

LETTER TO THE EDITOR

Low inorganic arsenic in hydrolysed rice formula used for cow's milk protein allergy

To the Editor,

Hypoallergenic formulas are recommended for use in young children with cow's milk protein allergy (CMPA), where breastmilk is not available,¹ with the choice between both extensively hydrolysed casein/whey or amino acid-based products. More recently, hydrolysed rice protein-based formulas (HRF) have become available and are now commonly used in Europe for CMPA. Some of these formulas have gone through the clinical trials required for hypoallergenicity according to European Academy of Allergy and Clinical Immunology guidelines and have shown their suitability for children with CMPA.^{2,3} However, concerns have been raised with respect to the arsenic content in infant rice products.^{4,5}

Arsenic is a ubiquitous metalloid present at low concentrations in rocks, soil and natural groundwater, mainly in inorganic forms.⁶ The International Agency for Research on Cancer classifies inorganic arsenic [As(V)] as carcinogenic to humans, and concerns have been raised with respect to exposure, particularly in early childhood (where relative exposure is greater due to smaller body mass). A publication from the United States in 2012 found that non-dairy-based infant formulas had significantly more As(V) than cow's milk-based equivalents.⁷ HRF are gaining popularity, due to both palatability and cost. We therefore sought to assess levels of arsenic in commonly used HRF in Europe.

For this study, HRF were sourced from Italy, France and Belgium and analysed at the Institute for Global Food Security, Queen's University Belfast. For each brand, we analysed samples taken from 2 different batch numbers, testing 2 samples (from separate tins) for each batch. We used the method of Meharg et al⁴ for analysis. In brief, 100 mg of each sample was microwave-digested at 95°C in 10 mL of 1% nitric acid. A certified reference material (CRM), rice flour NIST1568b, was used for quality control in each analytical batch (variance 2.1% for AS(V)). Samples, blanks and CRMs were tested in triplicate for arsenic content using ion chromatography-inductively coupled plasma mass spectrometry (Thermo Scientific iCap Q ICP-MS coupled to Thermo IC5000 Ion Chromatograph) with a gradient mobile phase for separation of all arsenic species. The results of the analysis are shown in Table 1.

We analysed dry formula powder rather than reconstituted formula to eliminate confounding due to arsenic present in household water. Levels of inorganic arsenic in all the HRF samples tested were very low and similar to that reported by Vela et al⁸ for conventional cow's milk infant formula but slightly higher than that reported by Jackson et al⁷ using a different analysis platform. The average volume of consumption

of hypoallergenic formula at 0-6 months is 600-800 mL/d, which would require 90-120 g of powder (based on an average scoop size of 4.5 g for HRF). This would equate to 1.3-1.8 µg of As(V), which in an 8 kg infant (50th centile for weight, z score 0) is an exposure of 0.16-0.23 µg/kg body weight per day (b.w./d). This is well below the average exposure in childhood generated from data produced by European Food Safety Authority (EFSA) for both infants [0.24-0.43 µg/kg per b.w./d] and toddlers [0.32-0.45 µg/kg per b.w./d].⁶ The As(V) exposure based on an average infant would also be 10-fold less than the limit for exposure set by the World Health Organisation at 2 µg/kg per b.w./d. It is important to note that all these studies are based on analysis of formula powder; actual As(V) exposure is significantly influenced by the arsenic in the tap water used to reconstitute the formula, which (according to EFSA) is 1.1-2.0 µg/kg b.w. There is no maximum level set by EFSA for infant formulas currently, but water for human consumption is set at 10 µg/L (Council Directive 98/83/EC).

The main limitation of this study was that samples were not compared to extensively hydrolysed or amino acid formula, which are the mainstay of treatment formulas for CMPA. However, the latter have been used for the last 60 years in the treatment of CMPA and were assumed safe. In the light of current data, a future study establishing As(V) levels also in these formulas would be recommended.

In conclusion, this study found that As(V) levels in hydrolysed rice formulas are well within the safe range as stipulated by EFSA/WHO. However, it is important take the source of water into account when mixing formulas, which may affect levels.

AUTHOR CONTRIBUTION

RM wrote manuscript and sourcing of rice formulas in Europe used for cow's milk protein allergy. MC performed laboratory analysis and review of manuscript. PT involved in the critical review of manuscript. AM performed critical review of manuscript and direction of methodology of the study.

CONFLICT OF INTEREST

None of the authors declare any conflict of interest pertaining the current publication.

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TABLE 1 Summary of hydrolysed rice formulas analysed in this study and results of arsenic content

Name of feed	Origin	Characteristic	As(V) (µg/kg)	DMA (µg/kg)	Sum of species [As(V) + DMA] (µg/kg)
Modilac Expert Riz 1 (batch one)	France	Hydrolysed rice suitable from 0 to 6 mo	9	2	11
Modilac Expert Riz 1 (batch 2)	France	Hydrolysed rice suitable from 0 to 6 mo	20	15	35
Modilac Expert Riz 2 (batch 1)	France	Hydrolysed rice suitable from 6 to 12 mo	12	13	25
Modilac Expert Riz 2 (batch 2)	France	Hydrolysed rice suitable from 6 to 12 mo	13	14	27
Modilac Expert Riz AR 1 (batch 1)	France	Hydrolysed rice suitable from 0 to 6 mo thickened with carob and cornstarch	14	19	33
Modilac Expert Riz AR 2 (batch 2)	France	Hydrolysed rice suitable from 6 to 12 mo thickened with carob and cornstarch	12	6	18
Novalac Novarice (batch 1)	Belgium and France	Extensively hydrolysed rice from 0 to 12 mo	11	3	13
Novalac Novarice (batch 2)	Belgium and France	Extensively hydrolysed rice from 0 to 12 mo	11	3	13
Plasmon Risolac (batch 1)	Italy	Hydrolysed rice suitable from 0 to 12 mo	9	6	15
Plasmon Risolac (batch 2)	Italy	Hydrolysed rice suitable from 0 to 12 mo	10	5	15

As(V), inorganic arsenic; DMA, dimethylarsinic acid.

The limit of detection (LOD) for all species by HPLC-ICP-MS (calculated from DMA calibration) was 0.0003 mg/kg.

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REFERENCES

- Muraro A, Werfel T, Hoffmann-Sommergruber K, et al. EAACI food allergy and anaphylaxis guidelines: diagnosis and management of food allergy. *Allergy*. 2014;69:1008-1025.
- Vandenplas Y, De GE, Hauser B. An extensively hydrolysed rice protein-based formula in the management of infants with cow's milk protein allergy: preliminary results after 1 month. *Arch Dis Child*. 2014;99:933-936.
- Vandenplas Y, De GE, Hauser B. Safety and tolerance of a new extensively hydrolyzed rice protein-based formula in the management of infants with cow's milk protein allergy. *Eur J Pediatr*. 2014;173:1209-1216.
- Meharg AA, Deacon C, Campbell RC, et al. Inorganic arsenic levels in rice milk exceed EU and US drinking water standards. *J Environ Monit*. 2008;10:428-431.
- Signes-Pastor AJ, Carey M, Meharg AA. Inorganic arsenic in rice-based products for infants and young children. *Food Chem*. 2016;191:128-134.
- European Food Safety Authority. Dietary exposure to inorganic arsenic in the European population. *EFSA J* 2014;12:63.
- Jackson BP, Taylor VF, Punshon T, et al. Arsenic concentration and speciation in infant formulas and first foods. *Pure Appl Chem*. 2012;84:215-223.
- Vela NP, Heidkemper DT. Total arsenic determination and speciation in infant food products by ion chromatography-inductively coupled plasma-mass spectrometry. *J AOAC Int*. 2004;81:244-252.