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Review

Gastrointestinal absorption of uranium compounds – A review

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ABSTRACT

Uranium occurs naturally in soil and rocks, and therefore where it is present in water-soluble form it also occurs naturally in groundwater as well as in drinking water obtained from groundwater. Animal studies suggest that the toxicity of uranium is mainly due to its damage to kidney tubular cells following exposure to soluble uranium compounds. The assessments of the absorption of uranium via the gastrointestinal tract vary, and this has consequences for regulation, in particular the derivation of e.g. drinking water limit values. Absorption rates vary according to the nature and solubility of the compound in which uranium is presented to the test animals and depending on the animal species used in the test. No differences for sex have been observed for absorption in either animals or humans. However, human biomonitoring data do show that boys excrete significantly more uranium than girls. In animal studies neonates took up more uranium than adults or older children. Nutritional status, and in particular the iron content of the diet, have a marked influence on absorption, and higher uranium levels in food intake also appear to increase the absorption rate. If the pointers to an absorption mechanism competing with iron are correct, these mechanisms could also explain the relatively high concentration and chemical toxicity of uranium in the kidneys. It is here (and in the duodenum) that divalent metal transporter 1 (DMT1), which is primarily responsible for the passage of iron (or uranium?) through the cell membranes, is most strongly expressed.

Contents

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1. Introduction

Uranium occurs naturally in soil and rocks in many regions of the world. Concentrations in groundwater vary between geological formations, and they reach levels relevant to human health in some regions where groundwater is used as drinking water. In Germany ground water uranium concentrations range between 0.001 μg/l and approximately 10 μg/l, but usually are below 10 μg/l (Dienemann and Utermann, 2012). Concentrations in excess of 20 μg/l have been reported in groundwater e.g. from parts of New Mexico (USA), central Australia and Norway (WHO, 2012). The digestive tract is the entry route for uranium ingested with drinking water. Results of animal experiments show the small intestinal epithelium and a transmucosal passage to be the preferential pathway for uptake of uranium (Dublineau et al., 2006).

Results of animal studies suggest the toxicity of uranium to be mainly due to its damage to the kidneys, especially to the glomeruli and proximal tubule. It causes histological changes of the epithelial cells in the lower segment of the proximal tubule, in particular the loss of the brush border, vacuoles, increased numbers of lysosomes and necrosis. Functionally this damage leads to increased excretion of glucose, amino acids and proteins (e.g. β-microglobulin). Glomerulus damage can lead to a decrease of the glomerular filtration capacity recognizable through changes in clearance rates and through proteinuria. Studies with humans have shown trends towards increasing markers of kidney damage, i.e. excretion of urinary β2-microglobulin with increasing concentration of uranium in well water (up to 0.7 mg/l), a statistically significant association between increasing but normal levels of urine albumin and an exposure dependent uranium cumulative index (with U in drinking water up to 19.6 μg/l), a correlation between exposure with alkaline phosphatase and β2-microglobulin in urine and a significantly association of uranium in drinking-water (median 28 μg/l, max. 1920 μg/l) with fractional excretion of calcium (for more details see ATSDR, 2013; WHO, 2012).

A guideline value for uranium in drinking water of 10 μg/l was proposed in 2005 as the maximum acceptable lifetime level compatible with health and protective for individuals against its chemically toxic effects (Konietzka et al., 2005), and a limit of 10 μg/l was introduced in the 2011 revision of the German Drinking Water Ordinance. This value is lower than some other health-based limits recommended for uranium in drinking water (e.g. WHO, 2012; U.S.-EPA, 2009, who both set values at 30 μg/l, the WHO on the basis of human data). Setting guideline values may draw on both human and animal data, and where animal data are used, differences in absorption in the gastrointestinal tract between species can be highly relevant for setting health-based guideline values or limits.

As early as 1986, Berlin and Rudell reported that adsorption of uranium compounds in the intestinal tract varies with solubility and, on the basis of daily intake and daily urinary excretion, they estimate a relatively high adsorption. They also suggest that the uranium uptake could be higher in the newborn, and that there could be a dose dependence for adsorption or the existence of highly absorbable uranium compounds in food (Berlin and Rudell, 1986).

The following review therefore collates and assesses absorption data and findings relevant to understanding the absorption behaviour of uranium compounds. It analyses data from animal and human studies with respect to the influence of the solubility, dose, age, species, sex, organ specificity, the nutritional status as well as a possible absorptions mechanism.

2. Data from animal tests

2.1. Dependence of uranium absorption on the solubility of the compound

Uranium (U, CAS no. 7440-61-1) can occur as various compounds, see Table 1 for some examples. Uranium acid salts, known as uranates, include the anion UO_4^{2-}, $U_2O_7^{2-}$ (diuranate) and substances known as polyuranates. Salts with the cation UO_2^{2+} are known as uranyl compounds.

The absorption of uranium compounds increases with their solubility, as shown by Leggett and Harrison (1995) in their comparison of the absorption capacity data found in animal studies (Table 1). Uranium tetrafluoride appears to be an exception with respect to the dependence on water solubility, as its absorption is low as compared to other uranium compounds. Data on dogs obtained by Fish et al. (1960) and unpublished, cited in Leggett and Harrison (1995) show that dogs absorb uranium administered as fluoride only twice as well as a uranium-nitrate compound (compound not specified in further detail, Table 2).

2.2. Species differences

From the data presented in Table 1 we can assume that hamsters absorb around 10 times as much uranium dioxide as rats and dogs, and that rats absorb uranium tetrafluoride 7 times better than mice. Table 2 gives a more comprehensive overview of absorption rates in various animal species. Rabbits absorb the lowest amounts of uranium nitrate (0.06%), rats and mice absorb a little more (<0.1%) and hamsters and dogs absorb much higher amounts (0.8% and up to 1.5% respectively). Absorption rates of uranium offered as bicarbonate differed significantly between mice (0.07%) and baboons (0.5%), although in part this may also be due

Table 1
Comparison of the relative absorption capacity of various uranium compounds following oral ingestion relative to uranyl nitrate hexahydrate (which is set as 1; from Leggett and Harrison, 1995, modified and expanded with data on solubility).

Compound formula (CAS no.)	Water solubility (g/l)[a]	Mice	Rats	Dogs	Hamsters
Uranyl nitrate hexahydrate $UO_2(NO_3)6H_2O$ (10102-06-4)	Soluble; 550 (20 °C)[b]	1	1	1	1
Uranyl fluoride UO_2F_2 (13536-84-0)	Soluble[c]	1	1	1	
Sodium diuranate $Na_2U_2O_7$ (13721-34-1)	No data available	1			
Uranyl peroxide UO_4 (12036-71-4)	No data available	0.5			
Uranium trioxide UO_3 (1344-58-7)	Approx. 0.01	0.5			
Uranium tetrachloride UCl_4 (10026-10-5)	No data available	0.1			
Triuranium octaoxide U_3O_8 (1344-59-8)	Poorly soluble	0.01		0.01	
Uranium tetrafluoride UF_4 (10049-14-6)	Very slightly soluble[c]; 0.1 (25 °C);	0.003	0.02		
Uranium dioxide UO_2 (1344-57-6)	Poorly soluble/practically insoluble[b]		0.01	0.01	0.1

[a] See also Table 1 in Konietzka et al. (2005).
[b] GESTIS (2009).
[c] U.S. Department of Energy (2001).