Review of Potentially Toxic Rare Earth Elements, Thallium and Tellurium in Plantbased Foods

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Review of Potentially Toxic Rare Earth Elements, Thallium and Tellurium in Plant-based Foods

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Abstract

In the last decades, there is an increasing inclusion of various trace metals and metalloids such as thallium, tellurium and rare earth elements (REEs; lanthanides, scandium, and yttrium) in the composition and production of alloys, in agricultural and medicinal applications, as well as in the manufacturing of hi-tech products. All these activities have led to an accumulation of the aforementioned elements both in soil and water bodies and consequently in the food chain, through discharges from mining and mineral processing, liquid industrial waste or disposal of urban and industrial products. It has been demonstrated that chronic exposure to some of these elements, even at low doses, might lead to a wide range of adverse health effects, even from the early stages of life, such as neurotoxicity, neurodevelopmental toxicity and hepatic alterations. Particularly in children, there have been studies suggesting that some of these elements might negatively affect the children's spatial learning and memory ability indirectly. Such effects are triggered by processes like the production of reactive oxygen species (ROS), lipid peroxidation and modulation of antioxidant activities. Nevertheless, the limited data from toxicological studies and their so-far naturally low occurrence levels in the environment acted as a deterrent in measuring their concentrations during routine analyses of metals in foodstuff. Thus, it is important to collect information on their occurrence data both in adults and in children's daily diet. This review summarises the current knowledge on the concentration of these elements, in plant-based food products to identify whether a potential health risk occurs. As side projects, this Fellowship provided hands-on training on the evaluation of new biocides application and participation in the given advice to the Danish Food and Veterinary Administration, Danish Environmental Protection Agency, the Danish Medical Agency and the European Chemicals Agency.

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Keywords: Rare Earth Element, thallium, tellurium, plant-based food, toxicity, trace element

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1. Introduction

The history of human kind has been closely connected with metals and metalloids. Most attention has so far been paid to heavy metals and their toxicity to humans, through the food consumption. Nevertheless, in the last decades, the use of various trace metals and metalloids has increased in medicinal, industrial and agricultural applications (Du and Graedel, 2011). As a result, there has been an elevation in their accumulation in the ecosystem (atmosphere, water, soil), resulting in potential human contamination via food, through discharges from mining and mineral processing, liquid industrial waste or disposal of urban and industrial products (Cheng et al., 2015).

In the current review, we focus on the rare earth elements, thallium, and tellurium. It has been documented that they can pass through the gastrointestinal tract and accumulate in the human body causing short- or long-term structural or functional alterations that can eventually lead to a toxic effect.

1.1. Rare Earth Elements

The REEs are 17 f-block inner transition elements of the periodic table, consisting of the 15 lanthanides: lanthanum (La), cerium (Ce), praseodymium (Pr), neodymium (Nd), promethium (Pm), samarium (Sm), europium (Eu), gadolinium (Gd), terbium (Tb), dysprosium (Dy), holmium (Ho), erbium (Er), thulium (Tm), ytterbium (Yb), and lutetium (Lu), and scandium (Sc) and yttrium (Y) (Connelly and Damhus, 2005). They have similar physicochemical properties and are classified into light (Ce, La, Pr and Nd), medium (Sm, Eu and Gd) and heavy (Tb, Dy, Ho, Er, Tm, Yb, Lu and Y) REEs, according to their ionic radii, which for the trivalent REEs is similar to the one of calcium (Ca). Despite their name, most of the REEs are abundant in Earth’s crust, with Ce being more plentiful than copper (Cu). Due to their geochemical properties though, they are dispersed and not found highly concentrated in minerals (Haxel et al., 2020). The REEs and alloys containing them are used in many technological devices, like cell phones, computers and rechargeable batteries for phones, cameras, electric and hybrid vehicles (Zhou et al., 2017).

REEs are distributed to and accumulated at elevated concentrations in the liver, eyes, bone, spleen, lungs, kidneys, testis, brain, heart and adipose tissue (Fei et al., 2011; Kawagoe et al., 2005). The distribution ratio in the organs is higher for the heavier REEs (Nakamura et al., 1997). More specifically, it has been proved that the lighter lanthanides, as well as Eu, accumulate in the microsomal fraction of the liver, in the spleen and other organs rich in reticuloendothelial cells (Ohnishi et al., 2011; Magnusson, 1963; Haley, 1965; Durbin et al., 1956). Yb has been shown to accumulate in the brain, liver and femur, while Tb has been found in liver, lung and spleen, with a very slow elimination rate (Feng et al., 2007; Shinohara et al., 1997).

Seven out of the seventeen REEs (Y, La, Ce, Nd, Gd, Tb and Yb) have been reported to have oxidative stress-related negative impacts. The most analysed endpoints were the lipid peroxidation, reactive oxygen species (ROS) production and formation of antioxidant activities, such as superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GPx) (Marubashi et al., 1998; Tseng et al., 2012; Huang et al., 2011; Wu et al., 2013; Zhao et al., 2011b; Xia et al., 2011; Kumari et al., 2014b).

Furthermore, exposure to elements like Ce and La can lead to a decrease in body weight, accumulate in the liver and brain, and lead to alterations in the histopathology and organ function (Aalapati et al., 2014; Hong et al., 2014; Kumari et al., 2014a; Peng et al., 2014; Sang et al., 2013; Zhao et al., 2011b). La has been shown to affect the spatial learning ability and memory of rats, potentially because of the inhibition of the signalling pathway in the hippocampus (Liu et al., 2014). Another study on La administration, during and after the pregnancy in mice resulted in smaller brain size and indication that this element is a potentially behavioural teratogen (Briner et al., 2000).

The REEs have already been found in edible plant-based foodstuff, like fresh edible fungi, vegetables (leafy, fruiting, legume, root, brassica, and bulb), and cereals (corn, rice and wheat flour) (Jiang et al., 2012; Zhuang et al., 2017; Howe et al., 2005).

1.2. Thallium

Thallium (TI) is an element belonging to the same family as aluminium, gallium and indium. It has been used as a pesticide for rodents and insects. Nowadays, it is used in the manufacturing of optic lenses and glass, in pharmaceuticals, medicine, alloys and electronics (International Programme on Chemical Safety, 1996; NLM, 1998; EPA, 1991b; Agency for toxic substances and disease registry,
1992). While, naturally, it is found in small concentrations, thallium accumulation in soil has been increased because of human activity, like copper mining, during the smelting of ores (lead, copper, zinc) and petroleum-refining processes (Nriagu, 1998; Queirolo et al., 2009; Kazantzis, 2000). It is considered a highly toxic element and once it enters the body, it is absorbed via gastrointestinal and respiratory tracts and widely distributed. It accumulates in the bone, liver, heart, muscle, lung, central nervous system and renal medulla (Léonard and Gerber, 1997; John Peter and Viraraghavan, 2005; Galvan et al., 2000).

Several mechanisms and modes of action have been proposed to explain the toxicity of Tl. Its chemical properties are similar to those of potassium (K). Thus, Tl can replace K and modify enzymatic activation of the Na+/K+ ATPases, pyruvate kinase and other proteins, to move via the membrane system and accumulate in the cell (Britten and Blank, 1968; Kayne, 1971). Another mechanism proposes that Tl inactivates sulfhydryl groups, responsible for increasing the permeability of mitochondria, leading to water influx and swelling (Spencer et al., 1973; Maya-López et al., 2018). Exposure to Tl during pregnancy has been linked to decreased mitochondrial DNA in neonates (Wu et al., 2019).

Tl concentrations have been detected in grain and cereal, leafy vegetable (cabbage, lettuce, and kale), oilseed rape, bean and potato samples (Asami et al., 1996; Maluszynski, 2009; Liu et al., 2019; Xiao et al., 2014).

1.3. Tellurium

Tellurium (Te) is a metalloid included in the same group as oxygen, sulfur, selenium and polonium. It has been used as catalyst and pigment for ceramics, in metallurgy as an additive to other metals, in glass optical fibres for telecommunications, as well as in magnetic disk and solar panel manufacturing. Its alloys with other metals are used for nanomaterials, such as quantum dots (Fairhill, 1969; Kominkova et al., 2017; Nishii et al., 1992). Te is distributed to the kidneys, liver, bone, brain and testes (MEDITEXT, 1997). It has been reported that plants that accumulate selenium, can accumulate also Te. Therefore, there is a risk of Te exposure, after consuming a contaminated edible plant (onions, garlic) (Cowgill, 1988). Furthermore, Te’s chloride accumulates in brain cells, called astrocytes, and causes cytotoxicity (Roy and Hardej, 2011).

In addition to onions and garlic, Te has been found in baby food samples, citrus fruits, cereals, vegetables, legumes and potatoes (Filippini et al., 2019; Ruiz-de-Cenzano et al., 2017).

2. Description of work programme

2.1. Aims

The main aim of the present work programme was to provide an overview of an area, still not completely explored. More specifically, this report reviews the current literature of the REEs, thallium and tellurium, regarding their potential toxicity after short- or long-term exposure, along with their concentrations in plant-based food including baby food. Moreover, the current work programme allowed the fellow to become familiar with how to conduct assessments in response to a request (public authorities, stakeholders) in compliance with ethical standards to prevent conflicts of interest.

2.2. Activities/methods

The project is comprised of a literature review of relevant publications (scientific papers and reports) published since 1956 on numerous trace metals and metalloids. The search was based on two factors:

1) Their potential toxicity on humans, mainly after oral administration.
2) Their occurrence in the human diet, and more specifically in edible plants.

The initial plan was to perform chemical analysis and retrieve occurrence data of the aforementioned elements in plant-based food. Due to the COVID-19 crisis, there was a lockdown at the university and the performance of chemical analysis in the risk assessment of a specific scenario was not feasible. Therefore, a more theoretical approach, for the final part of the project, had to be adapted.

2.2.1. Secondary activities

Apart from the main project, the fellow participated in weekly group and monthly division meetings and consultations with other colleagues over the entire period of the EU-FORA fellowship programme.
Besides, the hosting institution encouraged the fellow to participate in the postgraduate course ‘Risk Analysis in Food Safety’, divided in microbiological and chemical risk assessment. The chemical risk assessment module included a group case study, with a final report and poster presentation, elaborating on the risk assessment on a chemical hazard.

The fellow was part of the evaluation of applications and requests, related to biocides’ products that meant to be used mainly as disinfectants. Furthermore, the fellow was taking part, monthly, in recommending and consulting the Danish Food and Veterinary Administration, the Danish Environmental Protection Agency, and the Danish Medical Agency regarding residues in food.

During the fellowship programme the fellow participated in numerous secondary activities, provided by EFSA and DTU (Appendix B).

3. Conclusions

The widespread application of the aforementioned elements in numerous industries and agriculture is increasing, by possibly leading to an increase of their concentrations into the environment and consequently our food. Therefore, the fact that these potentially toxic elements have been already detected in several plant-based foodstuff is of concern (Appendix A).

For some of these elements, we have acquired knowledge regarding their adverse effects in human health. However, most of the animal studies up to now are limited to few REE (mostly Ce and La), and short-/medium-term tests (Pagano et al., 2015a; Pagano et al., 2015b).

The little research regarding their potential on humans toxicity combined with their high request in the technological applications has led to an apparent need to extend the research on this field, including hazard evaluation and risk assessment. The same argument applies for Tl and Te, as studies of long-term exposures and life-long observations are yet lacking, while their occurrence in human’s diet is evident.

The present study constitutes just the first step of all the steps needed to establish a chemical risk assessment regarding the potential risks posed by REEs, Tl and Te present in plant-based foodstuff, including baby-food. Nevertheless, this is a key step to estimate the size of this risk, according to the current knowledge. The next step would be to evaluate their content in foods that are consumed by the general population and to estimate their actual dietary intake.

From a broader perspective, the EU-FORA programme provided the means to a fast and extensive first-hand knowledge and experience of food risk assessment. During the modules and hands-on training, the EU-FORA fellowship programme offered a unique opportunity of networking and enhancing the cooperation among the food safety agencies. In a multicultural atmosphere, the colleagues of the National Food Institute, DTU provided the expertise and mentoring, and creating the ideal environment for knowledge exchange on food safety. Therefore, National Food Institute makes a suitable host site for future EU-FORA fellows.

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Abbreviations

| Abbreviation | Full Form |
|--------------|-----------|
| AGES         | Austrian Agency for Health and Food Safety |
| BfR          | German Federal Institute for Risk Assessment |
| CAT          | catalase |
| DTU          | Technical University of Denmark |
| DW           | dry weight |
| ECHA         | European Chemicals Agency |
| EFET         | Hellenic Food Authority |
| EPA          | Environmental Protection Agency |
| EU-FORA      | European Union Food Risk Assessment |
| fw           | fresh weight |
| GPx          | glutathione peroxidase |
| REEs         | rare earth elements |
| ROS          | reactive oxygen species |
| SOD          | superoxide dismutase |
Appendix A – Occurrence data for REEs, Tl and Te in plant-based foodstuff

| Foodstuff (study)                                                                 | Element/concentration                                                                 |
|----------------------------------------------------------------------------------|---------------------------------------------------------------------------------------|
| Cereals (wheat, maize, legume) (Zhuang et al., 2017)                             | REEs: Ce, La, Nd > 90% of total REE for mining area + Gd, Y                             |
|                                                                                  | Mining area 74.22 μg/kg Control area 47.83 μg/kg                                       |
| Survey in the major foods in China (Jiang et al., 2012)                          | Cereals                                                                 | Total REEs                                    |
|                                                                                  |                                      | 0.039 mg/kg                                  |
|                                                                                  | Fresh vegetables                     | 0.052 mg/kg                                  |
| Survey of food crop categories: Fruits, Legumes, Vegetables (leafy & roots)      |                                                                                  | Ce: 0.24 mg/kg (Callaloo) Eu: 2.8 μg/kg (red kidney beans) La: 0.35 mg/kg (Callaloo) Sc: 21 μg/kg (Turnip) Sm: 27 μg/kg (Callaloo) |
| (Howe et al., 2005)                                                              |                                                                                  |                                                |
| Baby food (Ruiz-de-Cenzano et al., 2017)                                        | Puree of fruits (100 g/100 g), (peach, banana and grape juice from concentrate), corn starch and vitamin C | Te: 2 μg/kg (fw)                             |
|                                                                                  | Green beans (40%), skimmed milk (32%), potatoes (27%), onion, milk cream (3%)        |                                              |
|                                                                                  | Te: 2.94 μg/kg (fw)                                                                |
|                                                                                  | Skimmed milk (32%), water, beans (14%), peas (10%), onion (5%), pasta (4%), rice    | Te: 2.45 μg/kg (fw)                          |
|                                                                                  | Potatoes, skimmed milk, monkfish (10%), tomato, onion, butter, celery,              | Te: 2.58 μg/kg (fw)                          |
| Survey in Italian population (Filippini et al., 2019)                           | Cereals and cereal products                                                       |
|                                                                                  | Te (mg/kg): Tl (mg/kg):                                                             |
|                                                                                  | 0.168 0.055                                                                        |
|                                                                                  | 0.246 0.256                                                                        |
|                                                                                  | 0.382 0.001                                                                        |
|                                                                                  | 0.189 0.046                                                                        |
|                                                                                  | 0.185 0.001                                                                        |
|                                                                                  | 1.072 0.648                                                                        |
| Pyrite mining area: upstream, midstream and downstream zones (Liu et al., 2019) |                                                                                   |
| Green cabbage                                                                    | Tl: 2.78 ± 0.12 – 0.31 ± 0.01 mg/kg                                                |
| Sweet potato                                                                      |                                                                                   |
| Tl-rich sulfide mineralisation area (Xiao et al., 2014)                           | Green cabbage                                                                     | Tl: 338 mg/kg                                |
|                                                                                  | Carrot                                                                             | Tl: 22.1 mg/kg                               |
|                                                                                  | Shelled rice                                                                        | Tl: 2.4 mg/kg                                |
| Waste water-irrigated vegetables (Wang et al., 2013)                             | Sweet potato                                                                       | Tl: 176.7 mg/kg DW                           |
|                                                                                  | Green cabbage                                                                      | Tl: 110 mg/kg DW                             |
|                                                                                  | Soya beans                                                                         | Tl: 51.2 mg/kg DW                            |
|                                                                                  | Eggplant                                                                           | Tl: 56.3 mg/kg DW                            |
|                                                                                  | Lettuce                                                                            | Tl: 22.2 mg/kg DW                            |
## Appendix B – Secondary Activities/Training

| Training sessions provided by EFSA | Title                                                                 | Date          |
|-----------------------------------|-----------------------------------------------------------------------|---------------|
|                                   | 3-Week induction training at EFSA premises in Parma, Italy            | 1-20.9.2019   |
|                                   | 1-Week training module at the Austrian Agency for Health              | 25-29.11.2019 |
|                                   | and Food Safety (AGES) in Vienna, Austria                             |               |
|                                   | 1-Week online module organised by the German Federal Institute for    | 10-14.8.2020  |
|                                   | Risk Assessment (BFR)                                                 |               |
|                                   | 1-Week online module organised by the Hellenic Food Authority (EFET)  | 24-31.8.2020  |
| Training sessions                 | Workshop: Searching for life science and chemistry                     | 15.1.2020     |
|                                   | (Reaxys database – an alternative to SciFinder)                       |               |
|                                   | Webinar – Metals & their Toxicity                                     | 11.2.2020     |
|                                   | Webinar – Rapid Assessment of Contaminant Exposure (RACE) tool        | 27.4.2020     |
| Other activities                  | Course: Risk Analysis in Food Safety (Report, Poster presentation)    | Winter semester|
|                                   | Co-advisor of a Master student’s report on chemical risk assessment   | Spring semester|
|                                   | Hands-on training on new veterinary medicine and biocides applications | N/A           |
|                                   | Participation in the advice given to the Danish Food and Veterinary   | Once per month|
|                                   | administration, the Danish EPA and ECHA                              |               |
|                                   | Visit the animal facilities of DTU                                   | 19.2.2020     |