MAGNETICALLY MODIFIED BENTONITE AS POSSIBLE CONTRAST AGENT IN MRI OF GASTROINTESTINAL TRACT

H. Bartonkova, K. Kluchova, M. Mashlan,
I. Medrik, D. Jancik, R. Zboril

Research Centre of Nanomaterials
Palacky University, Olomouc

Objectives

- Preparation of magnetically modified clay mineral by two ways:

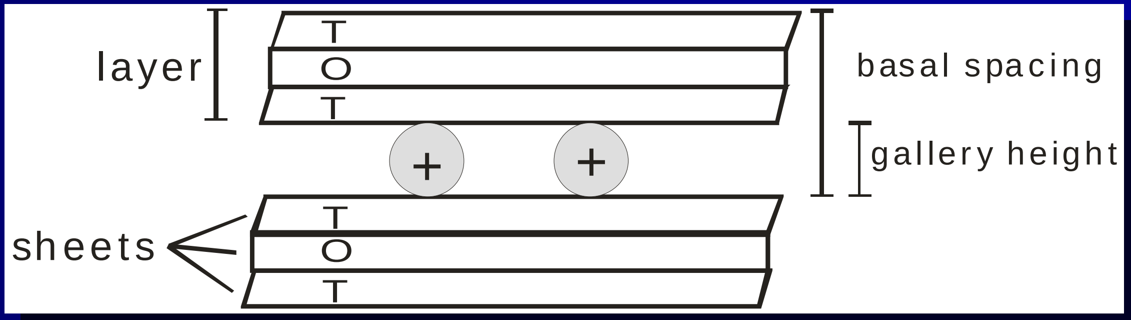
A) Magnetic modification of bentonite by precipitation process. Composite of bentonite and magnetite

B) Synthesis of maghemite nanoparticles termally induced oxidative decomposition of iron(II) acetate and mixed them with bentonite in water (fortrans)

- Characterization of properties of nanoparticles and composites by Mössbauer spectroscopy, XRD and TEM
- Finding potential applications of composite as contrast agent for MRI

What is bentonite?

- It is clay, consisting of smectite minerals, usually MONTMORILLONITE
- Smectites are sheet silicate minerals with diameter up to 2μm
- Layers have a slight negative charge, that is compensated by exchangeable cations (Na^+ or Ca^{2+})



Unit structure of montmorillonite

In the environment with high enough concentration of different cations (e.g. Fe2+) are original ions replaced by these new cations, maintaining charge balance

How to prepare the composite A ?

- Magnetic modification of natural bentonite is two step process:
  I. Replacing original interlayer cations by iron(II) ions and adsorption of another amount of iron (II) ions on the mineral surface
  II. Conversion of iron(II) cations to magnetite
  III. Depending on the used weight ratio of bentonite to iron several samples were obtained:

bentonite:iron

Sample 1:0 – pure bentonite

Sample 20:1

Sample 5:1

Sample 1:2

Sample 0:1 – pure iron oxide

Experiment A step by step

1. Preparation of 0.5% w/v suspension of bentonite in distilled water
2. Mixing the suspension with solution of iron(II) ions ($FeSO_4$)
3. Stirring of mixture for two hours
4. Adding solutions of KNO_3 and KOH, in this order
5. Heating the mixture up to 90°C
6. Slow cooling to room temperature
7. Separation of the product and drying on the air

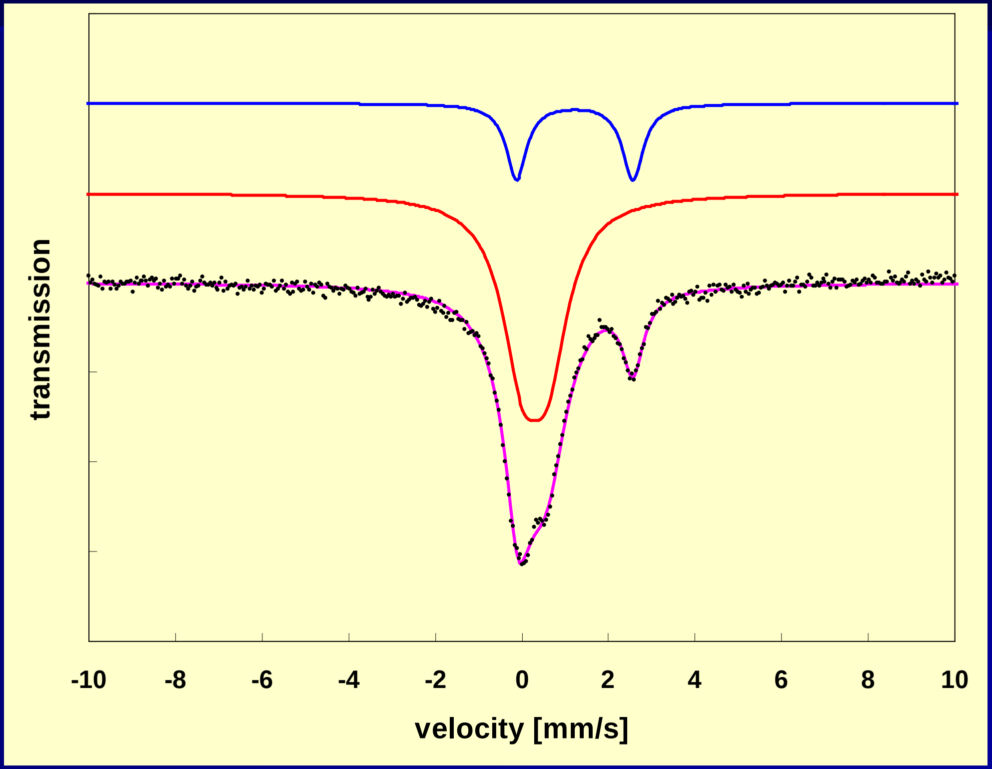
Mössbauer spectrum – natural bentonite

Natural bentonite (sample 1:0) contains low amount of iron, spectrum consists of

Fe^{2+} doublet (δ=1.22 mm/s, Δ=2.69 mm/s)

and

Fe^{3+} doublet (δ=0.30 mm/s, Δ=0.60 mm/s)



RT Mössbauer spectrum of bentonite

Mössbauer spectrum - magnetite

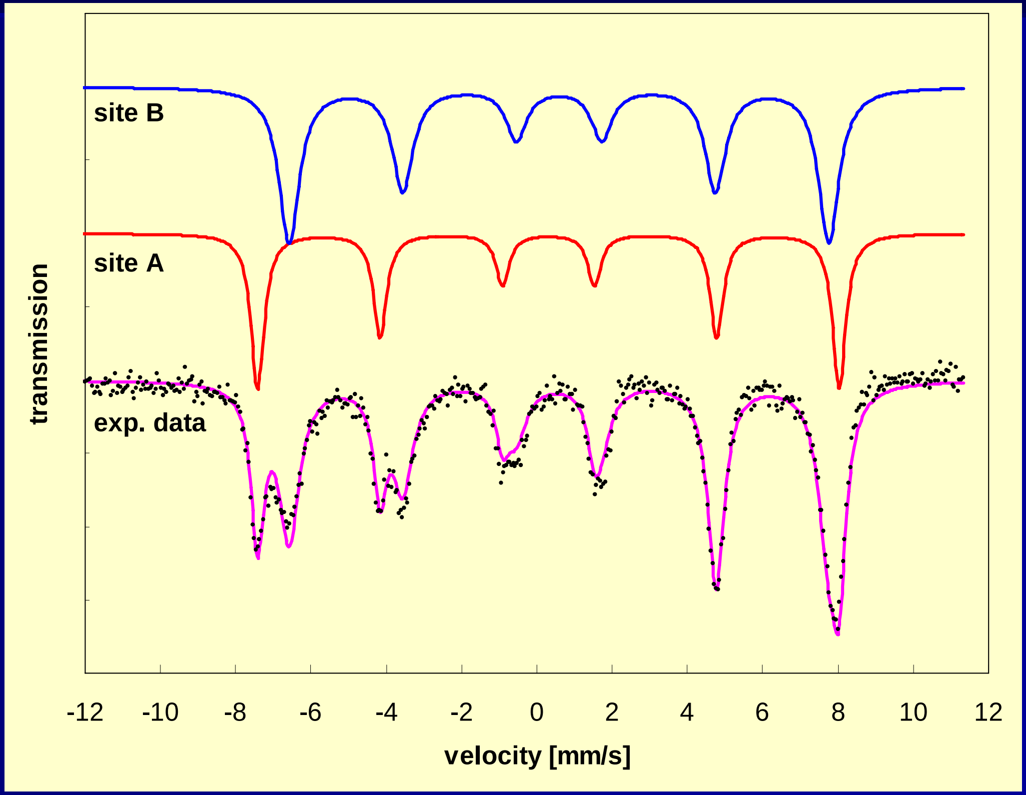
Spectrum of sample 0:1 verifies that pure magnetite was prepared.

Site A

sextet - δ=0.31 mm/s Δ=0 mm/s B=47.9 T

Site B

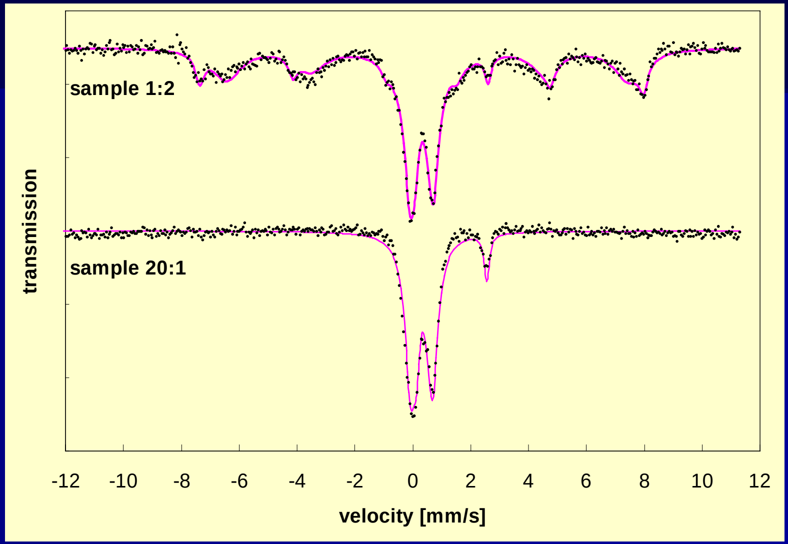
sextet - δ=0.59 mm/s Δ=0 mm/s B=44.5 T



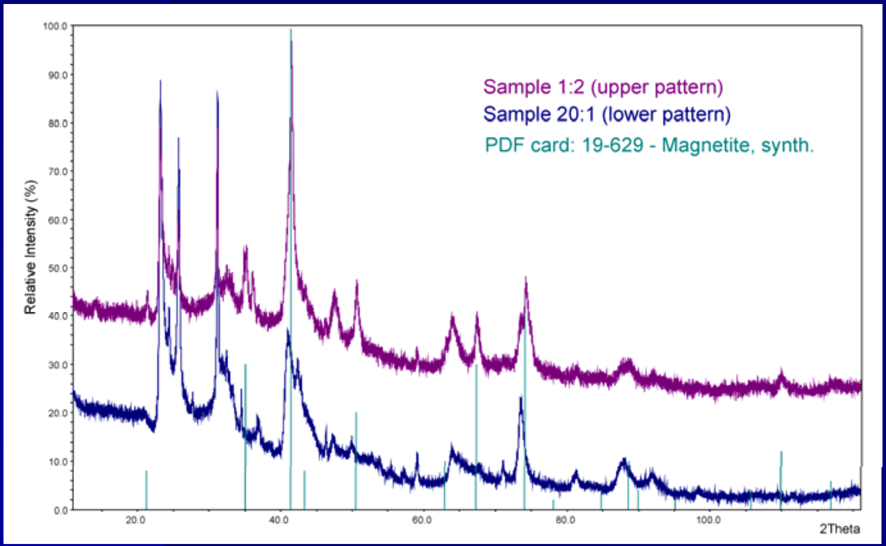
RT Mössbauer spectrum of sample 0:1

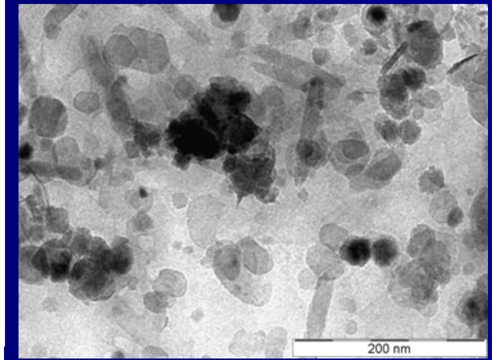
MS, TEM and XRD characterization composite A

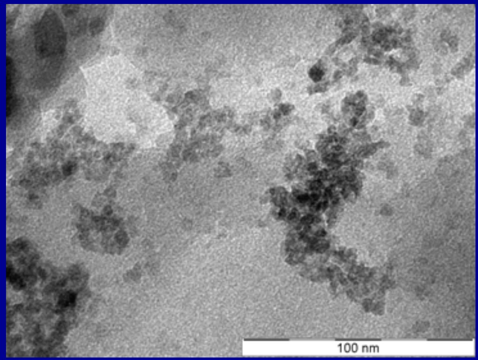
- **Spectrum of sample 1:2 consists of two doublets and two sextets**
- **spectrum of sample 20:1 consists of two doublets**



RT Mössbauer spectra of samples 20:1 and 1:2







TEM 1:2 and 20:1

Mössbauer spectra - composite A

Hyperfine parameters

sample	δ_{Fe} *mm/s*	ΔE_Q mm/s	B_{HF} *T*	*RA %*	*assignment*
1:2	0.31	0.78	-	40.4	Superparamagnetic magnetite
	1.34	2.52	-	4.1	Interlayer Fe^{2+}
	0.51	-	43.1	43.9	magnetite
	0.31	-	47.6	11.6	
5:1	0.33	0.76	-	52.1	Superparamagnetic magnetite
	1.30	2.57	-	11.8	Interlayer Fe^{2+}
	0.56	-	42.1	29.5	magnetite
	0.29	-	45.7	6.6	
20:1	0.31	0.73	-	88.0	Superparamagnetic magnetite
	1.34	2.42	-	12.0	Interlayer Fe^{2+}

Mössbauer spectra – composite A

- Samples 20:1, 5:1 and 1:2 contain iron in several states:

I. Interlayer cations Fe^{2+}, balancing the negative charge of mineral layers
II. Magnetically ordered magnetite
III. Superparamagnetically ordered magnetite

- Proportion of amounts of magnetically ordered magnetite and superparamagnetically ordered magnetite is changing in dependence on bentonite/iron weight ratio in composite

How to prepare the composite B ?

-Synthesis of magnetic nanoparticles Fe-O-based by thermally induced oxidative decomposition of iron(II) acetate

-Our precursor: Iron(II) acetate - $(CH_3COO)_2Fe$ (Sigma Aldrich)

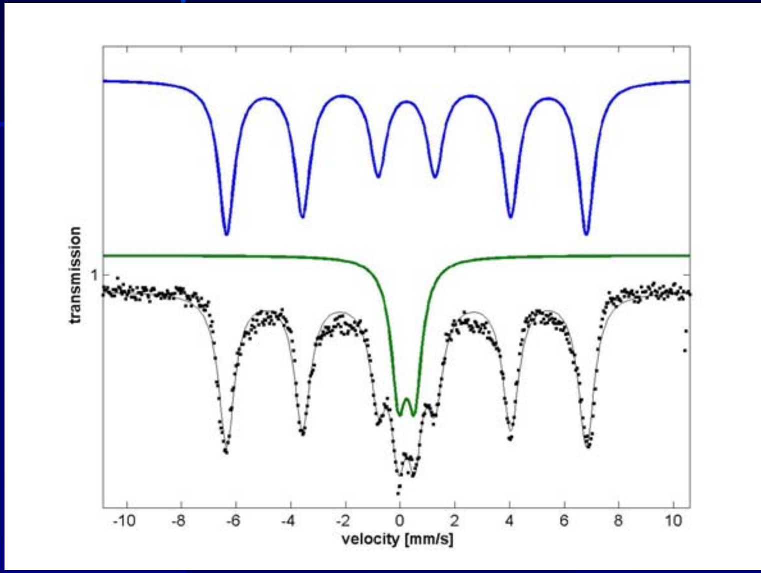
Synthesis : - the same kind of a ceramic bowl
- the same embankment of homogenized precursor: 1.2 g,
- thin layer of sample
- the oven LM 312.27 (LINN HIGH THERM)
- syntheses in air at 400 °C

Preparation of mixture of bentonite and maghemite nanoparticles :

-Mixing 30 mg γ-Fe_2O_3 and 200 mg bentonite in 50 ml of Fortrans

-Drying in air

Characterization of magnetic nanoparticles

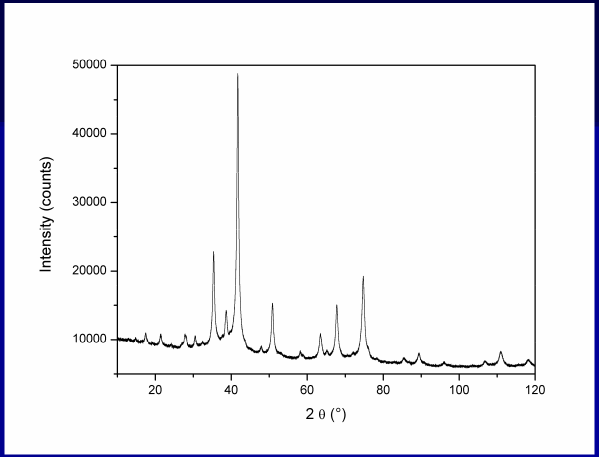


RT Mössbauer spectrum of maghemite synthesized at 400°C

Doublet: δ= 0.35 mm/s
ΔE_Q= 0.64 mm/s

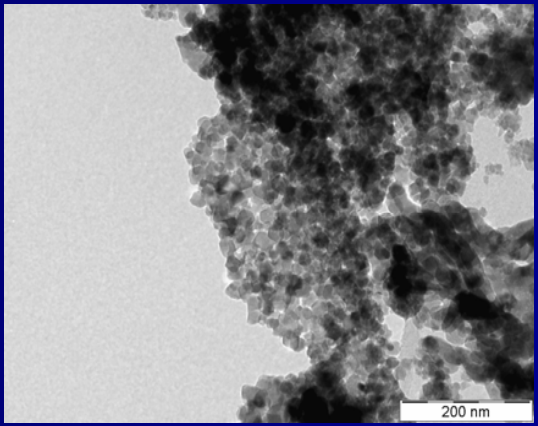
sextet(blue):
δ= 0.27 mm/s, ε_Q = 0

Only one chemical phase: Maghemite



XRD of the sample synthesized at 400 °C

- **narrow size distribution**
- **size of nanoparticles 20 nm**



TEM picture of maghemite

Contrast agents for MRI

$$SI = p \cdot e^{-\left(\frac{TR}{T1}\right)} \cdot \left[1 - e^{-\left(\frac{TE}{T2}\right)}\right]$$

In MRI, the signal intensity (*SI*) can be simplified in a spin-echo sequence by expression

- A lot of agents for MRI does exist, based on compounds of gadolinium (e.g. MAGNEVIST, DOTAREM), manganese (e.g. TESLASCAN) or iron (e.g. FERIDEX, RESOVIST)
- Special type of them are oral used contrast agents for MRI of gastrointestinal (GI) tract

Contrast agents for MRI of GI tract

Ideal contrast agent should meet these criteria:

- Good patient acceptance
- Uniform marking of GI tract
- Unchanged characteristics of contrast effects when diluted or concentrated throughout the GI tract
- No absorption of contrast material into the systemic circulation or adjacent tissues
- Complete excretion of agent from GI tract
- Increased sensitivity and specificity for diagnosis
- High margin of safety for the lowest effective dose
- Acceptable cost

Contrast agents for MRI of GI tract

- Existing oral contrast agents based on iron compounds:

I. LUMIREM (generic name ferumoxil) – made by Guerbet. It is a suspension of miscible superparamagnetic particles made by aggregates of maghemite and magnetite crystals, coated with siloxane

II. ABDOSCAN (generic name ferristene) – made by Nycomed-Amersham. It consists of superparamagnetic ferrite crystals incorporated into monodisperse polymer particles

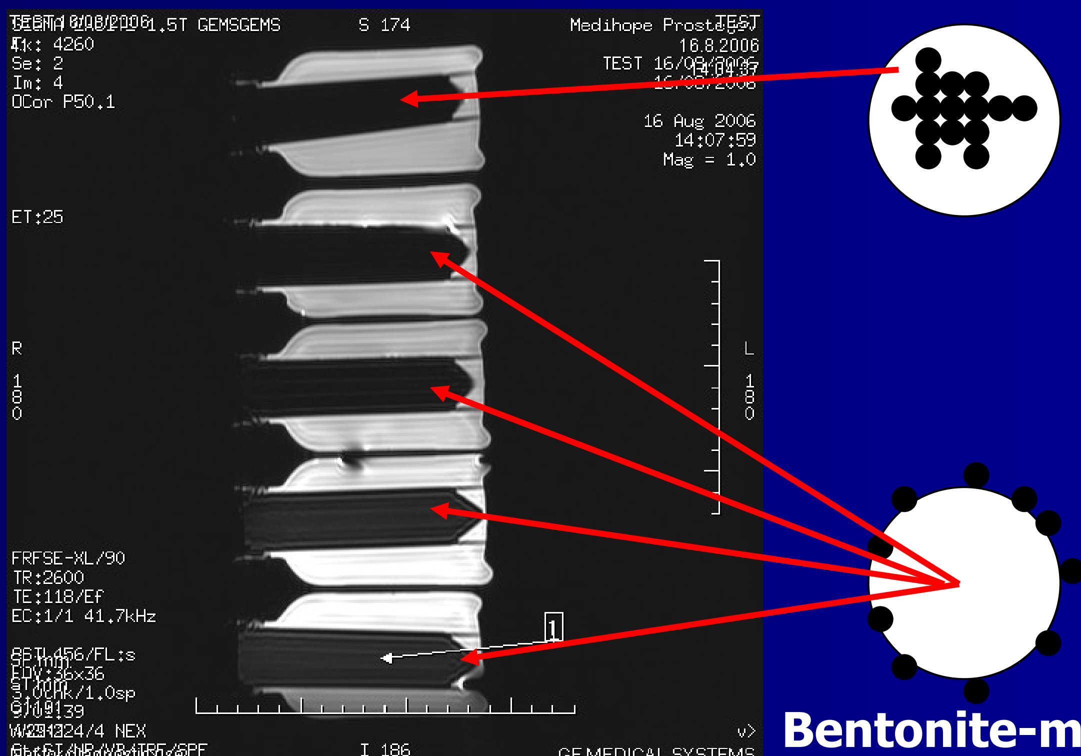
Could our composites act as contrast agent?

- Nanoparticles of magnetite or maghemite guarantee contrast effect
- Bentonite act as inert matrix preventing absorption of iron and improving dispersion of iron oxide particles
- Montmorillonite is used as antidiarrhoea medicament, iron oxide is used as pigment in some comercial medicaments – both components are non-toxic
- Both components are low-cost

Could our composite act as contrast agent?

- MRI pictures of samples: T2 weighted images

Lumirem



Bentonite-magnetite/maghemite

conclusions

- New types of composites were prepared and characterised
- Morphology, size and magnetic properties are determined by mineral-iron ratio in the initial mixture
- New composites were tested as negative MRI contrast agent
- The similar contrast with LUMIREM was obtained