

# CONSEQUENCES OF SHEEP BLOOD USED AS DILUTING AGENT FOR THE MAGNETOVISCOUS EFFECT IN BIOCOMPATIBLE FERROFLUIDS

J. NOWAK<sup>1\*</sup>, C. NOWAK<sup>2</sup>, S. ODENBACH<sup>1</sup>

<sup>1</sup>Chair of Magnetofluidynamics, Measuring and Automation Technology, Technische Universität Dresden, George-Baehr Strasse 3, 01062 Dresden, Germany

<sup>2</sup>Medical Sciences Department, Uppsala University, P.O. Box 1115, 751 41 Uppsala, Sweden

\* Corresponding author: [johannes.nowak@tu-dresden.de](mailto:johannes.nowak@tu-dresden.de)

Received: 10.4.2015, Final version: 1.7.2015

## ABSTRACT:

Magnetic nanoparticles suspended in suitable carrier liquids can be adopted for use in biomedicine. For this to be achieved, the biocompatibility of these ferrofluids needs to be ascertained. In cancer treatment, potential applications currently under investigation include, e. g. drug targeting by using magnetic fields and the destruction of diseased cells by applying alternating magnetic fields, which cause heating of magnetic nanoparticles. To enable the use of ferrofluids in the actual biomedical context, detailed knowledge of the flow characteristics is essential to ensure safe treatment. From ferrofluids used in the engineering context, a rise of viscosity when a magnetic field is applied – the magnetoviscous effect – is well known. This effect, which leads to an increased viscosity and profound alteration of a fluid's rheological behavior, has also been demonstrated for biocompatible ferrofluids used in the aforementioned applications. In biomedical applications, ferrofluids will be diluted in the blood stream. Therefore, the interaction between whole blood and the ferrofluid has to be investigated. This is the focus of the current experimental study, which makes use of two different ferrofluids diluted in sheep blood to gain a deeper understanding of the fluid mixtures primarily regarding the relative change in viscosity if an external magnetic field is applied. The results demonstrate a strong interaction between blood cells and structures formed by the magnetic nanoparticles and show a high deviation of results compared to ferrofluids diluted in water. These findings have to be taken into account for future research and applications of similar biocompatible fluids to guarantee safe and effective use in living organisms.

## KEY WORDS:

Magnetoviscous effect, ferrofluid, rotational rheometry, magnetic nanoparticles, biomedical materials

## 1 INTRODUCTION

Ferrofluids are suspensions of magnetic nanoparticles in suitable carrier liquids with a wide range of applications. The particles are prevented from agglomeration caused by e.g. van der Waals interaction by a surfactant layer of varying thickness [1, 2]. The resulting suspension can be considered as stable. Regarding applications, two areas are currently the focus of research: Ferrofluids used in the engineering context – an area which has been investigated in some detail in recent years [1, 3] as well as ferrofluids utilised in the biomedical context [4, 5]. The current study focuses on the investigation of ferrofluids used in the latter field of research. While for biomedical purposes such fluids have been used as contrast agents for magnetic resonance imaging (MRI) with success for several years [6], recent research has focused on magnetic drug targeting [7, 8], and magnetic fluid hyperthermia (MFH) [9].

Magnetic fluid hyperthermia is a novel approach for inducing cell death by concentrating ferrofluids within a tumor and applying a magnetic field that induces localised heat production. Initial results using, e.g. a breast cancer model [10], mice prostate tumor [11], ovarian cancer cells [12], and rat glioma [13] demonstrate its potential. Computed tomography (CT)-guided magnetic thermoablation of malignant kidney tumours in rabbits resulted in localised tumor necrosis [14]. It has been shown as well that MFH destroys tumor tissue whilst leaving healthy surrounding structures untouched [15].

Besides those promising examples of the use of ferrofluids in biomedicine, magnetic particle imaging (MPI) can be regarded as another continuously improving approach. This technique enables imaging of the spatial distribution of the magnetic nanoparticles [16]. Compared to non-invasive imaging using conventional X-ray or CT, it carries several advantages. Non-toxicity of contrast agents used in the treatment of chronic kid-

This is an extract of the complete reprint-pdf, available at the Applied Rheology website  
<http://www.appliedrheology.org>

## ACKNOWLEDGEMENTS

The authors would like to thank C. Rentsch of the Centre for Translational Bone, Joint and Soft Tissue Research (University Hospital Carl Gustav Carus, Dresden, Germany) for providing the sheep blood. Financial support by the Deutsche Forschungsgesellschaft under Grant no. OD18/23-1 is gratefully acknowledged.

## REFERENCES

- [1] Rosensweig RE: Ferrohydrodynamics, Cambridge University Press, New York (1985).
- [2] Odenbach S: Magnetoviscous effects in ferrofluids, Springer, Berlin (2002).
- [3] Berkovskici B, Medvedev V, Krakov M: Magnetic fluids: Engineering applications, Oxford University Press, Oxford (1993).
- [4] Lee Y, Chen D, Dodd SJ, Bouraoud N, Koretsky AP, Krishnan KM: The use of silica coated MnO nanoparticles to control MRI relaxivity in response to specific physiological changes, *Biomaterials* 33 (2012) 3560–3567.
- [5] Dürr S, Janko C, Lyer S, Tripal P, Schwarz M, Zaloga J, Tietze R, Alexiou C: Magnetic nanoparticles for cancer therapy, *Nanotechnol. Rev.* 2 (2013) 395–409.
- [6] Reimer P, Balzer T: Ferucarbotran (Resovist): A new clinically approved RES specific contrast agent for contrast-enhanced MRI of the liver: properties, clinical development, and applications, *Europ. Radiol.* 13 (2003) 1266–1276.
- [7] Alexiou C, Tietze R, Schreiber E, Jurgons R, Richter H, Trahms L, Rahn H, Odenbach S, Lyer S: Cancer therapy with drug loaded magnetic nanoparticles – magnetic drug targeting, *J. Magnet. Magnet. Mater.* 323 (2011) 1404–1407.
- [8] Tietze R, Lyer S, Dürr S, Struffert T, Engelhorn T, Schwarz M, Eckert E, Göen T, Vasylyev S, Peukert W: Efficient drug-delivery using magnetic nanoparticles – biodistribution and therapeutic effects in tumour bearing rabbits, *Nanomed.* 9 (2013) 961–971.
- [9] Dennis C, Jackson A, Borchers J, Hoopes P, Strawbridge R, Foreman A, van Lierop J, Grüttner C, Ivkov R: Nearly complete regression of tumors via collective behavior of magnetic nanoparticles in hyperthermia, *Nanotechnol.* 20 (2009) 395103.
- [10] Miaskowski A, Sawicki B: Magnetic fluid hyperthermia modeling based on phantom measurements and realistic breast model, *IEEE Trans. Bio. Med. Eng.* 60 (2013) 1806–1813.
- [11] Attaluri A, Ma R, Qiu Y, Li W, Zhu L: Nanoparticle distribution and temperature elevations in prostatic tumours in mice during magnetic nanoparticle hyperthermia, *Inter. J. Hyperther.* 27 (2011) 491–502.
- [12] Taratula O, Dani RK, Schumann C, Xu H, Wang A, Song H, Dhagat P, Taratula O: Multifunctional nanomedicine platform for concurrent delivery of chemotherapeutic drugs and mild hyperthermia to ovarian cancer cells, *Inter. J. Pharmaceut.* 458 (2013) 169–180.
- [13] Rabias I, Tsitrouli D, Karakosta E, Kehagias T, Diamantopoulos G, Fardis M, Stamopoulos D, Maris TG, Falaras P, Zouridakis N: Rapid magnetic heating treatment by highly charged maghemite nanoparticles on Wistar rats exocranial glioma tumors at microliter volume, *Biomicrofluid.* 4 (2010) 1–8.
- [14] Bruners P, Braunschweig T, Hodenius M, Pietsch H, Penzkofer T, Baumann M, Günther RW, Schmitz-Rode T, Mahnken AH: Thermoablation of malignant kidney tumors using magnetic nanoparticles: an in vivo feasibility study in a rabbit model, *Cardiovasc. Intervent. Radiol.* 33 (2010) 127–134.
- [15] Purushotham S, Ramanujan RV: Thermoresponsive magnetic composite nanomaterials for multimodal cancer therapy, *Acta Biomater.* 6 (2010) 502–510.
- [16] Ferguson RM, Minard KR, Krishnan KM: Optimization of nanoparticle core size for magnetic particle imaging, *J. Magnet. Magnet. Mater.* 321 (2009) 1548–1551.
- [17] Goodwill PW, Saritas EU, Croft LR, Kim TN, Krishnan KM, Schaffer DV, Conolly SM: X-Space MPI: Magnetic nanoparticles for safe medical imaging, *Adv. Mater.* 24 (2012) 3870–3877.
- [18] Laurent S, Forge D, Port M, Roch A, Robic C, Vander Elst L, Muller RN: Magnetic iron oxide nanoparticles: synthesis, stabilization, vectorization, physicochemical characterizations, and biological applications, *Chem. Rev.* 108 (2008) 2064–2110.
- [19] Ferguson RM, Khandhar AP, Krishnan KM: Tracer design for magnetic particle imaging, *J. Appl. Phys.* 111 (2012) 7B318–7B3185.
- [20] Thiele RH, Colquhoun DA, Gillies GT, Tiourine M: Manipulation of hyperbaric lidocaine using a weak magnetic field: A pilot study, *Anesth. Analg.* 114 (2012) 1365–1367.
- [21] Paschalis EI, Chodosh J, Sperling RA, Salvador-Culla B, Dohlman C: A Novel implantable glaucoma valve using ferrofluid, *PLoS ONE* 8 (2013) e67404.
- [22] Kami D, Takeda S, Itakura Y, Gojo S, Watanabe M, Toyoda M: Application of magnetic nanoparticles to gene delivery, *Inter. J. Mol. Sci.* 12 (2011) 3705–3722.
- [23] Odenbach S, Störk H: Shear dependence of field-induced contributions to the viscosity of magnetic fluids at low shear rates, *J. Magnet. Magnet. Mater.* 183 (1998) 188–194.
- [24] Odenbach S: Recent progress in magnetic fluid research, *J. Phys.: Cond. Mat.* 16 (2004) R1135–R1150.
- [25] Pop LM, Odenbach S: Investigation of the microscopic reason for the magnetoviscous effect in ferrofluids studied by small angle neutron scattering, *J. Phys.: Cond. Mat.* 18 (2006) S2785–S2802.
- [26] Meza M: Application of magnetic particles in immunoassays, *Scientific and Clinical Applications of Magnetic Carriers*, Plenum Press, New York (1997) 303–309.
- [27] Nowak J, Odenbach S: Magnetoviscous effect in a biocompatible ferrofluid, *IEEE Trans. Magnet.* 49 (2013) 208–212.
- [28] Nowak J, Wiekhorst F, Trahms L, Odenbach S: The influence of hydrodynamic diameter and core composition on the magnetoviscous effect of biocompatible ferrofluids, *J. Phys.: Cond. Mat.* 26 (2014) 176004.
- [29] Nowak J, Wolf D, Odenbach S: A rheological and microscopical characterization of biocompatible ferrofluids, *J. Magnet. Magnet. Mater.* 354 (2014) 98–104.
- [30] Ullrey D, Miller E: Sheep hematology from birth to matu-

This is an extract of the complete reprint-pdf, available at the Applied Rheology website

<http://www.appliedrheology.org>

rity I. Erythrocyte population, size and hemoglobin concentration, *J. Anim. Sci.* (1965) 135–140.

- [31] Merrill E: Rheology of blood, *Physiol. Rev* 49 (1969) 863–888.
- [32] Schmid-Schoenbein H, Wells R, Schildkraut R: Microscopy and viscometry of blood flowing under uniform shear rate (rheoscopy), *J. Appl. Physiol.* 26 (1969) 674–678.
- [33] Laurent A, Durussel JJ, Dufaux J, Penhou èt L, Bailly AL, Bonneau M, Merland JJ: Effects of contrast media on blood rheology: Comparison in humans, pigs, and sheep, *Cardiovasc. Intervent. Radiol.* 22 (1999) 62–66.
- [34] Weng X, Cloutier G, Pibarot P, Durand LG: Comparison and simulation of different levels of erythrocyte aggregation with pig, horse, sheep, calf, and normal human blood, *Biorheol.* 33 (1996) 365–377.
- [35] Alves MM, Rocha C, Goncalves MP: Study of the rheological behavior of human blood using a controlled stress rheometer, *Clin. Hemorheol. Microcirc.* 53 (2013) 369–386.
- [36] Baskurt OK: In vivo correlates of altered blood rheology, *Biorheol.* 45 (2008) 629–638.
- [37] Baskurt OK, Meiselman HJ: Erythrocyte aggregation: Basic aspects and clinical importance, *Clin. Hemorheol. Microcirc.* 53 (2013) 23–37.
- [38] Odenbach S, Rylewicz T, Heyen M: A rheometer dedicated for the investigation of viscoelastic effects in commercial magnetic fluids, *J. Magnet. Mater.* 201 (1999) 155–158.
- [39] Borin DY, Odenbach S: Magnetic measurements on frozen ferrofluids as a method for estimating the magnetoviscous effect, *J. Phys.: Cond. Mat.* 21 (2009) 246002.
- [40] Borin D, Odenbach S: Rheology of novel ferrofluids, *Inter. J. Mod. Phys. B* 25 (2011) 963–969.
- [41] Tao R, Huang K: Reducing blood viscosity with magnetic fields, *Phys. Rev. E* 84 (2011) 011905.
- [42] Yamamoto T, Nagayama Y, Tamura M: A blood-oxygenation-dependent increase in blood viscosity due to a static magnetic field, *Phys. Med. Biol.* 49 (2004) 3267–3277.
- [43] Smith JE, Mohandas N, Shohet SB: Variability in erythrocyte deformability among various mammals, *Am. J. Physiol.* 236 (1979) H725–H730.
- [44] Kwaan HC, Bongu A: The hyperviscosity syndromes, *Sem. Thromb. Hemost.* 25 (1999) 199–208.
- [45] Stone MJ, Bogen S: Evidence-based focused review of management of hyperviscosity syndrome, *Blood* 119 (2012) 2205–2208.
- [46] Simmonds MJ, Meiselman HJ, Baskurt OK: Blood rheology and aging, *J. Geriatr. Cardiol.* 10 (2013) 291–301.

