AN INTEGRATED MICROFLUIDIC DEVICE FOR THE PREPARATION AND EVALUATION OF MAGNETO-RESPONSIVE COMPOSITE PARTICLES

E. Rondeau, S. Holzapfel, P. Fischer, E. Windhab
ETH Zürich, Institute of Food, Nutrition and Health (IFNH), 8092 Zürich, SWITZERLAND

ABSTRACT
We present a microfluidic-based method allowing for the controlled production of lipid particles with encapsulated magnetic nanoparticles (MNPs). Within the same device, the magnetic properties of the composite particles are tested as they flow downstream. The effect of the fluid properties and flow parameters on the size of the microparticles containing MNPs is studied using standard flow visualization. The magnetic properties of the composite particles are characterized by studying their trajectory in a straight section of the channel, under a super-imposed magnetic field. Their deviation depends on their load, on the magnitude of the field, and on the flow conditions.

KEYWORDS: integrated microfluidic device, paramagnetic microparticle, miniaturized processing device.

INTRODUCTION
Functional magnetic (nano)particle composites have the potential to enhance the performance and economics of bioparticle separations, because of their high surface areas, rapid binding kinetics, and unique physical and chemical properties. A major barrier to implementing magnetic nano-particles and composites as adsorbents in the bio-processing industry is the lack of effective large-scale manufacturing of appropriately functionalized super-paramagnetic nanoparticles. We are developing a pilot-scale dynamic membrane-based emulsification process, using a rotating membrane device\cite{8}, in which fat or oil-based droplets of defined size and imparted with magnetic properties are generated. The resulting composite fat-particles (solidified by temperature quench) or oil droplets are to be used in separation processes such as magnetically-supported filtration, centrifugation, and extraction. At this stage of the project, the focus is set on the resulting magnetic properties of the particles, which need to be tuned specifically for their end application. The challenge leans not only in producing effective materials but also in systematically assessing their magnetic properties under flow conditions which are relevant to the application process. Microfluidic technology indisputably provides with flexible tools to investigate the fabrication, as well as to manipulate micro-structures in multiphase flow systems. In particular, microfluidic-based methods allow for the production and manipulation of very well defined droplet-based systems. A number of successful microfluidic-based syntheses of magnetic particles of varying size and shape have been reported\cite{2,3}. Microfluidic systems were also utilized to investigate possibilities for new developments in magnetic manipulation, separation, transport, and detection of magnetic microparticles and nanoparticles\cite{4}. In particular, the magnetically-driven migration\cite{5,6} and agglomeration\cite{7} of magnetic particles, in the presence of controlled laminar shear flow was studied in microfluidic channels. In this work, we demonstrate how specifically designed microfluidic devices are allowing us to 1) produce composite microparticles with precise control on their composition and size, and 2) investigate hydrodynamic behaviors combined with their magnetic properties, which is otherwise not observable in the pilot-scale devices.

EXPERIMENTAL

Solutions - Properties
All solutions used in this work were characterized thoroughly. In this short contribution, we only briefly discuss key data for a number of chosen properties. Reduced Palm Kernel Stearin (PKS) was used as the lipid matrix. It has a drop point of about 52°C. The SFC (solid fat content) varies with temperature and, for this particular fraction, is 45 - 55% at 30°C and 27 - 31% at 40°C. The steady shear viscosities of the fat in the liquid state, measured at different temperatures were found to be constant over a range of shear rates from 1 to 1000 s\(^{-1}\). As shown in Table 1, the effect of temperature on the viscosity of the liquid fat is significant and therefore the temperature at the droplet formation site has to be well-controlled. As a model system, sunflower oil (SFO) was also used as the disperse phase, in order to study the deflection of magnetic nanoparticle-dotted SFO droplets in the same channel under the same external magnetic field. As magnetic nanoparticles, maghemite nanoparticles coated with oleic acid (synthesized in the Laboratory of Magnetic Fluids, Romanian Academy by Vekas et al.\cite{8}) were used. They are dispersed in the liquid fat or oil phase prior to injection into the device. For the continuous phase, different formulations were tested. Glycerol was used to adjust the viscosity of the aqueous phase, using mass fraction \(m_{\text{glycerol}}/m_{\text{cont.phase}}\) ranging from 0.2 to 0.4. Tween 20 was used as a surfactant (Table 2). The system PKS+MNPs/Water + Glycerol + Tween 20 was assumed to be a Newtonian/Newtonian system.

Design and fabrication of the integrated microfluidic device - Experimental set-up
PDMS devices were fabricated using standard soft lithography. To create an oil in water emulsion, the channel walls required to be rendered hydrophilic. Surface treatment was achieved by coating the PDMS surface with Poly(acrylic acid) (PAA) using a UV polymerization technique described by Hu et al.\cite{9}. As shown in Figure 1, the microdevice prototype consists of three functional parts: a sheath-flow junction with an integrated heating system (1), where droplets are formed, a serpentine channel (2), in which the droplets harden, and a specifically designed section of the channel (3) for the sub-
sequent deviation of the resulting magneto-responsive particles with an integrated magnet to super-impose a magnetic field.

One of the main challenges is to ensure that the palm kernel stearin phase remains liquid until it reaches the droplet formation site. Lipid droplets solidify whilst flowing and can be analyzed in the flow chamber further downstream with no intermediate handling. The basic concept of the flow chamber is similar to the one described by Peyman et al.\textsuperscript{[5]}: Its application to the testing of magnetic properties under flow conditions is different. This is described in the following section.

RESULTS AND DISCUSSION

The effect of the flow parameters ($F_d$, $F_{c1}$, $F_d/F_{c1}$) and of the properties of the disperse and continuous phases on the droplet formation and ultimately on the size and shape of the lipid microparticles was studied in detail using a high-speed camera mounted on an optical microscope. PKS droplets containing MNPs were successfully formed and solidified downstream in the serpentine channel. As shown in Figure 2, the flow chamber where the magnetic properties of the particles are tested, is fed by three independent inlets for the generation of co-laminar streams inside the chamber. The same aqueous solution was injected in all three inlets and at the droplet formation site. The deflection of the particles across the straight channel results from the competition between hydrodynamic forces exerted by the carrier phase and the magnetic force imposed by the magnet. The fluid velocity profile in the chamber depends on the flow rates of all streams entering the chamber, i.e., on the corresponding flow rate ratios. The magnetic properties of MNP-dotted SFO droplets (or of the composite particles) were characterized by studying their trajectory at different positions $x_i$ along the straight channel. The effect on the trajectory of the droplets/particles can be investigated independently for different parameters. The most influential parameters were found to be the flow rate ratio $F_{c2}/F_{c1}$ (see Figure 2), the viscosity of the continuous phase, and the size of the particles/droplets. The effect of the MNPs content and of the strength of the magnet was not investigated here. Figure 2 illustrates the deviation of magnetic SFO droplets observed in the case of a particular set of experimental conditions ($F_{c2}/F_{c1} << 1$, $\eta = 10$ mPa s). The captions (A) show the comparison in between the trajectory of droplets without and with the imposition of a magnetic field. Figure 2 also illustrates the positive effect of the droplet size on the deflection from the droplet trajectory.

In the case of sufficiently small $F_{c2}/F_{c1}$ ratios, the droplets were found to shift along the y-axis just after exiting the feeding channel and entering the chamber. The same behavior was observed in the presence of a magnet and with no magnet. This is being investigated. The droplets deviate until they reach highest velocity stream lines and flow further along the x-axis. Due to the small dimensions of the microchannel, it is possible to operate with a hydrodynamic shear of substantial amplitude while keeping the flow laminar. A wide range of flow conditions can be thus tested and compared.
Figure 2: Magnetically-induced deviation observed in the case of SFO droplets containing MNPs. Images A and B correspond to SFO droplets with different sizes: B droplets are bigger than A droplets. Under the same flow conditions and magnet field, the magnitude of the deflection was bigger for the larger droplets.

CONCLUSION

We have designed, fabricated and tested a novel microfluidic device allowing for the production of composite particles containing magnetic nanoparticles and, without intermediate handling, for the evaluation of their magnetic properties. This miniaturized flow processing device is highly flexible and operating conditions are finely tunable. It allows investigating specific parameters independently under flow conditions which are relevant for the design and scale-up of pilot-scale separation processes to be further investigated.

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REFERENCES


CONTACT

*E. Rondeau, ETH-Zürich (IFNH), tel: +41-44-6327254; elisabeth.rondeau@ilw.agrl.ethz.ch