO-Fe bond and to the C=O of COOH group that interact with magnetite NPs, the C=O
 242 vibration from the free COOH group of CA at about 1700 cm⁻¹ [38, 40]. The
 243 functionalization with APTES is confirmed by the presence of a shoulder at about 970
 244 cm⁻¹ ascribable to Si-O stretching, a peak at about 1100 cm⁻¹ due to the Si-O-Si stretching
 245 and the shoulder at about 2870 cm⁻¹ is related to the stretching vibration C-H. Even if
 246 after the synthesis the NPs were washed, some characteristic peaks of ethanol (not
 247 reported in table 2) can be observed in the spectrum of MAe at about 1260-1000 cm⁻¹
 248 ascribable to the stretching of C-O and between 3400-3300 cm⁻¹ related to the OH
 249 stretching. Both the influence of the residual ethanol and the CA disturb the identification
 250 of the peaks relative to the C-N stretching vibration and, the free NH stretching vibration
 251 [41-43]. The spectrum of MAeG shows three peaks between 1600-1200 cm⁻¹ ascribable
 252 to the C=C bond and a very small peak at about 1700 cm⁻¹ relative to the C=O stretch of
 253 carboxylic group, the band at about 3400 cm⁻¹ relative to OH groups of GA in this case
 254 is poor visible [44, 45].

255

Assignment	Position (cm ⁻¹)	Remarks
------------	------------------------------	---------

Fe-O	500-600	Typical of iron-oxide NPs (M, MAw, MAwG, MAe, MAeG)
Si-OH, Si-O-Fe	850-950	A shoulder related to the stretch of Si-OH symmetric vibration or Si-O-Fe bond (MS, MSAw, MSAwG)
Si-O	960-970	A band due to the Si-O stretching (MAw, MAwG, MAe, MAeG)
Si-O-Si	1000-1150	A band belonging to the stretching of Si-O-Si groups (MAw, MAwG, MAe, MAeG)
C=C	1200-1600	A peak ascribable to the C=C bond (MAeG, MAeG)
C-O	1310	The asymmetric stretching of C-O from the COOH group of CA (M, MAw, MAwG, MAe, MAeG)
C-N	1330	The peak related to C-N stretching vibration (MAw, MAwG, MAe, MAeG)
COO-Fe, C=O	1400-1600	The large peak can be assigned both to COO-Fe bonding (in literature 1431 cm ⁻¹) and to the shift of peak characteristic of symmetric vibration of C=O due to the CA interaction with magnetite (M, MAw, MAwG, MAe, MAeG)
NH	1620	A broad band at 1628 cm ⁻¹ can be ascribed to the N-H stretching vibration (MAw, MAe)

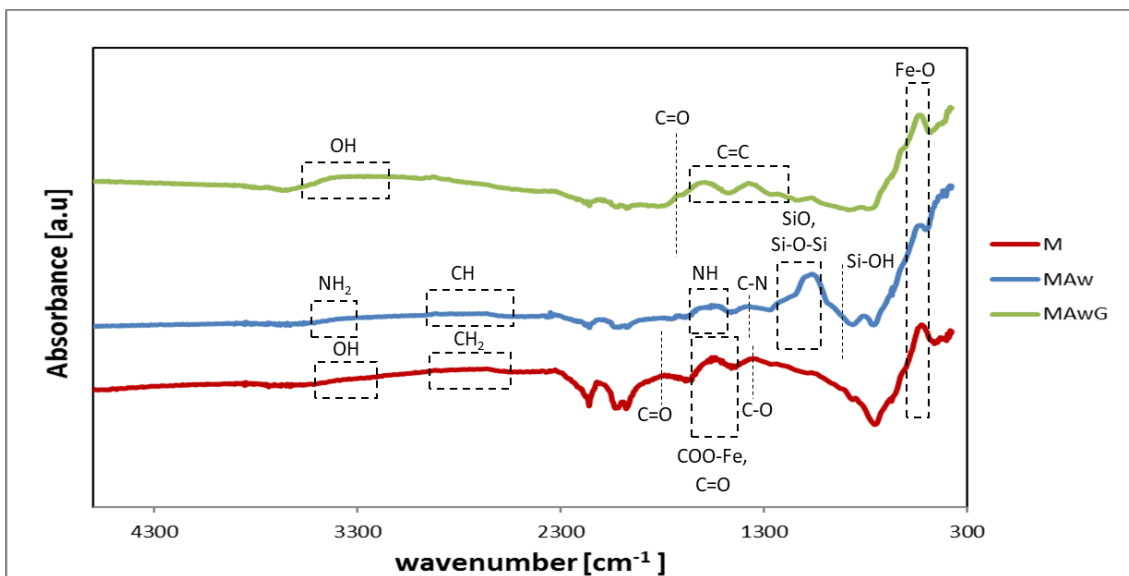
NH ₂	1640	The band attributable to NH ₂ bending mode of free NH ₂ groups (MAw, MAe)
C=O	1700	Stretching vibration from the free COOH group of CA (M, MAw, MAwG, MAe, MAeG)
C=O	1700	A small peak related to the C=O stretch of carboxylic group (MAwG, MAeG)
CH ₂	2600-2950	A band ascribable to CH ₂ stretching (M, MAw, MAwG, MAe, MAeG)
C-H	2850-2920	The band ascribable to the stretching and vibration of C-H (MAw, MAeG, MAe, MAeG)
OH	3300-3400	A band related to OH groups (M, MAw, MAwG, MAe, MAeG)
N-H	3445	The bands attributable to the N-H stretching vibration (MAw, MAwG, MAe, MAeG)

256

257 **Table 2:** List of the main peaks detected in the FTIR spectra of M, MAw, MAwG,

258 MAe, MAeG, MS, MSAw and MSAwG NPs.

259

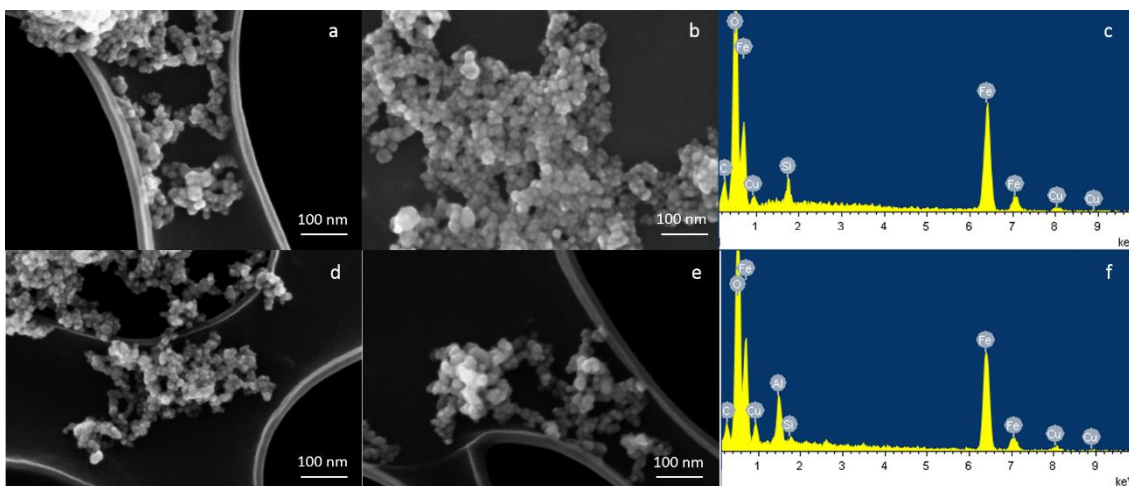


260

261 **Figure 3:** FTIR spectra of M, MAw and MAwG (NPs/GA 10:3) NPs.

262

263 The morphological and compositional analysis of MAeG (Figure 4a-c) shows the
 264 presence of spherical particles with a diameter between 5-20 nm. The EDS analysis
 265 (Figure 4c, MAeG with NPs/GA 10:1 as example) shows the Si peak ascribable to APTES
 266 functionalization. Analogously, the morphological analysis of MAwG (Figure 4d-e)
 267 reveals the presence of NPs with pseudo-spherical morphology and a diameter of about
 268 5-20 nm. Also in this case the compositional analysis performed on MAwG with NPs/GA
 269 10:1 (Figure 4f) evidences the peak of Si, due to the APTES functionalization.



270

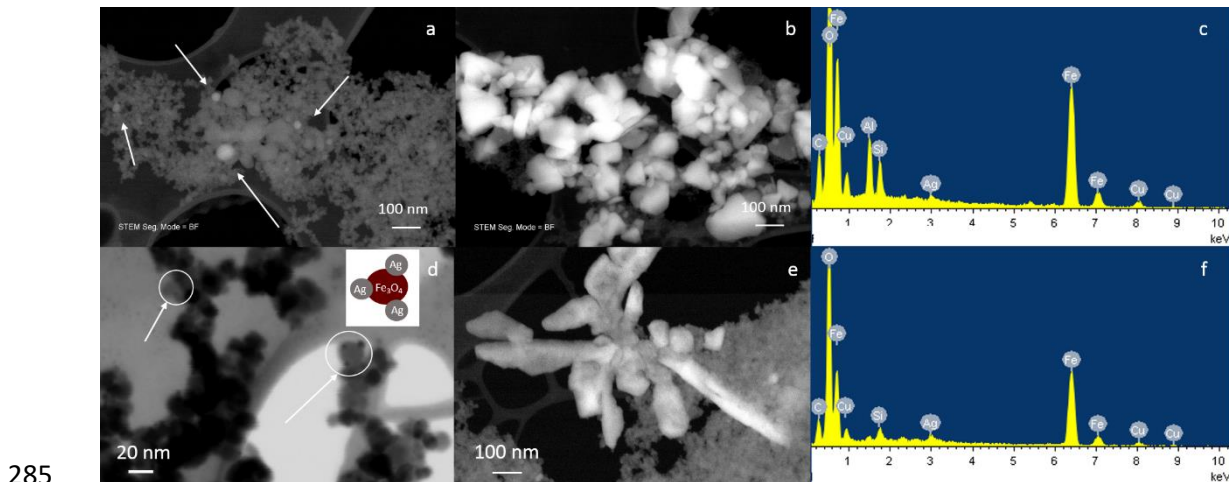
271 **Figure 4:** FESEM-EDS analysis of a) MAeG 10:1, b) MAeG 10:3, c) MAeG 10:1, d)
272 MAwG 10:1, e) MAwG 10:3, f) MAwG 10:1.

273

274 The STEM-EDS analysis of MAeGAg is reported in figure 5; as it can be observed
275 MAeGAg performed using NPs/GA ratio 10:1 show the presence of Ag nanometric
276 particles (< 50 nm) agglomerated with magnetite nanoparticles, evidenced with arrows in
277 figure 5a together with big silver particles (100-150 nm) with different shape (Figure 5b).

278 The EDS of area (Figure 5c) shows the peak of Ag, together with elements characteristic
279 of MAeG (Fe, Si and O) and elements acribable to sample holder (Cu, Al, C).

280 MAeGAg performed using NPs/GA ratio 10:3 show the presence of very small Ag NPs
281 (< 10 nm), which forms a nanoflower structure with magnetic NPs (Figure 5d, evidenced
282 by arrows and schematized in the inset). However, also in this case, in some area of the
283 sample big silver crystals were observed (Figure 5f and e) as confirmed by the EDS
284 analysis (Figure 5f).

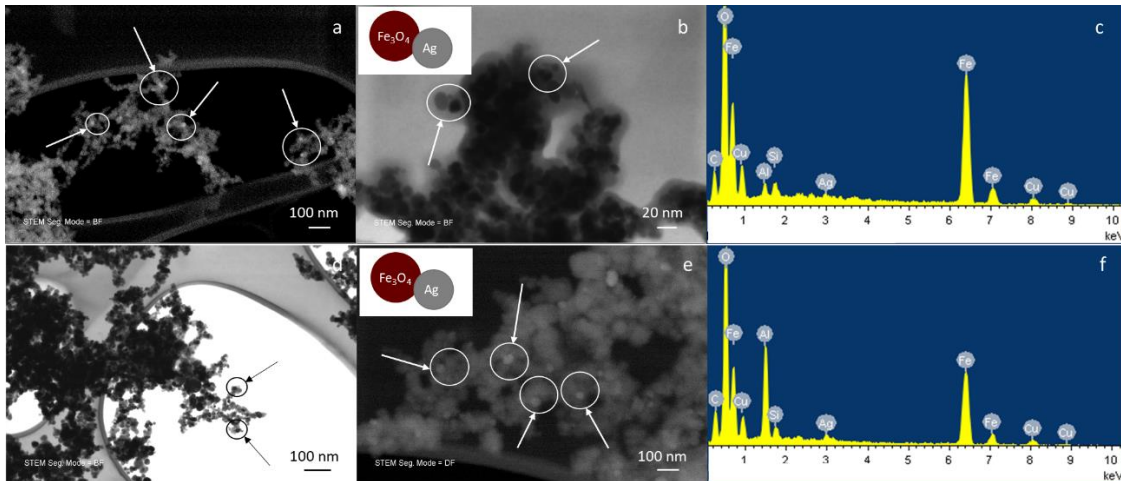


285

286 **Figure 5:** FESEM-EDS analysis of MAeGAg 10:1 (a-c) and MAeGAg 10:3 (d-f).

287

288 Figure 6 shows the STEM-EDS analysis of MAwGAg; in this case only Ag nanoparticles
 289 with dimension comparable with magnetite NPs were observed both for NPs/GA ratio
 290 10:1 (Figure 6a and b) and 10:3 (Figure 6d and e). Thus, in both NPs/GA ratio conditions,
 291 the synthesis in water allowed to obtain nanodumbbell structures with magnetite NPs
 292 connected with Ag NPs (Figure 6b and 6e). EDS analysis (Figure 6c and f) shows the Ag
 293 peak in addition to magnetic NPs peaks. As far as concerned the stability of composite
 294 NPs, their visual inspection suggests that they form a fairly stable suspension. Future test
 295 will be carried out to experimentally evaluate the stability of the nanostructures over time.
 296

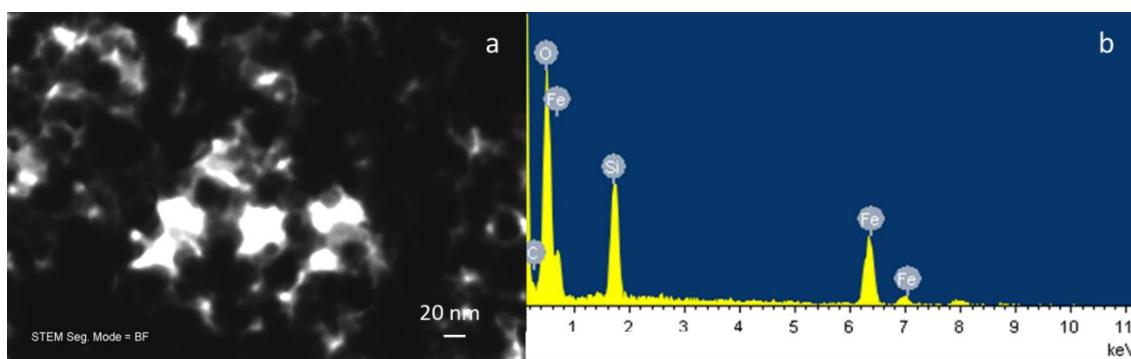


297
 298 **Figure 6:** STEM-EDS analysis of MAwGAg 10:1 (a-c) and MAwGAg 10:3 (d-f).
 299

300 3.2 Route B

301 The peaks obtained by means of FTIR analysis of MS, MSAw and MSAwG nanoparticles
 302 are reported in table 2. MS NPs evidence both the peak ascribable to Fe-O bond at about
 303 $500-600\text{ cm}^{-1}$ and the peak characteristic of silica shell: at 780 cm^{-1} the stretch of Si-OH,
 304 the broad band at about $850-990\text{ cm}^{-1}$ can be attributed to the Si-O symmetric vibration
 305 or to the Si-O-Fe bond and the peak at 1060 cm^{-1} the stretch of Si-O-Si [46, 47]. The

306 spectrum of MSAw shows an increase of the intensity of the peak related to Si-O-Si bond
307 attributable to the APTES functionalization, together with the peak of Fe-O bond. The
308 spectrum of MSAwG shows the peaks between 1600-1200 cm^{-1} ascribable to the C=C
309 bond, the peak at about 1700 cm^{-1} relative to the C=O stretch of carboxylic group, the
310 band at about 3400 cm^{-1} relative to OH groups of GA [44, 45].
311 The morphological analysis of MSAwG (Figure 7a) evidences the presence of pseudo-
312 spherical nanoparticles in the range 10-20 nm. The EDS spectrum (Figure 7b) shows a
313 very intense peak of Si ascribable to the silica shell, together with Fe and O peak; C peak
314 is due to the grid.



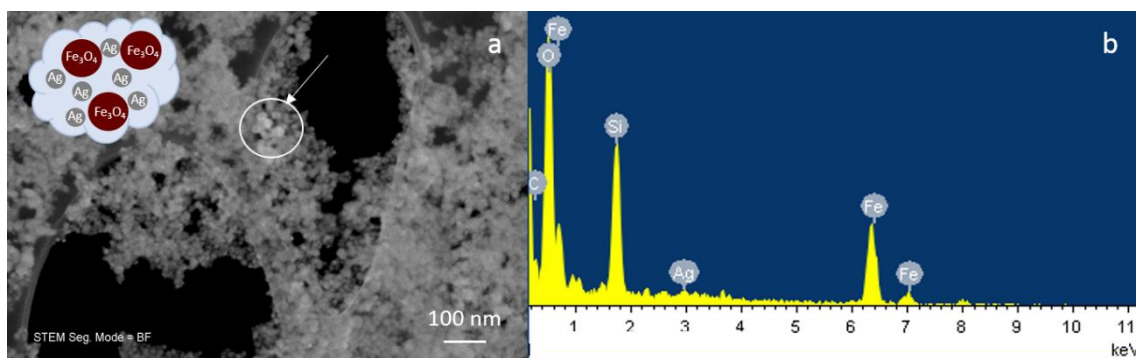
315

Figure 7: STEM image and EDS analysis of MSAwG.

316

317

318 The STEM analysis of MSAwGAg (Figure 8a) shows the formation of Ag NPs of ≤ 20
319 nm not well dispersed among magnetic NPs, but aggregated in some area (schematic
320 representation in Figure 8a); compositional analysis of an area (Figure 8b) shows the
321 effective presence of the Ag peak.



322

323 **Figure 8:** STEM-EDS analysis of MSAwGAg obtained using a NPs/GA ratio of 10:1.

324

325 4. Discussion

326 Aiming to improve the MNPs suspension stability, useful also for further
 327 functionalization steps, the prevention of their aggregation is a crucial aspect. In fact, the
 328 stability of MNPs in water is not optimal, due to anisotropic dipolar attraction [48] that
 329 could limit the nucleation of the metal nanoparticles on their surface [49]. For this
 330 purpose, CA was added to the MNPs suspension as stabilizing agent, promoting
 331 electrostatic repulsion, as reported also by several authors [48, 50, 51].

332 Concerning the functionalization with APTES and GA, no significant differences were
 333 noticed by FTIR analysis, although in the synthesis performed in ethanol it was difficult
 334 to identify some characteristic groups due to probable traces of residual ethanol.

335 The morphological and compositional analysis of samples synthesized in water evidenced
 336 the nucleation of smaller Ag nanoparticles by using a NPs/GA ratio of 10:3. We supposed
 337 that the higher amount of GA used in this synthesis introduced more nucleation sites
 338 allowing the formation of a lot of very small Ag NPs. In any case, even in this synthesis
 339 some larger Ag crystals, with a multibranch morphology, were noticed. These crystals
 340 could have been originated due to the seeding role of the nanoflowers-like structures, as

341 reported for ternary heterostructures by H. Zeng and S. Sun [52], further enhanced by
342 the excess of reducing agent in the synthesis environment.

343 The syntheses performed in water revealed the formation of small Ag nanoparticles both
344 using a NPs/GA ratio of 110:1 and 10:3. This result could be explained considering that,
345 as reported by [52], the partial exposure of Fe(II) on the nanoparticles to aqueous phase
346 could act as self-catalytic center for the reduction of Ag^+ ions to Ag° nanoparticles,
347 leading to the heterodimer morphology.

348 In summary, the synthesis in water allows to obtain more homogenous heterodimer
349 nanostructures, while the ethanol-based synthesis seems to have some critical aspects in
350 the control of the dimension and structure of silver NPs. Moreover, in the synthesis in
351 water, the different ratio between NPs and GA amount seems to not significantly
352 influence the amount and dimension of Ag NPs. For this reason, the route B was performed
353 only in water using a NPs/GA ratio of 10:1.

354 The NPs coating with a shell of silica seems to not improve the NPs functionalization and
355 most of all the *in situ* reduction of Ag NPs; in this case some small aggregates of Ag NPs,
356 not uniformly distributed were observed. As reported in other studies [47, 53], the
357 structure of nanocomposites is significantly influenced by charges, reactive groups or
358 functional moieties on the nanoparticles surface. The role of silica layer in the
359 precipitation of the above mentioned aggregates can be explained considering that bi-
360 component hybrid nanoparticles are generally obtained by sequential nucleation and
361 growth of the second component on a preformed seed of the first one [52]. The successful
362 synthesis of heterodimers strongly depends on the ability of suppressing the formation of
363 dispersed NPs of the second component (homogeneous nucleation) and promote their
364 seed-mediated heterogeneous nucleation on the first component NPs. This could be

365 achieved if the lattice spacing between the two components is well-matched to ensure
366 epitaxial growth of the second component on the first one, which often participate to the
367 reaction as catalyst, lowering the activating energy for heterogeneous nucleation. The
368 obtained results demonstrated that the silica shell seems to not positively influence the
369 decoration of MS NPs, probably due to its shield effect on the heterogeneous nucleation
370 of Ag NPs, while promoting their homogeneous nucleation in the synthesis medium and
371 their aggregated with the MS NPs, due to electrostatic interactions. Thus, the silver *in situ*
372 reduction by GA and the heterogeneous nucleation are promoted when magnetic NPs are
373 not coated by the silica shell; these two mechanisms are synergistic and lead to a better
374 decoration of magnetite NPs. In particular, if magnetic NPs are not coated by silica, they
375 are able to expose Fe(II) supporting the heterogeneous nucleation of Ag NPs, in addition
376 to the *in situ* reduction due to GA.

377

378 **5. Conclusions**

379 A novel method to prepare composite nanoparticles Fe₃O₄—Ag, by *in situ* reduction of
380 Ag on a magnetic core of Fe₃O₄ was developed. The synthesis allowed at first to prepare
381 Fe₃O₄ NPs stabilized by CA with spherical shape and size in the range 5 – 20 nm. The
382 obtained CA capped Fe₃O₄ NPs were successfully functionalized with APTES to graft
383 GA, as reducing agent for Ag NPs, in different media and with different NP/GA ratios.
384 Depending on the investigated synthesis conditions, different morphologies were
385 obtained, from polydispersed aggregates to nanoflower-like and nanodumbbell
386 nanocomposites. The best results were obtained in aqueous media, with NPs/GA ratio of
387 10:1, producing Fe₃O₄—Ag well defined nanodumbbells of about 20 nm size.

388 A further sol-gel coating of the CA-capped Fe₃O₄ NPs with a silica shell, functionalized
389 with APTES and GA in aqueous medium, was performed to assess its influence on the
390 nucleation of Ag NPs. In the presence of the silica coating, Ag NPs with size < 20 nm
391 nucleated as polydispersed aggregated among Fe₃O₄ NPs, evidencing that the silica shell
392 is not a key issue to optimize the morphology of Ag NPs nucleated on the magnetic core.
393 Further optimizations of synthesis parameters (such as time and reagent ratio) are still
394 necessary to improve the size and distribution of Ag NPs on Fe₃O₄ NPs. The
395 electromagnetic and optical characterizations are still in progress, as well as the
396 evaluation of suspensions stability.

397

398 **Summary Points**

- 399 1. Development of a novel method to prepare composite nanoparticles Fe₃O₄—Ag,
400 by in situ reduction of Ag on a magnetic core
- 401 2. Use of gallic acid, a green anti-inflammatory and anti-tumor phenolic compound,
402 as *in situ* reducing agent for Ag NPs
- 403 3. Evaluation of different synthesis media and functionalization steps
- 404 4. Estimation of different gallic acid/NPs ratios
- 405 5. Successfully functionalization of magnetic NPs with APTES and grafting with
406 GA, both in water and ethanol
- 407 6. Polydispersed aggregates, nanoflower-like and nanodumbbell nanocomposites
408 were obtained according to the synthesis conditions
- 409 7. Well-defined Fe₃O₄—Ag nanodumbbells (about 20 nm) were obtained using
410 aqueous media, a NPs/GA ratio of 10:1

411 8. The presence of a silica coating was not found to be useful to optimize the
412 morphology of Ag NPs nucleated on the magnetic core

413

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417

418 **References**

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589

590 **Table of Contents graphic**

**Gallic acid functionalized
magnetic NPs**

