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NOVEL BIOCOMPATIBLE MAGNETIC FLUIDS

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INTRODUCTION: Biocompatible magnetic fluids (MF) are composed of homogeneously dispersed magnetic core/shell nanoparticles in physiological aqueous carriers. The core material is mostly magnetite/maghemite and the non-magnetic shells are made of biocompatible or even biodegradable organic molecules. Typical shell materials are polysaccharides [1] such as dextran and starch. They can be modified by carboxy groups, dimercaptosuccinic acid or other reactive components.

MF are increasingly used in medical diagnostics and therapy as well as in biotechnology.

MF with a novel biocompatible shell:
A new generation of biocompatible MF [2] are presented composed of magnetic nanoparticles that are coated with cyclodextrin (CD). CD is formed by 6, 7 or 8 glucose units as a cycle (Fig. 1). These cycles generate subnanometer pores of 0.5-0.8 nm diameter.

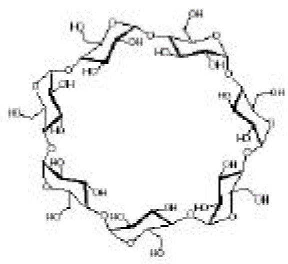

Fig. 1: Structure of b-cyclodextrin

Inclusion products with small molecules or components of molecules can be formed by incorporation into these pores [3]. Furthermore, the cyclodextrin shell can be functionalized in order to conjugate bioactive molecules such as antibodies.

METHODS: The preparation procedure has been divided into the following steps: First, carboxymethylated (CM) α-, β- and γ-CD were prepared by well-known methods [4]. The degree of substitution (DS) can be varied, but mostly in a range of 0.8 to 1.2 CM per glucose unit.
Then, magnetite nanoparticles were synthesized by co-precipitation with ammonia, and in a next step coated with carboxylated cyclodextrins (CM-CD). The CM-CD-MF were synthesized in high yields with iron concentrations of 5-10 % (w/w). Even higher concentrated MF were obtained after evaporation of the solvent.

The core size of the magnetic particles was determined by TEM (CM20 FEG Philips). The hydrodynamic size of the nanoparticles and their zeta potential were determined by photon correlation spectroscopy (PSC) using a Coulter N4 plus, and a Zetasizer 3000HS. Magnetization curves were obtained using coupled transformer spoils as the sensor. The saturation polarization Js and the initial susceptibility was evaluated from magnetization curves.
For the determination of the Fe(II) and Fe(III) concentration the particles were dissolved in hydrochloric acid and titrated with $KMnO_4$ and $Na_2S_2O_3$, respectively.

RESULTS: All measurements were executed with CM-β-CD (degree of substitution = 0.9) and the corresponding magnetic fluid, respectively.

The magnetic measurements (Fig. 2) yielded a very high saturation polarization that corresponded to 18 % (v/v) magnetite in the magnetic fluid.

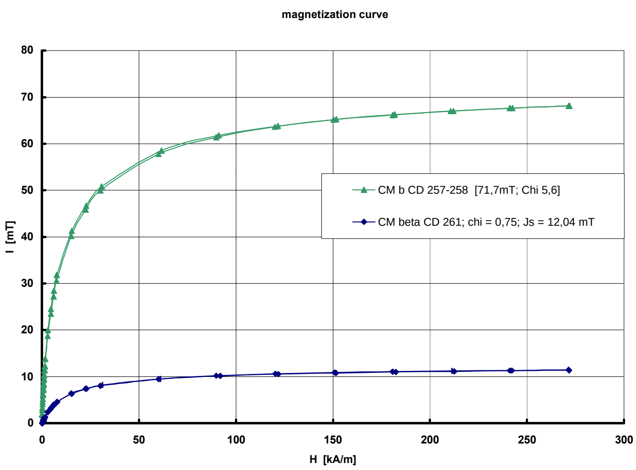

Fig. 2: *Magnetization curve of a high and low concentrated CM-b-CD-MF. Calculated saturation polarisation Is = 71.7 mT (12 mT) and initial susceptibility c = 5.6 (0.75) of the high (low) concentrated CM-b-CD- MF.*

The core particle size was determined by electron micrographs (Fig. 3). A mean particle diameter of 10.3 nm with the shown particle size distribution was found.

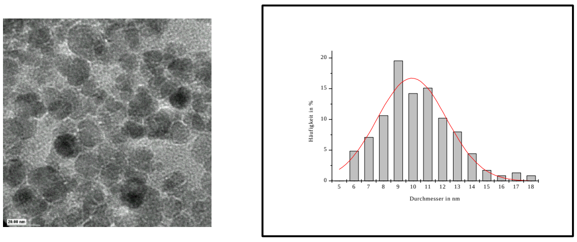

*Fig. 3: Electron micrograph and particle size histogram of stabilized CM-**b**-CD-magnetite particles.*

The zetapotential measurement (Fig. 4) showed that the diluted particles are negatively charged with a relatively high zeta potential of –30 to –50 mV in a pH range of 4-10 (titration with HCl and NaOH). This corresponds to the good colloidal stability of the particles.

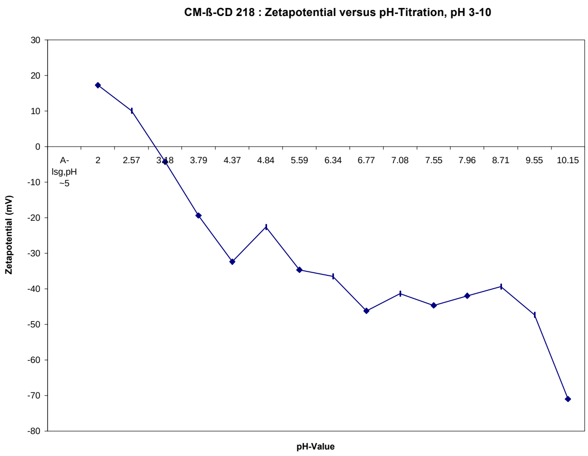

*Fig. 4: Zetapotential vs. pH of CM-**b**-CD-MF*

An average PCS hydrodynamic diameter of 65 nm of the very diluted *CM-**b**-CD-MF at pH = 7* with a polydispersity index of 0.22 was observed.

PCS measurements of the same CM-β-CD-MF at different pH were also executed (Fig. 5).

The hydrodynamic size of stable particles is 60-70 nm. But at strong acidic conditions the particles are not stable. Agglomerates were formed with higher PCS-values.

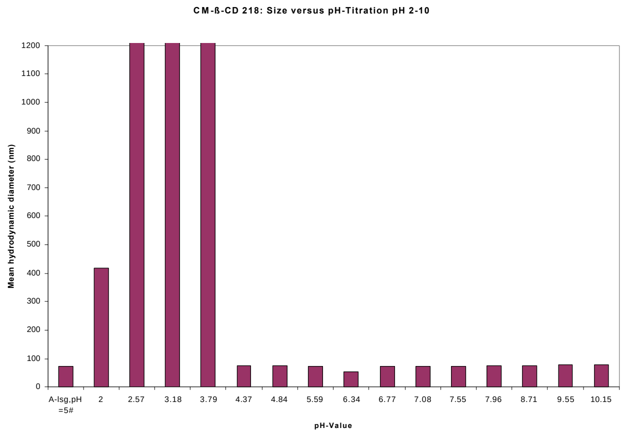

Fig. 5: Mean hydrodynamic diameter (PCS) versus pH-titration, pH 2-10, titrated with HCl and NaOH.

CONCLUSIONS: Novel magnetic fluids (MF) composed of nanosized magnetic iron oxide cores coated with biocompatible cyclodextrines (CD) and carboxylated cyclodextrins (CM-CD) were successfully prepared.

CM-β-CD-MF of high colloidal stability over a pH range of 4-10 in water and with magnetite volume concentration up to 18 % (v/v) (Js 71.7 mT) were synthesized. An average core size of the core/shell-particles of 10.3 nm with a size distribution ranging from 6 to 16 nm, and an average hydrodynamic diameter of 65 nm with a polydispersity index of 0.22 was observed.

The novel MF are intended for use in clinical and biochemical applications.

REFERENCES: [1] Th. Goetze, C. Gansau, N. Buske, M. Roeder, P.Görnert and M. Bahr *Biocompatible Magnetic Core/Shell Nanoparticles* 9. International Conference of Magnetic Fluids (2001) to be published in JMMM, in press. [2] C. Gansau, T. Götze and N. Buske: DE-patent pending 10154016.7. [3] W. Saenger, Angew. Chem. 92, 343-361 (1980). [4] S. Maruno, M. Hasegawa, EP 0928809A1 (1997).