Detoxification: Natural scavenger clinoptilolite for removal of heavy metals from the body - The use of naturally occurring clinoptilolite as a special preparation in a small scale pilot study recording the efficacy and safety in the human body-

ABSTRACT

The effect of natural clinoptilolites on lead and cadmium detoxification in smokers was analyzed in two observational studies.

In both proof of concept studies, five subjects were treated daily with 3x2 capsules and one stick preparation containing a milled zeolite clinoptilolite (Manc[©], FROXIMUN AG) after consumption of the last cigarette. The subjects were observed for 4 or 6/8 weeks.

Investigation of lead and cadmium levels in blood, urine and stool showed first evidence of an effect of clinoptilolites on detoxification processes inside the body. Treatment resulted in part in reduced cadmium levels in the blood and increased cadmium levels in urine and stool samples.

Due to the accumulation of cadmium and lead, the risk and intoxication potential is depending on the age of the person as well as the duration and amount of tobacco consume. Therefore, further studies are needed to verify the observations.

INTRODUCTION

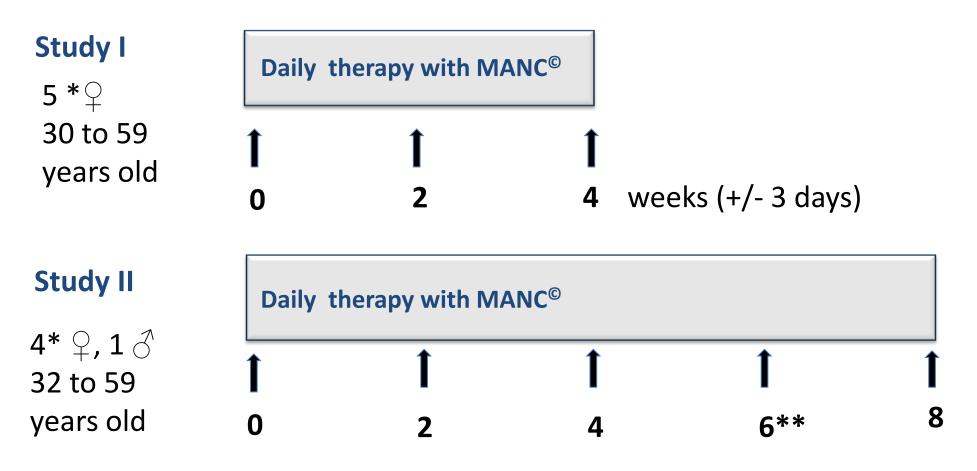
The natural zeolite clinoptilolite is among the aluminosilicate materials and finds diverse applications as adsorbent, ion exchanger and catalyst. In environmental protection, it is a commonly used measure against pollution with heavy metals such as lead (Pb) and cadmium (Cd). Both heavy metals are global contaminants, accumulating inside the body. Especially, smokers have a higher risk to develop diseases as beside food, tobacco smoke displays one of the major exposure sources for cadmium.

Cd and Pb are cancerogenic and teratogenic substances leading to premature births [1]. Cd may also cause nephrotoxic effects as it damages proximate tubule cells resulting in reduced resorption of low-molecular substances of the primary urine [2].

After uptake, Pb gets into the brain, lung, heart and kidney, where it may lead to organ damage. Particularly in children, the damage causes reduced intelligence, capacity of reaction and attention. Additionally, it may shift the hearing threshold and inhibits the synthesis of haemoglobin.

METHODS

The subjects received daily therapy with the zeolite clinoptilolites MANC[©] (FROXIMUM AG) in terms of daily 3x2 capsules and one stick preparation after consumption of the last cigarette. Blood, urine and stool were investigated every second week for Pb (study I only) and Cd levels as well as for liver and inflammation values (study II only). No control group was used and there were no dietary restrictions. Safety, acceptance parameter and compliance were daily documented by the subjects themselves in a diary.



* 3 subjects took part in both studies

** 2 subjects completed study II after 6 weeks

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Safety and compliance

Good tolerability:

- > 2 subjects reported light to moderate diarrhoea on 1 to 2 days
- > 2 subjects reported increased faeces amounts, which were not considered as disturbing
- 100% compliance of subjects from both studies

Effect of MANC[©] on Pb

- No detection in blood (< detection limit of 36 μ l/l)
- Pb in urine constant with a maximum of 1,6 μ l/l at all time points in a = 27 μg/l)
- Increased Pb values within the normal range in stool of 2 subject after treatment

Effect of MANC[©] on Cd in stool

Increased Cd values in stool of some subjects

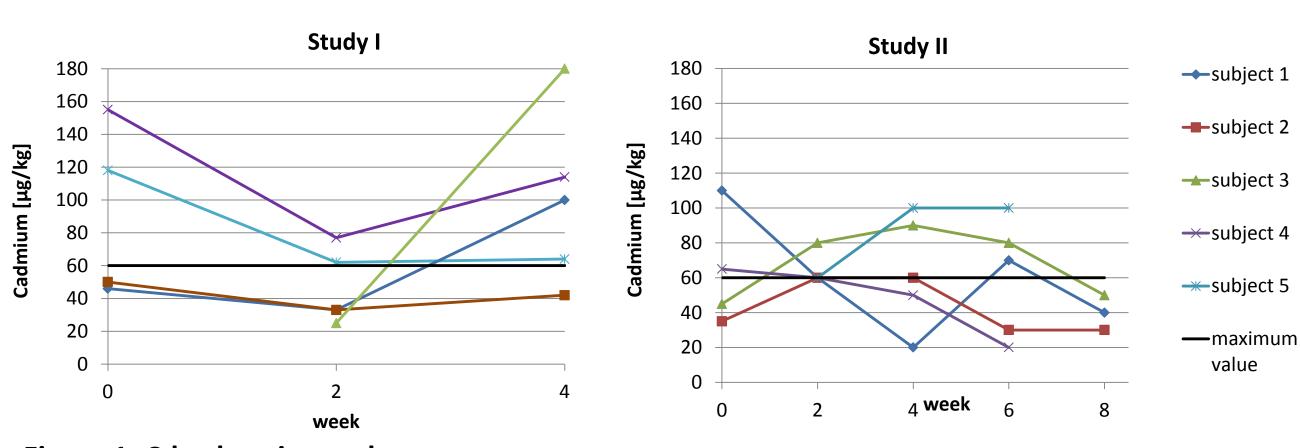
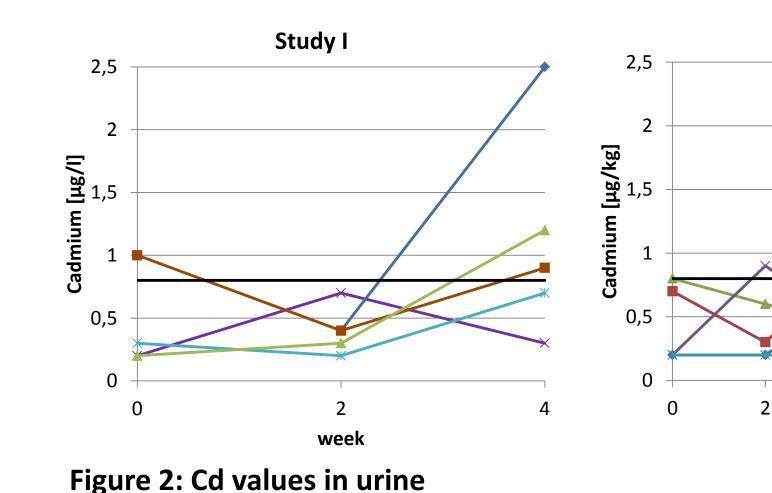
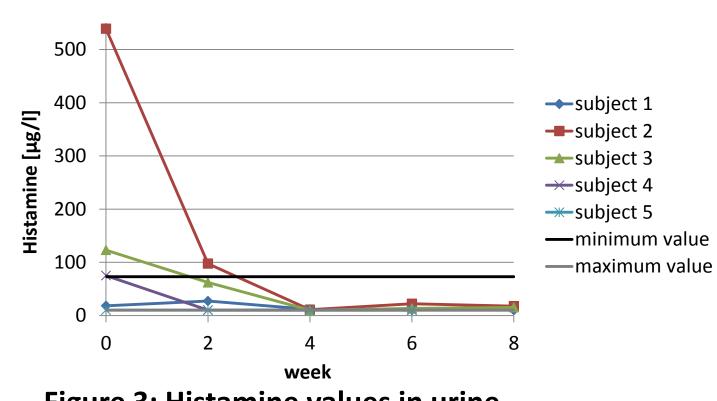


Figure 1: Cd values in stool

Effect of MANC[©] on parameter in urine

- Increased Cd values in urine of some subjects of both studies Decreased histamine levels in urine after treatment - Alternating creatinine values in urine during treatment period in subjects of both studies (data not shown)
- Cd/creatinine levels in urine of potential toxic effects detected in all subjects (cf. Table 1)





Study II

weeks (+/- 3 days)

Subject 5 <<u>0.8</u> <<u>0.9</u> <<u>0.9</u> n.d. Red numbers: values indicating potential toxic effects on: bones and skeleton $>0.5 \ \mu g \ Cd/g$ creatinine; nephrons >1 μ g Cd/g creatinine (1, 2)

0.2 **1.0** 0.5

<<u>2.0</u> <0.2 0.4 <0.2 <0.4

0.7 0.6 0.8 1.5 0.3

0.5 0.4 0.2 0.3 **0.9**

1.0 n.d.

Table 1: Cd/creatinine [µg/g]

0 2

Week

Subject 1

Subject 2

Subject 3

Subject 4

Figure 3: Histamine values in urine

RESULTS

Effect of MANC[©] on parameter in blood

- Significantly reduced (p=0.036) Cd levels in blood of subjects of study I (cf. Figure 4)

Table 2: Effect of MANC[©] on liver values (study II)

Week

all subjects	(max. value

		0	2	4	
	GOT (ASAT) (U/l)	22.0	21.0	24.0	
Subject 1	GPT (ALAT) (U/l)	21.0	18.0	22.0	
	De-Ritis-ratio*	1.0	1.2	1.1	
	γ-GT (U/I)	12.0	14.0	14.0	
	Creatinine (mg/dl)	0.7	0.6	0.6	
Subject 2	GOT (ASAT) (U/l)	23.0	25.0	29.0	
	GPT (ALAT) (U/l)	34.0	34.0	42.0	
	De-Ritis-ratio*	0.7	0.7	0.7	
	γ-GT (U/I)	29.0	31.0	34.0	
	Creatinine (mg/dl)	0.8	0.9	0.8	
Subject 3	GOT (ASAT) (U/l)	17.0	20.0	17.0	
	GPT (ALAT) (U/l)	15.0	17.0	19.0	
	De-Ritis-ratio*	1.1	1.2	0.9	
	γ-GT (U/l)	16.0	16.0	13.0	
	Creatinine (mg/dl)	0.6	0.7	0.6	
Subject 4	GOT (ASAT) (U/l)	29.0	33.0	34.0	
	GPT (ALAT) (U/I)	32.0	38.0	41.0	
	De-Ritis-ratio*	0.9	0.9	0.8	
	γ-GT (U/l)	54.0	57.0	52.0	
	Creatinine (mg/dl)	0.8	0.8	0.8	
Subject 5	GOT (ASAT) (U/l)	33.0	28.0	31.0	
	GPT (ALAT) (U/l)	21.0	22.0	24.0	
	De-Ritis-ratio*	1.6	1.3	1.3	
	γ-GT (U/l)	29.0	31.0	32.0	
	Creatinine (mg/dl)	0.9	0.9	0.8	

Threshold passing values are labeled red, * normal range: 0.6-0.8, Max. values GOT=35; GPT=35; γ-GT=40; creatinine=0.9



-----subject 1 ----subject 2 subject 3 \rightarrow subject 4 —maximum value

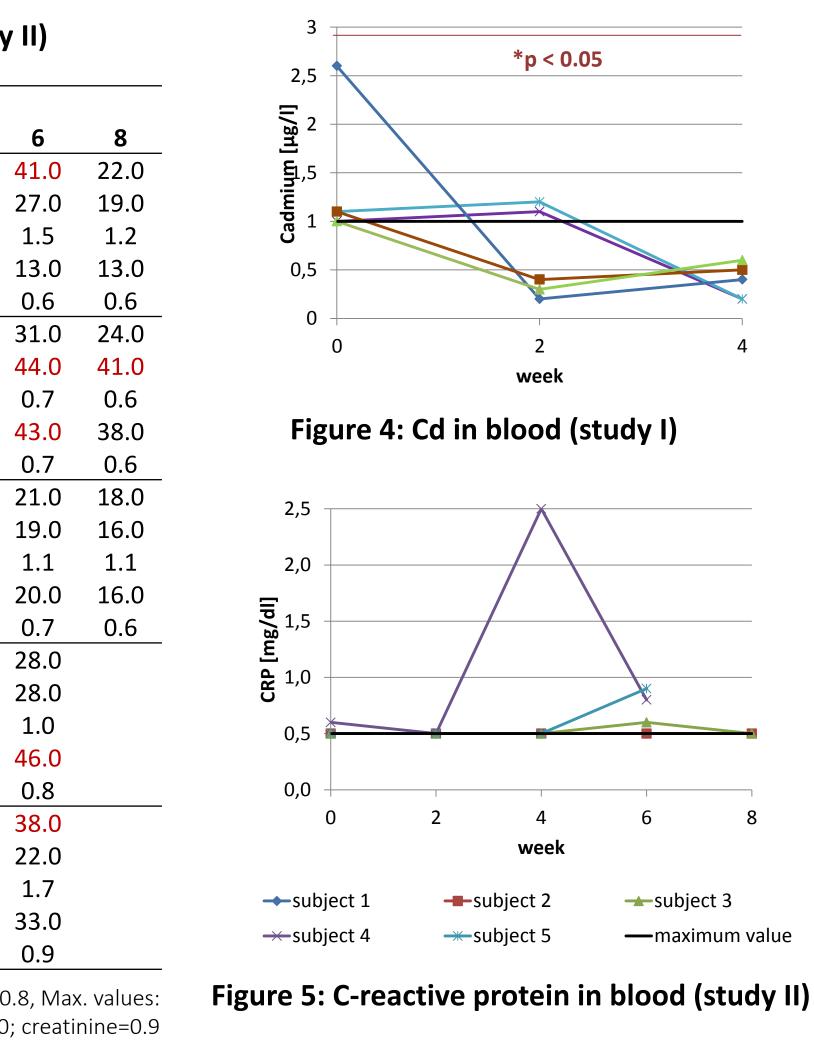
- participated in the first trial.
- like disease (e.g. hepatitis, cholangitis, alcoholic diseases) or drug intake.
- and stool of some subjects.

– MANC[©] therapy may reduce histamine and histamine/creatinine levels in urine.

References:

[1] Bayer W, Schmidt K, Schweizer T (2017) Kompendium Schwermetalle, synlab Holding Deutschland GmbH. [2] Bekanntmachung des Instituts für Wasser-, Boden- und Lufthygiene des Umweltbundesamtes, Kommission "Human-Biomonitoring" des Umweltbundesamtes (1998) Stoffmonographie Cadmium-Referenz- und Human-Biomonitoring-(HBM)-Werte. Bundesgesundhbl., Bd. 41 (5): 218-226. [3] Ewers U, Wilhelm M (1995) Cadmium. In: Wichmann/Schlipköter/Fülgraff (Hrsg.): Handbuch der Umweltmedizin. Ecomed-Verlag, Landsberg. [4]Lee DH, Lim JS, Song K, Boo Y, Jacobs DR (2006) Graded associations of blood lead and urinary cadmium concentrations with oxidative-stress-related markers in the U.S. population: results from the third National Health and Nutrition Examination Survey. Environ Health Perspect., 114(3):350-354.

- Cd values in blood were within the normal range in all subjects of study II (data not shown) Increased liver (see Table 2) and inflammation values (CRP, cf. Figure 5) in subjects of study II



CONCLUSIONS

MANC[©] is a safe medical device, as the therapy was well tolerated.

- Significantly reduced Cd levels in blood of study I could not be verified by study II, as values were in a normal range at all time points possibly resulting from a carry-over effect since 3 subjects also

- If increased γ-GT und CRP values in blood of some subjects may result from a nephrotoxic effect of Cd [3, 4] due to long term exposition needs to be clarified in a follow-up study excluding further reasons

- There is an evidence of detoxification processes as both studies revealed increased Cd values in urine