

**Institution: University of Aberdeen**

**Unit of Assessment: 8 (Chemistry)**

**Title of case study: Health policies for levels of inorganic arsenic in rice**

### 1. Summary of the impact

This case study describes how basic research to develop analytical methodologies for measuring inorganic arsenic in food, and its subsequent application to rice and rice-based food commodities, led directly to proposals to establish global agreements describing the maximum permissible level of a class I carcinogen, inorganic arsenic, in rice. The impact of the research conducted in Aberdeen is still to be fully developed, but as a result of our research has been identified as absolutely pivotal by food standards agencies in China, USA, the UK, and the European Union, in leading to policy decisions and changes to established practice amongst policy makers under the leadership of the Food & Agriculture Organisation (FAO) of the UN and the World Health Organization (WHO).

### 2. Underpinning research

Arsenic is regarded as a poison, and in areas where a large population has been exposed to arsenic-containing water, epidemiological studies have established that inorganic arsenic is a non-threshold class I carcinogen. All of the arsenic in water is inorganic, and its concentration is strictly regulated. Since the 1990s, the WHO, the European Union (EU), and the competent authorities in the USA have established a maximum permissible level of inorganic arsenic in drinking water of 0.01mg/l.

The environmental analytical chemistry group at the University of Aberdeen, led by Feldmann since 2003 (s), has worked for many years on the molecular forms of toxic elements in food, including arsenic. The concentration levels of arsenic in different food commodities are hugely variable. It was well known that seaweed used in Far East cuisine had the highest concentrations of arsenic, up to a factor 100 times higher than the levels permitted by UK legislation dating back to 1959 of 1.0 mg/kg. EU regulations are typically more onerous than national food policies, and as a result national legislation has long been subordinated to EU regulation levels although in the case of arsenic, these have never been established. In short, no maximum level for arsenic in foodstuffs exists. The reason behind this is that arsenic can occur in foodstuffs in different molecular forms, of which one organoarsenical (arsenobetaine) has been established to be benign while others, such as arsenosugars, are considered to be less toxic than inorganic arsenic. Hence introducing a legal limit has been more complex than stating a simple arsenic concentration level permissible in food commodities, and consequently, no levels were established for foodstuffs by organisations such as the WHO.

The research undertaken in Aberdeen focussed initially on determining the molecular forms in seaweeds, and studied how these are metabolised by mammals. In the first stage (1) a group of sheep was identified which roam the shoreline of the island North Ronaldsay in Orkney and whose only source of food is seaweed. Analytical methodologies were developed to determine the molecular forms of arsenic in the seaweed, and how these are metabolised by the sheep. Novel arrangements of analytical instrumentation were established by combining online liquid chromatography with arsenic-specific detectors (an elemental (ICP-MS) and molecular mass spectrometry (ESI-MS)). This hyphenation of mass spectrometers was the first of its kind and permitted the unambiguous determination of the molecular forms in complex matrices such as seaweed and urine (2). However, seaweed is not a major food commodity, and although extremely high concentrations of arsenic were identified, very little is in the form of inorganic arsenic, the class I carcinogen. Hence new analytical methods were developed which allowed the study of rice, a food commodity with lower arsenic concentration but consumed in large amounts. The reason for selecting rice was that it had been shown previously that the drinking water in shallow wells in Bangladesh contained significant levels of arsenic to which more than 60 million people are exposed. In collaboration with the group of Professor Meharg (School of Biological Sciences, University of Aberdeen) greenhouse-based experiments were designed to study how the irrigation of arsenic elevated groundwater would influence the arsenic concentration in rice (Abedin et al. ES&T 2002). Although the arsenic was two orders of magnitude lower in concentration in comparison to seaweed, a large proportion of the arsenic was in the inorganic form.

These initial findings provided impetus for further studies, resulting in the first paper to consider arsenic speciation (the identification of the chemical form of arsenic) in rice in a global context (3). The findings concluded that arsenic levels in rice produced in the USA were much higher than in rice from India and Bangladesh and most of the arsenic was in the form of inorganic arsenic. This work was published in 2005 and attracted not only specialist attention from food groups and the American Rice Federation, but also generated very considerable public awareness of the issue. The American Rice Federation accused the research team of bad science (Press Release USA Today) although the findings were later supported following confirmation by research on behalf of the US Environmental Protection Agency (US-EPA). The Aberdeen paper (3) also became the most influential paper related to the research on levels of arsenic in rice, cited 251 times to date (international recognition being identified by Thomson Reuters, *Essential Science Indicators*, November 2009: as the most cited paper in the fast moving area of "arsenic speciation"). This was followed up by a world-wide survey of polished white rice (4) which showed that high-rice consumption in regions with high arsenic in rice revealed elevated cancer risks based on cancer risk models from US-EPA using inorganic arsenic as the contaminant. Application of the same methods to rice-based products led to the identification of high levels of inorganic arsenic in baby rice (5) and rice milk (6).

### 3. References to the research

- 1: J. Feldmann, K. John, P. Pengprecha (2000) Arsenic metabolism of a seaweed-eating sheep in Northern Scotland using HPLC-ICP-MS, **Fresenius Journal of Analytical Chemistry** 368: 116-121. *The first paper to identify how arsenic in seaweed is metabolised in a mammal.* **Cit. 65**
- 2: H.R. Hansen, A. Raab, J. Feldmann (2003) New arsenosugar metabolite determined in urine by parallel use of HPLC-ICP-MS and HPLC-ESI-MS, **Journal of Analytical Atomic Spectrometry** 18: 474-479. *A demonstration of the novel arrangements of two parallel mass spectrometer used simultaneously for arsenic speciation in a complex matrix separated by HPLC.* **Cit. 43**
3. P.N. Williams, A.H. Price, A. Raab, S.A. Hossain, J. Feldmann, A.A. Meharg (2005) *Variation in arsenic speciation and concentration in paddy rice related to dietary exposure*, **Environmental Science & Technology** 39: 5531-5540. One paper of series of publications on characterizing arsenic in food-chains originating from Aberdeen was identified by **Thompson Reuters Essential Science Indicators: Essential Science Indicators, Nov 2009, Environment & Ecology category identified this as the most cited paper in the Fast Moving Front "Arsenic speciation".** <http://sciencewatch.com/dr/fmf/2009/09novfmf/09novfmfMeha/> **Cit. 251.**
- 4: A.A. Meharg, P.N. Williams, E. Adomako, Y.Y. Lawgali, C. Deacon, A. Villada, R.C.J. Campbell, G. Sun, Y.G. Zhu, J. Feldmann, A. Raab, F.J. Zhao, R. Islam, S. Houssain, J. Yanai (2009), Geographical variation in total and inorganic arsenic content of polished (white) rice. **Environmental Science & Technology** 43:1612-1617. *extended worldwide survey with more than 900 samples from 10 countries were analysed,* **Cit. 112**
- 5: A.A. Meharg, G. Sun, P.N. Williams, E. Adomako, C. Deacon, Y.G. Zhu, J. Feldmann, A. Raab (2008) Inorganic arsenic levels in baby rice are of concern, **Environmental Pollution** 152: 746-749. *triggered European Food Safety Authority to revisit arsenic levels in food.* **Cit. 36**
- 6: A.A. Meharg, C. Deacon, R.C.J. Campbell, A.M. Carey, P.N. Williams, J. Feldmann, A. Raab (2008), Inorganic arsenic levels in rice milk exceed EU and US drinking water standards **Journal of Environmental Monitoring** 10: 428-431. *Triggered a response from UK Food Standard Agency to investigate arsenic in rice milk which followed a recommendation that children < 4.5 should not drink rice milk.* **Cit. 23**

#### Relevant UK/EU funding:

- A; 2007-2010 EU Marie Curie Training programme awarded to joined PI Feldmann & Meharg £148k for arsenic loss from paddy field through biovolatilisation
- B: 2007-2011 BBSRC-DFID awarded to Meharg (PI), Feldmann & Price £650k to study genetic approaches to lowering inorganic arsenic in rice
- C: 2008 FSA awarded to Meharg & Feldmann £37k to study cooking practice affects arsenic removal
- D: 2010-2012 FSA awarded to Meharg & Feldmann £120k, to study arsenic speciation in vegetables
- E: 2012-2013 FSA awarded to Feldmann, Krupp & Meharg £146k to study bioimaging of metals in fruits, cereals and vegetables in the UK

**4. Details of the impact** (indicative maximum 750 words)

Prior to 2008, research in Aberdeen had already led to verification research by the US-EPA in the years after 2005. In parallel, Chinese Import Regulations (a) had also been revised to establish a maximum permissible level of arsenic in grain that could be imported. This Chinese hygiene regulation established, for the first time, not only a level for total arsenic, but also for inorganic arsenic in different grain types including rice (0.15 mg/kg) thereby acknowledging the different toxicity of the different molecular forms of arsenic in foodstuffs. No impact was witnessed at that time, however, on the regulatory levels of either the EU or the UK. Subsequent research in Aberdeen discovered that US rice has high levels of arsenic due to the use of arsenic containing herbicides on what were cotton fields but later converted in the Central Mid-West to rice fields. The extremely high arsenic prevalent in Bangladeshi rice grown in the dry season was due to irrigation using water containing arsenic; and that while rice accumulates large levels of arsenic, wheat or barley does not because rice is grown in flooded paddy soil, in which a different mobile form of arsenic occurs which is more easily taken up by the plant.

Subsequently, and as a result of the Chinese regulation, rice-based consumer products were analysed in Aberdeen, and it was found that most did not meet the Chinese standard. This triggered a study by the UK-Food Standard Agency (FSA) to conduct a study on rice-based drinks. Since the average rice milk had higher levels of inorganic arsenic than would be allowed for drinking water, public advice was issued in 2009 that children under 4 should not drink rice milk (b). So called “health foods” such as bran, analysed in Aberdeen, also showed elevated levels of arsenic. When the levels of inorganic arsenic in the consumer products were combined both with consumption data and with the toxicological assessments developed by the US-EPA for arsenic in water, the predicted excess cancer cases from eating rice were modelled. All exceeded the 1 case in 10,000 often used as a benchmark for an acceptable level of a contaminant in food. As a result the FSA began to support Aberdeen’s research (see grants listed in section 3). We investigated how the preparation of the rice has an influence on both the toxic form of the arsenic, and its amount (A). However it was only when the results of an analysis of baby-rice formula were published (5), which found that a significant number of products (35%) from the market did not pass the Chinese regulatory limit that European regulatory authorities began to pay attention. At this point (2009) an expert group of regulators, toxicologists and food scientists were contracted by the European Food Safety Authority (EFSA) to develop a scientific opinion paper related to levels of arsenic in foodstuffs, and whether there was scope to regulate it (c). This EFSA paper highlighted seaweeds and other marine foods, but principally the concern was about arsenic, and in particular inorganic arsenic, in rice and rice-based products. They concluded that there was insufficient data available regarding inorganic arsenic in foodstuffs. The authorities in their surveys only consider the total arsenic content, instead of identifying the specific molecular form of arsenic that is known to be a carcinogen, and only 2% of data contains the latter information. Hence, there was a pressing need to show that a robust analytical method existed to determine levels of inorganic arsenic in rice and rice-based products. Furthermore, it was noted at the FAO/WHO Joint Standard Program (2011) “... *that more accurate information on the inorganic arsenic content of foods as they are consumed is needed to improve assessments of dietary exposures of inorganic arsenic species. Analytical constraints to achieving this goal include the lack of validated methods for selective determination of inorganic arsenic species in food matrices and the lack of certified reference materials for inorganic arsenic in foods. The proportion of inorganic arsenic in some foods was found to vary widely, indicating that dietary exposures to inorganic arsenic should be based on actual data rather than using generalized conversion factors from total arsenic measurements*” (d).

Parallel to these developments Feldmann had been invited to join a discussion group in 2006 at the EU-JRC, IRMM (Institute of Materials & Measurements) to discuss how the lack of arsenic speciation data on consumer products could be alleviated. These discussions resulted in the organisation of a world-wide proficiency testing (PT) (e) and the development of rice as reference material (g) in which inorganic arsenic was certified for the first time. The Aberdeen researchers surveyed arsenic speciation in different rice products in the EU, provided a rice flour material, and studied the stability of a homogenised sample which could be sent out for worldwide PT to more than hundred laboratories to provide information about the concentration of arsenic and inorganic arsenic in this rice flour. Not only was Feldmann’s group chosen to provide the rice samples, it was also one of the five expert laboratories to identify the “true” value, and provide data

for the stability and homogeneity of the arsenic and arsenic speciation of the rice sample. Overall the proficiency testing was extremely successful, the analytical community demonstrating that more than 75% of the laboratories were able to analyse rice within an acceptable level (e). This led to the decision that the introduction of a maximum regulatory level of inorganic arsenic in rice should not be postponed due to concerns over constraints or validation of the analytical chemistry.

As a result, in 2012 the Joint (FAO/WHO) Food Standard Program with the Codex Committee for Contaminants in Foods tabled in their sixth session (26-30 March) a proposed draft maximum level of arsenic in rice and the Food and Drug Administration released their preliminary data of rice and rice based products (g).

In parallel Aberdeen worked together with the EU-JRC-IRMM to generate a rice flour reference material in which not only total arsenic but also its molecular forms especially the inorganic arsenic were certified. We provided the material and worked as the expert laboratory on the certification process. The process was successful and the material was released on 28<sup>th</sup> January 2013 (f) in which for the first time the molecular forms of arsenic were certified. This guarantees that sufficient high quality and transparent data for inorganic arsenic in rice and rice-based products will be produced over the next year to provide confidence for agreement on a maximum level of inorganic arsenic in rice and rice based product at the EU level and worldwide under the leadership of FAO of the UN and the WHO (h).

Claimed impact includes evidence of enhancement of the quality of data for contaminants in consumer products by the development of an analytical method and fostering a general acceptance of analytical methods for the carcinogenic chemical form of arsenic in foodstuff; public health and well-being has improved; and dietary guidelines have changed.

#### 5. Sources to corroborate the impact (indicative maximum of 10 references)

- a) Chinese Import Regulations (GAIN Report CH5080, GB2715-2005 Hygiene Standards for Grains, <http://www.fas.usda.gov/gainfiles/200510/146131382.pdf>)
- b) The UK Food Standard Agency, Survey of total and inorganic arsenic in rice drinks, Food Survey Information Sheet 02/09  
<http://food.gov.uk/science/research/surveillance/fsisbranch2009/survey0209>  
*FSA commissioned two studies one on rice milk and one on baby rice, directly following publication of Aberdeen studies (6, 7 in section 3) and their findings corroborating those of the Aberdeen group. It issued public advice for children younger than 4 not to drink rice milk*
- c) European Food Safety Authority, Panel on Contaminants in the Food Chain (2009), *Scientific Opinion on Arsenic in Food*, **EFSA Journal** 7: 1351.
- d) Joint FAO/WHO Food Standards Program Codex Comm. for Contaminants in Foods (21-25 Mar 2011) max. level of arsenic in food  
[ftp://ftp.fao.org/codex/meetings/CCCF/cccf5/cf05\\_INF.pdf](ftp://ftp.fao.org/codex/meetings/CCCF/cccf5/cf05_INF.pdf)
- e) European Commission-Joint Research Council -IRMM Report of the seventh inter-laboratory comparison organised by the European Union- Reference Laboratory for Heavy Metals in Feed and Food, IMEP 107: total and inorganic arsenic in rice (2010)  
[http://irmm.jrc.ec.europa.eu/EURLs/EURL\\_heavy\\_metals/interlaboratory\\_comparisons/imep-107/Documents/eur24314en.pdf](http://irmm.jrc.ec.europa.eu/EURLs/EURL_heavy_metals/interlaboratory_comparisons/imep-107/Documents/eur24314en.pdf)) *this is the report on the worldwide proficiency test, also subsequently published in a scientific paper co-authored by the Aberdeen group; M.B. de la Calle, H. Emteborg, T.P.J. Linsinger, R. Montoso, J.J. Sloth, R. Rubio, M.J. Baxter, J. Feldmann, G. Raber (2011) Trends in Analytical Chemistry 30:641-651.*
- f) Joint Research Centre (IRMM) reference material catalogue, reference to certificate, origin and certification report of the ERM-BC211 (rice):  
[http://irmm.jrc.ec.europa.eu/news/Pages/1301\\_ERM-BC211.aspx](http://irmm.jrc.ec.europa.eu/news/Pages/1301_ERM-BC211.aspx)
- g) Joint FAO/WHO Food Standards Programme Codex Committee for Contaminants in Foods (26-30 March 2012) a proposed draft maximum level of arsenic in rice  
[ftp://ftp.fao.org/codex/meetings/cccf/cccf6/cf06\\_08e.pdf](ftp://ftp.fao.org/codex/meetings/cccf/cccf6/cf06_08e.pdf).
- h) FDA releases preliminary data on arsenic levels in rice and rice products  
Full data collection to be complete by end of 2012, agency prioritizes further assessment to provide scientific basis for additional recommendations (9<sup>th</sup> Sept 2012)  
<http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm319972.htm>