High spatial resolution LA-ICP-MS demonstrates massive liver copper depletion in Wilson disease rats upon Methanobactin treatment.

Abstract:
Wilson disease (WD) is a rare genetic disorder of the copper metabolism leading to systemic copper accumulation, predominantly in the liver. The therapeutic approach in WD patients is the generation of a negative copper balance and the maintenance of copper homeostasis, currently by the use of copper chelators such as D-penicillamine (D-PA). However, in circumstances of delayed diagnosis, poor treatment compliance, or treatment failure, mortality is almost certain without hepatic transplantation. Moreover, even after years of D-PA treatment, high liver copper levels are present in WD patients. We have recently suggested the use of the bacterial peptide Methanobactin (MB), which has an outstanding binding affinity for copper, as potentially efficient and patient-friendly remedy against copper damage in WD. Here we substantiate these findings considerably, by demonstrating a significant removal of copper from liver samples of WD rats upon short, one week only, MB treatments. Using laser ablation-inductively coupled plasma-mass spectrometry with a spatial resolution down to 4 ?m, we demonstrate that only small copper hotspots remain in MB treated animal livers. We further demonstrate in WD rat liver, seven weeks after the stopped MB treatment, a lower liver copper concentration as compared to untreated control animals. Thus, MB
highly efficiently depletes liver copper overload with a sustained therapeutic effect.

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