**Supporting Information**

**Green and efficient determination of ʟ-dopa in complex polypill formulations using a magnetic microplate**

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1. **Synthesis of iron oxide (Fe3O4) nanoparticles**

The iron oxide nanoparticles were prepared from the chemical precipitation of ferric chloride and ferrous chloride using a solution of ammonium hydroxide; FeCl3·H2O (0.27 g), FeCl2·4H2O (0.1 g), and deionized water (25 mL) were mixed vigorously using ultrasonication for 10 min at room temperature (25–28 °C). The mixture was then purged with N2 and stirred using a Thermolyne® Cimarec®-top stirring hotplate (on speed 8) at room temperature (25±1 °C) for 5 min prior to the addition of NH4OH (4.5 mL), after which stirring continued for 2 min. The resulting product was magnetically separated and washed three times with deionized water, then washed once with 50% ethanol prior to drying under a vacuum at room temperature.

**2. Synthesis of the Fe3O4@SiO2 nanoparticles**

Iron oxide (0.03 g), deionized water (4 mL), and isopropyl alcohol (20 mL) were mixed vigorously using ultrasonication for 30 min at room temperature to give a homogeneous solution to which tetraethoxysilane (120 μL) was added. The resulting mixture was then stirred using a Thermolyne® Cimarec®-top stirring hotplate (on speed 8) at room temperature for approximately 2 min, then NH4OH (0.5 mL) was added and stirring continued for 3 h. The resulting product was magnetically separated and washed three times with 50% ethanol, prior to drying under a vacuum at room temperature. Figure S1 shows a transmission electron microscope (TEM) image of the resulting Fe3O4@SiO2 nanoparticles, which exhibited an average particle diameter of approximately 30 nm (Fig. S2).

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Figure S1**.** TEM images of the Fe3O4@SiO2 nanoparticles

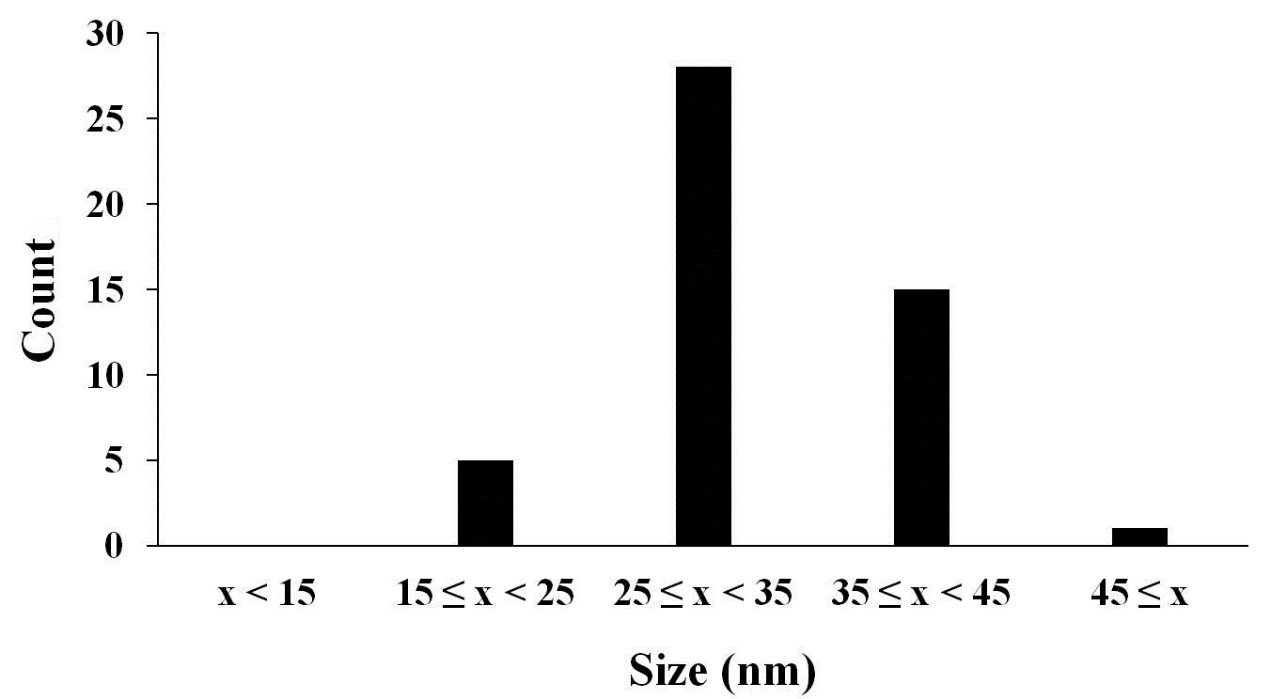
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Figure S2**.** Particle size distribution of the prepared Fe3O4@SiO2 nanoparticles

**3. Synthesis of the Fe3O4@SiO2-NH2 nanoparticles**

# The Fe3O4@SiO2 nanoparticles (30 mg), deionized water (4 mL), and isopropyl alcohol (20 mL) were mixed vigorously using ultrasonication for 5 min, after which time (3-aminopropyl)triethoxysilane (1 mL) was added. The resulting mixture was stirred using a Thermolyne® Cimarec®-top stirring hotplate (on speed 8) at room temperature for approximately 2 min, then NH4OH (1 mL) was added, and the mixture was stirred for a further 2 h. The resulting product was magnetically separated and washed three times with 50% ethanol, prior to drying under a vacuum at room temperature.

**4. FTIR spectra of iron oxide, silica (SiO2), and Fe3O4@SiO2**

The infrared spectra of iron oxide, silica (SiO2), and the Fe3O4@SiO2 nanoparticles are shown in Fig. S3. In all spectra, the broad absorption bands at 3200–3400 cm-1 correspond to O–H stretching mode, which indicates that many OH groups were present on the surface of the particles. The spectrum of SiO2 shows Si–O–Si stretching vibrations at 466 and 1093 cm−1. The spectrum of iron oxide (Fe3O4) shows absorption at approximately 586–631 and 1612 cm−1, which is assigned to Fe–O stretching vibration. The absorption also appears in the spectrum of Fe3O4@SiO2, but with lower intensity, likely due to the covering of SiO2 layers. The SiO2 layers in the Fe3O4@SiO2 spectrum are also indicated by the feature peaks at 466 and 1093 cm-1 corresponding to Si-O-Si stretching vibrations*(1)*.

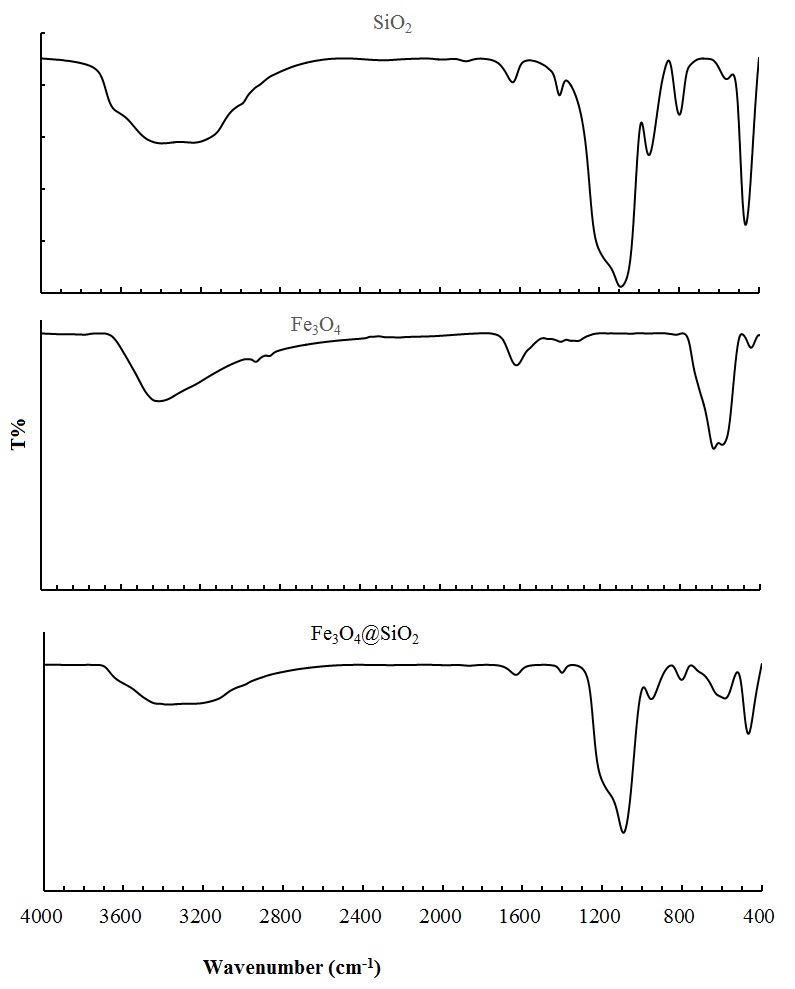


Figure S3**.** FTIR spectra of silica (SiO2), iron oxide (Fe3O4), and the Fe3O4@SiO2 nanoparticles, obtained using a Spectrum 100 FTIR Spectrometer (Perkin Elmer, Wellesley, UK).

**5. Immobilization of tyrosinase on the magnetic nanoparticles (TYR-MNPs)**

An aliquot of 2.5 % glutaraldehyde in 0.1 M phosphate buffer (PB) (10 mL, pH 6.0) and theFe3O4@SiO2-NH2 nanoparticles (MNPs, 1 mg) were added to a centrifuge tube, and the tube was gently rotated using a MACSmixTM tube rotator for 1 h at room temperature. The resulting glutaraldehyde-linked MNPs were washed three times with PB to remove any unreacted glutaraldehyde, and an aliquot of tyrosinase-containing PB (10 mL, 100 U ʟ-dopa activity) was added to the centrifuge tube, which was gently rotated again for 24 h at 4 °C. The resulting TYR-MNPs were magnetically separated, then washed three times with PB to remove any unreacted tyrosinase. Finally, the TYR-MNPs were reconstituted using PB (10 mL) and divided into aliquots of 1 mL, which were stored at 4 °C prior to use. TYR-MNPs were prepared twice (labelled batch 1 and batch 2) to verify the repeatability of the preparation.

**6. Preparation of the magnetic microplate**

Neodymiummagnets, 6 mm in diameter and 13 mm in length, were fixed into the wells of a 96-well microplate. The magnetic field strength of these magnets was 4.1 (±0.2) kG at the top of the microplate.

**7. Optimization of the reaction time between ʟ-dopa and the TYR-MNPs**

**Fig. S5.** Relationship between the formation of dopachrome and the reaction time

Reference

(1) Liu, L.; Yuan, M.; Huang, S.; Li, J.; Li, D.; Zhao, L., *Appl. Sci.* **2018**, 8, 158 ( doi:10.3390/app8020158)