Bioavailability of cadmium
Results from in-vivo and in-vitro studies using cocoa and linseeds

Hansen, Max; Rasmussen, Rie Romme; Herbst, Birgitte Koch; Sloth, Jens Jørgen

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Cadmium (Cd) is a toxic element found as an environmental contaminant, both through natural occurrence and from industrial and agricultural sources. Food is the main source of cadmium exposure for the non-smoking general population. Besides foods, tobacco smoking and work place air have been identified as potential significant contributors to cadmium exposure. Upon exposure cadmium is efficiently retained in the kidneys and liver in the human body, with a very long biological half-life ranging from 10 to 30 years. Cadmium is primarily toxic to the kidneys and may cause renal dysfunction. Cadmium can also cause bone demineralisation, either through direct bone damage or indirectly as a result of renal dysfunction. There is limited evidence for the carcinogenicity of cadmium following oral administration. In 2009 the CONTAM Panel of EFSA evaluated the dietary exposure to cadmium in the European population. Here a tolerable weekly exposure (TWI) value of 2.5 µg/kg bw/week was established, based on human studies on kidney effects (EFSA, 2009). This value was maintained in a statement from 2011 (EFSA, 2011) following a renewed evaluation due to a provisional tolerable monthly exposure (PTM) of 25 µg/kg bw/month established by the Joint FAO/WHO Expert Committee on Food Additives (JECFA) in 2010.

**DESIGN ANIMAL STUDY**

For the animal study four weaning Wistar rat mothers were acquired each with 10 pups. The pups went directly from breast feed to control feed during the period from day 0 to day 28. Subsequently, the rats were divided into 5 groups and given different diets for 21 days and thus sacrificed. Ethical approval was given by the Danish Animal Experiments Inspectorate. The experiments were overseen by the National Food Institutes in-house Animal Welfare Committee for animal care and use.

**ICPMS ANALYSIS**

*Feeding and kidneys* Subsamples (homogenized feed 0.2-0.4 g and whole single kidneys 0.6-1.5 g) were digested in high-pressure quartz vessels using microwaves (Multitwave 3000, Anton Paar) with 2 ml ultrapure water and 4 ml concentrated nitric acid (PlasmaPure, SCP Science). Prior to analysis the digests were further diluted to a volume of 40 ml with ultrapure water from a Millipore Element apparatus (Millipore).

*Simulated gastric juices* The simulated gastric juice suspensions were first centrifuged (4700 rpm, 10°C, 15 min) followed by filtration with single use hydrophilic syringe filters (0.45 µm, Minisart, Sartorious) and prior to analysis aliquots (0.4 ml) were further diluted to a volume of 5 ml with ultrapure water.

The cadmium content was subsequently determined at m/z 111 by ICP-MS using an Agilent 7500ce instrument (Agilent Technologies). Quantification was done by addition calibration with internal standardisation using 103Rh as internal standard at 1 µg/l in all blanks, standards and samples. The trueness was verified from the analysis of the certified reference material BCR186 Pig Kidney (Institute of Reference Materials and Measurements (IRMM), Geel) 2.83±0.17 mg/kg (N=6, mean ± 2sd), which results agreed well with the certified value (2.71±0.15 mg/kg).

**RESULTS**

The Cd amount in (both of) the rat kidneys following the exposure experiment was calculated from Cd concentration in the kidneys and kidney weight.

<table>
<thead>
<tr>
<th></th>
<th>Mean (µg)</th>
<th>% Mean (µg/kg)</th>
<th>% Mean (µg/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>21</td>
<td>13</td>
<td>-</td>
</tr>
<tr>
<td>Crushed linseed</td>
<td>23</td>
<td>25</td>
<td>-</td>
</tr>
<tr>
<td>Whole linseed</td>
<td>24</td>
<td>27</td>
<td>-</td>
</tr>
<tr>
<td>Cocoa</td>
<td>31</td>
<td>129</td>
<td>328</td>
</tr>
<tr>
<td>CdCl2</td>
<td>24</td>
<td>20</td>
<td>1622</td>
</tr>
</tbody>
</table>

1-2 % of the ingested Cd in the linseeds and cocoa was recovered in the kidneys.

**CONCLUSIONS**

1. The study design allowed the measurement of differences in the absorption of cadmium from foodstuffs in rats at human exposure levels.
2. Absorption of cadmium from linseed and cocoa is lower than the absorption from CdCl2.
3. The rat experiment did not indicate lower absorption from whole linseed compared to crushed linseed.
4. The in-vitro experiment indicate a much higher release of cadmium from crushed linseed compared to whole linseed at a pH similar to the pH in the human stomach.