Food Production, Processing and Nutrition

REVIEW

Open Access

Food additives and contaminants in infant foods: a critical review of their health risk, trends and recent developments

Swati Soni[1], Anvil Jennifer W.[1], Christine Kurian[1], Prapti Chakraborty[2] and Kuppusamy Alagesan Paari[1*]

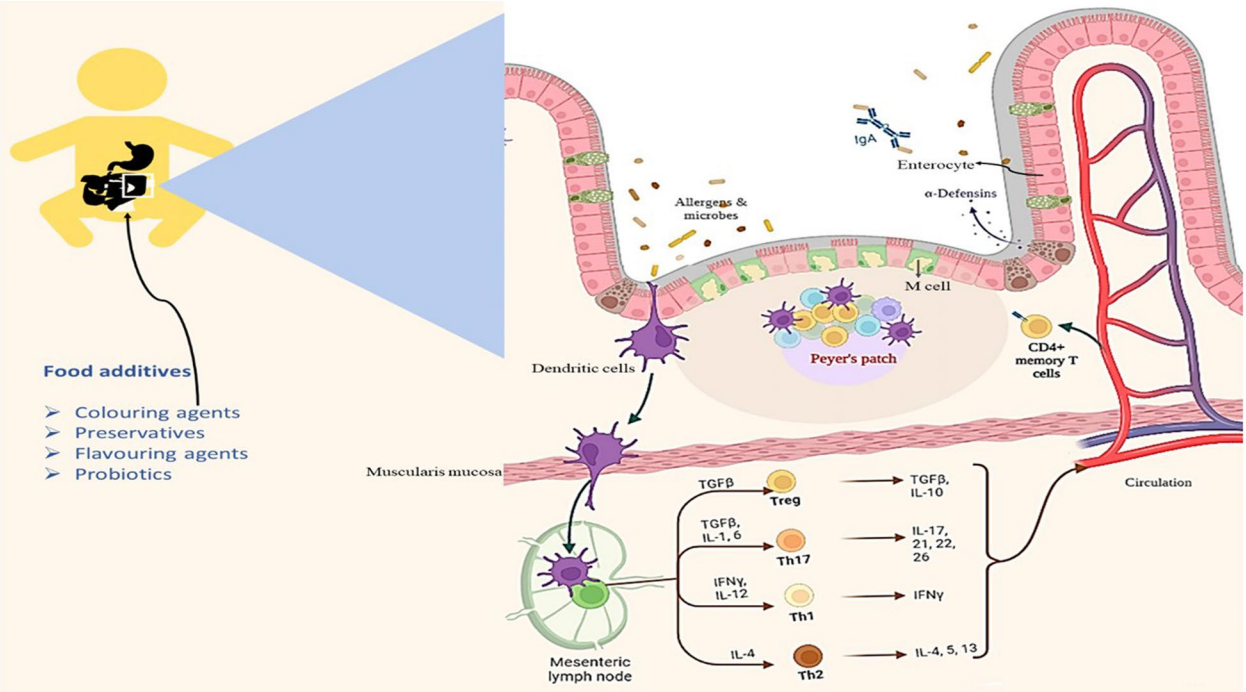
Abstract

The infant food market has expanded rapidly over the past two decades. However, the industry faces significant challenges, including concerns over the health effects of infant food additives and issues with food safety. However, new evidences suggest that certain food additives, such as those used to preserve and transport infant formula to keep it fresh for longer, should be avoided. Science into the effects of additives on human behavior makes up a sizable sector of the additives market. Problems such as hypernatremic dehydration, malnutrition, and obesity in infants are directly linked to faulty formula production. The Food and Drug Administration (FDA) has established the toxicity types and chemical tests necessary for evaluating the safety of food additives and GRAS (Generally Recognized as Safe) compounds. These tests are crucial in understanding the food safety aspects of food additives. The health effects of different types of food additives on infants are discussed in this context. The article gives an outline of various national and global agencies that provides recommendations and standards to gauge the quality of baby food. The immunological responses, allergic reaction pathways and other related health hazards among the infants and young children caused by the food additive are discussed in this article.

Keywords Health risk, Infant formula food, Food additives, Immunological responses, Child health

*Correspondence:
Kuppusamy Alagesan Paari
paari.ka@christuniversity.in
Full list of author information is available at the end of the article

Graphical Abstract



Introduction

The Sect. 201(s) of the United States Food, Drug and Cosmetic Act (US FDA FD & C Act) defines food additives as Substances that could potentially maintain or improve the safety, freshness, taste, texture, or appearance of food are termed as food additives. Some of the food additives are used from centuries for preservation such as salts in meats, sugars in marmalade, or sulfur dioxide in wine, etc. The use of food additives is only justifiable if there is a technological need in preserving the nutritional quality or enhance the stability of the foods. Additives are needed to ensure the processed food remains safe and in good condition throughout its journey from factories or industrial kitchens, or from manufacturer to consumers (Saltmarsh 2013). Globally, 70% of the food market is influenced by inventions in Infant formula. (Carocho et al. 2014). The market for infant food was estimated to be worth over USD 85.61 billion in 2021 and is anticipated to expand at a compound annual growth rate of more than 6% between 2022 and 2030. Over 200 million children, from economically developed and developing nations do not achieve their developmental potential in the first 5 years due to poverty, poor nutrition, inadequate health care and lack of psychosocial support (UNICEF 2021). Therefore, several preventive or therapeutic measures taken during this crucial period have a favorable impact on a person's short, medium and long-term health (Indrio et al. 2022). Food additives pose a significant impact on physiological metabolism that mediates growth and development of infants thereby causing a wide-ranging effect on metabolic diseases such as obesity, heart disorder, and lowered immunity (Sambu et al. 2022).

Over the past two decades, infant food industry has experienced tremendous growth due to growing urbanisation, increased awareness of infant nutrition, and an increase in the ratio of working-class mothers. However, issues on food safety, adherence to home-cooked food, and concern about infant food additives-related health issues are the industry's major challenges (Shashkova et al. 2021). The US Food and Drug Administration (FDA) has approved over 10,000 additives to preserve, pack, or modify food's taste, appearance, texture, and nutritional value (Ukwo et al. 2022). However, emerging research suggests that several chemicals used as food additives should be avoided in infant formula in some conditions, such as in preservation and long-term storage (Thakur et al. 2022). Food additives have been used to perform specific activities in foods, such as enhancing their appearance, aroma or flavour. In addition to

their usefulness in manufacturing food, some sensory additives (monosodium glutamate (MSG), NaCl, and sweeteners) are added strictly for flavour (Prescott 2013; Awuchi et al. 2020).

Infants' nutritional needs and sensitivities differ from those of adults due to their relatively less body mass and their tendency for higher pollutant absorption along with foods (Panseri et al. 2020). The Food and Drug Administration (FDA) has listed more than 3000 food additives which can be categorized into various groups on the basis of their functions and properties: as flavouring agents (sweeteners, natural and synthetic additives), coloring agents, preservatives, texturizing agents (emulsifier, stabilizer, phosphates) (Blekas 2016; Millstone & Van Zwanenberg 2003). Food additives deliberately introduced during processing may induce carcinogenicity or immunotoxicity. Sometimes materials in contact with food, such as plastics, adhesives, and polymers used in packaging, though not deliberately added to the food, can give rise to significant health issues such as hypernatremic dehydration and malnutrition (Trasande et al. 2018b). Thus, biological, chemical, and physical hazard risks must be monitored and addressed for the safety of infant food (Pettoello-Mantovani et al. 2022). In certain cases, the unethical pursuit for profit by businesses factors such as use of low-quality ingredients can lead to serious threats to the safety of food additives (Trasande et al. 2018c). Furthermore, novel milk processing technologies and the utilization of postbiotics provide efficient alternatives to milk consumption, contributing to improved immune tolerance in pediatric populations.

Types of food additives

Food additives are substances primarily added to processed foods, or other foods produced on an industrial scale, for technical purposes, e.g. to improve safety, increase the amount of time a food can be stored, or modify sensory properties of food (WHO 2023). Food additives can be gleaned from various genesis like environment, animals and agro based by-products (Fig. 1). The environmental or natural food additives are mostly derived from plants (herbs, fruits, vegetables). Animal-derived food additives such as gelatin and lecithin (extracted from animal skin/bones and animal fats respectively) are one of the authorised additives used in infant formula in European countries (Nunes et al. 2018). The environmental food additives can be further sorted based on the source from which they are obtained. Antimicrobials from the microorganisms, Ex: Bacteriocins such as Nisin (E-234), Natamycin (E-235) etc.; Antimicrobials from plants, Ex: Essential oils such as Oregano oil, Thymol, Carvacrol, Clove oil and Cinnamon oil etc.; are employed as food additives. However, the utilization of these components lacks authorization from

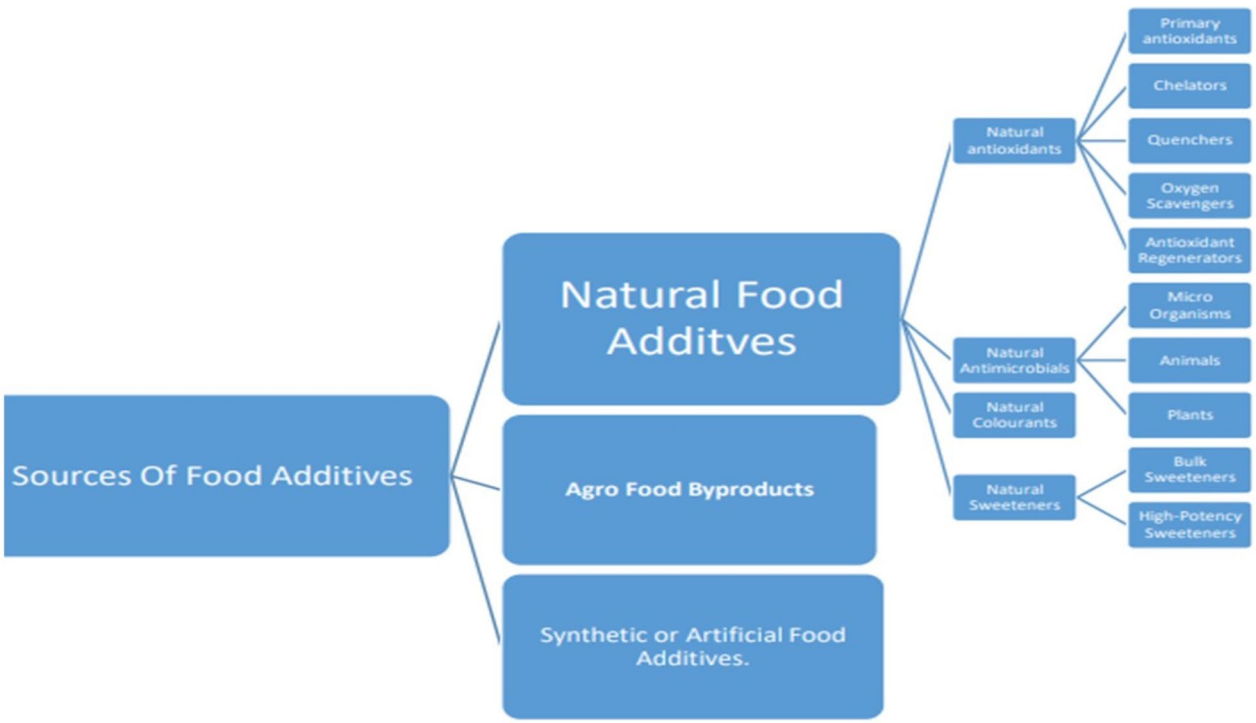


Fig. 1 Sources of food additive

diverse regulatory agencies. Consequently, strict control measures should be taken to safeguard consumer health, mitigating potential toxicities associated with the consumption of these molecules. Antimicrobials from Animals, Ex: Enzymes such as lysozyme (E-1105) and lactoperoxidase etc. Natural colorants are extracted from plants, algae and even insects. Natural flavouring agents extracted from plants namely *Terminalia ferdinandiana, Vanilla-planifolia* received more attraction in food industry (Chaliha et al. 2017; Rastogi & Bhatia 2019). Synthetic or artificial food additives are the food substances that are obtained as the product of a chemical reaction or an enzymatic reaction. Ex: Bisphenols are obtained when acetone and phenol are chemically treated on an ion-exchange catalyst or enzymatic reactions which involves mild conditions from ferulic, sinapic acids and mediated by lipase (Jeřábek et al. 1988; Hollande & Allais 2018). Secondary products procured from the derivative processes and extracts can be integrated with the food. Ex: Phenolic compounds present in the eggplant exhibit's antimicrobial, antifungal, and antioxidant properties and can serve as colorant and a versatile potential food additive, (Faustino et al. 2019). Some of the infant food additives and their function in infant foods preparation are highlighted in Table 1 along with their corresponding E numbers.

DHA (docosahexaenoic acid) and EPA (Eicosapentaenoic acid) are long-chain omega-3 fatty acids that are commonly found in fish and seafood (Tocher et al. 2019). These fatty acids are essential for human health and play important roles in various bodily functions, including brain development, cardiovascular health, and inflammation regulation (Calder 2015). DHA, AA- Arachidonic acid (essential fatty acid) and EPA are components present in the breast milk therefore in formulated milk, DHA, AA and EPA are often added as supplements to provide infants and young children with these essential nutrients (Ćwiek et al. 2023; Koletzko et al., 2020). However, supplementation of high levels of docosahexaenoic acid (DHA) in the absence of balanced arachidonic acid (AA) proportions may cause adverse outcomes for infants that include diminished concentrations of AA in brain tissue, suboptimal neurodevelopment, and cause potentially unfavorable effects on growth and the development of immune system (Koletzko et al. 2020).

Some of the health benefits associated with DHA are particularly important for the development of the brain and the retina in infants (Velumani et al. 2023). It is a critical component of cell membranes in the brain and helps support cognitive function and visual acuity (Silveira et al. 2023). Both DHA and EPA are known to have cardiovascular benefits (Koletzko et al. 2010). They can help reduce the risk of heart disease by lowering blood triglycerides, reducing inflammation, and promoting healthy blood vessel function (Liu et al. 2023). Both DHA and EPA have anti-inflammatory effects, which can be beneficial for conditions involving inflammation, such as arthritis and other inflammatory diseases. Even though, DHA and EPA are essential for health, excessive consumption of these fatty acids can have some potential risks, especially in the form of supplements (Lange et al. 2019). Omega-3 fatty acids have a blood-thinning effect, and high doses of DHA and EPA can increase the risk of bleeding and interfere with blood clotting (Ma et al. 2012). Similarly, overdosage of omega-3 supplements can cause gastrointestinal discomfort, including diarrhea (Barretto et al. 2023). High doses of DHA and EPA supplements may lead to increased oxidative stress in the body, potentially causing damage to cells and tissues (Pham-Huy et al. 2008).

Food additives are mainly classified into direct and indirect food additives as illustrated in Fig. 2. The direct food additives comprise of colorants, flavoring agent as well as preservatives. On the other side, indirect food additives are segregated based on a) processing equipment that includes adhesive, dyes and coatings and b) packaging processes that comprise paper and paper board. (Mwale 2023). Food adhesives are utilised in the packaging as well as to provide good bonding with the food material. Polyurethane is one of the most widely used food adhesives (Imam et al. 2013). Food coatings are usually carried using a flour-based liquid or powder that is coated or dusted on the food to make them look appetising and give a mild flavour (Raybaudi-Massilia et al. 2010). Food packaging materials such as cardboards and paper-based packages are also usually graded as non-permissible and permissible grade that are bleached with sulphates hence they contribute as indirect food additives (Deshwal et al. 2019) Table 2.

Food additives can be categorized based on the sources as: Natural food additives that can be grouped as **a) Natural Antioxidants** that prevent rancidity of the fats by inhibiting the peroxidation during the propagating stage. The antioxidants can be further categorized as i) Primary antioxidants that break chain, also gather the free radicals and hence known as radical scavengers. ii) Chelators that bind themselves to the metal moiety and intercept the formation of the radical during the radical formation phase. iii) Quenchers that make the high energy oxidant species inactive. iv) Oxygen scavengers which eliminate the oxygen present in the system and avert them from being unstable. v) Antioxidant generators, when radicalized generate antioxidants. **b) Natural antimicrobials** which inhibit the thriving microbes in the food. They are generally bactericidal and fungicidal. Benzoic acid (E210) is a bacteriostatic agent, synthetically obtained

Table 1 Common food additives with their E number and their use in baby foods

E Number	Additive	Function	Use in Infant Foods	Reference
E100	Curcumin	Colorant	Used in some baby purees and vegetable blends	Silva et al. (2022)
E270	Lactic Acid	Acidity regulator	Found in certain baby yogurts and dairy products	Ameen and Caruso (2017)
E300	Ascorbic Acid (Vitamin C)	Antioxidant	Added to some infant fruit purees for freshness	EFSA Panel Fernando et al. (2015)
E322	Lecithin	Emulsifier	Used in baby cereals and formula	Sandoval-Cuellar et al. (2020)
E330	Citric Acid	Acidity regulator	Found in baby fruit juices and purees	Lorenzoni et al. (2012)
E410	Locust Bean Gum	Thickener	Added to some baby foods for texture	EFSA Panel Mortensen et al. (2017)
E460	Cellulose	Bulking agent	Used in certain baby cereals and snacks	Gericke et al. (2013)
E500	Sodium Carbonates	Acidity regulator	Present in some baby biscuits and teething rusks	Chazelas et al. (2020)
E1200	Polydextrose	Bulking agent	Used in certain infant formula preparations	Stephen et al. (2017)
E1442	Hydroxypropyl Distarch Phosphate	Stabilizer	Found in some baby porridge and rice-based products	EFSA Panel Mortensen et al. (2017)
E101	Riboflavin (Vitamin B2)	Colorant	Added to certain infant cereals and snacks	EFSA Panel members Fernando et al. (2013)
E306	Tocopherol-rich Extracts of Natural Origin	Antioxidant	Used in some baby formulas for added nutritional value	EFSA Panel members Fernando et al. (2015)
E322	Lecithin	Emulsifier	Found in certain baby formula and dairy-based products	McSweeney (2019)
E375	Nicotinic Acid	Vitamin supplement	Added to some infant fortified cereals	Gargano et al. (2021)
E412	Guar Gum	Thickener	Used in certain baby purees and fruit gels	EFSA Panel members, Mortensen et al. (2017)
E551	Silicon Dioxide	Anti-caking agent	Present in some powdered infant formulas	EFSA Panel members Younes et al. (2018)
E951	Aspartame	Artificial sweetener	Found in certain sugar-free baby snacks and drinks	EFSA Panel members Fernando et al. (2013)
E160a	Carotenes (from Carrots)	Colorant	Used in some baby vegetable purees and snacks	Scotter et al. (2003)
E300	Ascorbic Acid (Vitamin C)	Antioxidant	Added to certain infant fruit purees for freshness	EFSA Panel Fernando et al. (2015)
E406	Agar	Gelling agent	Present in some baby fruit gels and desserts	EFSA Panel members Mortensen et al. (2016)
E160b	Annatto Extract (from seeds of the Achiote tree)	Colorant	Used in some baby cereals and dairy products	Scotter (2011)

and used as an antimicrobial preservative. It is preferred in a wide range of foods, such as sauces, pickles, acidic fruit juices, dried fruits, salty margarine, fruit and vegetable salads, sugary creams, and gums. **c) Natural colourants** that enhance the sensory quality and perception of the consumers about the food. Annatto (E-160b) is the most widely used and it exhibits yellow to Orange while Paprika (E-160c) displays orange to red colour. **d) Natural sweeteners** are the natural substances that are sweet in taste either with very low or high in calories. These are further classified based on the sucrose molecule as per the international standard for sweetness. i) Bulk sweeteners have potency lesser than that of one molecule of sucrose. Ex: Erythritol while ii) High potency sweeteners have potency that is above the standards of sweetness. Ex: Steviol Glycosides (Yadav & Guleria 2012). Sweetener such as sucrose and aspartame are non-caloric due to the reason that saccharin and sucralose because our bodies do not metabolize them. However, when we metabolize aspartame, it breaks down into chemicals that do have a caloric value, due to this reason its widely used as food additives to subside the sour tastes of pediatric foods. **e)**

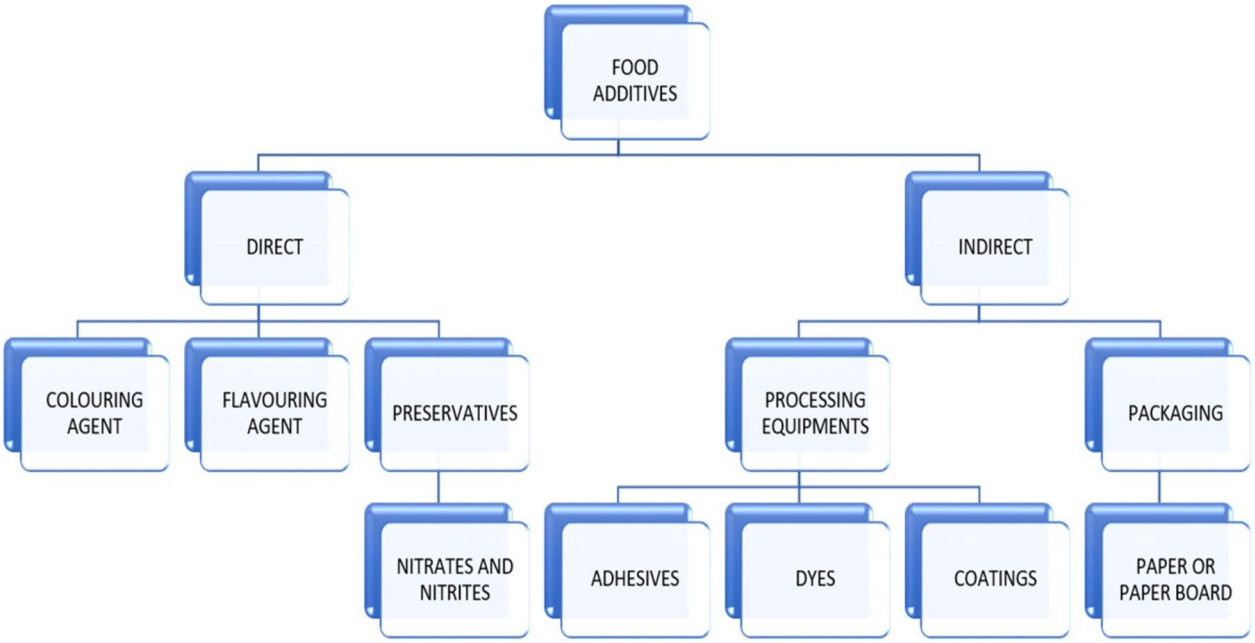


Fig. 2 Types of food additives and classification and example

Natural flavouring agents emulate the essence of the naturally available elements. Synthetic additives such as bisphenol, perfluoroalkyl, perchlorates cause detrimental effects to the body. Bisphenol triggers the pancreatic β-cell insulin in an estrogen-receptor dependent manner which leads to endocrine disruption (Alonso-Magdalena et al. 2006). Also, they are involved in the conversion of cells to adipocytes which may lead to obesity in infants. Perfluoroalkyl (PFCs) is persistent because of high-energy carbon-fluorine bonds and may stay in a child's body till 9 years of age, raising warning signs. Perfluoroalkyl compounds (PFCs) lead to immune toxicity mechanisms such as gene dysregulation and signal pathway disorders caused by Perfluorooctane sulfonic acid (PFOS) and perfluorooctanoic acid (PFOA) (Liang et al. 2022). Perchlorate alters the homeostasis of thyroid hormone and may cause neonatal hypothyroidism (Liang et al. 2022; Trasande et al. 2018a). Colourants added during processing, most notably nitrates and nitrites are used as food dyes. Oil can be dispersed throughout the food product with the help of emulsifiers. Food can be prevented from evaporation as well as deteriorations by adding stabilizers such as gums and carrageenan. Phosphates can alter the water holding capacity of foods containing proteins and starch thus helps in enhancement the texture of foods (Millstone & Van Zwanenberg 2003). The food additives were directly added as ingredients and are often listed with the chemical names: Salt, for example, may be described as sodium chloride, sugar as saccharin, ascorbic acid as vitamin C, and alpha-tocopherol as Vitamin-E. The possibility of protection of the gastrointestinal tract from bacterial invasion by supplementing with nitrite during the neonatal period appears to enhance its protective role (Jones et al. 2014).

Safety assessment of food additives

In order to ensure safety, any food or drug product must receive pre-marketing authorization from the Food and Drug Administration (FDA), unless it is generally recognized as safe (GRAS) by specialists with scientific expertise, who are qualified to evaluate its intended use under Federal Food, Drug, and Cosmetic Act (FFDCA). Since 1958, manufacturers have been required to submit Food additive petitions (FAPs) to the FDA, which collects data to assess the potential harm of additives before they are introduced into the food (Pressman et al. 2017). The FDA has established specific chemical tests and toxicity criteria to evaluate the safety of GRAS chemicals as well as food additives. An in-depth understanding of the safety assessment criteria for food additives is critical to differentiate between the safety evaluation of GRAS substances and food additives. Although both the types of substances share some similarities, they differ significantly in terms of their safety requirements. Therefore, it is imperative to analyse the safety data from both the sources to ensure the protection of public health (Pressman et al. 2017). In 1982, the safety assessment of food additives was documented in the booklet "Toxicological Principles

Table 2 Food additives and its health effect

Types of food additives	Chemical	Food-Related Activity	Health effect/Benefits	References
Indirect food additives	Bisphenols	Plastic containers of polycarbonate	Disruption of endocrine	(*Bisphenol A (BPA): Use in Food Contact Application	FDA*)
		Polymeric and epoxy resins in food cans	Obesogenic activity, disruption of neurodevelopmental	(*Bisphenol A (BPA): Use in Food Contact Application	FDA*)
	Phthalates	Food wrapper made for plastic	Disruption of endocrine	(Gärtner et al. 2009)
		Container used for storage in production, tubing made of plastic	Obesogenic activity	(Gärtner et al. 2009)
		Manufacturing equipment used for food	Oxidative stress, cardiotoxicity	(Gärtner et al. 2009)
	Perfluoroalkyl chemicals (PFCs)	Proof paper, cardboard	Immunosuppression, disruption of the endocrine, decrease in birth weight, Obesogenic activity	(Llorca et al. 2010)
	Perchlorate	Packaging materials of food	Disruption of thyroid hormone	(Li et al., 2022)
Direct food additives	Nitrites and nitrates	For preservation purposes and to enhance the colour	Disruption of thyroid hormone, cancer	(Maria et al. 2015)
	Artificial food color additives (AFCs)	Improve the appearance of food	Effect on child behaviour and attention	(Cheeseman 2012)
	Perchlorate and chlorate	Chemical is an additive that reduces static electricity in dry food packaging	Interference with the thyroid hormone, which can impair metabolism, digestion, heart health	(Li et al., 2022)
	Vitamin C (Ascorbic acid)	It serves to preserve jarred baby foods, and it's nutritious for your little one instead of harmful	Increased calcium absorption in the stomach, increased bone density and strength, and prevention of osteoporosis and rickets	(Leaf 2007)
	Vitamin B 12 (Cyanocobalamin)	Used in powdered food products and consumed by dissolving in water or milk	Brain development, neural myelination, and cognitive function	(Rychen et al. 2018)

for the Safety Assessment of Direct Food Additives and Colour Additives" commonly known as "The Redbook" (US FDA) (Kirschman 2010). It assumes that toxicological data is required to be analysed for each additive, and the amount of safety data available is referred to as the level of concern (LOC) which significantly determines additive's probable human intake (Krewski et al. 2010). Results of the toxicology study which are used to create an Acceptable Daily Intake (ADI) are compared with estimated daily intake (EDI). If ADI is more than EDI, the additive is deemed safe under the planned usage conditions (Howlett et al. 2003). The concept of LOC is comparable to that of risk assessment, as it involves evaluating the potential harm that a specific additive may cause (National Research Council 2003). Redbook II lists the degree of risk associated with expected direct additives, which is determined based on the chemical structure of the molecule (Pressman et al. 2017). The Redbook, which has since been renamed "Redbook 2000", which acts as a guidance document that is widely used by food manufacturers and developers, across the world (Redbook 2000: I Introduction | FDA 2007).

The European Food Safety Authority (EFSA) Scientific Committee, which includes the Panel on Food Additives and Nutrient Sources, conducts regular re-evaluations of scientific evidence related to food safety. Comparative analysis of the habitual nutrient intakes by the infant and young children in Europe raised serious concerns when evaluated for the Average Requirement (AR) and the Adequate Intake (AI) standards (EFSA 2013). Recently, the committee has recommended that additional information is necessary when assessing the safety of food additives and supplements for infants less than 16 week-age group (Nigel et al. 2017). The guidance framework basically encompasses exposure assessment concepts, consideration of organ system development status, toxicity report of existing chemicals, and applicable animal models that may fetch more data through safety studies (Hardy et al., 2017). Due to an increasingly varied diet, high intakes of additives exposure are more challenging

for infants. Experienced scientific judgment is required to approve all aspects of this safety assessment for evaluating new and existing food additives and constituents (F.A.O Joint 1987). The comprehensive testing parameters of baby foods is crucial and rigorous across various regulatory bodies to ensure the products' safety, nutritional adequacy, and adherence to regulatory standards. Some salient features of the parameters that are commonly tested for baby foods are Microbiological analyses, encompassing assessments of total plate count, coliforms, E. coli, as well as the detection of Salmonella and Listeria, are imperative for confirming microbiological safety (Mritunjay & Kumar 2017). Chemical contaminant evaluations, including scrutiny for pesticides, herbicides, heavy metals (such as lead, mercury, cadmium, and arsenic), and mycotoxins, serve to ascertain compliance with permissible limits and mitigate potential health risks (Tchounwou et al. 2012). Rigorous allergen testing, encompassing milk, egg, soy, wheat, peanuts, tree nuts, fish, and shellfish, ensures accurate labeling and addresses allergic considerations (National Academies of Sciences, Engineering, and Medicine et al. 2016). Nutritional profiling, covering vitamins, minerals, proteins, carbohydrates, and fats, is conducted to verify alignment with regulatory specifications and labeled values (Mondal et al. 2023). Physical attributes, such as texture, consistency, and particle size, are scrutinized to mitigate choking hazards and ascertain suitability for infant consumption. Attention is also directed towards packaging integrity, assessing seal integrity and compliance with food contact material regulations (Committee on Injury, Violence, and Poison Prevention 2010). Evaluation of additives, preservatives, and adherence to organoleptic properties, including color, flavor, and odor, is imperative. Thorough label scrutiny confirms the accuracy of nutritional information, allergen declarations, and feeding instructions. Stability and shelf-life testing validate the product's resilience under recommended storage conditions, while considerations of age-appropriate feeding guidelines and adherence to local and international standards underscore regulatory compliance. In sum, the systematic examination of these multifaceted parameters ensures the holistic quality assurance of baby foods, critical for safeguarding the health and well-being of the vulnerable infant demographic (Champeny et al. 2023).

To ensure the food safety, it is recommended that the amount of food additive added to food products should be kept to a minimum to achieve the intended technical effects. The maximum level of the additive to be used is also defined to avoid potential harm to consumers, when exceeds the ADI (Table 3). The recommended Tolerable Daily Intake (TDI) for direct food additives such as Nitrate (Sodium nitrate) ranges from 0–5 mg/kg body weight/day to 0–25 mg/kg body weight/day, and for Nitrite (Sodium Nitrite) is 0.1 mg/kg body weight/day. Perchlorate and chlorate have a recommended TDI of 0.3 µg/kg body weight/day, while ascorbic acid (Vitamin C) has a TDI of 200–300 mg/kg. Vitamin B12 has a lifelong daily intake recommendation of 500 µg for children. Among indirect food additives, bisphenols have a TDI of 4 µg /kg BW/day, phthalates have a TDI of < 0.1%, and infants can ingest 0.3 µg PFCs/day. Thickeners such as Guar Gum have a TDI of 10 g/L in liquid formulae with extensively hydrolysed proteins, while distarch phosphate has a TDI of 0.53 mg/kg body weight per day. Emulsifiers such as lecithin have a TDI of 1,000 mg/L, and Mono, diglycerides and fatty acids have a TDI of 4 g/L. Acidity regulators such as phosphates have a recommended TDI of 40 mg/kg birth weight per day. Flavours such as vanillin have a TDI of 5 mg. pH adjusting agents such as sodium carbonate has Good Manufacturing Practices (GMP). Citric acid has a recommended TDI of 9 g/L. Sodium hydrogen carbonate, sodium carbonate, potassium hydrogen carbonate, potassium carbonate, potassium hydroxide, and calcium hydroxide do not have specific TDIs listed. During infancy and early childhood, adequate nutrition is vital to ensure children's health and development (Lanigan & Singhal 2009).

EFSA panel on Dietetic Products, Nutrition, and Allergies (NDA), recommends an Adequate Intake of 100 mg of docosahexaenoic acid and 140 mg of AA for infants (> 6 months of age) and young children below 24 months of age, and 250 mg of DHA + EPA for the age range of 24–36 month (EFSA 2010; Koletzko et al., 2020). Food and Agriculture Organization/World Health Organization (FAO/WHO) provided a recommendation of 20 mg of docosahexaenoic acid (DHA) per kilogram of body weight per day for the optimal growth and development in infants aged 0 to 2 years, (Koletzko et al. 2010). The upper threshold for the combined intake of eicosapentaenoic acid (EPA) and DHA is advised to be maintained below 1.5% of total energy, (Uauy & Dangour 2009). Health Canada, in a published monograph, advises a recommended intake of up to 1.5 g of eicosapentaenoic acid (EPA) plus docosahexaenoic acid (DHA) for children between the ages of 1 and 8 years, (Mankad et al. 2015).

Recommendation Children are particularly susceptible to the effects of food additives as they have higher relative exposure than an adult. This is usually because the development of the metabolic systems will still be happening at a young age. The key organs also undergo multiple changes which makes them more susceptible. These maturations can be vulnerable to disruption because of the additives (Landrigan & Goldman 2011).

Table 3 Safety standards of food additives in the infant food

Sl. No.	Food additive	Recommended TDI (Tolerable daily intake)	References
1	**Direct Food additives**		
	Nitrate (Sodium nitrate)	Between 0–5 mg/kg body weight/day to 0–25 mg/kg body weight/day	(Walker 1990)
	Nitrite (Sodium Nitrite)	0.1 mg/kg body weight/day	Walker (1990)
	Perchlorate and Chlorate	0.3 µg/kg body weight/day	Vejdovszky et al. (2018)
	vitamin c ascorbic acid	200–300 mg/kg	Varvara et al. (2016)
	Vitamin B 12	lifelong daily intake of 500 µg for children	Allen et al. (2010)
2	**Indirect Food additives**		
	Bisphenols	Tolerable daily intake (TDI): 4 µg /kg BW/day	Almeida et al. (2018)
	Phthalates	< 0.1% to respective tolerable intakes of all kind of Phthalates	Amiridou and Voutsa (2011)
	Perfluoroalkyl	infants can ingest 0.3 µg PFCs/day	(Stahl et al. 2011)
3	**Thickeners**		
	Guar Gum	10 g/L L in liquid formulae with extensively hydrolysed proteins 1 g/L in liquid formulae that has partially hydrolysed protein 10 g/kg in all the weaning food 20 g/kg in cereal-based food that is free of gluten	Mortensen et al. (2017)
	Di starch phosphate	0.53 mg/kg body weight per day	Mortensen et al. (2017)
4	**Emulsifiers**		
	lecithin	1,000 mg/L	Younes et al. (2017)
	Mono, diglycerides, and fatty acids	4 g/L	Younes et al. (2020)
	citric acid	9 g/L	Claude Lambré et al. (2022)
5	**Acidity Regulators**		
	Phosphates	40 mg/kg bw per day	FSSAI Notification (2020)
	Sodium Hydrogen Carbonate	0.2 g	
	Sodium Carbonate		
	Potassium Hydrogen Carbonate		
	potassium Carbonate		
	Potassium Hydroxide		
	Calcium Hydroxide		
6	**Flavours**		
	Natural Fruit Extracts	5 mg	Arora et al. (2019)
	Vanillin		
7	**pH adjusting agents**		
	Sodium Carbonate	GMP (Good manufacturing practices)	Arora et al. (2019)

In December 2021, xanthan gum was incorporated into the General Standard for Food Additives (GSFA) during the 44th Codex Alimentarius Commission session (Kremer 2022). The use of locust bean gum (E 410) as a food ingredient in infant food before to 16 weeks of age is approved with a 1-week margin of exposure (EFSA, 2023). In addition, the EFSA periodically requests data in order to assess the safety and utility of a number of additives used in infant foods. Lactitol, a sugar alcohol obtained from lactose, finds application in newborn formula and follow-up formula where it functions as both a prebiotic and a sweetener. Human milk contains the glycoprotein lactoferrin, which possesses immunomodulatory, antibacterial, and anti-inflammatory effects. It can be used into newborn formula and follow-up formula as a functional element to promote infant health and development (Food standards 2022). Polydextrose is a synthetic glucose polymer that can be utilised in infant formula and follow-up formula as a bulking agent and soluble dietary fiber. It has the potential to enhance the gastrointestinal health and consistency of newborns' stools (Martin et al. 2016). It was granted GRAS status by the FDA in March 2023. Trehalose, a disaccharide consisting of two glucose molecules, finds application in infant formula and follow-up formula as both a sweetener and a stabiliser.

Health threat

To show the health hazards, many experimental studies have been done using the compounds of indirect and direct food additives as illustrated in Table 4. Bisphenol: have been linked to disruption of endocrine function and obesogenic activity. phthalates have been associated with disruption of endocrine function and for obesogenic activity. Perfluoroalkyl chemicals (PFCs): have been linked to immunosuppression, disruption of the endocrine system, decreased birth weight, and obesogenic activity. Perchlorate, nitrites and nitrates has been associated with disruption of thyroid hormone (Martyn et al. 2013). AFCs have been associated with effects on child behavior and attention. Perchlorate and chlorate have been linked to interference with thyroid hormone, impairing metabolism, digestion, and heart health. Vitamin C increase calcium absorption in the stomach, increase bone density and strength, and prevent osteoporosis and rickets (Martyn et al. 2013). Vitamin B12 has been associated with brain development, neural myelination, and cognitive function (Martyn et al. 2013). In preschool children, it has been observed that these additives can disrupt various mental processes like neural myelination, and cognitive function, when ingested at higher doses. Water-soluble additives such as artificial sweetener and vitamin B12, can easily penetrate the tissues in infants, potentially causing disease and disability like attention deficit or hyperactivity disorders (Martyn et al. 2013). In the pediatric population spanning 3 to 17 years of age, diminished levels of docosahexaenoic acid (DHA), eicosapentaenoic acid (EPA), coupled with an elevated arachidonic acid (AA)/EPA ratio, demonstrated a positive correlation with an increase in the symptom severity of ASD (autistic spectrum disorder) and ADHD (Attention deficit hyperactivity disorder). As per the omega-3 index, concentrations of EPA + DHA falling below 4% were associated with an elevated risk of mortality from cardiovascular disease, whereas levels within the range of 8–12% conferred optimal protection, (Parletta et al. 2016; Mankad et al. 2015).

Direct and Indirect additives come in contact with food during processing or packaging that may cause adverse effects as illustrated in Table 4 (Indrio et al. 2022). Titanium dioxide, a colourant is widely used to enhance and brighten the colour of the food and makes it appealing for consumption. The consumption of Titanium Dioxide (E-171) is considered to be the highly detrimental among the infants because of their lower body mass. This particular additive is mainly found in candies and icings used for toppings. In addition, the involuntary intake of toothpaste while brushing can be considered as another significant source of E171 consumption in children. Thus, high exposure to such nano-sized titanium dioxide raises concerns which induce the threat of potential intake in organs and causes unwanted effects on infant and child health (Bischoff et al. 2021). The pathway by which the adverse effects are induced is shown in Fig. 3.

Allergies by infant food

Food allergies are usually caused due to the response of the immune system against food components. Figure 4 illustrates the pathways of immune response triggered by food additives (coloring agents, preservatives, flavouring agents and probiotics) with allergenic potential. Allergens are absorbed by dendritic cells (DC) in the gut lumen, and subsequent events occur in the Peyer's patches/mesenteric lymph nodes. In healthy individuals, allergen-derived peptides are presented to naïve CD4+ T-cells via MHC-class II complex, leading to a tolerogenic immune response mediated by regulatory T cells and interleukin-10. However, in susceptible individuals, naive CD4+ T-cells polarize toward a Th-2 phenotype

Table 4 Outline of uses and health concerns related to some of the compounds in foods

Category	Chemical	Uses	References
Food additives (Indirect)	Perfluoroalkyl chemicals	In baking and cooking that provides a non-sticky texture (grease-proof paper)	Halldorsson et al. 2012
	Perchlorate	Packing of food particles	Ghassabian and Trasande 2018
	Bisphenols	In baby bottles and food storage container (polycarbonate)	Gore et al. 2015
	Phthalates	Equipment for food processing	Posnack et al. 2011
Food additives (Direct)	Nitrates and nitrites	Color enhancer and preservative	Tonacchera et al. 2004
Texturising agents	Emulsifier	Helps in oil dispersion in food items	Blekas 2016
	Stabilizer	Food can be prevented from evaporation as well as deteriorations	Blekas 2016
	Phosphates	Enhance water-holding capacity of the foods	Blekas 2016
Sweeteners	Saccharin	mitigates sour taste	Millstone and Van Zwanenberg 2003
Preservatives	Ascorbic acid	maintain the quality of food	Mwale 2023

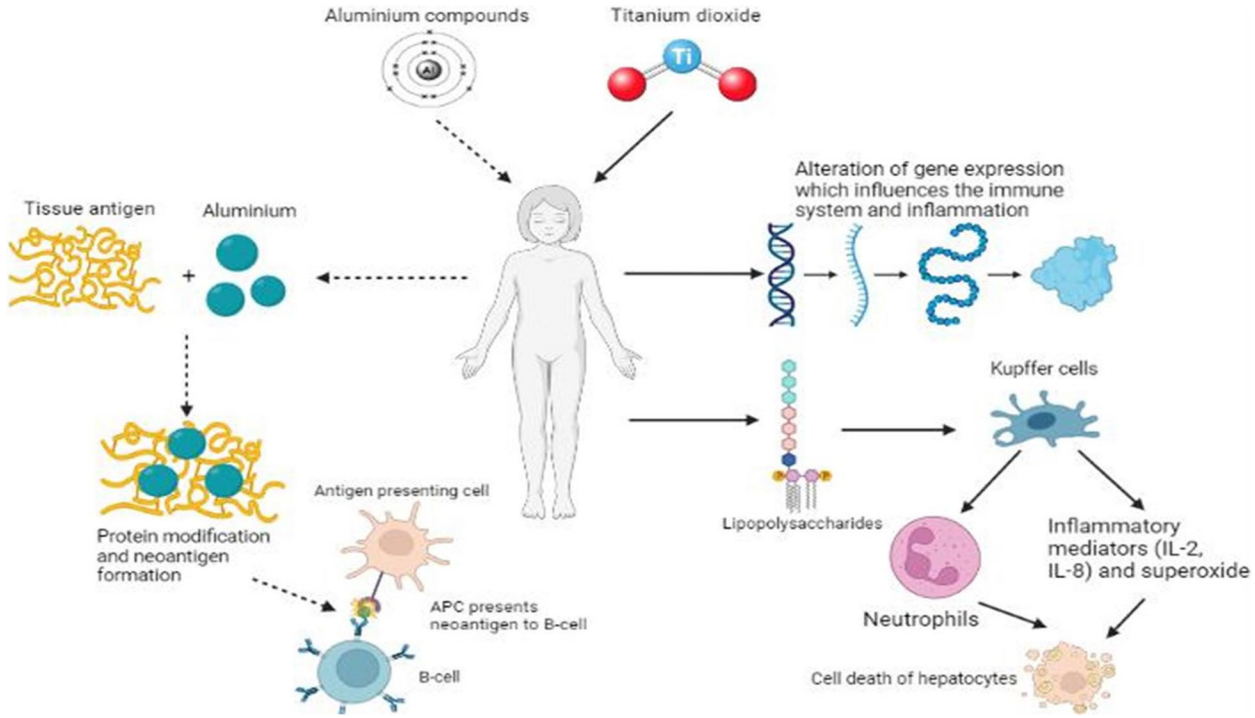


Fig. 3 Immunological response triggered by allergens and the pathway involved in it

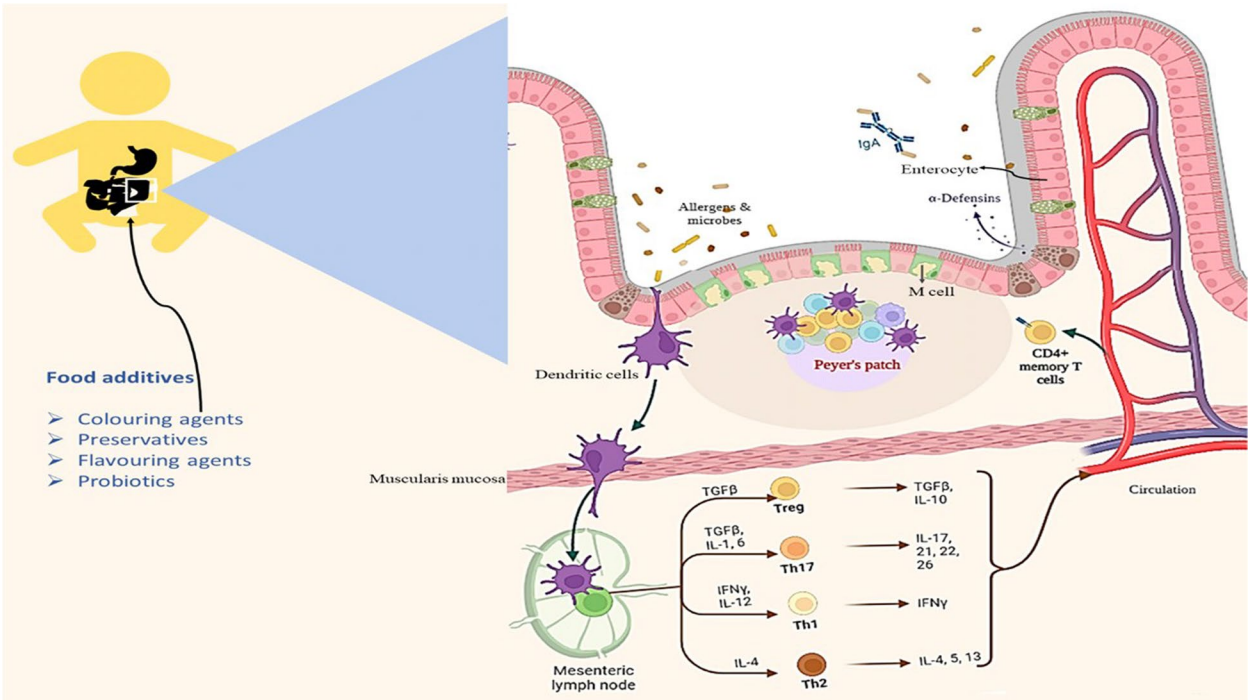


Fig. 4 Adverse outcome pathway of titanium dioxide after ingestion and related to inflammation and carcinogenicity

and produce IL-4, IL-5, and IL-13, stimulating allergen-specific IgE antibody production and clonal expansion by B cells. The release of chemical mediators such as histamine, cytokines, and prostaglandins are triggered by IgE binding to FcRI receptors on basophils and mast cells, leading to allergy symptoms. Late-phase allergic reactions are triggered by the recruitment of eosinophils and Th-2-cells in response to the release of cytokines like IL-4, IL-5, IL-6, IL-13, and TNF-α (Ali et al. 2020; Pratap et al. 2020).

Various symptoms of allergies include acute allergic reactions, anaphylaxis, proctocolitis, enterocolitis, Atopic dermatitis and intestinal barrier dysfunction (Sicherer et al. 2020). All the new ingredients which are used by the industries must be evaluated by the FDA (Food and Drug administration) for compliance before marketing (Vayda et al. 2021). The formation of these formulas usually comprises steps that can be subjected to a series of reactions that can cause a negative impact on the quality of the formula. One such process is the Maillard process (Nunes et al. 2019). Mycotoxins if present in formula, fruit products, and cereal-based products can lead to a synergistic health risk to the infant. Patulin which has been observed to be a mycotoxin has resulted in immunotoxicity and pulmonary congestion (Coppa et al. 2019). In the European Union, Patulin is restricted to 10 g/kg in apple-based products for infants and young children (apple juice and solid apple products, including apple compote and apple puree) for infants and young children (Juan et al. 2014). Partially hydrolysed whey protein dominant formula has shown proof of lower eczema or milk allergy in many regions for many years. However, this was shown to have no evidence and the UK Food Standards Agency's committee then concluded that there was actually no evidence for these whey-based formulas (Munblit et al. 2020). Atopic dermatitis is one of the most prevalent allergic diseases in infants and toddlers. It was seen that whey-based infant formulas helped in the reduction of atopic dermatitis (Holvoet et al. 2021). Linoleic Acid at high dietary concentration was seen to facilitate the development of allergic sensitization. If this linoleic acid was taken in higher intake as LA-rich vegetable oils there is a higher risk of allergic rections in infants (Carlson et al. 2021). Plant sterols are seen in infant formula in high concentrations especially when they are obtained from vegetable oil as the fat source. The associations between these steroids and eczema have been significant but there is yet more to be discovered regarding the relationship (Brakel et al. 2022). Breast-milk has its many benefits but for mothers who are unable to lactate it was seen that there was no consistency in the recommendation of soy milk for allergy reduction (Vale et al. 2021). For infants suffering from galactosemia, soy milk substitutes have been used for breast-milk (Ishola 2022).

Children with bronchial asthma, allergic rhinitis, chronic urticaria, angioedema, and hypersensitivity reactions may potentially have adverse reactions to various food additives. Some commonly reported food additives in various food products (cheese, cream, egg, glucose syrup etc.) and soft drinks that have been associated with these conditions include: Sulfites- sulfur dioxide (E 220), sodium sulfite (E 221), sodium bisulfite (E 222), sodium metabisulfite (E 223) (Silva & Lidon 2016). Sulfites can directly cause bronchoconstriction by activating the smooth muscle cells in the airways and by increasing the release of inflammatory mediators which can trigger an immune response and subsequent asthma symptoms or allergic reactions (Kaliner 1989). The European Food Safety Authority (EFSA) Panel on Food Additives has been recommended an ADI of 0.7 mg SO_2 equivalent/kg bw per day for all population groups. For infants, it is recommended that the introduction of wheat, egg, and fish be delayed until they are at least 12 months old (Chandra 1997). Consumption of fish rich in omega-3 fatty acids such as DHA and EPA during pregnancy, lactation, infancy or childhood opposes the actions of n−6 PUFAs that further minimize the allergic reactions and other associated clinical manifestations (Kremmyda et al. 2011). Similarly, the introduction of peanuts should be postponed until the child reaches the age of 36 months (Chandra 1997). Food colorings: Artificial food colorings, such as tartrazine, sunset yellow, and erythrosine, have been associated with hypersensitivity reactions in some children (Arnold et al. 2012). They may stimulate the release of inflammatory mediators, leading to symptoms such as bronchoconstriction, nasal inflammation, hives, and angioedema (Rao & Sudershan 2008). Studies found that low molecular weight compounds, such as artificial food dyes, have the potential to induce behavioral disorders in individuals who are susceptible (Vojdani & Vojdani 2015). Monosodium glutamate (MSG) is a flavor enhancer commonly used in processed foods that may stimulate the release of certain substances, such as histamine, which can trigger adolescent migraine in children (Millichap & Yee 2003). An acceptable daily intake (ADI) for MSG has been determined as 14 mg per pound (30 mg per kilogram of body weight per day) (Appaiah 2010). Aspartame: Aspartame is an artificial sweetener used in pediatric foods that can cause learning disabilities and behavioral disorders known as brain allergy. (Magnuson et al. 2007). The acceptable daily intake (ADI) for aspartame, as established by the FDA, is 50 mg per kilogram (mg/kg) of body weight per day, while the EFSA has set a lower ADI of 40 mg/kg per day. Concerns regarding the safety of aspartame and its potential side effects and

health risks have been raised, prompting discussions on its impact on pediatric health (Sardarodiyan & Hakimzadeh 2016).

Potential biohazards in infant and young children's food

Throughout the Food supply chain, from collection to transportation, biological, chemical, or physical risks may be present. Chemical risks can occur from food additives, food packaging materials, and environmental contaminants. Physical risks can arise from foreign objects such as metal fragments or broken glass from processing or packaging equipment, which can cause physical harm if ingested. Understanding the risks can dramatically mitigate the damage of contracting a foodborne ailment. An efficient food safety management system can prevent the addition of hazardous additives in infant food (Chinaza 2023). The safety of the food supply chain is crucial to public health. Foodborne illnesses are caused by consuming food or water contaminated with harmful microorganisms, such as bacteria, fungi, and parasites that can lead to acute gastrointestinal symptoms like vomiting and diarrhea (Bintsis 2017). These illnesses can have long-lasting impacts, particularly in infants during the first 1000 days of life, where it can result in potential biohazards such as behavioral disorders, language delays, and disturbance in mental and motor development, mutagenicity or carcinogenicity (Indrio et al. 2022). Probiotics are beneficial bacteria that are commonly added to foods such as yogurt, kefir, and other fermented products. While most probiotics are safe, some, such as *Streptococcus*, *Bacillus* and *Enterococcus*, can cause foodborne diseases such as lactose malabsorption and other associated ailments (Guandalini et al. 1989). Infant formula, soy milk, cereal-based follow up formula (FUF), rice soups, honey, liquid FUF, biscuits, beverages, nutrient supplements, and noodles were all analysed in detail to determine their prevalence and degree of pathogenic contamination in a study conducted in Korea. Some of these products, like cereal-based FUF and nutrient supplements, were found to have a very high aerobic plate count of *Cronobacter* spp. and *B. cereus* (Kim et al. 2011).

Contaminants in food can come from a variety of sources, including chemicals used for pest management, cleaning, and sanitizing surfaces that come into contact with food and equipment. Some contaminants, exemplified by persistent organic pollutants (POPs), pose a significant threat due to their ability to endure in the environment, accumulate within the food chain, and exert adverse effects on both humans and the environment, as demonstrated in Table 5 (Indrio et al. 2022). The use of synthetic food additives is widely increasing and it can achieve the shade which is not possible by natural colorants and are less expensive. However, since the consumption of synthetic or artificial food additive has increased in a larger ratio, it results in the major rise of numerous allergic reactions and other immunological disorders. Carrageenan is a natural additive that comes from red seaweeds. Carrageenan (CGN) has been largely used as a food additive in infant formula and this latter formula is used for infants having special medical needs. JECFA upholds the ADI for CGN as "Not specified" and they raised interests regarding the safety of CGN for the utilization in infant formula and the issues were raised based on lack of data on latent effects of CGN consumption on the new born immune system (Weiner 2014; Weiner et al. 2007, 2015). Food coloring agent such as the tartrazine has been considered as a spark for asthma

Table 5 Most common POP and related health hazards

POP	Health hazards	References
Polyaromatic hydrocarbons (PAHs)	Cancer and cognitive dysfunction among children, male fertility impairment, respiratory disorders	(Sabarwal et al. 2018)
Organochlorine pesticide (OCPs)	Neurological, disruption of endocrine, infertility and malformation of foetus, diabetes mellitus, cancer, reproductive and heart problems, high blood pressure	(Alharbi et al. 2018)
Polychlorinated biphenyls (PCBs)	Disruption of endocrine, neurological problems, liver injury, cancer, diabetes, heart disease, obesity	(Maqbool et al. 2016)
Polybrominated diphenyl ethers (PBDEs)	Cancer, problems in reproductive and cardiovascular, obesity, diabetes	(Hauser et al. 2015)
Perfluorinated compounds (PFCs/PFOS and PFOA)	Cancer in breast	(Garg et al. 2020)
Hexabromocyclododecanes (HBCDs)	Disruption of endocrine, problems in and heart problems and behaviour disorder	(Kim et al. 2019)
Polychlorinated naphthalene's (PCNs)	Cancer	(Niu et al. 2021)
Dioxins/furans	Mental disturbances and motor development, cancer, diabetes, disruption of endocrine, high blood pressure, intolerance level of glucose and heart problems	(Indrio et al. 2022)

where adverse reactions are observed. However, it is found that a high percentage of infants suffering from severe atopic dermatitis are sensitive to tartrazine. In addition, tartrazine and few other colorants have been identified to be involved in multiple chemical sensitivities that are not found to be IgE-mediated (MacDonald Baker et al. 2015). The allergic and immune reactivity to infant food additives can be intensively considered as aggravating factors in quite sensitive individuals. Thus, it is the responsibility of the clinicians to be aware of the allergic characteristics of infant food additives (MacDonald Baker et al. 2015). The consequences resulted by consuming products with highly concentrated additives are particularly found in pediatric population. The nitrate-nitrite pathway in pediatrics does not occur in the usual way as in aged population due to lesser bacterial conversion of nitrate to nitrite occurring in the mouth. The nitrates and nitrites mainly affect immune system of infants when it enters milk formulas via contaminated water and results in the depletion of adequate nutrition content. Excessive consumption can highly affect the immune system of the infants and all these functions can be impaired with the presence of nitrates and nitrites in the infant's formula (Savin et al. 2022). Perfluoroalkyl (PFA) chemicals are commonly used in food packaging, but their exposure can lead to immune disorders and developmental neurotoxicity. The risk associated with PFA exposure is linked to the suppression of immune function, increasing the risk of autoimmune diseases (Zhang et al. 2020).

Docosahexaenoic acid (DHA) and arachidonic acid (ARA) are essential components of breast milk, that plays crucial role in early infant development. Incorporating these fatty acids into infant formula (usually with ARA surpassing DHA, mirroring breast milk) is considered to be vital. At 16 weeks of age, infants fed formula enriched in ARA and DHA exhibited increased immune cell proliferation, T cell stimulation compared to those with unsupplemented formula. Furthermore, supplementation of formula enriched with AA and DHA resulted in a higher expression of IFN-γ/IL-4 ratio (indicative of a better Th1/Th2 response) after T cell stimulation. Notably, adjusting formula linoleic acid (LA) to alpha-linolenic acid (ALA) ratios cannot achieve plasma or red blood cell long-chain polyunsaturated fatty acid (lcPUFA) levels comparable to breastfed infants, (Lien et al. 2018).

Due to the vulnerability of infants to foodborne illnesses and contaminants, infants and young children require special attention to food safety. Table 3 enlists foreign chemical substances that may be unintentionally introduced into food products during production or processing. These substances include pesticides, veterinary drugs, and environmental contaminants. Table 4 includes materials that may be present in food products, such as food packaging materials and utensils that can release harmful chemicals into food. These materials may contain bisphenols, phthalates, and other harmful substances. Table 5 lists the POPs, which are toxic chemicals that persist in the environment and can accumulate in the food chain. Exposure to POPs can lead to developmental and neurological problems, among other health issues. Table 6 highlights the naturally occurring substances that are not separated along the food production line and should be avoided while consuming. This includes certain types of mushrooms and shellfish that can be toxic when consumed in large quantities. Metals, such as mercury, lead, cadmium, and arsenic, are also potential hazards in food products. Heavy metal exposure can lead to organ damage, particularly in young children who are more susceptible to their toxic effects. Therefore, the U.S. Food and Drug Administration (FDA) has taken measures to reduce exposure to heavy metal contaminants in baby and children's food (Bair 2022).

Regulations and challenges in the formulation of Infant food

Infant food additives are essential for ensuring the optimal growth and development of infants. it is critical to identify potential risk associated with many new

Table 6 Common sources of health hazards in food

Category	Sources	References
Metals	Blades, needles, staples, etc. from equipment's sections	(Das et al. 2019)
Glass	Containers, bulbs	(Teklemariam & Gotera 2019)
Stones	From crop fields, dust	(Garcia-Garcia et al. 2019)
Plastics	Packaging materials, utensils plastic pieces while cleaning the apparatus	(Braun et al. 2021)
Wood	Pieces of wooden structures and pallets while storing and transporting products and ingredients	(Braun et al. 2021)
Natural food components	A sharp or hard portion of food	(Gil-Martín et al. 2022)
Metallic contaminant	Heavy metal source contamination: pesticides application, contaminated water used for irrigation, municipal waste	(Ibe et al. 2021)

additives (Augustin & Sanguansri 2012). Development of appropriate infant food additives poses several challenges. One of the top significant challenges is ensuring the safety of the additives. The pursuit of Generally Recognized as Safe (GRAS) status in the United States or regulatory approvals within the European Union for baby foods necessitates a careful understanding of food safety regulations and compliance prerequisites. A foundational resource for U.S. regulatory processes is the "GRAS Self-Determination: A How-To Guide" provided by the U.S. Food and Drug Administration (FDA). Alongside, the "Code of Federal Regulations (CFR), Title 21, Part 170-199" summarizes FDA regulations relevant to food and drugs, including criteria for defining substances Generally Recognized as Safe according to U.S. FDA Resources: GRAS Notification Program Code of Federal Regulations (CFR), Title 21 (Driedger 2008).

European regulatory directives are clarified within documents circulated by the European Food Safety Authority (EFSA), illustrated by the "Guidance on the safety assessment of substances present in food intended for infants", which provides specialized insights into safety considerations connected to baby foods (Ververis et al. 2020). European Union Resources on European Food Safety Authority (EFSA) Guidance on the safety assessment of substances present in Books: "Food Safety Regulatory Compliance: Catalyst for a Lean and Sustainable Food Supply Chain by Preston W. Blevins and Richard L. Woteki". "Food Law and Regulation for Non-Lawyers" by Marc C. Sanchez". "EU Food Law: A Practical Guide" by Bernd van der Meulen and Gertjan van Midden".

In 2001, the FDA addressed manufacturers' request to designate the versions of omega-3 fatty acids, namely ARASCO and DHASCO, as Generally Recognized as Safe (GRAS), (Kent 2014). European Academy of Pediatrics and Child Health Foundation recently implemented regulatory standards to all marketed products to incorporate 20–50 mg of omega-3 docosahexaenoic acid (DHA; 22:6n–3) per 100 kcal in infant and follow-on formula. This requirement equals approximately 0.5–1% of fatty acids (FAs) that matches the typical levels found in human milk (Koletzko et al., 2020).

Engaging with consulting services specializing in food regulatory businesses is advised. These entities offer personalized counsel and support corresponding with the distinctive attributes characterizing baby food products. Some consultancies also provide caution with regards to the changes in guidelines and regulations which is important, given their susceptibility to periodic changes in amendments. Additionally, seeking the insights of regulatory professionals or legal experts proficient in food laws is vital for skillfully navigating the complex regulatory directives governing baby foods.

The American Academy of Pediatrics (AAP) focus on new prospects of food additives and the existing ingredient ratios that may be introduced to infant formulae to give potential health benefits within the first year of life; later in childhood; and possibly even during adulthood. AAP also focus on factors that control colour change, increasing shelf life, marketing adjustment and the method of manufacture that influence the impact of food additive on child health and development. A new technique such as 3D food printing or effective policy to observe the type of plastic container via recycling codes on the bottom of products, are being developed to improve the pediatric health (Azam et al. 2018; Leung et al. 2009; Trasande et al. 2018b).

The research studies discovered that inclusions of food additives such as food colorants in infant nutrition raises concerns due to their potential to cause food intolerance, asthma, urticaria and other adverse effects. However, the exact prevalence of reactions to the food colorants remains unknown. The quantity of food colorant consumed by infants or children on a regular basis, leads to unfavaouarble reactions. Wide variations were observed in the amount of colorant present in different infant foods products, ranging from 0.3 to 33 mg in candies, 9.4 to 41.3 mg in breakfast cereals, 1.9 to 6.0 mg in ice-creams and 2.8 to 14.4 mg in snack foods per serving size (Feketea & Tsabouri 2017). Moreover, a dose-response relationship was observed, as evidence by mood changes in children, such as restlessness and irritability during sleep after the ingestion of tartrazine (Feketea & Tsabouri 2017). Recent findings have also illustrated presence of chlorate in infant formula, originating from the use of potable water treated with oxyhalides during the manufacturing process. This chlorate content in food products arises from the utilisation of chlorinated potable water in various food additives. Furthermore, the addition of hydrophilic food surfactant allowed in the infant formulae within the permissible range of 50 mg/L had shown to increase the permeability of tight junctions (Kettlitz et al. 2016). The toxic effect of the additives increases with the uptake of food allergens by infants with immature intestinal barrier (Csáki 2011).

Over the last two decades, there has been an increasing concern about the potential negative effects of synthetic chemicals on infant health that are used as food additives. In the United States, more than 10,000 chemicals have been authorized for use in foods, either directly or indirectly, under the Federal Drug and Cosmetic Act (Neltner et al. 2011). Additionally, approximately 1,000 chemicals are being classified as GRAS without notification of United States Food and Drug Administration (USFDA) (Neltner et al. 2013). The Joint Food Agriculture Organization of the United Nations (FAO)/World

Health Organization (WHO) expert committee on food Additives along with Joint FAO/WHO Meeting on Pesticide Residues (JMPR) go along with the same general rules and procedures for in analyzing the risk assessment of chemicals. In addition, a term called Single portion exposure technique (SPET) was introduced as a new procedure of estimating the dietary exposure for category of flavoring agent (Ingenbleek et al. 2020). The European Food Safety Authority (EFSA) is responsible for implementing a complex system of standards governing the use of additives, purity of additives, the maximum number of additives that can be added, and labelling. The EFSA also provides independent scientific advice on various food-related risks. EFSA's work also includes gathering scientific data, communicating the scientific work to the public, boosting trust among consumers and boosting cooperation among the stakeholders and the countries. Many organizations, like the International Expert Committee on Food Additives and Food Standards Australia and New Zealand, fulfil equivalent functions. Before any authority allows the use of an addition, its safety for the relevant consumer group must be established. There is a rising concern about the overuse of chemicals in food production and processing. Intake levels of food additives must be determined to check whether these food additives constitute a health risk (NIGEL et al. 2017). The food colorants that are tested to be safe are banned by few other countries leaves the consumers with a state of disorder and anxiety. For instance, carmoisine, Ponceau and Quinoline Yellow are banned in US but permitted in EU. One of the clinical studies conducted revealed that 73% of the children with Hyperactivity ADHD exhibited lessened symptoms of hypersensitivity when food free of food dyes and preservatives were consumed (Stevens et al. 2011). FDA had recently banned the usage of 'Bisphenol A' (BPA) which was used as a convenient ingredient in the formulation of polycarbonate plastics present in certain products like infant bottles and other cups used for infants (Metz 2016). The developing food safety standards and improved worldwide product norms causes a high necessity in improving legislative system of India on the basis of codex Hazard Analysis Critical Control Point (HACCP).

The regulation of food safety in India is a complex process that involves multiple ministries. To streamline the process, the Food Safety and Standards Act was introduced to consolidate food safety laws in the country (Shukla et al. 2014). The HACCP based safety management standard for food and other associated certifications needs to be submitted by large food operators. The product standards are set for infant milk products with a particular upper limit of salts and microbiological limits especially for coliforms yeast and salmonella. In addition, oil products used for children food preparation that are categorized as vegetable and animal oil must be sorted into mandatory legislation (Shukla et al. 2014). The infant food additive manufacturers must make sure that the utilization of scientifically justified food additives such as the Food for Special Medical Purposes (FSMP) is in accordance to the proposition forwarded by the Codex Alimentarius Commission (CAC). Recently, few additives have been dispensed by the specialized industry for nutrition known as Joint FAO/WHO Expert Committee on Food Additives (JECFA) for the purpose of evaluation of these additives in infant foods (Barlow et al. 2015). Even though infant formulas are available commercially in late 19th century, within the span of few years the emergence of harmonized regulations in order to ensure the safety of food additives in infant formulas as well as the nutritional adequacy had raised. Also, the scientific and technological requirement for few of the food additives in infant foods was recognized by the Codex Alimentarius Commission (CAC) (Constable et al. 2017). Antioxidants such as citric acid and ascorbic acid are meant to be prevalent in pureed infant foods (Čížková et al. 2009). Flavors and thickeners are added in nutritive foods which help in enhancing the infant dietary foods (Teixeira 2018). The Codex Alimentarius Commission had proposed approaches based on Acceptable Daily Intake (ADI). This strategy involves collection of the relevant data whose comprehensiveness is ascertained and ineffective levels are set by employing an accurate indicator of the toxicity (Gibney & Lambe 1996). The mean intakes of a few artificial sweeteners were considered to be 1.5 mg/day whereas 3.5 mg/day for saccharin and cyclamates (Gibney & Lambe 1996). Security issues often arise due to some business's fanatical pursuit of profit and other considerations like using excess preservatives beyond the limit (example; for infant formula food: 20 kcal/ounce or 20 kcal/30 ml and 0.45 g of protein/ounce or 0.45 g of protein/30 ml) (Trasande et al. 2018c). The scientific outputs are connected to overarching opinions on nutrition, novel foods, nutrition sources, additives, enzymes, contact materials, pesticides, contaminants, biological risks, and food consumption surveys.

Future prospects of food additives in infant food

Novel technologies in food processing have revolutionized the preservation of nutritional value in functional foods, thereby reducing the need for harmful preservatives for infant food making. As demand rises for functional foods in children, enhancing these products with functional ingredients, such as probiotics, proteins, peptides, and lipophilic bioactive compounds (BACs) that are not naturally retained becomes a challenge. Recently, introduction of a promising potential in the field of

functional foods in children can be attained through 3D food printing (3DP). This technique efficiently prepares three-dimensional food products consisting of various flavors, nutritional compositions, and shapes, allowing for the development of personalized nutritional characteristics for the desired target population of children (Tomašević et al. 2021). Using 3DP, a fruit-based functional food for infants can be prepared consisting of skim milk, *Boletus edulis* mushrooms, and white beans, providing a good source of vitamin D, iron, and calcium, and fulfilling the RDI for the mentioned compounds (Derossi et al. 2018). Furthermore, 3DP is used to develop orange concentrate with the preferred compound to streamline dietary supplementation, as only a limited number of food carriers are available for the fortification of Vitamin D (Azam et al. 2018). The unique chemical constituents of microalgal biomass, such as high content of minerals, pigments, antioxidants, and proteins, make it a suitable option for functional food fortification with 3DP. In the field of food technology, 3D printing—also referred to as "food 3D printing" or "edible 3D printing"—is the process of piling edible materials into specialised 3D printers to create three-dimensional, edible structures or objects. *Chlorella vulgaris* and *Arthrospira platensis* are highly considered for integration to preserve the coloration of the product (Pina-Pérez et al. 2019). Therefore, 3DP is considered as a favourable technology for the enhancement with probiotics, proteins as well BACs to enrich functional characteristics especially health benefits to fruits and other functional food products in children (Uribe-Wandurraga et al. 2020).

Bovine colostrum (BC), an initial mammary secretion after parturition, is significantly prosperous in biologically active antioxidants, peptides, and growth-promoting factors that differ from normal mature milk. It is highly preferred in children's food formulas and plays a crucial role in treating GI tract diseases in children. It is observed in the recent studies that lactoferrin present in BC is highly preferred in preventing gastric infections, late-onset sepsis in newborn children, inflammatory bowel disease, autoimmune disorders, some cancer types, and necrotizing enterocolitis (Mehra et al. 2022). Novel technologies for milk processing as an alternative to conventional medications provide the industry with highly efficient, reliable, and hygienic equipment for drinking milk products. The implementation of a large-scale technology typically follows a batch processing approach, However the introduction of devices specifically designed for continuous in-flow application aids in the smooth transition of this technology to the industrial production of milk for consumption (Di Paolo et al., 2023). Additionally, postbiotics refer to the soluble components, such as organic acids, bacteriocins, vitamins, short-chain fatty acids (SCFAs), polyphosphates, and quorum sensing molecules, produced by live probiotic cells in the process of fermentation or can be synthetically produced in laboratory conditions. Recent studies suggest that postbiotic components can be considered as a novel food additive that can improve children's immune tolerance with no undesirable side effects, particularly in pediatrics (Homayouni Rad et al. 2021).

Conclusion

Inclusion of novel food additives in infant formula is a serious concern that must be carefully monitored to ensure the health and safety of new-born. Early nutritional intake is crucial for infant growth and development, and any nutritional deficiencies can have long-term consequences. Thus, it is essential to analyse the potential risks associated with their utilisation in infant food formulation. To reduce concerns about the safety of these additives, it is necessary to have adequate quality control, pediatric clinical and post-market surveillance data, and a comprehensive weight-of-evidence approach has to be executed. Consumers of infant formula should also be aware of the components and the potential negative outcomes of the products they purchase. National authorities should set guidelines for harmful chemicals in baby food products, and a frequent monitoring system should be in place to assess potential hazards. In conclusion, monitoring the quality of infant food products and ensuring that conventions and regulations are followed in their preparation, transport, storage, and sale is of utmost importance to protect the health and well-being of newborns.

Abbreviations

CAGR	Compound Annual Growth Rate
FDA	Food and Drug Administration
EFSA	European Food Safety Authority
DHA	Docosahexaenoic acid
AA/ARA	Arachidonic acid
EPA	Eicosapentaenoic acid
lcPUFA	Long-chain polyunsaturated fatty acid
UNICEF	United Nations International Children's Emergency Fund
ADI	Acceptable Daily Intake
WHO	World Health Organisation
FAO	Food Agriculture Organisation
JMPR	Joint Meeting on Pesticide Residues
JECFA	Joint FAO/WHO Expert Committee on Food Additives
MSDI	Maximum Survey-Derived Intake
SPET	Single Portion Exposure Technique
GRAS	Generally Recognised As Safe
FFDCA	Federal food, Drug and Cosmetic Act
FAPs	Food Additive Petitions
LOC	Level Of Concern
EDI	Estimated Daily Intake
POP	Persistent Organic Pollutants
DC	Dendritic cells
FUF	Follow up formula
CML	Carboxy-Methyl-Lysine
AD	Atopic Dermatitis

LA	Linoleic Acid
ALA	Alpha Linoleic acid
BPA	Bisphenol A
PFCS	Perfluoroalkyl Chemicals
CGN	Carrageenan
PFA	Perfluoroalkyl
HACCP	Hazard Analysis Critical Control Point
USFDA	United States Food and Drug Administration
ADHD	Attention Deficit Hyperactivity Disorder
ASD	Autistic spectrum disorder
CAC	Codex Alimentarius Commission
FSMP	Food for Special Medical Purposes

Acknowledgements
The authors acknowledge the support received from the Department of Life Sciences and Centre for Research (MRP-DSC 1936), CHRIST (Deemed to be University), India.

Authors' contributions
Mrs. Swati Soni, Mrs. Anvil Jennifer W., Mr. Christine Kurian and Ms. Prapti Chakraborty contributed in methodology, validation, and formal analysis of results and wrote the original draft. Dr K. A. Paari contributed to the conceptualization, methodology, and analyze the data. The author(s) read and approved the final manuscript.

Funding
The authors acknowledge the support received from Centre for Research (MRP-DSC 1936), CHRIST (Deemed to be University), India.

Availability of data and materials
The datasets used and analyzed during the present study are available from the corresponding.

Declarations

Ethics approval and consent to participate
Not applicable.

Consent for publication
All authors have no conflicts of interest to disclose and have approved the manuscript for publication.

Competing interests
The authors declare that they have no competing interests.

Author details
[1]Department of Life Sciences, CHRIST (Deemed to be) University, Central Campus, Hosur Road, Bangalore, Karnataka 560029, India. [2]Netaji Subhas Open University, Regional Centre, Durgapur, Paschim Bardhaman, India.

Received: 1 September 2023 Accepted: 25 January 2024
Published online: 05 September 2024

References

Alharbi, O. M. L., Basheer, A. A., Khattab, R. A., & Ali, I. (2018). Health and environmental effects of persistent organic pollutants. *Journal of Molecular Liquids*, *263*, 442–453. https://doi.org/10.1016/J.MOLLIQ.2018.05.029

Ali, A., Tan, H. Y., & Kaiko, G. E. (2020). Role of the intestinal epithelium and its interaction with the microbiota in food allergy. *Frontiers in Immunology*, *11*, 604054. https://doi.org/10.3389/FIMMU.2020.604054/FULL

Allen, L. H., Rosenberg, I. H., Oakley, G. P., & Omenn, G. S. (2010). Considering the case for vitamin B12 fortification of flour. *Food and Nutrition Bulletin*, *31*(1_suppl1), S36–S46.

Almeida, S., Raposo, A., Almeida-González, M., & Carrascosa, C. (2018). Bisphenol A: Food exposure and impact on human health. *Comprehensive Reviews in Food Science and Food Safety*, *17*(6), 1503–1517.

Alonso-Magdalena, P., Morimoto, S., Ripoll, C., Fuentes, E., & Nadal, A. (2006). The estrogenic effect of bisphenol A disrupts pancreatic beta-cell function in vivo and induces insulin resistance. *Environmental Health Perspectives*, *114*(1), 106–112. https://doi.org/10.1289/ehp.8451

Ameen, S.M., Caruso, G. (2017). The importance of lactic acid in the current food industry. An introduction. *Lactic Acid in the Food Industry*, 1–5.

Amiridou, D., & Voutsa, D. (2011). Alkylphenols and phthalates in bottled waters. *Journal of Hazardous Materials*, *185*(1), 281–286.

Appaiah, K. M. (2010). Monosodium glutamate in foods and its biological effects. In *Ensuring global food safety* (pp. 217–226). Academic.

Arnold, L. E., Lofthouse, N., & Hurt, E. (2012). Artificial food colors and attention-deficit/hyperactivity symptoms: Conclusions to dye for. *Neurotherapeutics: The Journal of the American Society for Experimental NeuroTherapeutics*, *9*(3), 599–609. https://doi.org/10.1007/s13311-012-0133-x

Arora, M., Kaur, N., Bansal, P., & Baldi, A. (2019). Emergence of traditionally used foods as today's probioticslong journey. *Current Traditional Medicine*, *5*(2), 114–125.

Augustin, M. A., & Sanguansri, L. (2012). Challenges in developing delivery systems for food additives, nutraceuticals and dietary supplements. In *Encapsulation technologies and delivery systems for food ingredients and nutraceuticals* (pp. 19–48). Elsevier. https://doi.org/10.1533/9780857095909.1.19

Awuchi, C. G., Twinomuhwezi, H., Igwe, V. S., & Amagwula, I. O. (2020). Food additives and food preservatives for domestic and industrial food applications. *Journal of Animal Health*, *2*(1), 1–16.

Azam, R. S. M., Zhang, M., Bhandari, B., & Yang, C. (2018). Effect of different gums on features of 3D printed object based on vitamin-D enriched orange concentrate. *Food Biophysics*, *13*(3), 250–262. https://doi.org/10.1007/s11483-018-9531-x

Bair, E. C. (2022). A narrative review of toxic heavy metal content of infant and Toddler Foods and evaluation of United States policy. *Frontiers in Nutrition*, *9*, 919913.

Barlow, S. M., Boobis, A. R., Bridges, J., Cockburn, A., Dekant, W., Hepburn, P., Houben, G. F., König, J., Nauta, M. J., Schuermans, J., & Bánáti, D. (2015). The role of hazard- and risk-based approaches in ensuring food safety. *Trends in Food Science and Technology*, *46*(2), 176–188. https://doi.org/10.1016/j.tifs.2015.10.007. Elsevier Ltd.

Barretto, J. R., da Cruz Gouveia, M. A., & Alves, C. (2023). Use of dietary supplements by children and adolescents. *Jornal De Pediatria*. https://doi.org/10.1016/j.jped.2023.09.008

Bintsis, T. (2017). Foodborne pathogens. *AIMS Microbiology*, *3*(3), 529–563. https://doi.org/10.3934/microbiol.2017.3.529

Bischoff, N. S., de Kok, T. M., Sijm, D. T. H. M., van Breda, S. G., Briedé, J. J., Castenmiller, J. J. M., Opperhuizen, A., Chirino, Y. I., Dirven, H., Gott, D., Houdeau, E., Oomen, A. G., Poulsen, M., Rogler, G., & van Loveren, H. (2021). Review possible adverse effects of food additive e171 (Titanium dioxide) related to particle specific human toxicity, including the immune system. *International Journal of Molecular Sciences*, *22*(1), 1–35. https://doi.org/10.3390/ijms22010207. MDPI AG.

Blekas, G. A. (2016). Food additives: Classification, uses and regulation. In *Encyclopedia of food and health* (pp. 731–736). https://doi.org/10.1016/B978-0-12-384947-2.00304-4

Braun, T., Ehrlich, L., Henrich, W., Koeppel, S., Lomako, I., Schwabl, P., & Liebmann, B. (2021). Detection of microplastic in human placenta and meconium in a clinical setting. *Pharmaceutics*, *13*(7), 921. https://doi.org/10.3390/PHARMACEUTICS13070921

Calder, P. C. (2015). Functional roles of fatty acids and their effects on human health. *Journal of Parenteral and Enteral Nutrition*, *39*, 18S-32S. https://doi.org/10.1177/0148607115595980

Carlson, S. E., Schipper, L., Brenna, J. T., Agostoni, C., Calder, P. C., Forsyth, S., … & Muhlhausler, B. (2021). Perspective: Moving toward desirable linoleic acid content in infant formula. *Advances in Nutrition*, *12*(6), 2085–2098.

Carocho, M., Barreiro, M. F., Morales, P., & Ferreira, I. C. (2014). Adding molecules to food, pros and cons: A review on synthetic and natural food additives. *Comprehensive Reviews in Food Science and Food Safety*, *13*(4), 377–399.

Chaliha, M., Williams, D., Edwards, D., Pun, S., Smyth, H., & Sultanbawa, Y. (2017). Bioactive rich extracts from Terminalia ferdinandiana by enzyme-assisted extraction: A simple food safe extraction method. *Journal of Medicinal Plants Research*, *11*, 96–106.

Champeny, M., Yuen-Esco, K., Juniza, E., Sy, N. Y., Kane, R., Badham, J., Mulder, A., & Pries, A. M. (2023). Accuracy of declared nutrient content on labels of commercial complementary food products in Cambodia,

Indonesia and Senegal. *Maternal & Child Nutrition*, *19*(3), e13504. https://doi.org/10.1111/mcn.13504
Chandra, R. K. (1997). Food hypersensitivity and allergic disease: A selective review. *The American Journal of Clinical Nutrition*, *66*(2), 526S-529S. https://doi.org/10.1093/ajcn/66.2.526S
Chazelas, E., Deschasaux, M., Srour, B., Kesse-Guyot, E., Julia, C., Alles, B., & Touvier, M. (2020). Food additives: distribution and co-occurrence in 126,000 food products of the French market. *Scientific Reports, 10*(1), 3980.
Cheeseman, M. A. (2012). Artificial food color additives and child behavior. *Environmental Health Perspectives*, *120*(1), a15. https://doi.org/10.1289/EHP.1104409
Chinaza, G. A. (2023). HACCP, quality, and food safety management in food and agricultural systems. *Cogent Food & Agriculture*, *9*, 1. https://doi.org/10.1080/23311932.2023.2176280
Čížková, H., Ševčík, R., Rajchl, A., & Voldřich, M. (2009). Nutritional quality of commercial fruit baby food. *Czech Journal of Food Sciences*, *27*(special issue), 134–137.
Committee on Injury, Violence, and Poison Prevention. (2010). Prevention of choking among children. *Pediatrics*, *125*(3), 601–607. https://doi.org/10.1542/peds.2009-2862
Constable, A., Mahadevan, B., Pressman, P., Garthoff, J. A., Meunier, L., Schrenk, D., Speijers, G., O'Sullivan, A., & Hayes, A. W. (2017). An integrated approach to the safety assessment of food additives in early life. *Toxicology Research and Application*, *1*, 239784731770737. https://doi.org/10.1177/2397847317707370
Coppa, C. F. S. C., Khaneghah, A. M., Alvito, P., Assunção, R., Martins, C., Eş, I., … & Oliveira, C. A. F. (2019). The occurrence of mycotoxins in breast milk, fruit products and cereal-based infant formula: A review. *Trends in Food Science & Technology*, *92*, 81–93. https://doi.org/10.1016/j.tifs.2019.08.014
Csáki, K. F. (2011). Synthetic surfactant food additives can cause intestinal barrier dysfunction. *Medical Hypotheses*, *76*(5), 676–681. https://doi.org/10.1016/j.mehy.2011.01.030
Ćwiek, D., Zimny, M., Szymoniak, K., Czechowska, K., & Sipak-Szmigiel, O. (2023). Assessment of fatty acid content in the milk of women from the West Pomeranian region of Poland with regard to supplementation and the amount of adipose tissue. *Nutrients*, *15*(5), 1110. https://doi.org/10.3390/nu15051110
Das, A. K., Nanda, P. K., Das, A., & Biswas, S. (2019). Hazards and safety issues of meat and meat products. In *Food safety and human health* (pp. 145–168). Academic. https://doi.org/10.1016/B978-0-12-816333-7.00006-0
Derossi, A., Caporizzi, R., Azzollini, D., & Severini, C. (2018). Application of 3D printing for customized food. A case on the development of a fruit-based snack for children. *Journal of Food Engineering*, *220*, 65–75. https://doi.org/10.1016/j.jfoodeng.2017.05.015
Deshwal, G. K., Panjagari, N. R., & Alam, T. (2019). An overview of paper and paper based food packaging materials: Health safety and environmental concerns. *Journal of Food Science and Technology*, *56*, 4391–4403.
Di Paolo, M., Vuoso, V., Ambrosio, R. L., Balestrieri, A., Bifulco, G., Anastasio, A., & Marrone, R. (2023). Role of feeding and novel ripening system to enhance the quality and production sustainability of curd buffalo cheeses. *Foods, 12*(4), 704.
Driedger, A. (2008). 8.3 Relevant US Legislation. *Chemistry and Technology of Surfactants*, 294. https://doi.org/10.1002/9780470988596
EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA). (2013). Scientific Opinion on nutrient requirements and dietary intakes of infants and young children in the European Union. *EFSA Journal*, *11*(10), 3408.
EFSA Panel on Dietetic Products, Nutrition, and Allergies (NDA). (2010). Scientific opinion on dietary reference values for fats, including saturated fatty acids, polyunsaturated fatty acids, monounsaturated fatty acids, trans fatty acids, and cholesterol. *Efsa Journal*, *8*(3), 1461.
EFSA Panel on Food Additives and Nutrient Sources added to Food (ANS), Mortensen, A., Aguilar, F., Crebelli, R., Di Domenico, A., Frutos, M. J., & Dusemund, B. (2017). Re-evaluation of konjac gum (E 425 i) and konjac glucomannan (E 425 ii) as food additives. *Efsa Journal, 15*(6), e04864.
EFSA Panel on Food Additives and Nutrient Sources added to Food (ANS), Younes, M., Aggett, P., Aguilar, F., Crebelli, R., Dusemund, B., & Gott, D. (2018). Guidance on safety evaluation of sources of nutrients and bioavailability of nutrient from the sources. *EFSA Journal, 16*(6), e05294.
EFSA Panel on Food Additives Nutrient Sources added to Food (ANS), Mortensen, A., Aguilar, F., Crebelli, R., Di Domenico, A., Frutos, M. J., & Dusemund, B. (2017). Re-evaluation of locust bean gum (E 410) as a food additive. *Efsa Journal, 15*(1), e04646.
EFSA Panel, Aguilar, Fernando, Crebelli, R., Dusemund, B., Galtier, P., Gott, D., Gundert-Remy, U., König, J., Lambré, C., Leblanc, J.-C., Mortensen, A., Mosesso, P., Oskarsson, A., Parent-Massin, D., Rose, M., Stankovic, I., Tobback, P., Waalkens-Berendsen, I., Woutersen, R. A., & Wright, M. (2013). Scientific opinion on the re-evaluation of aspartame (E 951) as a food additive. *EFSA Journal, 11*(12), 3496. https://doi.org/10.2903/j.efsa.2013.3496
EFSA Panel, Aguilar, F., Crebelli, R., Di Domenico, A., Dusemund, B., Frutos, M. J., Galtier, P., Gott, D., Gundert-Remy, U., Lambré, C., Leblanc J. C., Lindtner, O., Moldeus, P., Mortensen, A., Mosesso, P., Parent-Massin, D., Oskarsson, A., Stankovic, I., Waalkens-Berendsen, I., Woutersen, R. A., Wright, M., & Younes, M. (2015). Scientific opinion on the risk assessment for peri- and post-menopausal women taking food supplements containing isolated isoflavones. *EFSA Journal*, *13*(10), 4246, 342 pp. https://doi.org/10.2903/j.efsa.2015.4246
EFSA Panel, Aguilar, F., Crebelli, R., Di Domenico, A., Dusemund, B., Frutos, M. J., Galtier, P., Gott, D., Gundert-Remy, U., Lambré, C., Leblanc, J.-C., Lindtner, O., Moldeus, P., Mortensen, A., Mosesso, P., Parent-Massin, D., Oskarsson, A., Stankovic, I., Waalkens-Berendsen, I., … Younes, M. (2015). Scientific opinion on the safety of the extension of use of steviol glycosides (E 960) as a food additive. *EFSA Journal, 13*(6), 4146. https://doi.org/10.2903/j.efsa.2015.4146
EFSA Panel, Mortensen, A., Aguilar, F., Crebelli, R., Di Domenico, A., Frutos, M. J., & Dusemund, B. (2016). Re-evaluation of agar (E 406) as a food additive. *EFSA Journal, 14*(12), e04645.
EFSA Panel, Mortensen, A., Aguilar, F., Crebelli, R., Di Domenico, A., Dusemund, B., & Lambré, C. (2017). Re-evaluation of glutamic acid (E 620), sodium glutamate (E 621), potassium glutamate (E 622), calcium glutamate (E 623), ammonium glutamate (E 624) and magnesium glutamate (E 625) as food additives. *EFSA Journal, 15*(7), e04910.
European Food Safety Authority (EFSA), Gkrintzali, G., Georgiev, M., Matas, R. G., Maggiore, A., Merten, C., & Bottex, B. (2023). *EFSA's activities on emerging risks in 2021* (Vol. 20, No. 9, pp. 8233E).
Faustino, M., Veiga, M., Sousa, P., Costa, E. M., Silva, S., & Pintado, M. (2019). Agro-food byproducts as a new source of natural food additives. *Molecules*, *24*(6), 1056. https://doi.org/10.3390/molecules24061056
Feketea, G., & Tsabouri, S. (2017). Common food colorants and allergic reactions in children: Myth or reality? *Food Chemistry*, *230*, 578–588. https://doi.org/10.1016/j.foodchem.2017.03.043. Elsevier Ltd.
Food standards. (2022). A1253 - bovine lactoferrin in infant formula products. A1253 - Bovine lactoferrin in infant formula products. https://www.foodstandards.gov.au/code/applications/Pages/A1253-Bovine-lactoferrin-in-infant-formula-products.aspx
Garcia-Garcia, G., Stone, J., & Rahimifard, S. (2019). Opportunities for waste valorisation in the food industry – A case study with four UK food manufacturers. *Journal of Cleaner Production*, *211*, 1339–1356. https://doi.org/10.1016/J.JCLEPRO.2018.11.269
Garg, S., Kumar, P., Mishra, V., Guijt, R., Singh, P., Dumée, L. F., & Sharma, R. S. (2020). A review on the sources, occurrence and health risks of per-/poly-fluoroalkyl substances (PFAS) arising from the manufacture and disposal of electric and electronic products. *Journal of Water Process Engineering*, *38*, 101683. https://doi.org/10.1016/J.JWPE.2020.101683
Gargano, D., Appanna, R., Santonicola, A., De Bartolomeis, F., Stellato, C., Cianferoni, A., & Iovino, P. (2021). Food allergy and intolerance: a narrative review on nutritional concerns. *Nutrients, 13*(5), 1638.
Gärtner, S., Balski, M., Koch, M., & Nehls, A. (2009). Analysis and migration of phthalates in infant food packed in recycled paperboard. *Journal of Agricultural and Food Chemistry*, *57*(22), 10675–10681. https://doi.org/10.1021/JF902683M
Gericke, M., Trygg, J., & Fardim, P. (2013). Functional cellulose beads: preparation, characterization, and applications. *Chemical Reviews, 113*(7), 4812–4836.
Ghassabian, A., & Trasande, L. (2018). Disruption in thyroid signaling pathway: A mechanism for the effect of endocrine-disrupting chemicals on child

neurodevelopment. *Frontiers in Endocrinology*, *9*(APR). https://doi.org/10.3389/fendo.2018.00204. Frontiers Media S.A.

Gibney, M. J., & Lambe, J. (1996). Estimation of food additive intake: Methodology overview. *Food Additives and Contaminants*, *13*(4), 405–410. https://doi.org/10.1080/02652039609374424

Gil-Martín, E., Forbes-Hernández, T., Romero, A., Cianciosi, D., Giampieri, F., & Battino, M. (2022). Influence of the extraction method on the recovery of bioactive phenolic compounds from food industry by-products. *Food Chemistry*, *378*, 131918. https://doi.org/10.1016/J.FOODCHEM.2021.131918

Gore, A. C., Chappell, V. A., Fenton, S. E., Flaws, J. A., Nadal, A., Prins, G. S., Toppari, J., & Zoeller, R. T. (2015). Executive Summary to EDC-2: The Endocrine Society's second Scientific Statement on endocrine-disrupting chemicals. *Endocrine Reviews*, *36*(6), 593–602. https://doi.org/10.1210/er.2015-1093. Endocrine Society.

Guandalini, S., Ecuba, P., Corvino, C., & di Martino, L. (1989). Lactose malabsorption in children with symptomatic Giardia lamblia infection: Feasibility of yogurt supplementation. *Journal of Pediatric Gastroenterology and Nutrition*, *9*(3), 295–300.

Halldorsson, T. I., Rytter, D., Haug, L. S., Bech, B. H., Danielsen, I., Becher, G., Henriksen, T. B., & Olsen, S. F. (2012). Prenatal exposure to perfluorooctanoate and risk of overweight at 20 years of age: A prospective cohort study. *Environmental Health Perspectives*, *120*(5), 668–673. https://doi.org/10.1289/ehp.1104034

Hardy, A., Benford, D., Halldorsson, T., Jeger, M. J., Knutsen, H. K., & Mortensen, A. (2017). Guidance on the risk assessment of substances present in food intended for infants below 16 weeks of age. *EFSA Journal, 15*(5), e04849.

Hauser, R., Skakkebaek, N. E., Hass, U., Toppari, J., Juul, A., Andersson, A. M., Kortenkamp, A., Heindel, J. J., & Trasande, L. (2015). Male reproductive disorders, diseases, and costs of exposure to endocrine-disrupting chemicals in the European Union. *The Journal of Clinical Endocrinology & Metabolism*, *100*(4), 1267–1277. https://doi.org/10.1210/JC.2014-4325

Hollande, L., & Allais, F. (2018). Ferulic acid-and sinapic acid-based bisphenols: Promising renewable and safer alternatives to bisphenol A for the production of bio-based polymers and resins. In *Green polymer chemistry: New products, processes, and applications* (pp. 221–251). American Chemical Society.

Holvoet, S., Nutten, S., Dupuis, L., Donnicola, D., Bourdeau, T., Hughes-Formella, B., … & Blanchard, C. (2021). Partially hydrolysed whey-based infant formula improves skin barrier function. *Nutrients*, *13*(9), 3113.

Homayouni Rad, A., Aghebati Maleki, L., Samadi Kafil, H., & Abbasi, A. (2021). Postbiotics: A novel strategy in food allergy treatment. *Critical Reviews in Food Science and Nutrition*, *61*(3), 492–499. https://doi.org/10.1080/10408398.2020.1738333. Bellwether Publishing, Ltd.

Howlett, J., Edwards, D., … A. C.-… journal of food, & 2003, undefined. (2003). The safety assessment of novel foods and concepts to determine their safety in use. *Taylor & Francis*, 54(SUPPL.). https://doi.org/10.1080/09637480310001610308

Ibe, F. C., Opara, A. I., Amaobi, C. E., & Ibe, B. O. (2021). Environmental risk assessment of the intake of contaminants in aquifers in the vicinity of a reclaimed waste dumpsite in Owerri municipal, Southeastern Nigeria. *Applied Water Science*, *11*, 1–19. https://doi.org/10.1007/S13201-020-01355-4

Imam, S. H., Bilbao-Sainz, C., Chiou, B. S., Glenn, G. M., & Orts, W. J. (2013). Biobased adhesives, gums, emulsions, and binders: Current trends and future prospects. *Journal of Adhesion Science and Technology*, *27*(18–19), 1972–1997.

Indrio, F., Mestrovic, J., Carrasco-Sanz, A., Vural, M., Namazova-Baranova, L., Giardino, I., Pop, T. L., & Pettoello-Mantovani, M. (2022). Overview on child health, nutrition and food hazards during the first thousand days of life. *Global Pediatrics*, *2*, 100018. https://doi.org/10.1016/J.GPEDS.2022.100018

Ingenbleek, L., Lautz, L. S., Dervilly, G., Darney, K., Astuto, M. C., Tarazona, J., … & Dorne, J. L. C. M. (2020). *Risk assessment of chemicals in food and feed: principles, applications and future perspectives*. pp. 1–38.

Ishola, I. S. (2022). Development of complimentary food from soy bean and soy by–products. *Journal of Food Technology & Nutrition Sciences*, *SRC/JFTNS/158*(4), 142, 2–4. https://doi.org/10.47363/JFTNS/2022

Jeřábek, K., Odnoha, J., & Setinek, K. (1988). Kinetics of the synthesis of bisphenol A. *Applied Catalysis*, *37*, 129–138.

Joint, F. A. O., World Health Organization, & WHO Expert Committee on Food Additives. (1987). *Principles for the safety assessment of food additives and contaminants in food*. World Health Organization.

Jones, J. A., Hopper, A. O., Power, G. G., & Blood, A. B. (2014). *Dietary intake and bio-activation of nitrite and nitrate in newborn infants*. https://doi.org/10.1038/pr.2014.168

Juan, C., Raiola, A., Mañes, J., & Ritieni, A. (2014). Presence of mycotoxin in commercial infant formulas and baby foods from Italian market. *Food Control*, *39*, 227–236.

Kaliner, M. (1989). Asthma and mast cell activation. *Journal of Allergy and Clinical Immunology*, *83*(2), 510–520.

Kent, G. (2014). Regulating fatty acids in infant formula: Critical assessment of US policies and practices. *International Breastfeeding Journal*, *9*(1), 1–10.

Kettlitz, B., Kemendi, G., Thorgrimsson, N., Cattoor, N., Verzegnassi, L., le Bail-Collet, Y., Maphosa, F., Perrichet, A., Christall, B., & Stadler, R. H. (2016). Why chlorate occurs in potable water and processed foods: A critical assessment and challenges faced by the food industry. *Food Additives and Contaminants - Part A Chemistry, Analysis, Control, Exposure and Risk Assessment*, *33*(6), 968–982. https://doi.org/10.1080/19440049.2016.1184521

Kim, S. A., Oh, S. W., Lee, Y. M., Imm, J. Y., Hwang, I. G., Kang, D. H., & Rhee, M. S. (2011). Microbial contamination of food products consumed by infants and babies in Korea. *Letters in Applied Microbiology*, *53*(5), 532–538. https://doi.org/10.1111/J.1472-765X.2011.03142.X

Kim, Y. R., Pacella, R. E., Harden, F. A., White, N., & Toms, L. M. L. (2019). A systematic review: Impact of endocrine disrupting chemicals exposure on fecundity as measured by time to pregnancy. *Environmental Research*, *171*, 119–133. https://doi.org/10.1016/J.ENVRES.2018.12.065

Kirschman, J. C. (2010). Effective regulatory approval process for food ingredient technologies. *Critical Reviews in Food Science and Nutrition*, *38*(6), 465–510. https://doi.org/10.1080/10408699891274282

Koletzko, B., Uauy, R., Palou, A., Kok, F., Hornstra, G., Eilander, A., … & Innis, S. (2010). Dietary intake of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) in children–A workshop report. *British Journal of Nutrition*, *103*(6), 923–928.

Koletzko, B., Bergmann, K., Brenna, J. T., Calder, P. C., Campoy, C., Clandinin, M. T., … & Carlson, S. E. (2020). Should formula for infants provide arachidonic acid along with DHA? A position paper of the European Academy of Paediatrics and the Child Health Foundation. *The American Journal of Clinical Nutrition*, *111*(1), 10–16. https://doi.org/10.1093/ajcn/nqz252

Kremer, J. C. (2022). Xanthan gum in formulas for special medical purposes for infants. ISDI. https://www.isdi.org/xanthan-gum-in-formulas-for-special-medical-purposes-for-infants/

Kremmyda, L. S., Vlachava, M., Noakes, P. S., Diaper, N. D., Miles, E. A., & Calder, P. C. (2011). Atopy risk in infants and children in relation to early exposure to fish, oily fish, or long-chain omega-3 fatty acids: A systematic review. *Clinical Reviews in Allergy & Immunology*, *41*, 36–66.

Krewski, D., Acosta, D., Andersen, M., Anderson, H., Bailar, J. C., Boekelheide, K., Brent, R., Charnley, G., Cheung, V. G., Green, S., Kelsey, K. T., Kerkvliet, N. I., Li, A. A., McCray, L., Meyer, O., Patterson, R. D., Pennie, W., Scala, R. A., Solomon, G. M., … & Zeise, L. (2010). Toxicity testing in the 21st century: A vision and a strategy. *Journal of Toxicology and Environmental Health. Part B, Critical Reviews*, *13*(0), 51. https://doi.org/10.1080/10937404.2010.483176

Lambré, C., Baviera, J. M. B., Bolognesi, C., Chesson, A., Cocconcelli, P. S., Crebelli, R., & Castle, L. (2022). Identification and prioritisation for risk assessment of phthalates, structurally similar substances and replacement substances potentially used as plasticisers in materials and articles intended to come into contact with food. *EFSA Journal, 20*(5).

Landrigan, P. J., & Goldman, L. R. (2011). Children's vulnerability to toxic chemicals: A challenge and opportunity to strengthen health and environmental policy. *Health Affairs*, *30*(5), 842–850.

Lange, K. W., Nakamura, Y., Gosslau, A. M., & Li, S. (2019). Are there serious adverse effects of omega-3 polyunsaturated fatty acid supplements? *Journal of Food Bioactives*, *7*. https://doi.org/10.31665/JFB.2019.7192.

Lanigan, J., & Singhal, A. (2009). Early nutrition and long-term health: A practical approach: Symposium on 'Early nutrition and later disease: Current concepts, research and implications.' *Proceedings of the Nutrition Society*, *68*(4), 422–429. https://doi.org/10.1017/S002966510999019X

Leaf, A. A. (2007). Vitamins for babies and young children. *Archives of Disease in Childhood*, *92*(2), 160. https://doi.org/10.1136/ADC.2006.109066

Leung, C., Chang, W. C., & Yeh, S. J. (2009). Hypernatremic dehydration due to concentrated infant formula: Report of two cases. *Pediatrics & Neonatology*, *50*(2), 70–73. https://doi.org/10.1016/S1875-9572(09)60036-X

Li, M., Xiao, M., Xiao, Q., Chen, Y., Guo, Y., Sun, J., & Lu, S. (2022). Perchlorate and chlorate in breast milk, infant formulas, baby supplementary food and the implications for infant exposure. *Environment International, 158*, 106939.

Liang, L., Pan, Y., Bin, L., Liu, Y., Huang, W., Li, R., & Lai, K. P. (2022). Immunotoxicity mechanisms of perfluorinated compounds PFOA and PFOS. *Chemosphere*, *291*(Pt 2), 132892. https://doi.org/10.1016/j.chemosphere.2021.132892

Lien, E. L., Richard, C., & Hoffman, D. R. (2018). DHA and ARA addition to infant formula: Current status and future research directions. *Prostaglandins, Leukotrienes and Essential Fatty Acids*, *128*, 26–40.

Liu, Q., Qiao, W., Liu, Y., Zhao, J., Fan, X., Li, Z., & Chen, L. (2023). Effects of lipids from multiple sources on glyceride composition, concentration, and structure of infant formulas benchmarked to human milk. *Heliyon*, e21611. https://doi.org/10.1016/j.heliyon.2023.e21611

Llorca, M., Farré, M., Picó, Y., Teijón, M. L., Álvarez, J. G., & Barceló, D. (2010). Infant exposure of perfluorinated compounds: Levels in breast milk and commercial baby food. *Environment International*, *36*(6), 584–592. https://doi.org/10.1016/J.ENVINT.2010.04.016

Lorenzoni, A. S. G., Oliveira, F. A., & Cladera-Oliveira, F. (2012). Food additives in products for children marketed in Brazil. *Food and Public Health, 2*(5), 131–136.

Ma, Y., Lindsey, M. L., & Halade, G. V. (2012). DHA derivatives of fish oil as dietary supplements: A nutrition-based drug discovery approach for therapies to prevent metabolic cardiotoxicity. *Expert Opinion on Drug Discovery*, *7*(8), 711–721. https://doi.org/10.1517/17460441.2012.694862

MacDonald Baker, S., Bauer, B. A., Monti, D. A., Jefferson, T., Mullin, G., Hopkins, J., Neely, J., Nicolson, G. L., Plumlee, L. A., Rea, W. J., Health Center -Dallas Sandeep Saluja, E., Ashram Hospital, S., Eric Secor Jr, D. R., Campbell, A. W., Balick, M., Hyman, M., Bland, J., Lee, R., & Low Dog, T. (2015). *Optimal Health and Prevention Research Foundation*.

Magnuson, B. A., Burdock, G., Doull, J., Kroes, R. M., Marsh, G. M., Pariza, M. W., … & Williams, G. M. (2007). Aspartame: A safety evaluation based on current use levels, regulations, and toxicological and epidemiological studies. *Critical Reviews in Toxicology*, *37*(8), 629–727. https://doi.org/10.1080/10408440701516184

Mankad, D., Dupuis, A., Smile, S., Roberts, W., Brian, J., Lui, T., … & Anagnostou, E. (2015). A randomized, placebo controlled trial of omega-3 fatty acids in the treatment of young children with autism. *Molecular Autism*, *6*, 1–11.

Maqbool, F., Mostafalou, S., Bahadar, H., & Abdollahi, M. (2016). Review of endocrine disorders associated with environmental toxicants and possible involved mechanisms. *Life Sciences*, *145*, 265–273. https://doi.org/10.1016/J.LFS.2015.10.022

Maria, L. C., Lucia, V., Maria, F. P., Raffaele, M., & Raffaelina, M. (2015). Determination of nitrate and nitrite levels in infant foods marketed in Southern Italy. *CyTA - Journal of Food*, *13*(4), 629–634. https://doi.org/10.1080/19476337.2015.1035337

Martin, C. R., Ling, P. R., & Blackburn, G. L. (2016). Review of infant feeding: Key features of breast milk and infant formula. *Nutrients*, *8*(5), 279. https://doi.org/10.3390/nu8050279

Martyn, D. M., McNulty, B. A., Nugent, A. P., & Gibney, M. J. (2013). Food additives and preschool children. *Proceedings of the Nutrition Society*, *72*(1), 109–116. https://doi.org/10.1017/S0029665112002935

McSweeney, S. L. (2019). *Emulsifiers in infant nutritional products*. Food emulsifiers and their applications, 255–284.

Mehra, R., Garhwal, R., Sangwan, K., Guiné, R. P. F., Lemos, E. T., Buttar, H. S., Visen, P. K. S., Kumar, N., Bhardwaj, A., & Kumar, H. (2022). Insights into the research trends on bovine colostrum: Beneficial health perspectives with special reference to manufacturing of functional foods and feed supplements. *Nutrients*, *14*(3). https://doi.org/10.3390/nu14030659. MDPI.

Metz, C. M. (2016). Bisphenol A: Understanding the controversy. *Workplace Health & Safety*, *64*(1), 28–36. https://doi.org/10.1177/2165079915623790

Millichap, J. G., & Yee, M. M. (2003). The diet factor in pediatric and adolescent migraine. *Pediatric Neurology*, *28*(1), 9–15.

Millstone, E., & Van Zwanenberg, P. (2003). Food and agricultural biotechnology policy: How much autonomy can developing countries exercise? *Development Policy Review*, *21*(5–6), 655–667. https://doi.org/10.1111/j.1467-8659.2003.00230.x

Mondal, D. D., Chakraborty, U., Bera, M., Ghosh, S., & Kar, D. (2023). An overview of nutritional profiling in foods: Bioanalytical techniques and useful protocols. *Frontiers in Nutrition*, *10*, 1124409. https://doi.org/10.3389/fnut.2023.1124409

Mortensen, A., Aguilar, F., Crebelli, R., Di Domenico, A., Dusemund, B., Frutos, M. J., Galtier, P., Gott, D. M., Gundert-Remy, U., Lambré, C., Leblanc, J., Lindtner, O., Moldeus, P., Mosesso, P., Parent-Massin, D., Oskarsson, A., Stankovic, I., Waalkens-Berendsen, I., Wright, M., & Woutersen, R. A. (2017). Re-evaluation of oxidised starch (E 1404), monostarch phosphate (E 1410), distarch phosphate (E 1412), phosphated distarch phosphate (E 1413), acetylated distarch phosphate (E 1414), acetylated starch (E 1420), acetylated distarch adipate (E 1422), hydroxypropyl starch (E 1440), hydroxypropyl distarch phosphate (E 1442), starch sodium octenyl succinate (E 1450), acetylated oxidised starch (E 1451) and starch aluminium octenyl succinate (E 1452) as food additives. *EFSA Journal*, *15*(10). https://doi.org/10.2903/j.efsa.2017.4911

Mritunjay, S. K., & Kumar, V. (2017). Microbial quality, safety, and pathogen detection by using quantitative PCR of raw salad vegetables sold in Dhanbad city, India. *Journal of Food Protection*, *80*(1), 121–126. https://doi.org/10.4315/0362-028X.JFP-16-223

Munblit, D., Crawley, H., Hyde, R., & Boyle, R. J. (2020). Health and nutrition claims for infant formula are poorly substantiated and potentially harmful. *BMJ*, *369*, m875. https://doi.org/10.1136/bmj.m875

Mwale, M. (2023). *Health risk of food additives: Recent developments and trends in the food sector*. https://doi.org/10.5772/intechopen.109484

National Academies of Sciences, Engineering, and Medicine, Health and Medicine Division, Food and Nutrition Board, Committee on Food Allergies: Global Burden, Causes, Treatment, Prevention, and Public Policy, Oria, M. P., & Stallings, V. A. (Eds.). (2016). *Finding a path to safety in food allergy: Assessment of the global burden, causes, prevention, management, and public policy*. National Academies Press (US). Available from: https://www.ncbi.nlm.nih.gov/books/NBK435951/

National Research Council (US) Committee on Occupational Health and Safety in the Care and Use of Nonhuman Primates (2003) *Occupational health and safety in the care and use of nonhuman primates*. National Academies Press (US). https://doi.org/10.17226/10713. Available from: https://www.ncbi.nlm.nih.gov/books/NBK43451/

Neltner, T. G., Kulkarni, N. R., Alger, H. M., Maffini, M. V., Bongard, E. D., Fortin, N. D., & Olson, E. D. (2011). Navigating the U.S. food additive regulatory program. *Comprehensive Reviews in Food Science and Food Safety*, *10*(6), 342–368. https://doi.org/10.1111/j.1541-4337.2011.00166.x

Neltner, T. G., Alger, H. M., O'Reilly, J. T., Krimsky, S., Bero, L. A., & Maffini, M. V. (2013). Conflicts of interest in approvals of additives to food: Determined to be generally recognized as safe: Out of balance. *JAMA Internal Medicine*, *173*(22), 2032–2036. https://doi.org/10.1001/jamainternmed.2013.10559

Nigel, B., Danika, M., & Phipps, K. R. (2017). Safety assessment of additives and ingredients for infants and young children - Article. *Agro FOOD Industry Hi Tech*, *28*(6), 22–25. https://www.intertek.com/WorkArea/DownloadAsset.aspx?id=34359769752.

Niu, S., Tao, W., Chen, R., Hageman, K. J., Zhu, C., Zheng, R., & Dong, L. (2021). Using polychlorinated naphthalene concentrations in the soil from a southeast China e-waste recycling area in a novel screening-level multipathway human cancer risk assessment. *Environmental Science and Technology*, *55*(10), 6773–6782. https://doi.org/10.1021/ACS.EST.1C00128/SUPPL_FILE/ES1C00128_SI_001.PDF

Nunes, L., Martins, E., Perrone, I. T., & de Carvalho, A. F. (2019). The Maillard reaction in powdered infant formula. *Journal of Food and Nutrition Research*, *7*(1), 33–40.

Nunes, C. S., Kunamneni, A., Kumar, V., & Habte-Tsion, H. M. (2018). Registration of food and feed additives (enzymes) in the United States, Canada, and China. In *Enzymes in human and animal nutrition* (pp. 457–480). Academic. https://doi.org/10.1016/B978-0-12-805419-2.00024-1

Panseri, S., Nobile, M., Arioli, F., Biolatti, C., Pavlovic, R., & Chiesa, L. M. (2020). Occurrence of perchlorate, chlorate and polar herbicides in different baby food commodities. *Food Chemistry*, *330*, 127205. https://doi.org/10.1016/j.foodchem.2020.127205

Parletta, N., Niyonsenga, T., & Duff, J. (2016). Omega-3 and omega-6 polyunsaturated fatty acid levels and correlations with symptoms in children with attention deficit hyperactivity disorder, autistic spectrum disorder and typically developing controls. *PLoS One*, *11*(5), e0156432.

Pettoello-Mantovani, M., Mestrovic, J., Carrasco-Sanz, A., Hoey, H., Pop, T. L., Somekh, E., Vural, M., Mujkic, A., Giardino, I., & Namazova-Baranova, L. (2022). Introduction to the Special Issue on Safe food for infants: The importance of pursuing integrated approaches to monitor and reduce the risks of biological, chemical, and physical hazards in infant food during the key developmental years. *Global Pediatrics*, *2*, 100008. https://doi.org/10.1016/J.GPEDS.2022.100008

Pham-Huy, L. A., He, H., & Pham-Huy, C. (2008). Free radicals, antioxidants in disease and health. *International Journal of Biomedical Science: IJBS*, *4*(2), 89.

Pina-Pérez, M. C., Brück, W. M., Brück, T., & Beyrer, M. (2019). Microalgae as healthy ingredients for functional foods. In *The role of alternative and innovative food ingredients and products in consumer wellness* (pp. 103–137). Elsevier. https://doi.org/10.1016/B978-0-12-816453-2.00004-8

Posnack, N. G., Lee, N. H., Brown, R., & Sarvazyan, N. (2011). Gene expression profiling of DEHP-treated cardiomyocytes reveals potential causes of phthalate arrhythmogenicity. *Toxicology*, *279*(1–3), 54–64. https://doi.org/10.1016/j.tox.2010.09.007

Pratap, K., Taki, A. C., Johnston, E. B., Lopata, A. L., & Kamath, S. D. (2020). A comprehensive review on natural bioactive compounds and probiotics as potential therapeutics in food allergy treatment. *Frontiers in Immunology*, *11*, 996. https://doi.org/10.3389/FIMMU.2020.00996/BIBTEX

Prescott, J. (2013). *Taste matters: Why we like the foods we do*. Reaktion Books.

Pressman, P., Clemens, R., Hayes, W., & Reddy, C. (2017). *Food additive safety*. https://doi.org/10.1177/2397847317723572

Putta, S. (2020). *FSSAI guidance and notification on nutraceuticals–An insight*. FnBnews.com.

Rao, P., & Sudershan, R. V. (2008). Risk assessment of synthetic food colours: A case study in Hyderabad, India. *International Journal of Food Safety, Nutrition and Public Health*, *1*(1), 68–87.

Rastogi, H., & Bhatia, S. (2019). Future prospectives for enzyme technologies in the food industry. In *Enzymes in food biotechnology* (pp. 845–860). Academic.

Raybaudi-Massilia, R. M., Mosqueda-Melgar, J., & Tapia, M. S. (2010). Edible coatings as carriers of food additives on fresh-cut fruits and vegetables. *Stewart Postharvest Review*, *3*(3), 1–7.

Redbook 2000: I Introduction | FDA. (2007). Retrieved December 21, 2022, from https://www.fda.gov/regulatory-information/search-fda-guidance-documents/redbook-2000-i-introduction

Rychen, G., Aquilina, G., Azimonti, G., Bampidis, V., Bastos, M. D. L., Bories, G., Chesson, A., Cocconcelli, P. S., Flachowsky, G., Gropp, J., Kolar, B., Kouba, M., López-Alonso, M., López Puente, S., Mantovani, A., Mayo, B., Ramos, F., Saarela, M., Villa, R. E., … & Wallace, R. J. (2018). Safety and efficacy of vitamin B12 (in the form of cyanocobalamin) produced by Ensifer spp. as a feed additive for all animal species based on a dossier submitted by VITAC EEIG. *EFSA Journal*, *16*(7), 5336. https://doi.org/10.2903/J.EFSA.2018.5336

Sabarwal, A., Kumar, K., & Singh, R. P. (2018). Hazardous effects of chemical pesticides on human health–Cancer and other associated disorders. *Environmental Toxicology and Pharmacology*, *63*, 103–114. https://doi.org/10.1016/J.ETAP.2018.08.018

Saltmarsh, M. (Ed.4th). (2013). *Essential guide to food additives*. Royal Society of Chemistry. https://books.google.co.in/books?id=V4p77KU8BE0C&lpg=PA1&ots=ZuCZXDuqbP&dq=What%20are%20food%20additives%3F%20WHO&lr&pg=PA9#v=onepage&q=What%20are%20food%20additives?%20WHO&f=false

Sambu, S., Hemaram, U., Murugan, R., & Alsofi, A. A. (2022). Toxicological and teratogenic effect of various food additives: An updated review. *BioMed Research International*, *2022*, 6829409. https://doi.org/10.1155/2022/6829409

Sandoval-Cuellar, C. E., de Jesus Perea-Flores, M., & Quintanilla-Carvajal, M. X. (2020). In-vitro digestion of whey protein-and soy lecithin-stabilized High Oleic Palm Oil emulsions. *Journal of Food Engineering, 278*, 109918.

Sardarodiyan, M., & Hakimzadeh, V. (2016). Artificial sweeteners. *International Journal of PharmTech Research*, *9*, 357–363.

Savin, M., Vrkatić, A., Dedić, D., Vlaški, T., Vorgučin, I., Bjelanović, J., & Jevtic, M. (2022). Additives in children's nutrition—A review of current events. *International Journal of Environmental Research and Public Health*, *19*(20), 13452. https://doi.org/10.3390/ijerph192013452. MDPI.

Scotter, M. J. (2011). Methods for the determination of European Union-permitted added natural colours in foods: a review. *Food Additives and Contaminants, 28*(5), 527–596.

Scotter, M. J., Castle, L., Croucher, J. M., & Olivier, L. (2003). Method development and analysis of retail foods and beverages for carotenoid food colouring materials E160a (ii) and E160e. *Food Additives & Contaminants, 20*(2), 115–126.

Shashkova, N., Ushkarenko, I., Soloviov, A., Osadchyi, O., & Nitsenko, V. (2021). Behavioral segmentation of baby food consumers: Risk areas, possible solutions. The case of Ukraine. *European Journal of Sustainable Development*, *10*(1), 349–349.

Shukla, S., Shankar, R., & Singh, S. P. (2014). Food safety regulatory model in India. *Food Control*, *37*(1), 401–413. https://doi.org/10.1016/j.foodcont.2013.08.015

Sicherer, S. H., Warren, C. M., Dant, C., Gupta, R. S., & Nadeau, K. C. (2020). Food allergy from infancy through adulthood. *The Journal of Allergy and Clinical Immunology: In Practice*, *8*(6), 1854–1864.

Silva, E., Aroso, I. M., Silva, J. M., & Reis, R. L. (2022). Comparing deep eutectic solvents and cyclodextrin complexes as curcumin vehicles for blue-light antimicrobial photodynamic therapy approaches. *Photochemical & Photobiological Sciences, 21*(7), 1159–1173.

Silva, Maria Manuela, & Lidon, F. (2016). Food preservatives–An overview on applications and side effects. *Emirates Journal of Food and Agriculture, 28*(6), 366–373. https://doi.org/10.9755/ejfa.2016-04-351

Silveira, R. C., Corso, A. L., & Procianoy, R. S. (2023). The influence of early nutrition on neurodevelopmental outcomes in preterm infants. *Nutrients*, *15*(21), 4644. https://doi.org/10.3390/nu15214644

Stahl, T., Mattern, D., & Brunn, H. (2011). Toxicology of perfluorinated compounds. *Environmental Sciences Europe*, *23*(1), 38.

Stephen, A. M., Champ, M. M. J., Cloran, S. J., Fleith, M., Van Lieshout, L., Mejborn, H., & Burley, V. J. (2017). Dietary fibre in Europe: current state of knowledge on definitions, sources, recommendations, intakes and relationships to health. *Nutrition Research Reviews, 30*(2), 149–190.

Stevens, L. J., Kuczek, T., Burgess, J. R., Hurt, E., & Arnold, L. E. (2011). Dietary sensitivities and ADHD symptoms: Thirty-five years of research. *Clinical Pediatrics*, *50*(4), 279–293. https://doi.org/10.1177/0009922810384728

Tchounwou, P. B., Yedjou, C. G., Patlolla, A. K., & Sutton, D.J. (2012). Heavy metal toxicity and the environment. In A. Luch (Ed.) *Molecular, clinical and environmental toxicology. Experientia supplementum* (vol. 101). Springer. https://doi.org/10.1007/978-3-7643-8340-4_6

Teixeira, A. Z. A. (2018). Sodium content and food additives in major brands of brazilian children's foods. *Ciencia e Saude Coletiva*, *23*(12), 4065–4075. https://doi.org/10.1590/1413-812320182312.21812016

Teklemariam, T. A., & Gotera, J. (2019). Application of laser induced breakdown spectroscopy in food container glass discrimination. *Spectrochimica Acta Part B: Atomic Spectroscopy*, *155*, 34–43. https://doi.org/10.1016/J.SAB.2019.03.005

Thakur, K., Singh, D., & Rajput, R. (2022). Effects of food additives and preservatives and shelf life of the processed foods. *Journal of Current Research in Food Science*, *3*(2), 11–22.

Tocher, D. R., Betancor, M. B., Sprague, M., Olsen, R. E., & Napier, J. A. (2019). Omega-3 long-chain polyunsaturated fatty acids, EPA and DHA: Bridging the gap between supply and demand. *Nutrients*, *11*(1), 89. https://doi.org/10.3390/nu11010089

Tomašević, I., Putnik, P., Valjak, F., Pavlić, B., Šojić, B., Bebek Markovinović, A., & Bursać Kovačević, D. (2021). 3D printing as novel tool for fruit-based functional food production. In *Current opinion in food science* (vol. 41, pp. 138–145). Elsevier Ltd. https://doi.org/10.1016/j.cofs.2021.03.015

Tonacchera, M., Pinchera, A., Dimida, A., Ferrarini, E., Agretti, P., Vitti, P., Santini, F., Crump, K., & Gibbs, J. (2004). Relative potencies and additivity of perchlorate, thiocyanate, nitrate, and iodide on the inhibition of radioactive iodide uptake by the human sodium iodide symporter. *Thyroid, 14*(12), 1012–1019.

Trasande, L., Shaffer, R. M., Sathyanarayana, S., Lowry, J. A., Ahdoot, S., Baum, C. R., & Woolf, A. D. (2018a). Food additives and child health. *Pediatrics*, *142*(2), e20181410. https://doi.org/10.1542/peds.2018-1410

Trasande, L., Shaffer, R. M., & Sathyanarayana, S. (2018b). Food Additives and Child Health. *Pediatrics*, *142*(2). https://doi.org/10.1542/PEDS.2018-1410

Trasande, L., Shaffer, R. M., & Sathyanarayana, S. (2018c). Food additives and child health. *Pediatrics*, *142*(2). https://doi.org/10.1542/PEDS.2018-1410/37583

Uauy, R., & Dangour, A. D. (2009). Fat and fatty acid requirements and recommendations for infants of 0–2 years and children of 2–18 years. *Annals of Nutrition & Metabolism*, *55*(1/3), 76–96.

Ukwo, S. P., Udo, I. I., & Ndaeyo, N. (2022). Food additives: Overview of related safety concerns. *Food Science & Nutrition Research*, *5*, 1–10.

United Nations Children's Fund. (2021). *The state of the world's children 2021: On my mind – promoting, protecting and caring for children's mental health*. UNICEF.

Uribe-Wandurraga, Z. N., Zhang, L., Noort, M. W. J., Schutyser, M. A. I., García-Segovia, P., & Martínez-Monzó, J. (2020). Printability and physicochemical properties of microalgae-enriched 3D-printedsnacks. *Food and Bioprocess Technology*, *13*(11), 2029–2042. https://doi.org/10.1007/s11947-020-02544-4

Vale, S. L., Lobb, M., Netting, M. J., Murray, K., Clifford, R., Campbell, D. E., & Salter, S. M. (2021). A systematic review of infant feeding food allergy prevention guidelines–Can we AGREE? *World Allergy Organization Journal*, *14*(6), 100550.

Van Brakel, L., Thijs, C., Mensink, R. P., Lütjohann, D., & Plat, J. (2022). Non-cholesterol sterols in breast milk and risk of allergic outcomes in the first two years of life. *Nutrients*, *14*(4), 766.

Varvara, M., Bozzo, G., Celano, G., Disanto, C., Pagliarone, C. N., & Celano, G. V. (2016). The use of ascorbic acid as a food additive: technical-legal issues. *Italian Journal of Food Safety, 5*(1), 4313. https://doi.org/10.4081/ijfs.2016.4313

Vayda, M. E., Walsh, H., Zhang, W., & Guo, M. R. (2021). Infant formula analysis. In *Human milk biochemistry and infant formula manufacturing technology* (pp. 317–364). Woodhead Publishing

Vejdovszky, K., Grossgut, R., Unterluggauer, H., Inreiter, N., & Steinwider, J. (2018). Risk assessment of dietary exposure to perchlorate for the Austrian population. *Food Additives & Contaminants: Part A*, *35*(4), 624–632.

Velumani, K., Arasu, A., Issac, P. K., Kishore Kumar, M. S., Guru, A., & Arockiaraj, J. (2023). Advancements of fish-derived peptides for mucormycosis: A novel strategy to treat diabetic compilation. *Molecular Biology Reports*, 1–23. https://doi.org/10.1007/s11033-023-08882-8

Ververis, E., Ackerl, R., Azzollini, D., Colombo, P. A., de Sesmaisons, A., Dumas, C., ... & Gelbmann, W. (2020). Novel foods in the European Union: Scientific requirements and challenges of the risk assessment process by the European Food Safety Authority. *Food Research International*, *137*, 109515. https://doi.org/10.1016/j.foodres.2020.109515

Vojdani, A., & Vojdani, C. (2015). Immune reactivity to food coloring. *Alternative Therapies*, *21*, 1–100.

Walker, R. (1990). Nitrates, nitrites and N-nitrosocompounds: A review of the occurrence in food and diet and the toxicological implications. *Food Additives & Contaminants*, *7*(6), 717–768.

Weiner, M. L. (2014). Food additive carrageenan: Part II: A critical review of carrageenan in vivo safety studies. *Critical Reviews in Toxicology*, *44*(3), 244–269. https://doi.org/10.3109/10408444.2013.861798

Weiner, M. L., Nuber, D., Blakemore, W. R., Harriman, J. F., & Cohen, S. M. (2007). A 90-day dietary study on kappa carrageenan with emphasis on the gastrointestinal tract. *Food and Chemical Toxicology: An International Journal Published for the British Industrial Biological Research Association*, *45*(1), 98–106. https://doi.org/10.1016/J.FCT.2006.07.033

Weiner, M. L., Ferguson, H. E., Thorsrud, B. A., Nelson, K. G., Blakemore, W. R., Zeigler, B., Cameron, M. J., Brant, A., Cochrane, L., Pellerin, M., & Mahadevan, B. (2015). An infant formula toxicity and toxicokinetic feeding study on carrageenan in preweaning piglets with special attention to the immune system and gastrointestinal tract. *Food and Chemical Toxicology: An International Journal Published for the British Industrial Biological Research Association*, *77*, 120–131. https://doi.org/10.1016/J.FCT.2014.12.022

World Health Organization. (2023). Food additives. Retrieved from https://www.who.int/news-room/fact-sheets/detail/food-additives#:~:text=Food%20additives%20are%20substances%20primarily,modify%20sensory%20properties%20of%20food

Yadav, S. K., & Guleria, P. (2012). Steviol glycosides from Stevia: Biosynthesis pathway review and their application in foods and medicine. *Critical Reviews in Food Science and Nutrition*, *52*(11), 988–998.

Younes, M., Aggett, P., Aguilar, F., Crebelli, R., Dusemund, B., Filipič, M., Frutos, M. J., Galtier, P., Gott, D. M., Gundert-Remy, U., Kuhnle, G. G. C., Leblanc, J., Lillegaard, I. T. L., Moldeus, P., Mortensen, A., Oskarsson, A., Stankovic, I., Waalkens-Berendsen, I., Woutersen, R. A., … & Lambré, C. (2017). Re-evaluation of mono- and di-glycerides of fatty acids (E 471) as food additives. *EFSA Journal*, *15*(11). https://doi.org/10.2903/j.efsa.2017.5045

Younes, F., Aquilina, M., Castle, G., Engel, L., Fowler, K., Fernandez, P., Fürst, M. L., Gürtler, P., Gundert-Remy, R., Husøy, U., Mennes, T., Shah, W., Waalkens-Berendsen, R., Wölfle, D., Boon, D., Tobback, P., Wright, P., Horvath, M., Moldeus, Z., (2020). Re-evaluation of acetic acid, lactic acid, citric acid, tartaric acid, mono- and diacetyltartaric acid, mixed acetic and tartaric acid esters of mono- and diglycerides of fatty acids (E 472a-f) as food additives. *EFSA Journal*, *18*(3). https://doi.org/10.2903/j.efsa.2020.6032

Zhang, M., Wang, P., Lu, Y., Lu, X., Zhang, A., Liu, Z., Zhang, Y., Khan, K., & Sarvajayakesavalu, S. (2020). Bioaccumulation and human exposure of perfluoroalkyl acids (PFAAs) in vegetables from the largest vegetable production base of China. *Environment International*, *135*. https://doi.org/10.1016/j.envint.2019.105347

Publisher's Note