Original Research

Manganese Content of Soy or Rice Beverages is High in Comparison to Infant Formulas

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Key words: manganese, soy beverages, rice beverages, infant formula

Objective: Well-meaning but inadequately informed parents may perceive plant-based beverages such as soy beverages (SB) or rice beverages (RB) as an alternative to infant formula. Manganese (Mn) is an essential mineral nutrient found at high levels in plants such as soy and rice. Excessive Mn exposure increases the risk of adverse neurological effects.

Methods: We analysed, by atomic absorption spectrometry, the Mn content of 36 SB, 5 RB, 6 evaporated milks (EM), 14 soy-based infant formulas (SF) and 16 milk-based infant formulas (MF), obtained from commercial outlets in Ottawa, Canada.

Results: SB had the highest levels of Mn (16.5 ± 8.6 μg/g dry wt, mean ± s.d.), followed by RB (9.9 ± 1.7 μg/g dry wt). Mn levels of individual SB/RB ranged from 2 to 17 times the mean Mn content of SF (2.4 ± 0.7 μg/g dry wt) and 7 to 56 times that of MF (0.70 ± 0.35 μg/g dry wt). EM contained very little Mn (0.02 ± 0.03 μg/g dry wt). Calculated mean Mn intakes from SB/RB by infants up to 6 months of age, assuming complete substitution of these products (0.78 L/day), approached the Tolerable Upper Intake Level (UL) for 1–3 year olds (no UL for Mn is available for infants under 1 year of age). Expressed as μg Mn/100 kcal, SB/RB exceeded the range derived from ULs and typical energy intakes of 1–3 year olds.

Conclusions: SB/RB should not be fed to infants because they are nutritionally inadequate and contain Mn at levels which may present an increased risk of adverse neurological effects if used as a sole source of nutrition.

INTRODUCTION

Manganese is an essential mineral nutrient with diverse metabolic functions in bone formation, amino acid and energy metabolism and as an antioxidant [1]. The U.S. National Academy of Sciences has recently established Dietary Reference Intake (DRI) values for Mn. These include Adequate Intake (AI) and Tolerable Upper Intake Level (UL) values determined for various life stage and gender groups. For infants in their first year of life, AI values were derived but not ULs; it was concluded that to minimize the risk of adverse effects of excessive Mn intakes by infants, the only source of Mn for infants should be from mother's milk, food or formula [1]. Selected DRIs for Mn are summarized in Table 1.

Plants such as soy and rice are naturally rich in Mn as they accumulate Mn from the soil [2]. Soy protein preparations including soy protein isolate (SPI) contain relatively high levels of Mn. As a result, soy-based infant formulas may contain up to 50 times more Mn than human breast milk (which has a mean Mn content of 6 μg/L) [3,4], even without fortification of the formulas with Mn. High levels of Mn in soy infant formulas have been a concern in the past, leading to recommendations to limit the maximum concentration of Mn allowable in infant formulas to 0.35–0.6 μg Mn/mL [5,6] or 100 μg Mn/100 kcal [7]. The issue of potential adverse effects of Mn consumption from soy-based infant formula still receives some media attention [e.g., 8]. Rice protein preparations similarly contain more Mn than may be desirable in a nutritional product intended for infant feeding [9].

It is widely recognized that breast-feeding is the optimal

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Table 1. Selected Dietary Reference Intake values for manganese derived by the Food and Nutrition Board, U.S. National Academy of Sciences [1]

Age group	Adequate Intake (AI) (mg/d)	Tolerable Upper Intake Level (UL) (mg/d)
Infants 0–6 mo	0.003	**
7–12 mo	0.6	**
Children 1–3 yr	1.2	2
4–8 yr	1.5	3
Men 19–70+ yr	2.3	11
Women 19–70+ yr	1.8	11

** Not established; "to prevent high levels of manganese intake, the only source of Mn intake for infants should be from food or formula" [1].

mode of nutrition for infants [10]. However, there are circumstances where this may not be possible or desired, and commercially available infant formulas provide a suitable alternative. In some areas, for reasons of "cost, convenience and tradition", homemade infant formulas based on evaporated milk continue to be used [11], though these are not generally recommended by pediatric authorities as they may not meet all of an infant's vitamin and mineral needs.

Well-meaning but inadequately informed parents may perceive plant-based beverages such as "soy milk" or rice-based beverages as an alternative to infant formula. This can have severe consequences due to the low energy density and imbalanced nutrient profiles of these products relative to breast milk or infant formula leading to "failure to thrive" [12–14], or to other complications such as rickets or hypocalcemia [14,15]. While the prevalence of such feeding practices is not known, the small number of case reports available in the literature probably represent under-reporting of the phenomenon. Currently, several (but not all) soy or rice beverage products bear label statements that the product is not a substitute for infant formula, and reviews of the subject targeted to dietitians specifically state that "commercial soymilk should not be the primary beverage until after age 1 year," as these products do not provide adequate nutrition for infants [16]. Other concerns exist regarding excessive exposure of infants to substances such as phytoestrogens which are found in soy products [17]. One U.S. manufacturer of soy-based beverage products recently issued a statement that the Mn content of these products might pose a risk of neurotoxicity to infants because of the unique sensitivities of this group [18]. While no direct toxic effects of oral Mn intake in human infants have been reported to date [1,6], Mn overexposure in infancy has been associated with long-term effects on learning ability [19].

We undertook to survey the Mn content of a variety of soy- or rice-based beverage products available commercially in Ottawa, Canada, in comparison to the levels in soy-based and milk protein-based infant formulas and evaporated milk. Phosphate compounds, particularly phytic acid (phytate, hexaphosphoinositol) which is found in plant foods such as soy and rice, are known to decrease the bioavailability of some mineral nutrients through the formation of insoluble complexes in the gut lumen [20]. Decreased bioavailability might "protect" against the effects of exposure to higher levels of Mn such as are found in SB/RB. To assess this possibility we also analysed the phosphorus (P) content of these products.

MATERIALS AND METHODS

Sample Collection and Analyses

A variety of soy- or rice-based beverage products, evaporated milks and infant formulas were obtained from commercial outlets in Ottawa, Canada (Table 2). Each product was represented in this study by a single package and consequently a single product lot number, from which triplicate subsamples were analysed. These triplicate subsamples (~10 mL liquid or ~1 g powder) were accurately weighed and dry ashed at 450°C using concentrated nitric acid as an oxidizing agent until a pure white ash was obtained. Mn was analysed by flame atomic absorption spectroscopy (Perkin-Elmer 5100PC, Perkin-Elmer, Norwalk, CT). P content was determined using a colorimetric assay [21]. NIST standard reference materials (National Institute of Standards and Technology, Gaithersburg, MD) representing milk powder and plant flour matrices were analysed for Mn and P in triplicate, yielding recoveries within the certified ranges. Analytical standards for Mn and P were prepared from certified single-element stock solutions (SPEX Chemical, Metuchen, NJ). A composite control sample was used to assure consistency between analytical runs for Mn and P [22].

Calculations

A. Estimation of Daily Mn Intakes by Infants (Table 2):

1. To convert dry matter concentration to liquid concentration (μg Mn/mL) as consumed:

For liquid products, the specific volume dispensed for analysis was used. Values for liquid concentrate forms of MF and SF were divided by two to account for normal dilution of these products for use.

For SB powders, an estimated value of 10% dry matter was used, based on analysis of SB liquids.

For powdered infant formulas, product label statements of typical volume yield (mL) per weight of product mixed (g) were used.

2. Estimated Mn intakes by infants were calculated from liquid concentrations using the assumption of 780 mL as the typical daily intake by infants, as used in DRI calculations [1].

B. Estimation of Mn content per 100 kcal (Fig. 1):

Estimated Mn content per 100 kcal was derived from label information of energy density, where available. For SB powders, label information or product-specific information from a website referred to on the product label were used. Where these

Table 2. Analysed Mn and P Content of Beverage and Infant formula Products Analysed, per Unit Dry Matter, Calculated Mn Concentration per mL and Intakes for Infants if Fed Each Product as a Sole Source of Nutrition (Assuming Intake of 780 mL/Day, as Used in the DRI Process [1]

Product category	Form	Abbreviation	# Samples*	Mn content		Calculated Mn Intake by Infants (μg/day)	P Content (μg/g dry wt)
				Dry Weight (μg/g)	As Consumed (μg/mL)		
Evaporated milk	liquid	EM	6	0.02 ± 0.03^{a}	0.01 ± 0.01	4.2 ± 5.8	8000 ± 1719^{c}
Milk-protein-based infant formula	liquid concentrate	MFC	6	0.68 ± 0.36^{a}	0.09 ± 0.04	66 ± 33	3006 ± 739^{a}
	powder	MFP	5	0.71 ± 0.36^{a}	0.10 ± 0.05	76 ± 38	3528 ± 481^{a}
	ready-to-use	MFRTU	5	0.72 ± 0.40^{a}	0.09 ± 0.05	69 ± 37	3214 ± 988^{ab}
Soy-based infant formula	liquid concentrate	SFC	5	2.35 ± 0.42^{ab}	0.31 ± 0.06	243 ± 43	3961 ± 570^{ab}
	powder	SFP	6	2.63 ± 0.85^{a}	0.34 ± 0.11	268 ± 86	4294 ± 572^{ab}
	ready-to-use	SFRTU	3	2.16 ± 0.69^{abc}	0.27 ± 0.08	215 ± 66	4124 ± 616^{abc}
Rice-based beverage	liquid	RB	5	9.95 ± 1.74^{abc}	1.36 ± 0.39	1058 ± 301	3021 ± 2008^{a}
Soy-based beverage	liquid, flavoured	SBF	16	13.06 ± 3.64^{bc}	1.60 ± 0.43	1249 ± 333	5186 ± 2286^{abc}
	liquid, unflavoured	SBU	13	15.53 ± 5.65^{c}	1.39 ± 0.51	1082 ± 400	7103 ± 2438^{bc}
	powder	SBP	7	26.00 ± 13.95^{d}	2.47 ± 1.33	1927 ± 1036	8243 ± 1470^{c}

* Each product sample consisted of an individual package (a single product lot number) obtained from commercial outlets in Ottawa, Canada; each sample was analysed in triplicate (see text for details).

Results presented as mean ± SD.

[a,b,c,d] Values within a column sharing a common superscript are not significantly different by ANOVA and Tukey's HSD (unequal N) ($p > 0.05$). Only primary analytical data (Mn and P concentrations per unit dry wt) were analyzed statistically. See text for details.

were not available, estimates of energy density based on product type (e.g. soy flour, soy milk powder) were obtained from the USDA Nutrient Database for Standard Reference, Release 14 [23].

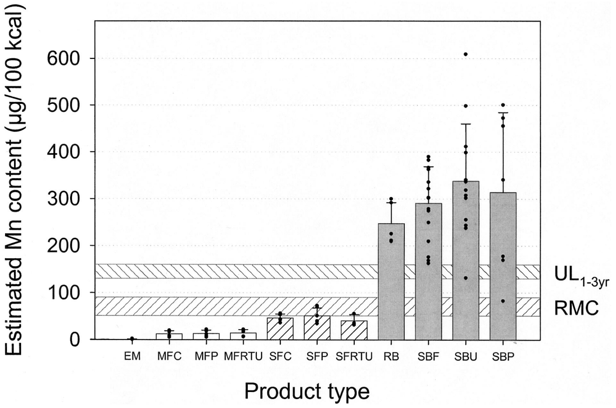

Fig. 1. Estimated manganese content of beverage products per 100 kcal of food energy. $UL_{1\text{–}3\ yr}$ = estimated range of the Tolerable Upper Intake Level (UL) for 1–3 year old children [1], expressed per 100 kcal, derived using energy intakes by 1 and 3 year old children from the Food and Nutrient Intakes by Children Surveys: 1994–96, 1998 [24]. RMC = range of recommended maximum manganese concentrations for infant formulas [5, 6]. EM = evaporated milks, MF = cow milk-based infant formulas, SF = soy-based infant formulas, RB = rice beverages, SB = soy beverages, C = concentrated liquid, P = powder, RTU = ready-to-use liquid, F = flavoured liquid, U = unflavoured liquid.

C. Estimation of phytic acid P content of soy formulas and plant-based beverages from analysed total P concentration (Table 3):

1. Phytic acid P content of soy-based infant formulas was estimated based on the product label statement of protein content assuming soy protein isolate to be 90% protein and 9.8 mg P/g protein [23] with 62% of P present in the form of phytic acid [24].
2. Based on ingredient lists on product labels, liquid SB could be stratified into two groups: those containing >6000 μg P/g dry wt had added inorganic phosphate salts (e.g. tricalcium phosphate); while those with <6000 μg P/g dry wt, with one exception, were assumed to contain only native P compounds. The phytate P content of liquid SB was estimated from the total P content of the latter group (without added inorganic P salts), assuming a phytate P content of 50–70% of total P for soybeans [24].
3. Powdered SB could be distinguished according to label indication of soy protein source: the four powdered SB containing >30 μg Mn/g dry wt (Fig. 2) were based on soy flour, with an assumed phytate P content of 87% of total P; the remaining three were based on soy protein isolate, with an assumed phytate P content of 62% [24]. One product from this last group contained only 57% SPI, and was omitted from further calculations.
4. The 5 RB products analysed were categorized according

Table 3. Total Mn and P (by Analysis) and Calculated Phytate P Content of Soy-Based Infant Formula (SF), Soy Beverages (SB) and Rice Beverages (RB)

Product Description	n	Analysed Total Mn* (μg/g dry wt)	Analysed Total P* (μg/g dry wt)	Calculated Phytate P* (μg/g dry wt)
SF	14	2.4 ± 0.7	4139 ± 554	970 ± 78
SB liquid (no phosphate added)	15	15.2 ± 3.6	4023 ± 986	2012 ± 493 to 2816 ± 690
SB powder (soy protein isolate)	2	12.3 ± 6.1	8706 ± 120	5398 ± 74
(soy flour)	4	36.9 ± 1.6	8754 ± 941	7616 ± 819
RB liquid (no phosphate added)	2	8.9 ± 0.5	890 ± 187	721 ± 152

* Mean ± s.d. (n as shown).

Products included in these calculations are only those with no added inorganic phosphate salts specified in the ingredients listed on the product label.

Proportions of phytate P to total P used in these calculations are based on Reddy (2002).

Note that two value ranges are provided for SB liquid with no added phosphate salts; Reddy (2002) indicates that phytate P in soybeans ranges from 50–70%; values derived using both ends of this range are shown here. See text for details of calculations.

to label statements of added inorganic P salts. Phytate P content of RB was estimated based on the total P content of the two products without added inorganic P salts, assuming a phytate P content of 81% of total P for brown rice [24].

Statistical Analyses

Primary analytical data (dry weight concentrations of Mn and P) were analysed by ANOVA and Tukey's Honestly Significant Difference test for unequal N, using $p < 0.05$ to show significance. Statistical analyses were performed using Statistica for Windows, Version 6.1 (StatSoft, Inc., Tulsa, OK). All values presented are mean ± s.d. and are compared qualitatively to reference values calculated as described below. Individual data for each product tested are also shown in Figs. 1 and 2.

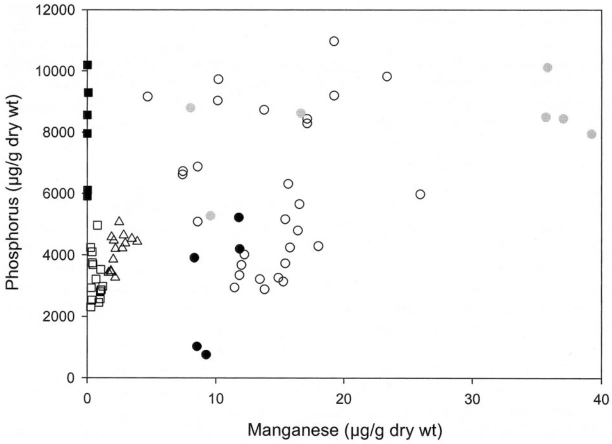

Fig. 2. Scatter plot of analysed P and Mn concentrations of individual beverage products, per unit dry wt. ■ Evaporated milks (EM), □ milk-based infant formula (MF), △ soy-based infant formula (SF), ● rice-based beverages (RB), ○ liquid soy-based beverages (SB), grey circles, powdered soy-based beverages (SBP).

Derivation of Reference Values used for comparison in Fig. 1.

Because no Tolerable Upper Intake Limit (UL) has been derived for infants [1], the UL for 1–3 year olds (2000 μg Mn/day) was used for comparison. It is assumed that tolerable upper intakes for infants will not be higher, and may be lower, than for this older age group. Estimated UL equivalents expressed per 100 kcal in Fig. 1 were derived using mean energy intakes by 1 and 3 year olds (1256 kcal/day for 1 year olds and 1545 kcal/day for 3 year olds) taken from the Food and Nutrient Intakes by Children: 1994–96, 1998 [25]. The reference UL equivalent range so derived is 130–160 μg Mn/100 kcal.

The "Recommended Maximum Concentration" (RMC) range shown in Fig. 1 is based on recommendations made by Lönnerdal [5] and Hambidge and Krebs [6] for upper limits for Mn concentration in infant formulas. The RMC range is 0.35–0.6 μg Mn/mL, equivalent to 270–470 μg Mn/day or 50–90 μg Mn/100 kcal.

RESULTS

Expressed on a dry weight basis, SB had the highest mean Mn content, followed by RB (Table 2). SB/RB products as a group contained 2 to 16 times the level of Mn found in SF and 7 to 56 times that of MF. No difference was noted in Mn content of flavoured versus unflavoured liquid SB products (Table 2), although four of the powdered SB had much higher Mn content than the liquid SB products. EM contained relatively little Mn.

Calculated mean Mn intakes by infants 0–6 months of age, assuming consumption of 780 mL/day of the SB/RB product as the sole source of nutrition approached the UL of 2000 μg Mn/day for 1–3 year olds (Table 2). Calculated Mn intakes by infants 0–6 months of age for four of the individual powdered SB products tested exceeded the UL for 1–3 year olds.

Expressed as estimated Mn concentration per 100 kcal, the mean Mn concentrations of SB/RB were 5 to 7 times the mean levels found in SF, exceeding the estimated UL range for 1–3 year olds of 130–160 μg Mn/100 kcal (Fig. 1). Values calculated for individual SB/RB products, when expressed as μg Mn/100 kcal, almost all exceeded the derived UL equivalent range for 1–3 year olds.

The total P content of all beverage product categories was quite variable (Table 2). Similar mean total P levels were found in SB and EM. Mean total P content of the RB products analysed was similar to that of MF or SF. Calculated phytate P content of liquid SB (based only on those products without added phosphate salts) was 2 to 3 times that of SF (Table 3). SB powders based on SPI had calculated phytate P contents on the order of 5.6 times that of SF, while those based on soy flour were 7.8 times. RB had slightly lower calculated phytate P content than SF (Table 3).

DISCUSSION

The levels of Mn found in SB/RB in the present study were similar to levels reported for Mn-supplemented infant formulas two decades ago [26], before limits on Mn fortification of infant formulas began to be put in place [5]. When converted to liquid concentrations, all of the SB/RB analysed exceeded the RMC for infant formula of 0.35–0.6 μg Mn/mL [5,6]. None of the SF, MF or EM exceeded this range.

The calculated mean Mn intakes by infants 0–6 months of age (in mg/day, based on a standardized consumption estimate of 780 mL/day for this age group [1]) approached, and for four of the individual SB products exceeded, the UL for 1–3 year olds. While no UL has been derived for infants under one year of age, it may be reasonable to assume that such a value would not be higher than for 1–3 year olds, and might be lower. In particular, 1–3 year olds do not typically rely on a single food for all their nutrition, while infants commonly do so.

Expressed on the basis of energy density (μg Mn/100 kcal), 34 of the 36 SB/RB products analysed exceeded the range derived from the UL for 1–3 year olds [1] and mean energy intakes by 1 and 3 year olds in the USA [25]. All but one of the individual SB/RB exceeded the 100 μg Mn/100 kcal maximum Mn content for infant formulas recommended by an expert panel of the Life Sciences Research Office of the American Society for Nutritional Sciences [7]. This apparently greater excess of Mn when expressed per 100 kcal is a reflection of the generally lower energy density of SB/RB compared to infant formulas. Some 60% of the SB/RB products in this study had less than 80% of the energy density of the infant formulas, based on label statements from the packages of product analysed in this study (data not shown). The lower energy density of SB/RB products relative to breast milk or infant formula has been listed as a causal factor in case studies of infant malnutrition resulting from prolonged (weeks to months) feeding of SB/RB as the sole source of nutrition [12–14].

In addition to the risk imparted by their reliance on a small number of food sources, infants may also be more susceptible than older children to the adverse effects of elevated Mn intakes. Animal studies have demonstrated that absorption and retention of Mn are higher during early life [27]. The same appears to be true of humans [28,29]. Following oral exposure, Mn is rapidly cleared from circulation by the liver, within a few minutes [30]. Mn is predominantly excreted in bile [31]. Immaturity of biliary excretion in human neonates thus places them at additional risk from elevated oral Mn exposures because of diminished excretory capacity in addition to higher absorption [32].

The critical adverse effect used in determining the UL for Mn was neurotoxicity [1]. This too points to infants as a group of particular concern, given the rapid neurological development that occurs at this life stage. Here again there is congruency between animal and human studies. Neonatal rats have been shown to be more sensitive to Mn-induced neurotoxicity than adult rats at the same oral dosing level [33]. Excessive oral Mn intakes during infancy and/or childhood, from soy-based infant formulas before limits of Mn content were recommended [19] or from localized environmental contamination of food and drinking water [34], have been associated with learning disability in humans.

The bioavailability of Mn has been shown in some studies to be somewhat lower from SF than from human milk, cow milk or MF when tested in human adults, though not by enough to compensate for the much higher level of Mn in SF. As a result, the total amount of Mn absorbed from SF was much higher [32]. Lower bioavailability of mineral nutrients from plant-based food products is largely attributed to the presence of phytic acid, which represents approximately 60% of the total phosphorus in soybeans [24]. Phytic acid in soybeans is not significantly degraded during processing to soy flour or soy protein isolates [35] such as would have been used to prepare the beverage and formula products analysed here. Neither phytate nor phosphate significantly affected Mn absorption when added to MF fed to human adults [36]. Dephytinization of SF was shown to increase the geometric mean Mn absorption in human adults [37], though the difference was small [38]. The effect of phytic acid on Mn absorption has been described as modest in comparison to the well-known effect on zinc [38].

In the analyses reported here, liquid SB contained on average more than 6 times the Mn level of SF and only 2 to 3 times the phytate P. SB powders based on SPI had roughly 5 times the Mn and phytate P, while SB powders based on soy flour had more than 15 times the Mn and only 7 to 8 times the phytate P. These proportions suggest that phytate would be less "protective" in SB than in SF. The same would appear to be true of RB, which had 3.7 times the Mn level of SF, with slightly lower phytate P than the SF. The most critical factor may be the very high levels of Mn in the SB/RB. Fractional absorption of Mn does not appear to vary much with dose [36], suggesting that infants exposed to high Mn intakes through consumption of SB/RB would take up higher amounts of Mn.

With the introduction of solid foods, young children are no longer reliant upon a single food for their nutrition. This "dilutes" the relatively high Mn content of SB/RB, such that these would not pose the same degree of risk to older infants and children when consumed as a part of a mixed diet.

Although no direct adverse effects of excessive oral Mn exposure to infants have been reported to date, the Mn content of the soy and rice beverages analysed in this study approach or exceed the available reference values (UL, RMC). Soy- or rice-based beverages like those analysed in this study should not be used to replace breast-feeding or infant formula as a sole source of nutrients for infant feeding. In addition to being nutritionally incomplete for such purposes, they contain Mn at a level which may present an increased risk of adverse neurological effects in infants.

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