BIH Innovations
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Technology Offer

Novel Iron-(III)-*t*CDTA-based contrast agents for MRI and methods for producing them

Ref. No.: CH879

Background

Intravenously applied gadolinium based contrast agents (GBCA) are the most used contrast agents in magnetic resonance imaging (MRI) for detecting acute and chronic inflammation, tumors and new vascularization. Although the heavy metal gadolinium is complexed, renal excretion is incomplete. Gadolinium deposits have been detected in liver, bone and brain of healthy humans. Potentially decomplexed gadolinium is toxic and renal systemic fibrosis is a rare but severe side effect of less stable GBCA in patients with restricted renal function. Therefore, there is a strong medical need for alternatives to GBCA. In addition, novel agents with pH-dependent contrast effects would be desirable for new diagnostic possibilities.

Technology

Novel iron-III-*t*CDTA-based contrast agents have been developed for use as alternatives to GBCA in MRI as well as a method for producing them with chemical two-step modifications of *t*CDTA. The four investigated iron-III-*t*CDTA derivatives have similar high stabilities as unmodified [Fe-(*t*CDTA)]$^-$. Two of the complexes have relaxivities in the same range as GBCA at field strength of 3 Tesla and higher relaxivities than unmodified [Fe-*t*CDTA]$^-$ that increase with increasing field strength. The dimer-complex has the highest T1 relaxivity of 6.8 l/mmol/s per molecule. One of the four complexes ("[Fe(en-tCDTA)]$^+$-complex") is a pH sensor at weakly acidic pH levels, which therefore is useful in diagnostic imaging of cancer tissue, which have a weakly acidic environment.

Benefits

- ✓ Potentially less risk of long term toxicity compared to gadolinium
- ✓ Increased T1 relaxivities at higher magnetic field strength
- ✓ Avoiding excretion of heavy metal gadolinium to the environment
- ✓ pH-dependent contrast agent: Novel diagnostic use aspects
- ✓ Dimer / Multimer contrast agents: Reduced osmolality

Application

Contrast agent for magnetic resonance imaging e.g. in tumor diagnostic

Further Reading

Eyk Schellenberger, Jing Xie et al. 2021: "Iron(III)-tCDTA derivatives as MRI contrast agents.."; Eyk Schellenberger, Philipp Böhm-Sturm et al. 2018: „Low-Molecular-Weight Iron Chelates…"

Commercial Opportunity

Searching for a licensing or developing partner

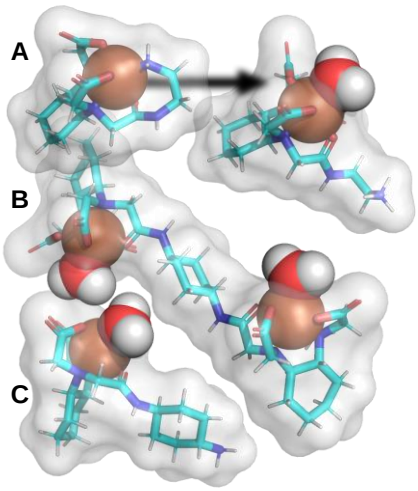

Fig. 1: Three of the novel iron-III-tCDTA based contrast agents. A: pH-Sensor, B: Dimer *Trans*-1,4 diaminocyclohexane-Di-*t*CDTA, C: Monomer *Trans*-1,4-diaminocyclohexane-*t*CDTA

Key words

Iron(III)-*t*CDTA, contrast agent, MRT, MRI, magnet resonance imaging, diagnostic, tumor, pH sensor

Developmental Status

in vitro / in vivo

IP Status

EP patent application (09/2018)
PCT patent application (06/2019): WO2020001950
Regionalization in US and EP
PCT/EP2020/079182 (10/2020)

Patent Owner

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