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High-Flow System to Trap and Separate Magnetic Particles from Liquid Mixtures

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Abstract

Bio-separation of natural as well as biomedical molecules has been constantly developed in last decades. Even though several techniques are available, the majority of them present drawbacks such impossibility to work at industrial scale. Main up scaling limitations is linked to high costs and to the fact that devices are based on microfluid dynamic. In this scenario, magnetic bio-separation is considered the most prone to be applied for large scale preparation. Herein, we propose a proof of concept of a simple magnetic separation method that is not based on microfluid dynamics and can work in a semi-continuous high-flow rate. Furthermore, the proposed system could be easily automated in order to be used for standard separation purposes. The functional principia are based on the use of an anisotropic flexible magnetic strip, teflon hoses and a pumping device. We show the modelling of the separation process along with an experimental test on iron oxide magnetic particles. The results showed that it is possible to remove, and separately collect, more than 92% of magnetic particles from a liquid solution of 100 ml in roughly 15 minutes with just one passage.

Keywords: Bio-separation; Magnetic separation; Magnetic particles; High-flow

Introduction

In recent decades the application of magnetic iron oxide micro- and nano-particles has been established in various technological fields, such as magnetic separation of biomolecules and ions, biosensors, biofuel production and others [1-4]. Working with iron oxide particles is becoming main stream subject thanks to the facility such kind of materials can be functionalized with a variety of chemical groups which confer them specific selective or catalytic properties [5]. Furthermore, iron oxide Nano-particles present magnetic properties, and in particular superparamagnetism, which allows to remotely control them making their manipulation easy and cost-effective [6]. In addition, a new method of synthesis has been recently proposed, which can guarantee a cost-effective production of magnetic particles that may further reduce the running cost of separation methods based on magnetism [7]. Nevertheless, biotechnological applications of iron oxide particles are still confined to research level (lab scale devices) or for low-throughput clinical applications [8,9]. Indeed, most systems based on the use of magnetic elements are design to work with microfluid dynamic or are able to process samples in bath-based fashion, therefore discontinuously. The need of robust and high-productive methods is demanded especially in bioscience where, independently from the reaction or process involving magnetic particles, once such composite materials are mixed or added to a given solution, inevitably at the end of workflow they must be separated/harvested from the reaction vessel. Therefore, it is vital for a good productivity and processivity of reactions involving magnetic particles to ensure that large volumes of solution can be treated, and magnetic particles withdrew in the most fast and accurate way. To address this issue, in this paper it is investigated whether it is possible to operate a magnetic particle trapping and separation system is using a flexible magnetic surface and a spiral-arranged hose to separate particles from a liquid solution, whose volume is in the order of 100 ml. It is presented herein, the experimental test of the magnetic separation system, together with a modelling of the separation process. The system proposed has the potential to be fully automated and could be further exploited to concentrate magnetic particles dispersed in large volume of solvent with a rate in the order of ml per second.

Materials and Methods

A Teflon hose 100 mm length with a 4 mm external diameter and 3 mm internal diameter was used for the experiment. 80 mm of the teflon hose were coiled into 8 turns around a 50 ml tube. The magnetic field was generated by striped North-South magnetic lines Figure 1a. The anisotropic flexible ferric magnetic strip (Neodymium Iron Boron, NdFeB) was 40 mm wide with adhesive surface and has been purchased from Magnitech, Greece. The magnetic core (Figure 1b) can easily be inserted into the tube with the coiled Teflon hose. A peristaltic pump PLP 380 Dullabo was used together with a pump head of 10 rolling cylinders and a specific hose with a diameter of 4 mm, and a 3 way splitter with a manually adjustable valve. For the liquid solution we used ethanol ≥ 98% (Honeywell, Germany), oleic acid 90% (Alfa Aesar, Germany), Iron oxide (Fe_3O_4) magnetic particles containing large poly-domains with an average size of 200-400 µm (Figure 2), purchased from Chemical Store, USA. The alchol-oleic acid solvent was use to better dissolve Fe3O4 particles and obtain a colloidal solution. Ethanol and Oleic acid have been purchased with the maximum grade of purity indicated by their percentage.

Results

Design of a spiral magnetic separator

Finite element software (ANSYS fluent) was used in order to

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simulate the fluid flow inside the spiral hose. As seen in Figure 3, there is laminar flow all over the tube with no turbulences in the fluid dynamics.

Based on such simulation of the fluid dynamic, we assumed that the magnetic particles that are close to the hose walls move slower than those in the center and thus, they can be retained easier by the magnetic field. However, due to the fact that a spiral geometry was used, the mixing of the particles was allowed and statistically, the majority of the particles could be trapped. Thus, it can be assessed that the purity of the solution depends not only on the velocity of the fluid, but also on the number of the turns of the helical coil and the concentration of the particles in the solution. By defining the velocity of the fluid, it is also possible to define the fluid force applied on the magnetic particles by using Stokes' law:

$$F_d = 6\pi\mu Ru$$

where: μ is the viscosity of the solution; R is the radius of the particle; u is the velocity of the fluid.

Therefore, having determined the fluid force applied on magnetic particles, it is possible to define the magnetic force needed in order to retain the magnetic particles in the spiral hose. The alternating polarity magnetic sheet (Figure 4) propagates a high gradient magnetic field only from one side close to its surface that allows to retain particles evenly at the inner part of the spiral hose.

The equation of the magnetic force applied on a spherical magnetic particle is given:

$$F_M = \frac{4\pi}{3}\frac{\mu_o\chi}{1+\frac{\chi}{3}}\vec{H}\frac{d\vec{H}}{d\vec{x}} = \frac{2\pi\alpha^3}{3}\frac{\mu_o}{1+\frac{\chi}{3}}\nabla(|\vec{H}|^2)$$

where: α is the radius of the particle; χ is the magnetic susceptibility; μ_o is the vacuum's magnetic permeability; H is the magnetic field intensity; $\frac{d\vec{H}}{d\vec{x}}$ is the magnetic field gradient.

Thus, by asserting the equilibrium between the magnetic and the fluidic forces, it is possible to define the highest velocity over which the particles are not able to be retained in the spiral hose laid over the magnetic core.

Trapping, separation and concentration of magnetic particles by a spiral magnetic separator

To test the system, we used magnetic particles dissolved in ethanol containing 5% of oleic acid. Specifically, oleic acid was used to obtain a colloidal solution of dispersed magnetic particles. 0.1 grams of magnetite (Fe_3O_4) particles have been dissolved in 100 ml of alcoholic solvent by thoroughly shaking the flask (Figure 5a and Supplementary Figure S1). The resulting solution was homogenous, with magnetite particles well dispersed and showed an intense dark color; however sedimentation of particles occurred when the solution was left un-stirred for long time. The peristaltic pump was set to a pumping rate of roughly 0.1 ml/sec and one side of the propelling hose was immerse in alcoholic solution containing particles, whereas the other side connected to the inlet pipe of the spiral separator (Figure 5b and Supplementary Figure S2). The system was turned on and, as the solution started to reach the pipe wrapped around the magnetic surface, the magnetic particles initiated to be trapped by means of magnetic force along the entire spiral (Figure 5c). In Figure 4c is shown how magnetic particles accumulate gradually, with the majority at the inlet side, as the solution was moving from the inlet towards the outlet side. Eventually, at the end of the process, the majority of the magnetic particles were trapped near the inlet side (Figure 5d). This was due to the progressive impoverishment of magnetic particles inside the solution since they were gradually attracted as they were travelling along the spiral system. Once all alcoholic mixture was pumped through the spiral hose the peristaltic pump was let to run for a few seconds more in order to empty all the piping system. The solution deprived of magnetic particles was collect in a specific flask, and almost all magnetic particles were trapped by the spiral hose (Figure 6).

It is important to mention that even without any liquid phase covering magnetic particles; they remained firmly attached to the spiral hose. To assess the trapping capacity of our method, we used a spectrophotometer assay. We arbitrarily chose to measure the alcoholic solution's absorbance at a light wavelength of 600 nm before and after passing it through the spiral system. The result showed that more than 90% of magnetite was retained in the hose facing the magnetic core after only one passage (Figure 7).

Finally, to elute magnetic particles from the system, we first separated the magnetic core from the spiral hose (Figure 8a) and subsequently used 20 ml of alcoholic solution (Figure 8b and Supplementary Figure S2) to remove and collect magnetic particles in a separate flask (Figure 8c). After passing the 20 ml of fresh alcoholic solution, the magnetic particles were completely removed from the spiral hose (Figure 8d).

Discussion

Our group has recently demonstrated that by using properly configurated magnetic nanoparticles it possible to remove ions from seawater [2]. The state-of-the-art of magnetic separators available today in the market, though, does not offer solutions to separate magnetic materials from large amount of liquid mixture. Indeed, all systems are

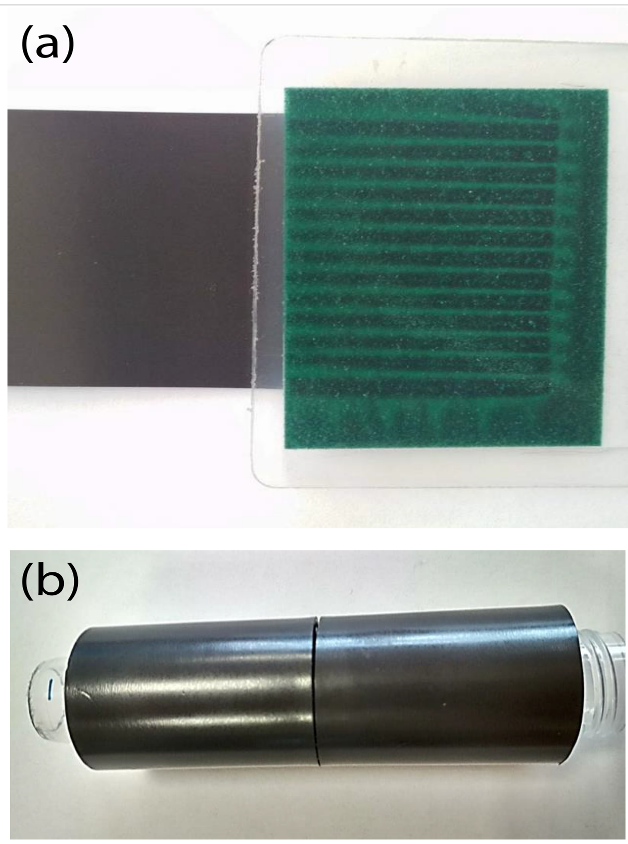

Figure 1: (a) anisotropic NdFeB magnetic strip with a magnetic field viewer. The distance between the alternating poles was roughly 4 mm, which creates a magnetic force able to trap magnetic particles at a distance of few mm, **(b)** Magnetic core assembled with the magnetic strip.

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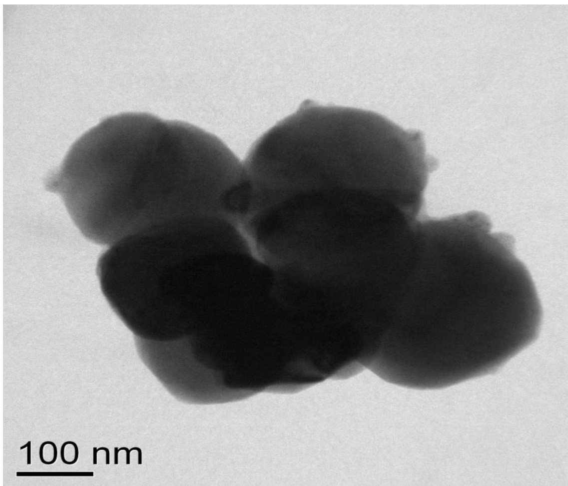

Figure 2: Transmission electron microscope (TME) image of iron oxide (Fe_3O_4) magnetic nanoparticles. The cluster formed as results of sample preparation due to dried environment.

based on microfluid devices or on the use of permanent/electromagnet able to attract magnetic materials towards a specific side of the reaction vessel. Concerning experimental machineries, in the last decade interesting lab prototypes have been proposed. Garcia and colleagues proposed an improved rotor stator prototype with 1 L chamber volume able to perform adsorption, separation, washing, elution and magnetic particles recovery in a cycling way [10]. Others interesting devices has been proposed by the group of Dr. Thomas O. in 2013 and 2018 named High-gradient magnetic fishing (HGMF). The model's setup published on 2018 consisted of a stirred batch adsorption reactor; a 70 kg permanent "ON OFF" magnet and magnetic filter canister and two peristaltic pumps [11,12]. We proposed in this work a much simple and reliable solution to remove magnetic particles from a given liquid mixture at a rate of ml per minute and in a semi-continuous flow fashion. However, it is import to mention that by varying the number of hose turns, strength of the magnetic core, hose's length, and eventually performing extra passage of the solution, it will possible to achieve much higher processing rates as well as increase the trapping percentage.

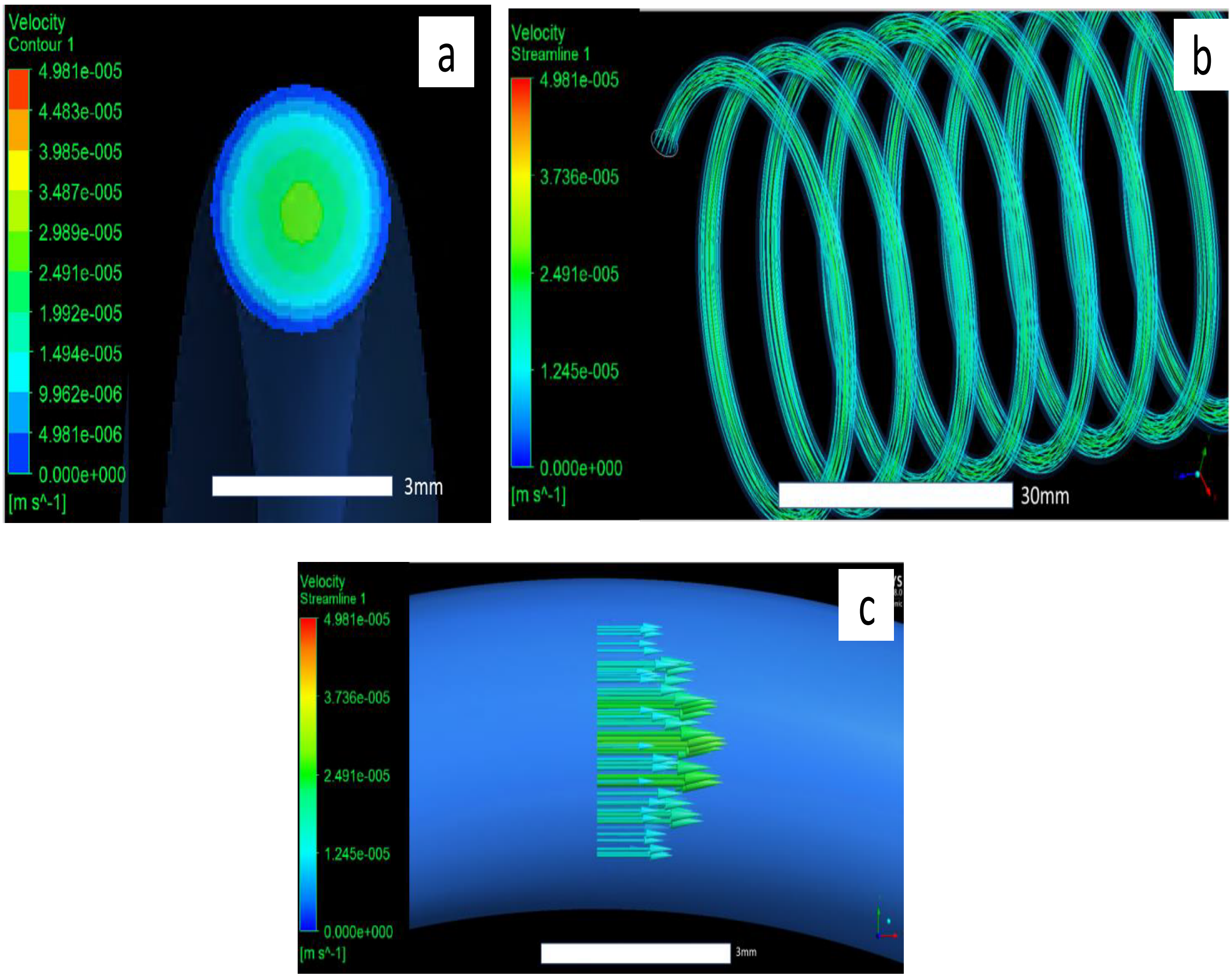

Figure 3: **(a)** cross section view-velocity contours; **(b)** laminar flow distribution in the spiral hose; **(c)** lateral view-velocity vectors.

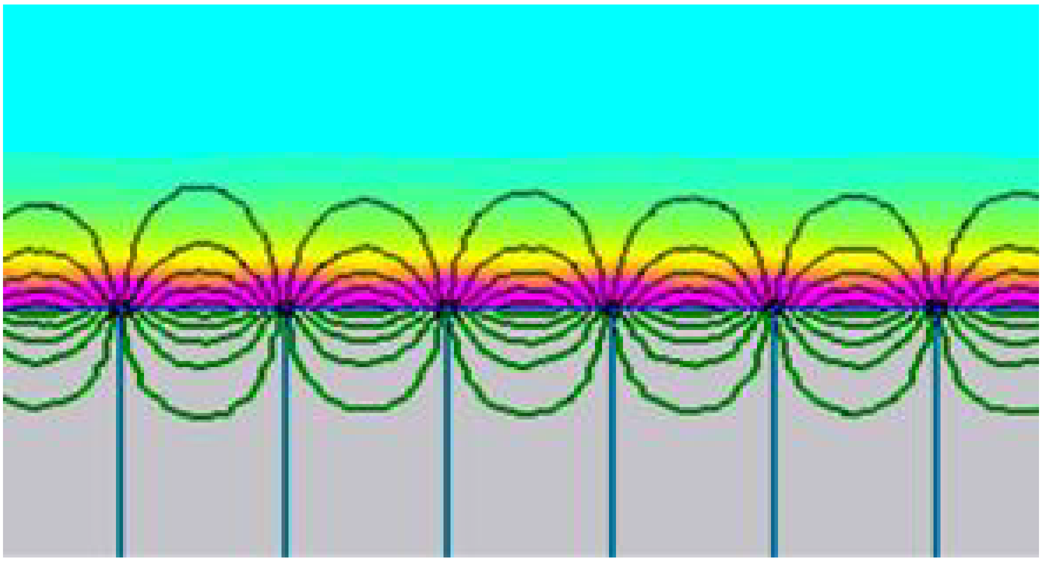

Figure 4: Schematic representation of the magnetic field generated by anisotropic NdFeB magnetic strip. Only one side of the strip is highly magnetized (purple color), and magnetic field intensity decreases exponentially with the distance (yellow and green colors). Curved magnetic lines are also represented.

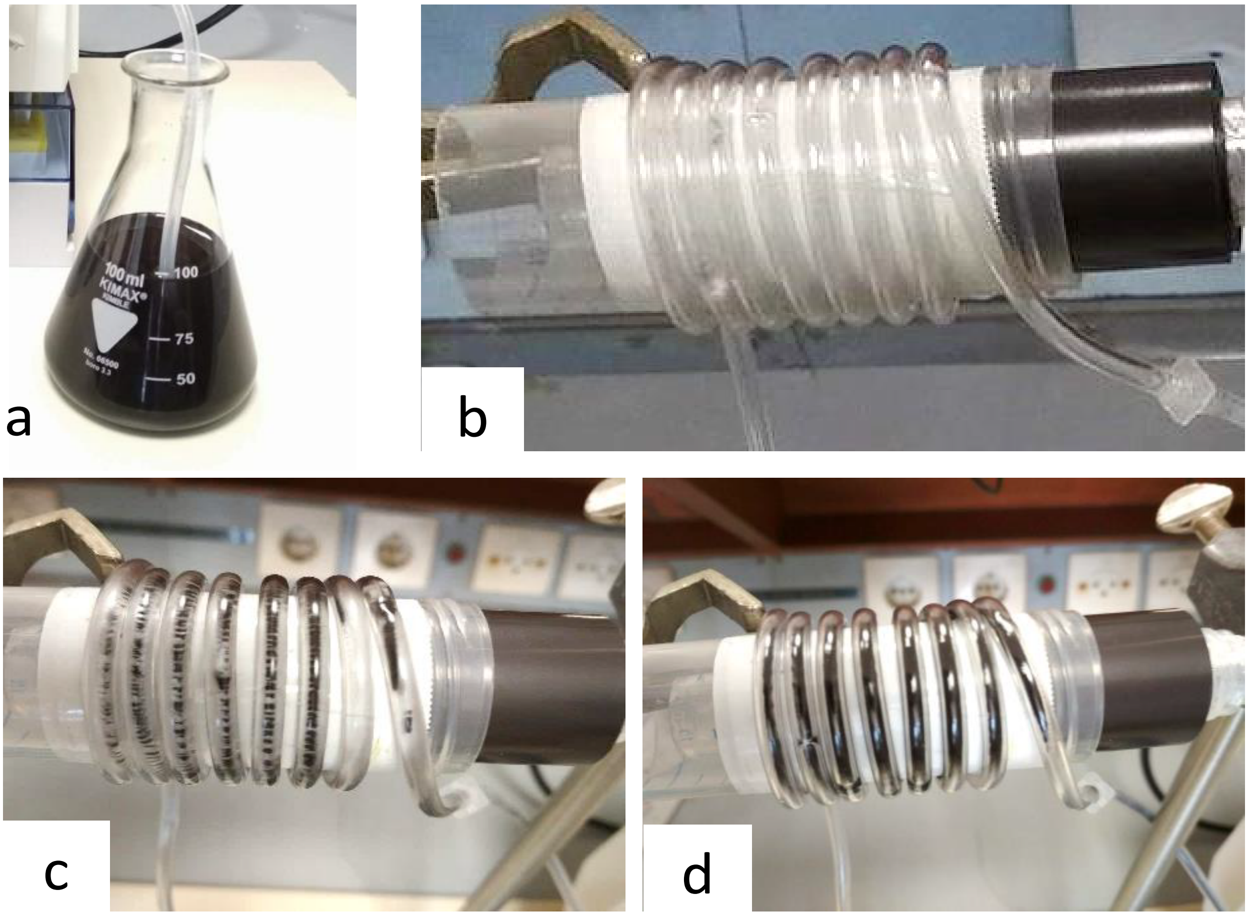

Figure 5: (a) alcoholic solution with magnetic particles; (b) spiral teflon hose coiled over the magnet core; (c) gradual accumulation of magnetic particles; (d) final accumulation of magnetic particles.

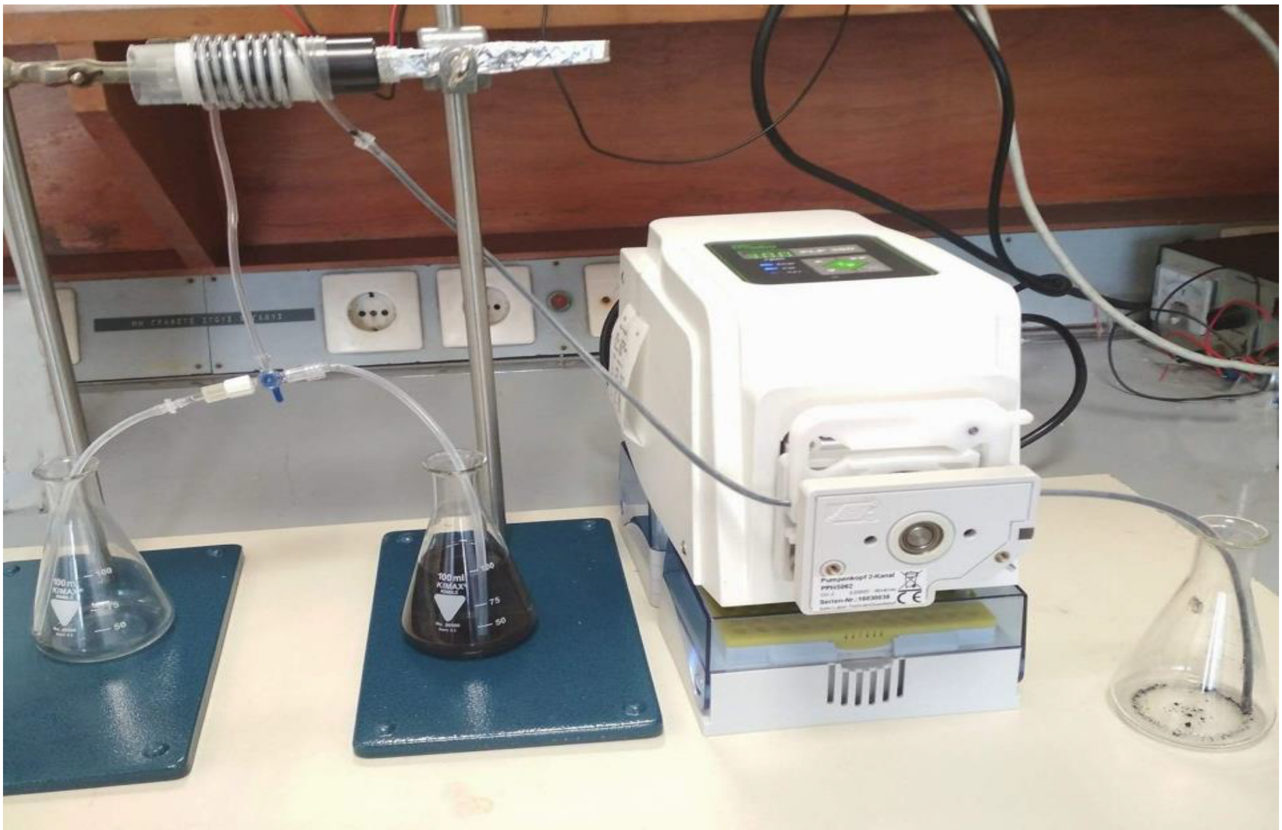

Figure 6: Complete apparatus after magnetic separation. Magnetic particles are trapped on the spiral hose without liquid covering them.

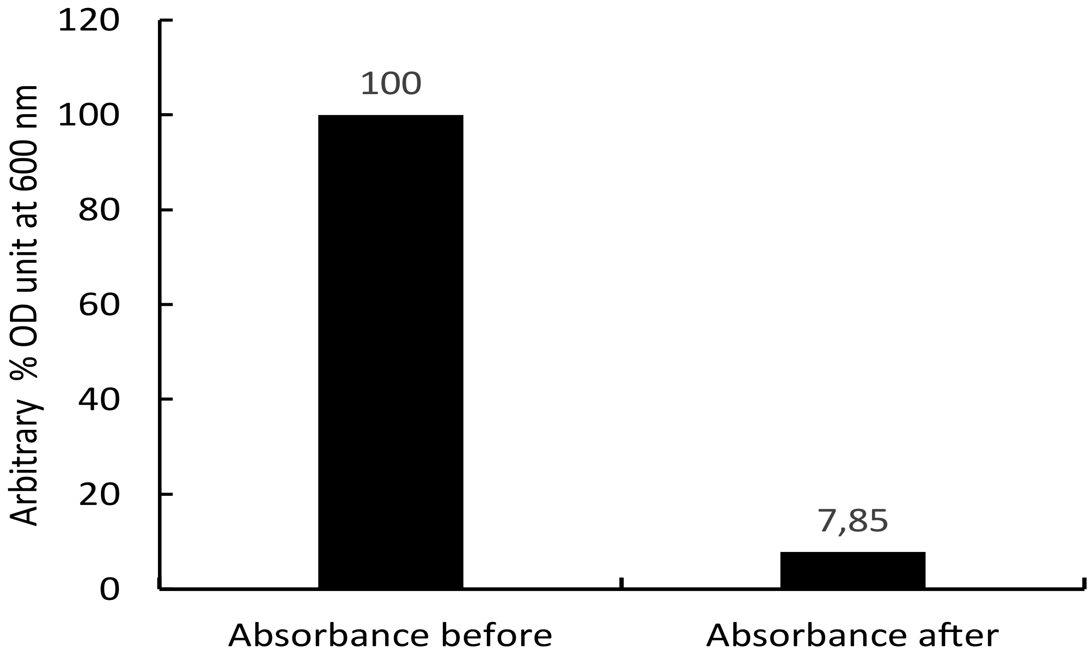

Figure 7: Spectrophotometer analysis of the optical density (OD) of alcoholic solutions before and after magnetic separation measured at light wavelength of 600 nm.

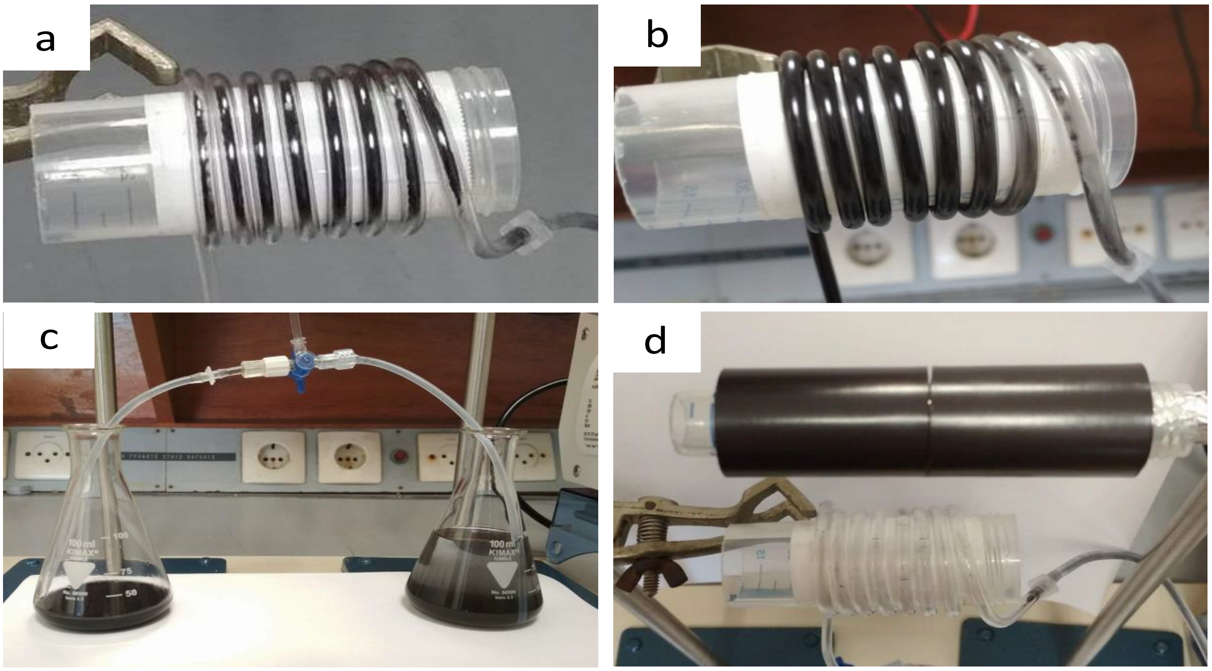

Figure 8: (a) magnetic core removal; **(b)** harvesting of magnetic particles form spiral hose; **(c)** magnetic particles collection into separate flasks; **(d)** spiral hose completely clean after magnetic particles harvesting.

The method principle is based on the use of an anisotropic flexible NdFeB magnet folded over a cylindric shape (magnetic core) around which a teflon hose is wrapped in order to form a spiral structure that surrounds the magnetic core itself. These two main components are in closed contact, nonetheless they can be easily separated apart from each other since the magnetic core can be ejected from the support of the spiral hose. This arrangement guaranties a big trapping surface in small volume compared to a linear tube. Such a method can be fully automated and by implementing its design it could be possible not only to trap and elute magnetic particles in a small volume, but also perform washing septs, routinely used when biomolecules are isolated by means of magnetic procedures. Indeed, by adding automated multiway valves it could be possible to pass over the magnetic particles trapped in the spiral hose additional solvents or buffers, which may remove impurities and not bound molecules. It is also important to mention that the trapping ability could be increased to near 100%, by few technical implementations. As it has been showed by the fluid flow simulations, the velocity of the solution inside the hose cross-section is not constant. Indeed, it increases moving from the hose walls towards the center. This phenomenon limits the trapping potential of the magnetic surface. Indeed, particles that are running in the center experience a different fluid force than those near the wall hose. To overcame this phenomenon, it could be enough to alter the constant fluid flow in order to increase solution mixing. This could be achieved, e.g., by just introducing in the spiral hose babbles of air which will alter the fluid flow providing a constant mixing.

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Author Contributions

G Banis executed all simulations using dedicated software; G Banis and M Kouli performed experiments and draft the paper; P Svec performed TEM analysis and reviewed the paper; E Hristoforou and A Ferraro design the work and substantively revised data and manuscript.

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