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RESEARCH ARTICLE

BABY FOODS CAN ALSO HAVE TOXIC SIDE EFFECTS: A REVIEW

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ABSTRACT

Popularity of baby foods and infant formula is increasing day by day as they are easy to use and claim to be very nutritive for babies. The safety of these products should be checked before introducing them to the market. Many contaminants are a challenge to food safety and can enter the food chain at any stage of manufacturing from raw material to finished food product. The contamination of food can also be caused by food additives like flavoring agents, preservatives, food colors etc. It has been indicated by many studies that flavoring agents and food additives like acrylamide, azodicarbonamide, semicarbazide, MSG etc are causing serious toxicity among the kids. Bisphenol A found on plastic packaging and metal cans as coating has been shown to migrate into the food inside. It is a known genotoxic and carcinogenic compound. Many toxins like mycotoxins, plant toxins and microbial toxins have been detected in the baby foods which come from vegetables and fruits used during their preparation. Microbial junk has also been detected in baby food which can be very harmful for the babies. The purpose of this review is to highlight the ingredients and contaminants which might harm the baby and cause serious health issues.

INTRODUCTION

Safe and adequate nutrition is a necessary requirement for a child's growth. Baby foods are an important part of a baby's diet other than breast milk. Baby foods like formula milk, infant food, cooked/mashed and canned fruits and vegetables etc are attracting parents in urban localities. They are available in powdered, liquid concentrate and ready-to-eat forms. They are mostly cow milk or soy milk based. They are available in flavours usually like by babies like chocolate, apple strawberry etc. Infant formulas, according to the medical community are acceptable for infants under the age of 1 year where breast feeding is not possible. These are formulated based on the scientific evidence about the nutritive needs of the infants. Baby food, on the other hand, is any food that can be given to the infants between the age of 6 months to 2 years and can be taken as a part of the baby's diet during the third year. These foods are soft textured purees or liquid concentrates (Joeckel and Phillips, 2009). The nutritional quality and physicochemical properties of baby foods depend on their formulation, handling and storage of baby foods (Nasirpour *et al.,* 2006). According to the Food and Drug Administration (FDA) an infant formula and baby food must contain essential nutrients whose upper limits should also be set (N.R.O' Connor 2009).

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These food products on the other hand can also be harmful and might contain contaminants causing harm to baby's health. Acrylamide (Fohgelberg *et al.* 2005), semicarbazide (Maranghi *et al.* 2010), phthalate (Booker 2001), pesticides (Turconi *et al,* 2004; Campbell, 2014) etc. are certain food additives causing serious toxicity among the babies. Bisphenol A which is found on plastic and metal cans as a surface coating has been shown to migrate into the food in contact with the bottle or can and is a known genotoxic and carcinogenic compound (Fasano 2012). Toxins released by living cells like mycotoxins(C. Juan, *et al.* 2014), plant toxins (Meneely, *et al.* 2010) and microbial toxins (Fallick, 2014) have been detected in the baby foods. These toxins might come from vegetables and fruits used during their preparation. Microbial junk has also been detected in baby food which can be very harmful for the babies.

Parents who are the end users of these products should be made aware of their possible harmful side effects. Different chemicals being used for flavor enhancement and preservation; as additives and food colors and as plastic coatings on the food container can be very harmful for the baby's health. These compounds might lead to genotoxicity, cytotoxicity, neurotoxicity, reproductive toxicity. Many of these compounds can cause carcinogenicity leading to development of cancer in different parts of body during childhood or in later stages of life. The purpose of this review is to bring light on possible factors which might cause serious risk to baby's health because of regular intake of baby foods.

Genotoxicity and cytotoxicity

Genotoxicity is the property of a chemical to damage the genetic information within a cell which may cause mutations in somatic or germ cell line. It can be assayed by many sophisticated in vitro and *in vivo* assays. It is however often confused with mutagenicity. All mutagens are genotoxic, whereas all genotoxic substances are not mutagenic. Mutations are the permanent heritable changes affecting the cells that can be passed on to future generations. Cells have mechanisms called DNA repair and apoptosis to prevent the expression of genotoxic mutations. Sometimes the damage cannot be fixed by these mechanisms leading to mutagenesis (Mukhopadhyay *et al* 2004; Aardema, *et al* 2006; Aubrecht *et al* 2007; Kirkland *et al*, 2006). Cytotoxicity is the quality of a chemical of being toxic to the cells. It can be assayed by evaluating the levels of ATP. Some recently developed *in vitro* assays utilize standard fluorescence and luminescence plate readers (Riss *et al*; 2011). Cytotoxicity can also be assayed by various cell based assays which rely on the endpoint readings in cell number and cell viability after treatment with the toxic compounds (Yu *et al*; 2013).

Major Toxicants detected in Baby Foods

The contaminants most commonly present in processed and packaged baby foods are

A) Chemicals used as flavoring agents and food additives

Acrylamide

It is an α, β unsaturated (conjugated) reactive molecule. Acrylamide is a potent genotoxic compound. Heavy exposure to acrylamide can be very dangerous to baby's health (P. Erkekoglu and Baydar, 2010). Acrylamide is produced in baked foods by reaction between aspargines and reducing sugars (fructose and glucose) and reactive carbonyls. Boiling does not produce acrylamides but frying, baking, microwaving and over cooking produces them in large amounts (Choe and Min, 2006). Acrylamide is classified as ‘probably carcinogenic to humans (grp 2A) by the International Agency for Research on Cancer (International Agency for research on cancer; 1994). Acrylamide causes genotoxic effects like gene mutations, chromosomal aberrations, somatic mutation etc *in vivo* and *in vitro.* (Rice 2005). It also causes cumulative neurotoxicity through a direct inhibitory effect on presynaptic function (LoPachin and Gavin, 2012). In their two important studies, Cengiz and Gunduz have shown presence of acrylamide in baby foods and also suggested a method for its quantification. A study on turkish toddlers that cereal based foods that contribute to acrylamide exposure were aligned from high to low as bread, crackers, baby biscuits, powdered baby based cereal foods, baby bread rusks and breakfast cereals (Cengiz and Gunduz, 2013). An eco- friendly method for acrylamide quantification suggested by them includes defatting with n-hexane, precipitation of proteins and their extraction into ethyl acetate followed by injection into GC/MS system (Cengiz and Gunduz, 2014). According to a study by Fan and Mastovska the treatment of food with ionizing radiation of 1.5 kGy degrades most of the acrylamide present in water; however it has very limited effects on oil and potato chips even at a dose of 10 kGy (Fan and Mastovska 2006). Another study claims 40% reduction in the level of acrylamide in a non-optimized system using synergy of different treatments (Henley *et al* 2006). The Food and Drug administration (FDA) has released data on acrylamide levels in more than 750 food samples. FDA has also released a final version of its action plan describing how the risk associated with acrylamide can be evaluated and in what ways can the levels of acrylamide in foods be reduced (Cosum, 2004)

Arsenic

Arsenic is a metalloid and is ubiquitously present. According to the WHO, it is found in almost all foodstuffs (WHO, 2001). Rice is one of the major sources of arsenic in South Asian areas where arsenic contaminated water is used for irrigation and cooking. This contamination causes big harm to people’s health as rice is staple food in these areas (Azizur Rehman and Hasegava, 2011). Arsenic has been classified as a class 1 carcinogen by the International Agency for Research on Cancer (IARC, 1987). It can also cause nausea, vomiting etc. prolonged exposure to arsenic can cause damage to liver, lung and kidney (Zand *et al*, 2012). Acute health effects of arsenic intake include gastrointestinal, neurological and skin effects, and in some cases facial edema cardiac arrhythmia and dermatoses etc. (Tsuji *et al;* 2004). Inorganic arsenic levels can be determined by Ion Chromatography Inductively Coupled Plasma Mass Spectrometry (IC- ICPMS), which is considered a valuable tool in evaluating arsenic in baby foods (Llorente- Mirandes *et al*, 2014). In June to August 1955, mass arsenic poisoning of infants occured in western areas of Japan including Kinki, Chugoku, Shikoku and Kyushu due to contaminated milk powder. 12131 newborn infants were poisoned and 130 died in this incident. The infants poisoned during this period showed pancreatic and haematopoietic cancer (Yorifuji *et al*, 2011). Arsenic intake during infancy also shows long term neurotoxic effects. Among 600 of the survivors from the above incidence in Japan, who are mostly in their 50’s now; many suffer from mental retardation, neurological diseases and other disabilities (Dakeishi *et al,* 2006). According to a recent study conducted on children suffering from celiac disease; these children consume lot of rice based food as they cannot tolerate gluten intake. Rice based products unfortunately have high levels of arsenic which can be very harmful for the children therefore proper legislations should be made for labelling of food products manufactured for celiac patients. (Munera- Picazo *et al*, 2014) Another study indicates that infant milk formulas are low in total arsenic (2.2-12.6 ng g(-1)) while non dairy formulas were significantly higher in arsenic. Arsenic concentration in purees and stage 3 foods ranges between 0.3- 22 ng g(-1). Rice fortified foods have significantly higher concentration of arsenic than non rice foods (Jackson *et al,* 2012). A spanish study indicates a positive correlation between rice and arsenic levels in foods which is extremely important for children below 1 year of age and children with celiac disease as their diet mostly consists of rice based foods (Burlo *et al*, 2012).

Azodicarbonamide and semicarbazide

Azodicarbonamide is used as foaming and blowing agent for food packaging in glass jars while its use as a food additive is not permitted. Jar sealing technology called Press On-Twist Off or Push Twist (PT) uses azodicarbonamide for the formation of a hermatic, plastisol seal. Semicarbazide (SEM) is the degradation product of azodicarbonamide. Azodicarbonamide is responsible for asthamagenecity and respiratory sensitization (Da la Calle and Anklam, 2005) while SEM is a potent carcinogen (Becalski *et al,* 2004; Ye *et al*, 2011). SEM also is an endocrine disruptor. It shows a weak anti- estrogenic activity and alteration of testosterone catabolism in a gender related way in rats (Maranghi *et al*, 2010). In a study SEM levels are determined by using reversed phase LC- MS/MS in fresh egg and egg powder based samples (Szilagyi and De la Calle, 2006). A direct competitive enzyme-linked immunosorbent assay (ELISA) has also been developed based on polyclonal antibodies specific for SEM. (Vass *et al*, 2008).

Mono Sodium Glutamate

Glutamate is present in all living organisms as principal excitatory neurotransmitter in CNS. It has been used as flavour enhancer since 1200 years and being marketed since last 100 years. Glutamate in high concentration has been shown to cause neurodegeneration in infant rodents. However, the joint FAO/WHO expert committee on Food Additives has declared Glutamate as an additive in food (Mallick, 2007) but it can be harmful for the poorly developed infant system. A Gas Chromatographic procedure is described for determining MSG levels in foods (Nakanishi, 1983). The Chinese restaurant Syndrome characterized by flushing, tightness of chest, difficulty in breathing etc can be caused by MSG. It also might cause asthamatic response in adults and children (Zhou *et al,* 2012). Long term MSG administration has shown to cause gastritis, gastric and duodenal ulcers and obesity in rats (T.M. Falalieieva *et al*, 2010). The Acceptable Daily Intake (ADI) for glutamate and its salts is not specified by any of the food committies (Walker and Lupien, 2000). Food and Drug Administration has classified MSG as Generally recognized as safe (GRAS) (Geha *et al*, 2000). Few food additives like Hydrolyzed Vegetable Protein, Plant Protein Extract, Calcium Caseinate, Sodium Caseinate, Yeast Extract, and Corn Oil etc always contain MSG. It is a known neurotoxin causing damage to the brain of infants leading to learning and emotional difficulties during later development. Possible addition of MSG to infant food has been reported to cause no increase in plasma glutamic acid levels in 24 premature newborn babies until 5-90 mins after the feed in a study report (Salmona *et al*, 1980). It is advised to keep MSG out of the baby food, still many reports show MSG content in baby foods of many leading brands. The protective effect of N-acetylcysteine (NAC) on MSG induced toxicity has been seen in C6 astrocytic cells. NAC prevented the changes of Bcl-2 expression level. (Park and Yu, 2014).

Furan

Furan is small cyclic ether; and is formed in foods during heat processing. Furan is known to have carcinogenic effect (Crews and Castle, 2007). Furan is a potent hepatotoxin and hepatocarcinogen in rodents. It is a risk to human health and has shown genotoxic and carcinogenic properties at dose level lower than 2mg/kg body weight (Moro and Chipman, 2012). It is classified as possible human carcinogen by European and US authorities but studies are still going on for assessing the risk of furan in human food (Bakhiya and Appel, 2010). The presence of ascorbic acid, vitamin C (ascorbic acid + Dehydroascorbic acid), and furfural as potential precursors of furan in commercial fruit based baby foods has been studied and it was found that the higher furfural content could lead to high furan content in vegetable based baby foods as compared to the fruit based ones (Mesias Garcia *et al*, 2010). Occurrence of furan in complementary foods has been detected using headspace-gas chromatography/ mass spectrometry (HS-GC/MS). Average furan content in fruit, vegetables, meat/vegetables, fish/vegetables and dairy containing baby foods were 5.0, 37.8, 25.2, 33.8 and 30.5µg/kg (E. Ruiz *et al*, 2010). Furan can be reduced in food samples by irradiating them with an ionizing radiation (Fan and Mastovska, 2006).

Nitrates and nitrites

Nitrates and nitrites are usually found in vegetable based baby foods and are used as food additives and preservative, providing the food with specific color and flavor. Their intake by babies might result in Methaenemoglobinemia or blue baby syndrome. At higher pH, they form nitrosamines which are known carcinogens and might cause colorectal cancer. A study indicates ion chromatographic determination of nitrites and nitrates in vegetable and fruit based baby foods (S.E. McMullen *et al*, 2005). Nitrates get converted into Methaemoglobin producing nitrite before and/or after ingestion. Methemoglobin cannot bind oxygen and thus shifts the oxygen dissociation curve towards left causing hypoxaemia. Infants under 3 months of age are particularly susceptible to this disease. Pureeing the vegetables leads to increase in nitrite concentration due to release of endogenous nitrate reductase (Chan, 2011). In an important study, impact of food processing and storage conditions was seen on nitrite and nitrate contents of vegetable based infant foods. The results show that steps like peeling and washing decrease the content. During processing also, the nitrate content further decreases, while it increases after 24 hours after storage at refrigerated conditions or room temperature. Therefore it should be empathized that raw material is good (T. Tamme *et al,* 2009)*.* Nitrates and nitrites can also be tranported to milk of dairy cows through their digestive system which can harm the human health as well as can cause many problems in milk processing industries (Baranova *et al*, 1993).

B) Chemicals entering the food through packaging

Bisphenol A (BPA)

It is a chemical agent coated on plastic bottles, cans and jars used for packaging of baby foods. It is known to migrate into the baby's body alongwith the food which comes in contact with coated material. It is used in the production of epoxy resins and polycarbonate plastic products. It can also cause obesity and heart diseases. More stringent regulatory actions are needed to protect the public health against the ill effects of this chemical. (Fjeldel *et al*, 2003; Liao and Kannan, 2013; L. Barraza, 2013). Bisphenol A is an estrogen mimicker and it binds the estrogen recptors and thus disrupts the endocrine system. This study states that BPA is toxic to humans at the levels it is being used (Teeguarden and Hansen Drury, 2013). A new kind of fluorescent sensor for BPA detection was established based on the fluorescent conjugated polymer PPESO3. The oxidative product of BPA is able to quench PPESO3 in the presence of HRP and H2O2, and the quenched PL intensity of PPESO3 was proportionally to the concentration of BPA (Huang *et al*, 2015). The phenomenon of release of BPA into food is due to hydrolysation of polycarbonate under alkaline conditions by residual alkaline detergents and boiled water. The release is not because of brushing of cans and bottles as it is shown that old ones release more BPA than the new ones (E.J. Hoekstra and C. Simoneau, 2013).

Pthalates

Pthalates are used as plasticizers in the plastic products. Plastisizers or dispensers are additives that increase flexibility, transparency, durability, and longevity of plastic material. Pthalates are the most commonly used plasticizers. Babies might be exposed to pthalates through leaching and general environmental contamination. In general, children's exposure to phthalates is greater than that of adults. According to a pilot study done in Canada, it was estimated that daily exposure to bis(2-ethylhexyl) phthalate (DEHP) was 9 µg/kg bodyweight/day in infants and 19 µg/kg bodyweight/day in toddlers while it was 6 µg/kg bodyweight/day in adults. Infants and toddlers are therefore at the greatest risk of exposure, because of their mouthing behavior. Plastic products containing phthalates are a source of exposure for infants (Heudorf *et al.,* 2007*;* Sathyanarayana *2008*)*.* Li *et al* have performed the detection of migration of phthalates from disposable table wares to drinking water Hexafluoroisopropanol (HFIP)-induced sodium dodecyl sulfate/dodecyltrimethylammonium bromide (SDS/DTAB) catanionic surfactant coacervate extraction method coupled with high performance liquid chromatography (HPLC) (Li *et al,* 2016).

C) Toxins from fruits, vegetables and oils and other Microbial Junk

Mycotoxins

Mycotoxins are toxic secondary metabolites by different fungal species. They can enter the baby food through use of contaminated raw material. Aflatoxin B1 and Ochratoxin A are mutagenic, teratogenic and carcinogenic; Patulin found especially in baby foods with apple flavor is genotoxic and carcinogenic while Fumonisin found in sorghum, rice and mung beans is found in cereal based baby foods. Aflatoxins are usually associated with hepatitis, immunodepression, impairement of fertility and cancer (Tchana *et al;* 2010). Aflatoxins also participate in the pathogenecity of primary liver cancer (Bauer, 2004). The mycotoxin contamination in the baby foods should therefore be regulated to increase the safety of these foods (Erkekoglu *et al*, 2008). A stable isotope dilution assay and liquid chromatography tandem mass spectrometry (LC- MS/MS) were used to study 12 mycotoxins in milk based infant formula and foods (Zhang and Wong, 2013). In a study aflatoxin M1 was analysed using ELISA from different milk samples from the Greek market (Tsakiris *et al*; 2013).

Phycotoxins and Plant toxins

Toxins of this category might be present in canned baby vegetables. Plants are major sources of allergens, defensive toxins and antimetabolites. The crops treated with extremely toxic pesticides can act as allergens to human population. Sensitivities to these allergens can probably persist even after the industrial chemical has been eliminated (Balachandran *et al*, 1991).

Poly Aromatic Hydrocarbons (PAH's)

This class includes a large class of organic compounds composed of two or more fused aromatic rings. They show clear evidence of mutagenicity/genotoxicity and carcinogenic effects in somatic cells in experimental animals *in vivo* (Hyoun-Kyoung and Hang-Seung, 2012; Ciecierska and Obiedziński, 2010). They are present in oils and coal and therefore can be present in cooked baby vegetables and fruits and other canned and barbequed food stuffs. A study was conducted to estimate PAH levels in 322 commercial as well as homemade meat products and it was found that highest levels were found in smoked meat and ham and home grilled pork (Reinik *et al*, 2007). PAH binds covalently to the DNA to form a DNA adduct which indicates DNA damage and a potential cancer risk. Many genes including cytochrome 450 genes like *CYP1A1* and *CYP1B1* and Glutathione S Transferase (GST) genes. Polymorphisms in these genes lead to susceptibility to the adverse effects of PAH (S. Wang and S. Chanock, 2008).

Heavy metals

Mercury has been found in the fish and cereal based baby foods (Carla Martins and Elsa Vasco *et al*; 2013). High levels of mercury are very harmful for infants and young babies and can even be life threatening. Most reports find that mercury has dangerous effects on brain, kidney and lungs of infants. In an important study, cadmium (Cd), copper (Cu), iron (Fe), mercury (Hg), manganese (Mn), nickel (Ni), lead (Pb), selenium (Se), and zinc (Zn) were determined in most consumed baby foods in European market including infant formulae and solid foods and beverages (M. Pandelova *et al*., 2012). Another recent study suggests a method based on atomic spectroscopy for determining the levels of heavy metals in baby foods (Dasbası *et al.,* 2016).

Microbial Contamination

High temperature and over sterilization required for the stringent manufacturing process of canned and other packaged foods might lead to development of thermotolerant organisms. One such report has shown the presence of an opportunistic pathogen, *Cronobactersakazakii* SP291, associated with meningitis in neonates. The report provides complete genome along with the sequences of three plasmids identified in this organism. (Karen A. Power, Qiongqiong Yan *et al*., 2013) High temperature and over sterilization required for the stringent manufacturing process of canned and other packaged foods might lead to development of thermotolerant organisms.

D) Chemicals used as preservatives

BHA (butylatedhydroxyanisole) and BHT (butylatedhydroxytoluene)

These are antioxidants, and they scoop up oxygen before it makes the fat rancid. Some studies have shown that these two compounds can cause cancer and tumors in lab animals and DNA damage in gastrointestinal organs. Both these compounds were banned in U.S., Japan, Romania, Sweden, and Australia (Sasaki *et al*, 2002).

Paraben: The family of parabens have shown adverse effects on reproductive system and are carcinogenic (Liu *et al*, 2013).

They are estrogen mimickers and may cause breast cancer. In addition, they also cause many skin problems (Kirchhof and Gannes , 2013). On the other hand few chemicals can be taken as a better choice for baby foods

Epoxide Soyabean Oil (ESBO

ESBO and its derivatives are used as plastisizer and stabilizer and are very common in packaging of baby foods. They can migrate into the food but are neither carcinogenic nor genotoxic. Though, overexposure to them might cause slight irritation in eyes. (Bueno *et al*, 2011)

'Narine' Lactobacilli

According to an interesting report the *'Narine' Lactobacilli* (LB, *Lactobacillus Acidophilus*, strain 317/402) have shown to have anti- genotoxic effect. It is being used for milk fermentation for baby foods in many countries. This fact was proved using comet assay (Narsesyan, 2001).

Good preservatives

Preservative free food might contain Sorbic Acid and Benzoic Acid (Ruziye Cakir and Arzu Cagri- Mehmetoglu, 2012). These two compounds can be categorised as good preservatives. They show good antimicrobial properties; they are tasteless, harmless and have no side effects. They should be chosen as preservatives, if necessary, atleast where baby foods are concerned.

Conclusion

Considering the range of baby products available in the market, the buyers need to made aware about the harmful side effects of the ingredients used in these products. The baby food buyers should check the ingredients of the products and also should be aware of their ill fates. These products must also catch more attention of the research field and more work should be done on them. The National Authorities of all the countries should also decide the limits for these toxic compounds for the baby care products.

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