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Compositional differences between organically manufactured dairy products, infant formula and toddler milk and conventionally manufactured products. Implications for health in infants and young children: a narrative review

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Introduction and background

Global sales of all organic food have recently been reported as having reached 97 billion Euros in 2018 (1). The organic fresh produce market is therefore the fastest growing such market in world agriculture (2).

Data showing organic food revenue and per capita consumption in various countries (2) around the world are shown in tables 1 and 2 below. Clearly the production and consumption of organic foods are major economic and nutritional considerations for many industries and organisations.

COUNTRY	REVENUE (BILLION EUROS)
USA	40.56
GERMANY	10.91
FRANCE	9.14
CHINA	8.09
ITALY	3.48
CANADA	3.12
SWITZERLAND	2.66
UK	2.54
SWEDEN	2.30
SPAIN	1.90

Table 1. Organic food revenue in 2018. (Adapted from Rahman SME et al, Foods. 2021. 10. 105. Doi.org/10.3390/foods10010105)

COUNTRY	PER CAPITA CONSUMPTION (EUROS)
DENMARK	312
SWITZERLAND	312
SWEDEN	231
LUXEMBOURG	221
AUSTRIA	205
FRANCE	136
GERMANY	132
USA	124

Table 2. Organic food per capita consumption in 2018. (Adapted from Rahman SME et al, Foods. 2021. 10. 105. Doi.org/10.3390/foods10010105)

Numerous reasons are cited in the contemporary literature to account for this burgeoning consumption of organic foods, including the perceived potential harmful effect of what is usually termed chemically grown food, on both the environment and human health (3-6). Some of this reasoning is based on reported community and consumer beliefs that organic foods are more environmentally friendly (7) and healthier (8) than chemically grown foods.

A key factor here is that there have been many reports that there are relationships between health consciousness and positive attitudes towards organic foods as well as a willingness to purchase such foods and the frequency of purchases (9-12).

Compositional differences between conventional dairy and organic dairy products

A limited number of studies have evaluated potential differences in the composition of conventional dairy products and organic dairy products. The vast majority of such studies have focused on milk and potential differences in fat composition between such milks. There are clear and obvious reasons for this focus.

Milk and other dairy products have long been known to be rich in saturated fatty acids (SFA) and for many years both these and trans fatty acids (TFA) have been linked in many reports and recommendations to a greater risk of coronary heart disease (13,14).

However, more recent publications have suggested that in fact that milk fat may be beneficial when related to mortality, ischemic heart disease, stroke and diabetes (15), as well as risk of cardiovascular disease (16) and colorectal cancer (17).

Also, there is a burgeoning literature that suggests that n-3 and 18:2 conjugated linoleic acid fatty acids have important health benefits (18-21) and that the ratio of n-3 to n-6 fatty acids in the diet is equally as important as the patterns of consumption of total fat, monounsaturated fat and saturated fat (22,23).

As part of a larger study in Italy, Bergamo and colleagues (24) compared the composition of organic cow's milk fat with that found in cow's milk that have been produced by, what they termed, a conventional management system. The analyses focused on the fatty acid composition of both organic and conventional cow's milk. Differences in the concentration of fat soluble vitamins between the milks were also assessed. Whilst milk was the major focus, a number of milk products such as parmigiano, mozzarella, butter, ricotta, crescenza and fontina were also examined.

There were statistically significant ($p<0.05$) greater amounts of both alpha-tocopherol and beta carotene in the organic products, when expressed per gram of total fat, whilst there was no difference found in the concentration of retinol between the products. Bergamo et al, believed their 2003 publication was the first to show differences in fat soluble vitamins between organic and conventional dairy products and pointed out that dietary intakes of alpha tocopherol may be protective against cardiovascular disease (25), as well as mutagenic alteration (26) and cancer (27).

Concentrations of conjugated linoleic acid, trans vaccenic acid and linolenic acid were all reported as being statistically significantly higher in organic milk when compared to conventional milk. In contrast, organic milk had significantly lower levels of linoleic acid than conventional milk. Bergamo and co-workers stated that their data confirmed the findings of a German study by Jahreis and colleagues, (28) who had previously reported higher levels of conjugated linoleic acid, trans vaccenic acid and linolenic acid in milk produced via organic management. Ellis and colleagues (29) focused on potential differences in fatty acid composition between organic and conventional milk. This work was based on the premise that no large-scale longitudinal studies had, at that time, evaluated possible differences in fatty acid composition due to organic farming that often used clover silage as a forage crop. Consumption of clover silage had previously been shown to effect fatty acid profiles in milk (30). Over a 12 months period bulk tank milk was collected monthly from 17 organic and 19 conventional farms in the UK. The organic milk had a higher proportion of PUFA to monounsaturated acids and of n-3 fatty acids than the conventional milk. The organic milk also had a lower n-6:n-3 fatty acid ratio compared to conventional milk. The authors also considered other factors that were identified as affecting fatty acid composition and were able to conclude that organic dairy farms in the UK produced milk throughout the year with a higher PUFA content, notably n-3 fatty acids. Ellis and co-workers referenced previous work that had linked n-3 fatty acids to improved neurological function, and protection against coronary heart disease and some forms of cancer.

An important paper was published in 2012. Palupi et al, undertook a meta-analysis of previously published papers that considered differences in nutritional quality between organic and conventional dairy products (31).

The meta-analysis considered articles published between March 2008 and April 2011. The rationale for this choice of time period was that a previous review cited by Palupi and colleagues (32) had already covered the period of January1958 to February 2008.

However, should be pointed out that this paper by Dangour and co-workers (32) in 2009 published what they described as a systematic review investigating differences in nutrient content of organically and conventionally produced food stuffs. Their review, that initially examined over 50,000 articles between 1958 and 2008, focused primarily on crops and livestock and not on dairy products, resulted in 55 papers being of sufficient quality to use in their systematic review. As described in their conclusions they found no evidence to support the selection of organically produced foods above conventionally produced foods to increase the dietary intake of specific nutrients.

Palupi et al in 2012, suggested that a review of organic dairy products was timely as sales of such foods had risen by as much as 30% in some European countries following what they described as the BSE crisis. A literature search resulted in 994 papers being identified. After initial screening and subsequent review this number was reduced to 13 articles providing data from 29 studies that were included in the meta-analysis. Of these 29 studies the majority were from the UK (n=12) with 4 from Italy, 3 from Poland, 2 from the USA, Greece and Sweden and 1 from Denmark, Switzerland, the Netherlands and Germany. Twenty six of the 29 studies assessed differences in whole milk, 2 considered differences in curd and 1 assessed Grana Padano cheese. Possible seasonal differences were taken into consideration with 34.5% of the studies using data collected in both winter and summer, 20.7% using data from summer only and the remaining 44.8% using data from winter only

Information was extracted from these studies on a number of key nutrients. These included, fat content, protein content, and some vitamins (α-tocopherol and β-carotene). The analysis mainly focused on the fat components and these were: total saturated fatty acid (SFA), total monounsaturated fatty acid (MUFA), total polyunsaturated fatty acid (PUFA), stearic acid (C18 : 0), oleic acid (C18 : 1 n-9), linoleic acid (C18 : 2 n-6), α-linolenic acid (ALA, C18 : 3 n-3), omega-3 fatty acid (n-3), omega-6 fatty acid (n-6), conjugated linoleic acid 9 (CLA9, cis-9,trans-11 C18 : 2), vaccenic acid (VA, trans-11 C18 : 1), eicosapentanoic acid C20 : 5 n-3 (EPA), and docosapentanoic acid C22 : 5 n-3 (DPA). Docosahexaenoic acid was reported as being excluded from analysis as the number of studies that included this acid was not large enough for quantification.

The effect size was applied to quantify parameter difference between the above nutrients in conventional and organic dairy products. A positive effect size for any nutrient showed that the organic dairy product had a greater concentration or amount of that nutrient, whilst a negative effect size showed greater amounts in the conventional dairy products. Moreover, another statistical approach was used to determine what is called a "fail safe number" which can be used to determine "robust" findings between organic and conventional dairy products. The results of these calculations are shown in table 3, with the "robust" findings shown in red. It should be noted that the determination of a "robust" finding is not simply a function of the effect size. Further, it was reported that organic dairy product had a significantly ($p < 0.001$) higher ratio of omega-3 to omega-6 (n-3/n-6) than that of the conventional dairy products, and a significantly ($p < 0.001$) higher delta 9- desaturase index, where this was calculated as being equal to (CLA9)/(VA) + (CLA9). Palupi and colleagues concluded that the significantly higher amounts of protein, ALA, n-3, CLA9, VA, EPA and DPA in the organic dairy products when compared to the conventional dairy products, coupled with the higher ratio of n-3 to n-6 and the difference in delta 9-desaturase index, indicated that the organic dairy product may have a premium nutritional quality.

They also reported that the most plausible reason for these nutritional differences was the difference in feeding regime between organic and conventional dairy production systems.

Positive Effect	Negative effect
Large Effect Size (>0.8) Alpha Linolenic acid Total Omega-3 fatty acids	**Large Effect Size (>0.8)** Oleic acid
Medium Effect Size (>0.5 <0.8)	**Medium Effect Size (>0.5 <0.8)**
Protein Conjugated linoleic acid Docosapentanoic acid Vaccenic acid	Linoleic acid Omega 6 fatty acids
Small Effect Size (>0.2<0.5)	**Small Effect Size (>0.2<0.5)**
Fat Saturated fatty acids Poly unsaturated fatty acids Eicosapentanoic acid	Mono unsaturated fatty acids Stearic acid

Table 3. Classification of nutrient differences by strength of effect size reported by Palupi E, Jayanegara A, Ploeger A, Kahl J. Comparison of nutritional quality between conventional and organic dairy products: a meta-analysis. J Sci Food Agric 2012. 92. 2774-2781. Robust findings are shown in red.

More recently, the potential use of nuclear magnetic resonance based metabolomics to evaluate the lipid fractions of organic and conventional milk has been described (33). This relatively new approach (34) is believed to have advantages over standard traditional methods such as gas chromatography (GC), GC-mass spectrometry, GC-tandem mass spectrometry and liquid chromatography mass spectrometry (33). The underlying hypothesis of this work was that as milk fatty acid profiles are very sensitive to changes in the diet of animals, there may be differences in fatty acid profiles between organic and conventional milk which may offer potential health benefits to consumers. It has been long known that about 50% of bovine milk fat is derived from plasma lipids of which close to 90% are of dietary origin (35).

Translation of differences in milk composition to differences in infant formula and toddler milk composition manufactured using organic milk

A detailed and comprehensive literature search revealed only two publications that addressed possible differences in the composition of infant formula and/or toddler formula made with organic and conventional milk (36,37). Moreover, these papers are recent (2019 and 2020) and together cite 89 other pieces or work, none of which on close examination, described previous studies assessing possible differences in the composition of infant formula and/or toddler formula made with organic and conventional milk.

Both of these papers where from Italy and both used previously described nuclear magnetic resonance based metabolomics in their analyses. The first publication by Corbu and colleagues (36) contended that their publication was the first to use magnetic resonance based metabolomics in organic infant formula. In this study a total of 15 commercial milk samples were obtained of which 10 were labelled as being suitable from birth to 1 year and 5 being described as being suitable for infants aged 6-12 months. Of these 15 samples, 6 were produced from organic materials. Corbu and co-workers concluded that within the comparison between organic and conventionally produced formulas, the only metabolite that had significantly different concentrations was methionine, which was higher ($p=0.001$) in the organic formula.

Methionine is described as an essential amino acid and must be obtained via the diet as humans lack the ability to synthesise it. Methionine is vital in metabolism and is a substate of other amino acids including taurine and cysteine. Nevertheless, methionine has also long been described as being the most toxic amino acid when consumed in excess (38,39). Thus, as both methionine deficiency and excess can have significant detrimental health effects, quantities in the diet of infants and young children need to be carefully determined (40).

The second recent publication using nuclear magnetic resonance based metabolomics (37) in 2020, acknowledged that little is known about the differences in nutritional profile of formula produced using organic milk when compared with formula made using conventionally produced milk. In this study 5 different brands of both infant formula and toddler milk available in Italy where assessed. Of these 5 brands 2 were labelled as organic. As another comparison 4 human milk samples were also collected and analysed. Significantly different levels of metabolites found between organic and conventional infant formula and toddler milks are shown in Table 4.

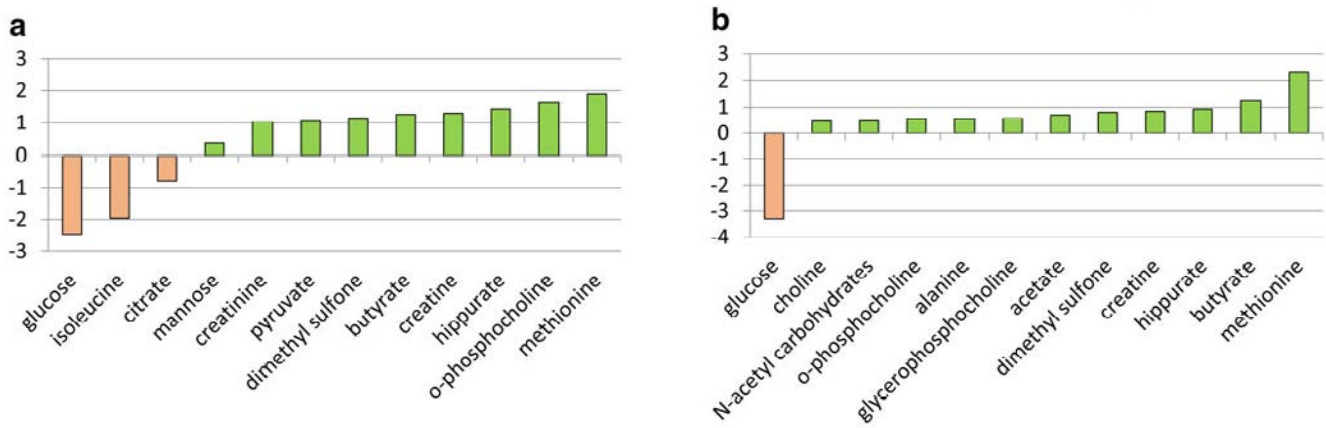

Table 4. Bar plots of Log2FC values of the statistically significant metabolites (FDR p-value <0.05) showing different levels in the organic (positive Log2FC values labeled in green) and non-organic milk formulations (negative Log2FC values labeled in orange). (a) Infant milk formulae; (b) toddler milk formulae. Changes in metabolite levels are calculated as the Log2FC ratio of the normalized median intensities of the corresponding signals in the spectra of the two groups. FDR, false discovery rate; Log2FC, Log2 fold- change.

Taken from Meoni G, Tenori L, Luchinat C. Nuclear magnetic resonance based metabolomic comparison of breast milk and organic and traditional formula brands for infants and toddlers. J. Int. Biol 2020. 24.7. doi:10.1089/omi.2019.0125.

Meoni and colleagues actually reported the differences in numerous metabolites between infant formula and toddler milk produced using organic milk and conventional milk as effect sizes, in similar fashion to Palupi et al (31), although it should be noted that the cut offs to determine large, medium, small and negligible differed. As shown in table 4, the only metabolites that were higher in concentration in conventionally produced infant formula were Isoleucine, citrate and glucose. For toddler milk only glucose concentrations were higher in conventionally produced milk. The classification of all other metabolites by their effect sizes is shown in Table 5.

The primary conclusion of Meoni and colleagues related to the promising nature of their NMR based metabolomics approach to assessing the composition of milk from various sources. Nevertheless they went on to suggest that the variation and differences that they found in some metabolites such as glucose, methionine, o-phosphocholine, butyrate, hippurate, creatine, and di- methyl sulfone could be due to the organic feeding regimen given to some cows that provided milk. However, their views are tempered as they also suggested that as numerous factors affect formula composition, further information, such as the diet composition, breed of cows, and the different processes that milk undergoes to produce formula, is needed to better determine which metabolites could be unequivocally attributed to organic farming practices.

Infant Formula	**Toddler Milk**
Large Effect size >0.474	**Large Effect size >0.474**
Valine	Lactate
Lactate	Alanine
Butyrate	Butyrate
Acetate	Acetate
Methionine	n-acetyl carbohydrate
Pyruvate	Methionine
Glutamine	Creatine
Creatine	Dimethyl sulfone
Creatinine	Choline
Dimethyl sulfone	o-phosphocholine
o-phosphocholine	Glycerophosphocholine
mannose	Hippurate
Hippurate	
Nicotinamide	
Medium Effect Size <0.474	**Medium Effect Size <0.474**
n-acetyl carbohydrate	Valine
Choline	Riboflavin
Glycerophosphocoline	Citrate
Ascorbate	Betaine
Fumarate	Lactulose
Formate	Maltodextrin
Phenylalanine	Sucrose
Tryptophan	
Small Effect Size <0.330	**Small Effect Size <0.330**
Riboflavin	Isoleucine
Tyrosine	Acetone
Histidine	Pyruvate
Negligible effect size <0.147	Glutamine
Alanine	Creatinine
Acetone	Lactose
Succinate	Ascorbate
Betaine	Mannose
Lactose	Fumarate
Lactulose	Tyrosine
Raffinose	Formate
Orotate	Nicotinamide
	Negligible effect size <0.147
	Succinate
	Raffinose
	Orotate

Table 5. Classification of nutrient differences by strength of effect size reported by Meoni G, Tenori L, Luchinat C. Nuclear magnetic resonance based metabolomiccomparison of breast milk and organic and traditional formula brands for infants and toddlers. J. Int. Biol 2020. 24.7. doi:10.1089/omi.2019.0125.

Possible health benefits of organic food consumption in infants and young children

There are few data in the literature that relate to the possible health benefits of consuming organically produced food per se, or organically produced dairy foods or infant formula or toddler milks. Indeed, in 2008, Kummeling and co-workers described their publication (41) as "the first prospective study to evaluate the role of organic food consumption on human health". Specifically, in this study the relationship between early life consumption of organic food and atopic manifestations in the first 2 years of life was investigated in a large birth cohort. In around 2700 two year old children, organic food consumption was measured via parental report of the child's diet in their second year of life. Parents were asked about the consumption of a wide range of food groups such as meat, dairy, fruit, vegetable etc, and when consumed, whether the foods were organically produced or not.

Three diet categories were defined: 'conventional' (i.e organic in less than 50 % of the occasions that the food was consumed) 'moderately organic' (i.e organic in 50 – 90 % of the occasions that the foods were consumed); and 'strictly organic' (organic in more than 90 % of the occasions that the foods were consumed). Each of the seven food groups was given a score, depending on the percentage organic. The scores were summed and divided by the number of food groups that had been eaten. After multiplying by 100 a score between 0 and 100 % was achieved for each child.

The occurrence of eczema and wheezing were assessed by questionnaires, adapted from the International Study of Asthma and Allergies in Childhood (42). At age 7, 12 and 24 months, parents were asked whether their child had ever had an intermittent itchy rash in the past months. If a positive response was recorded for this question, infants were classified as having developed eczema in the first 2 years of life. Wheezing was also recorded in the 7, 12 and 24 months questionnaires. Recurrent wheeze was defined as the reported presence of wheezing with at least four episodes in the first 2 years, whilst prolonged wheeze was recorded if the child had ever been awake due to wheezing in both the first and second year of life.

Kummeling et al reported but there was no association between the consumption of organic meat, fruit, vegetables or eggs, or the proportion of organic products within the total diet and the development of eczema, wheeze or atopic sensitisation. However, they did find that consumption of organic dairy products was associated with lower eczema risk (OR 0·64 (95 % CI 0·44, 0·93)) in those children whose diet had been classified as strictly organic. They also suggested that further studies were needed to support or refute their data. Whilst this study was the first prospective study to evaluate the role of organic food consumption on human health, as previously described, Kummeling and co-workers acknowledge a cross sectional study in older children (5-13 years) from 5 European countries that also showed differences in atopic outcomes based upon diet. This study (43) is complex and cannot provide definitive conclusions as the children were divided in three groups according to the nature of their diet, namely, conventional, biodynamic, or a mixture of conventional, biodynamic and organic foods. Since the latter group consumed foods from a mixture of production methods, the isolated effect of organic foods could not be assessed.

Kummeling et al also pointed out that the mechanism by which organic dairy product consumption may protect against the development of eczema is unknown. Nevertheless, they suggest that n-3 long-chain PUFA have anti-inflammatory properties and can contribute to the maintenance of the skin barrier. They refer to studies already referenced in this current document that show that the levels of n-3 PUFA and conjugated linoleic acid are substantially higher in organic cows' milk when compared to conventionally produced milk (24,28).

Summary and conclusions

There is **substantial and convincing evidence** that sales of organically produced foods of all kinds have accelerated dramatically in recent years (1-2) and that this is a result, at least partially, to consumers beliefs that such foods are less harmful to the environment and health than conventionally produced foods (3-8).

There is **strong evidence from a limited number of studies**, to show that there are differences in composition between conventional dairy (mainly milk) products and organic dairy products (24,28,29,31,33,34). There is **some evidence from a very limited number of publications** (36,37) that there is translation of the differences above into differences in infant formula and toddler milk composition manufactured using organic milk.

There are few data in the literature that relate to the possible health benefits of consuming organically produced dairy foods, per se, (41) and no data/evidence could be found that supported possible health benefits of consuming organically produced infant formula or toddler milks when compared to conventionally produced such formula and/or milks.

Possible future directions

There is a need to complete **more studies** that assess possible differences in composition between organically produced infant formula and toddler milks and conventionally manufactured such products. In the two studies that have reported such differences to date (36,37) the number of samples assessed is relatively small. Corbu and colleagues (36) reported assessments in only 15 formula milks, of which 6 were labelled as being organically produced whilst the remaining 9 were conventionally produced. Meoni et al (37) reported data from a total of 45 packs of formula and toddler milk, from 5 different brands. Of these 2 brands were declared organic and the other 3 were conventionally produced.

It has long been known that the typical characteristics of dairy products, including infant formula and toddler milks, are closely linked to the origin and quality of the milk used in the preparation (44). As a consequence, information relating to all aspects of milk production including animal feeding regimes, breed, season etc should be **documented in detail** to allow these relationships to be better understood.

Assuming such studies confirm and strengthen our knowledge of compositional differences between organically produced infant formula and toddler milks and conventionally made products, **hypotheses could be generated** that relate these differences to potential **health outcomes** that might be seen in groups of infants and young children. These outcomes could be based on biochemical, physiological or morbidity data. Existing data could be used to determine appropriate sample sizes in order to show statistical, biological and clinically relevant differences between feeding groups in a **community setting**.

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