Risks and Benefits of Food Additives - Review

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Abstract

Food additives are substances of natural or synthetic origin, which are added to foods to serve a certain technological or sensory function, for example, to counter food perishability and bacterial degradation, give or restore color or impart flavor to foods.These additives generally provide some type of benefit for the food producer, processor or consumer. For example: acids that may be added to prevent the growth of microorganisms that cause spoilage may also prevent the growth of microorganisms that can cause foodborne illness. Some additives are directly added to food and ingredients, while others are added indirectly through contact with packaging materials as are, for example the preservatives BHA and BHT on the inside of breakfast cereal bags.

The benefit of some food additives is enhancing health status or prevents disease; most benefits reflect economic considerations for food processors and sensory attributes and convenience for consumer.

Keywords: artificial food additives, benefits, hazards, natural additives

INTRODUCTION

The safety or risk evaluation of food additives, residues of pesticides and veterinary drugs, and food contaminants is based on hazard identification, hazard characterization and assessment of exposure (Kuiper *et al.*, 2001). FAO/WHO and the International Program on Chemical Safety (IPCS) have developed strategies for the safety evaluation of these types of chemicals which may be present in food (WHO, 1987; WHO, 1990). The concept of food safety excluded elements of nutrition, such as: anti-nutrients, toxicants, contaminants and other potentially dangerous elements (dioxin, *E.coli)* components that are known risk factors for certain chronic diseases (FAO, 2005c) and nutrients in the form of additives, functional foods and supplements. After that, requests have been made at international forums to include these elements in risk and safety activities (FAO/WHO, 2006; Burlingame B., 2001b).

Within the EU, food additives are divided into many functional classes, depending on their function in food: sweeteners, colorants, preservatives, antioxidants, carriers, acids, acidity regulators, anticaking agents, antifoaming agents, bulking agents, emulsifiers, emulsifying salts, firming agents, flavor enhancers, foaming agents, gelling agents, glazing agents, humectants, modified starches, packaging gases, propellants, raising agents, sequestrants, stabilizers, thickeners, and flour treatment agents (Council Regulation (EC) 1333/2008).

The Codex Alimentarius defines a food additive as "any substance not normally consumed as a food itself and not normally used as a typical ingredient of the food, whether or not it has nutritive value, the intentional addition of which to food for a technological (including organoleptic) purpose in the manufacture, processing, preparation treatment, packing, packaging, transport or holding of such food results, or may be reasonably expected to result, (directly or indirectly) in it or its by-products becoming a component of or otherwise affecting the characteristics of such foods. The term does not include contaminants, or substances added to food for maintaining or improving nutritional qualities, or sodium chloride" (Codex Alimentarius; Motarjemi *et al.,* 2014; Carocho *et al.,* 2015).

Since 2010, European Commission Regulation and EFSA have started a program to re-evaluate all the existing approved food aditives (Carocho *et al.,* 2014). The 1st evaluation includes food colorants and preservatives (including antimicrobials and antioxidants), which has to be concluded before 2015. The 2nd group to be evaluated, comprising texturizing agents (including emulsifiers, stablizers and gelling agents) by 2018, and the last group, sweeteners, to be revised until 2020 (Lodi *et al.,* 2011).

Other research demonstrated that factors such as whether the risk is perceived to be involuntary, unnatural or potentially catastrophic, and whether the risk may affect health rather than the environment, drive public risk perception (Gaskell, 2005; Siegrist *et al.*, 2007b; Rollin *et al.,* 2011). Acceptance of a technology is also partly driven by perception of the potential benefits (Ronteltap *et al.,* 2007). A lack of perceived benefits leads the majority of people to question the need for, and usefulness of, novel food technologies, and may even accentuate perceived risks and moral concerns (Gaskell, 2005).

Despite the various classes of additives, Carocho *et al.* mentioned in 2014 that the additives can be divided in four fundamental groups with regard to their origin and manufacture: natural additives (obtained directly from animals and plants); similar to natural additives (produced synthetically imitating natural ones); modified from natural (natural additives that are then modified chemically) and finally artificial additives (synthetic compounds).

This bibliographic study aims to present a brief review of the most important scientific findings and research regarding risks and benefits of certain classes of food additives.

PRESERVATIVES

European Food Safety Authority (EFSA) has issued a scientific opinion on the safety of: ascobyl palmitate (E304), tocopherol-rich extract (E306), α-tocopherol (E307), γ-tocopherol (E308), δ-tocopherol (E309), lecithins (E322), when used as food additive for some food categories like infants below 16 weeks of age, and now the European Commission has asked EFSA to re-evaluate these additives. The E numbers of the preservatives range from E200 to E399. The antimicrobials are added to food for two purposes: to control natural spoilage of food and/or to avoid /control contamination by microorganisms, including pathogenic ones (of food safety concern) (*Tajkarimi et al.,* 2010). Among the most used antimicrobial additives are benzoic acid and benzoates (E210-E219; ADI 5 mg/kg bw), sorbic acid and sorbates (E200-E209; ADI 25 mg/kg bw); propionic acid and propionates (E280-E289; quantum satis), nitrites (potassium nitrite E249; ADI 0.07 mg/kg bw, sodium nitrate E250; ADI 0.1 mg/kg bw), nitates (sodium nitrate E251 and potassium nitrate E252; both with ADI 3.7 mg/kg bw), and parabens (E214-E219; ADI 10 mg/kg bw) table 1 (Carocho *et al.*, 2014).

Nitrites and nitrates are widely used as preservatives in processed meats (eg. frankfurters, salami). These agents have not been associated with hypersensitivity reactions, but can provoke vascular headache; their metabolic products (nitrosamines) are known carcinogens (Simon, 2003).

Sodium benzoate is a closely related substance and may cross-react with other parabens. There has been only one subject reported in the medical literature to be benzoate sensitive, in a double-bind, placebo-controlled study of additive-provoked asthma (Flynn *et al.,* 1992); this patient was not aspirin-sensitive and did not experience amelioration of asthma symptoms while on a benzoate-free diet (Simon, 2003).

Benzoic acid produced by oxidation of toluene, is a widespread antimicrobial agent, employed against yeast, bacteria and fungi. It acts through membrane distruption and inhibition of metabolic reactions, stress and accumulation of toxic aninons inside the microbial cell (Brul and Coote, 1999; Carocho *et al.,* 2014).

Some *in vitro* studies have related the conjugated double bonds present in sorbic acid`s structure as being prone to nucleophilic attack, turning

Table 1. Antimicrobial food additives with their ADI quantities (mg/kg bw) (Carocho *et al.,* 2014)

Name	E number	ADI	Legislation
Benzoic acid	E210	5 mg/kg bw	Code of Federal Regulations 21 Sec.184.1021 EU Regulation No. 1129/2011
Sodium benzoate	E211	5 mg/kg bw	Code of Federal Regulations 21 Sec.184.1733 EU Regulation No. 1129/2011
Ethyl-p-hydroxy-benzoate (paraben)	E214	10 mg/kg bw	Code of Federal Regulations 21 Sec.175.105 EU Regulation No. 1129/2011
Sodium ethyl p-hydroxybenzoate (parabens)	E215	10 mg/kg bw	Code of Federal Regulations 21 Sec.175.105 EU Regulation No. 1129/2011
Methyl p-hydroxybenzoate (parabens)	E218	10 mg/kg bw	Code of Federal Regulations 21 Sec.150.141 EU Regulation No. 1129/2011
Sodium methyl p-hydroxybenzoate (paraben)	E219	10 mg/kg bw	Banned in the United States EU Regulation No. 1129/2011
Sorbic acid	E200	25 mg/kg bw	Code of Federal Regulations 21 Sec.182.3089 EU Regulation No. 1129/2011
Sodium sorbate	E201	25 mg/kg bw	Code of Federal Regulations 21 Sec.182.3089- Not approved in the EU
Potassium sorbate	E202	25 mg/kg bw	Code of Federal Regulations 21 Sec.182.3640 EU Regulation No. 1129/2011
Sulfites	E220-E228	0.7 mg/kg	Code of Federal Regulations 21 Sec.182.3616, 3637, 3739, 3766, 3798 EU Regulation No. 1129/2011
Potassium nitrite	E249	0.7 mg/kg bw	Code of Federal Regulations 21 Sec.172.160 EU Regulation No. 1129/2011
Sodium nitrate	E250	0.1 mg/kg bw	Code of Federal Regulations 21 Sec.172.175 EU Regulation No. 1129/2011
Sodium propionate	E281	Not specified	Code of Federal Regulations 21 Sec.184.1784 EU Regulation No. 1129/2011

Note: ADI=acceptable daily intake

it into mutagenic compound. The interaction between sorbic acid and various amines was tested by Ferrand *et al.* (2000) for mutagenic and genotoxic activities on HeLa cells and plasmid DNA, resulting in negative values, while another study found sodium sorbate toxic toward human peripheral blood lymphocytes at 400 and 800 µg/ml (Mamur *et al.,* 2012)

There are not many studies regarding the toxicity of propionic acids or its salts, (sodium propionate, E281), calcium propionate (E282) and potassium propionate (E283), although it has been considerated to suppress, in a dose-dependent manner, Th1-type immune response in human peripheral blood mononuclear cells *in vitro.* Sodium propionate has been stated as inducing abnormalities on the root tips of onion, while calcium propionate has been related to irritability, restlessness, inattention, and sleep disturbance in some children (Dengate and Ruben, 2002; Turkoglu, 2008; Maier *et al.,* 2010; Carocho *et al.,* 2014).

It has recently been determined that phosphate additives in food may harm the health of persons with normal renal function (Sullivan *et al.,* 2009). This judgment has been made on the basis of large-scale epidemiological studies and is supported by the latest findings of basic research. It was first recognized in patients with renal disease that a high serum phosphate concentration is a major risk factor for elevated cardiovascular and overall mortality (Block *et al.,* 2004; Kestenbaum *et al.,* 2005).

The antioxidants are another subgroup of the preservatives; they prevent the oxidation of molecules by donating a hydrogen atom or an electron, becoming themselves reduced, in the radical form, but contrary to other radicals, antioxidants when in radical form are more stable and do not allow further reactions to take place, therefore preserving the *status quo* of the system (Carocho and Ferreira, 2013a,b). The most commonly used antioxidants with *quantum satis* status are: ascorbic acid (E300), sodium ascorbate (E301), calcium ascorbate (E302), fatty acid esters of ascorbic acid (E304), tocopherols (E306), α-tocopherol (E307), γ-tocopherol (E308), δ-tocopherol (E309), lecithins (E322), sodium lactate (E325), potassium lactate (E326), calcium lactate (E327), citric acid (E330), sodium citrate (E331), potassium citrate (E332), calcium citrate (E333), tartaric acid (E334), sodium potassium tartrate (E337), sodium malate (E350), potassium malate (E351), calcium malate (E352), calcium tartrate (E354) and triammonium citrate (E380); Table 2 (Carocho *et al.*, 2014).

They are known to reduce the risk of cancer, heart disease, and diabetes; to inhibit plasma platelet aggregation, cyclooxygenase (COX) activity, and histamine release, as well as to exert antibacterial, antiviral, anti-inflammatory, and anti-allergenic activities (Shahidi and Ambigaipalan, 2015). The benefits towards many of these conditions arise in part through the antioxidant characteristic of phenolics; therefore, it is important to quantify, identify and evaluate their antioxidant activities (Cevallos-Casals and Cisneros-Zevallos, 2010).

Ethoxyquin is a quinolone-based antioxidant that is not permitted to be added to human food, only used in domestic and farm animal feed. This compound has been reported to induce dermatitis in animals and humans, as well as being a promoter of certain types of cancer. (Blaszczyk *et al.,* 2013; EFSA, 2013a,b). BHA and BHT are antioxidants commonly used in break-fast cereals and other grain producys to maintain crispness and prevent rancidity. There is one well-documented report of cronic urticarial, confirmed by double-blind, placebo-controlled challenges, exacerbated by these agents (Goodman, 1990; Simon, 2003).

TBHQ is commercially available as a beige coloured powder and may be used alone or in combination with BHA or BHT at a maximum

Table 2. Antioxidant food additives with their ADI quantities (mg/kg bw) (Carocho *et al.,* 2014)

Name	E number	ADI	Legislation
Propyl galate (PG)	E310	1.4 mg/kg bw	Code of Federal Regulations 21 Sec.184.1660 EU Regulation No. 1129/2011
tert-butylhydroquinone (TBHQ)	E319	0.7 mg/kg bw	Code of Federal Regulations 21 Sec.172185 EU Regulation No. 1129/2011
Butylated hydroxyanisole (BHA)	E320	0.5 mg/kg bw	Code of Federal Regulations 21 Sec.175.110 EU Regulation No. 1129/2011
Butylated hydroxytoluene (BHT)	E321	0.05 mg/kg bw	Code of Federal Regulations 21 Sec.175.115 EU Regulation No. 1129/2011
Ethoxyquin (EQ)	E224	0.005 mg/kg bw	Code of Federal Regulations 21 Sec.172.140 EU Regulation No. 1129/2011

Note: ADI=acceptable daily intake

concentration of 0.02% or 200 ppm, based on the fat content of foods, including essential oils (Shahidi and Naczk, 2004). Khan and Shahidi (2001) reported that amongst synthetic antioxidants,TBHQ was more effective than BHA and BHT and served as the strongest antioxidant in borage and evening primrose oil triacylglycerols (TAG). Anothers studies have shown that TBHQ causes DNA cleavage *in vitro* and the formation of 8-hydroxydeoxyguanosine in calf thymus DNA due to the generation of ROS such as superoxide radical anion and hydrogen peroxide (Shahidi and Ambigaipalan, 2015). In 2009, Han and Park demonstrated that PG inhibits the growth of microorganisms by inhibiting respiration and nucleic acid synthesis; it also decreases hepatic microsomal hydrolase and demethylase activities and inhibits the activity of some redox enzymes. So, in 2015 studies shown that the antioxidative and cytoprotective propertiesof propyl gallate may change to prooxidative, cytotoxic and genotoxic in the presence of Cu(II).

NATURAL ANTIMICROBIALS

Natural antimicrobials that can be added to food (but are not considered additives in the sense of Codex Alimentarius definition) are mainly terpens (carvacrol, thymol and menthol), peptides, polysaccharides, and phenlolic compounds. Also in 2014, Abbaszadeh *et al.,* used various compounds from essential oils as alternative agents to control the growth of food-relevant fungi. They shown that the MICs of thymol ranged from 100 to 500 mg/mL (mean value: 263.3 mg/mL) for different fungal isolates. The most growth inhibition was associated with *Cladosporium spp.,* followed by *Aspergillus spp., Fusarium oxysporum, Botrytis cinerea, Penicillium spp., Alternaria alternata* and *Rhizopus oryzae.* For carvacrol the MICs ranged from 50 to 350 mg/mL (mean value: 154.5 mg/mL) for tested fungi, and growth inhibition of *Aspergillus spp.* was higher than that of other fungal isolates. Generaly, the antifungal effect of thymol was higher than that of carvacrol according to some previous reports (Numpaque *et al.*, 2011). Perez-Alfonso *et al.* (2012) indicated that both thymol and carvacrol were effective in inhibiting fungal growth, with the predominant efficacy by thymol. The World Health Organization (WHO) has stated that thymol and carvacrol residues in food are without danger to the consumer as long as they do not exceed 50 mg/kg (WHO, 2002; WHO, 2012).

Eugenol ($C_{10}H_{12}O_2$) is a clear to pale yellow oil extracted as a major component (approximately 85%) from buds and leaves of clove (Abbaszadeh *et al.*, 2014). According to previous studies (Wang *et al.*, 2005; Yen *et al.*, 2008), eugenol has been demonstrated as an excellent fungicide against foodborne pathogens. Campanniello *et al.* (2011) found that eugenol at concentrations of 100—150 mg/mL is an effective antifungal compound against phytopathogenic *Aspergillus, Penicillium, Emericella,* and *Fusarium* species.

The most potent inhibitory activity of menthol was found for *Cladosporium spp*. and *Aspergillus spp*., followed by *Fusarium oxysporum, Penicillium spp., Rhizopus oryzae, Botrytis cinerea* and *Alternaria alternata.* MIC values for menthol ($C_{10}H_{20}O$) ranged from 100 to 450 mg/mL (mean value: 211.4 mg/mL) (Abbaszadeh *et al.,* 2014).

In conclusion, the naturally occurring compounds, such as thymol, carvacrol, eugenol and menthol, showed toxic effects *in vitro* on fungal growth of all fungal species but different levels of potency.

NATURAL ANTIOXIDANTS

Antioxidants present in plants, algae, and mushrooms are excellent natural addtitives such as: α-tocopherol (E307), γ-tocopherol (E308), δ-tocopherol (E309), xanthan gum (E415), pectin (E440i) should be added to food stuffs for their iron on hydrogen donating, metal chelating, and chain breaking capabilities. Also, the most antioxidant natural molecules are vitamins, polyphenols, and carotenoids (Ferreira *et al.,* 2009; Carocho *et al.,* 2014). The main foods where antioxidants are used are meats, oils, fried foods, dressings, dairy products, baked goods and extruded snacks (Baines and Seal, 2012). Polyphenols are some of the most interesting groups of natural compounds in the vegetable kingdom, and due to their strong antioxidant capacity they display interesting effects towards human health, namely against cancer, osteoporosis, cataracts, cardiovascular dysfunctions, brain diseases, and immunological conditions (Carocho & Ferreira, 2013). In another study Carocho *et al.* (2015) reported that use carotenes, ascorbic acid or vitamin E (tocopherols) are used to benefit from synergies. Carotene mixes and b-carotene have been reviewed by the EFSA's scientific panel and ruled out any toxicity arising from its consumption, whether from synthetic provenance or extraction from plants and fruits. Carotenoids are also known for their antioxidant potential as food additives, although their use is always limited by being very susceptibility to oxidation by light. In the same year, the EFSA gathered a scientific opinion regarding ascorbic acid and determined there was no risk in its consumption, not defining an ADI (Baines and Seal, 2012; EFSA, 2015a).

ANTIBROWNING AGENTS

Enzymatic browning of raw fruits and vegetables is a PPO-catalyzedoxidation reaction leading to the formation of polymerized dark-colored pigments from oxidation of *o*-quinones, which can significantly affect the functional, nutritional, and organoleptic properties of the product (Mogol *et al.,* 2010). There are some chemical compounds for inhibiting PPO activity. The most widely studied compounds are halide salts, carboxylic, and other organic acids, as well as chelating agents that act on the enzyme. In addition, others are mainly reducing agents, including ascorbic acid and its derivatives, SH-compounds, and sulfites, which act on the reaction products through *o*-quinones reduction to *o*-diphenols (their precursors), and formation of colorless compounds by reacting with *o*-quinones (Billaud *et al.,* 2003; Nooshkam *et al.,* 2019).

The different mechanisms for antioxidant potency of MRPs like metal chelation, scavenging of free radicals, breakdown of hydrogen peroxide, and radical chains have been proposed by the

Table 3. Azo-compounds and triarylmethane compounds of dyes with their ADI quantities (mg/kg bw) (Carocho et al., 2014)

Name	E number	ADI	Legislation
Tartrazine-FD&C Yellow No.5.	E102	7.5 mg/kg bw	Code of Federal Regulations 21 Sec.74.1705 EU Regulation No. 1129/2011
Sunset yellow-FD&C Yellow No.6.	E110	2.5 mg/kg bw	Code of Federal Regulations 21 Sec.74.1706 EU Regulation No. 1129/2011
Carmoisine	E122	4 mg/kg bw	No permission sought in the United States EU Regulation No. 1129/2011
Amaranth	E123	0.8 mg/kg bw	Banned in the United States EU Regulation No. 1129/2011
Allura red-FD&C Red No.40	E129	7 mg/kg bw	Code of Federal Regulations 21 Sec.74.340 EU Regulation No. 1129/2011
Patent blue	E131	15 mg/kg bw	Banned in the United States EU Regulation No. 1129/2011
Brilliant blue-FD&C Blue No.1.	E133	10 mg/kg bw	Code of Federal Regulations 21 Sec.74.101 EU Regulation No. 1129/2011
Brilliant green	E142	5 mg/kg bw	No permission sought in the United States EU Regulation No. 1129/2011
Fast green-FD&C Green No.3.	E143	25 mg/kg bw	Code of Federal Regulations 21 Sec.74.203- Banned in the EU
Brilliant black	E151	5 mg/kg bw	No permission sought in the United States EU Regulation No. 1129/2011

Note: ADI=acceptable daily intake

common and available antioxidative assays. Additionally, these functional compounds have been successfully applied to improve the oxidative stability of diverse foods such as bakery, pasta, meat, oil, and dairy products. As well, they have potential to be used as antibrowning agents in place of sulfite compounds, to inhibit enzymatic browning in fruits and vegetables. Maillard-type conjugates have some functionality, including improved antioxidant, solubility, and heat stability of proteins over a wide range of temperatures, pH values, and ionic strengths. They also provide a continuous and viscoelastic layer around oil particles, which make them excellent foodgrade carriers for the controlled release of biologically active compounds (Nooshkam *et al.,* 2019).

COLORING AGENTS

Coloring agents or food dayes are used to alter or confer colors to food, in order to increase its attractiveness toward consumers. There are 5 groups of coloring agents: the azo compounds, the chinophthalon derivatives of quinolone yellow, the triarylmethane group, xanthenes, and the indigo colorants (Sarikaya *et al.,* 2012); Table 3. The only dye with *quantum satis* status is calcium carbonate (E170), which confers a white color to food and also, calcicum carbonate (E170) need to be re-evaluated by the European Food Safety Authority (EFSA) intended to be used in foods for infants below 16 weeks of age. And also, calcicum carbonate (E170) need to be re-evaluated by the European Food Safety Authority (EFSA) intended to be used in foods for infants below 16 weeks of age.

Some dyes, like amaranth (E123), carmosine (E122) and others are banned in some countries; for instance, both these compounds are banned in the Unites States and not in the EU, while fast green (FD&C Green No.3) is forbidden to be used within the EU and legally added to food in the United States (Carocho *et al.,* 2014).

Furthermore, given the low rate of absorption, harm to human health is unlikely. However, in light of new findings, is it necessary to regularly assess potential toxicity of food colorants by regulatory authorities and consequently revise guidelines for their use (Amchova *et al.,* 2015).

In the last decades, an increase in the incidence of allergies and asthma has been observed. Besides the well-known hygiene theory, other factors, such as administration of antioxidant supplements, food preserving agents and colorants, have also been suggested to be correlated with the increase in the incidence of allergies and asthma (Vojdani and Vojdani, 2015). Previous researches shown contradictory results on this topic, as erythrosine was shown to inhibit hematopoietic prostaglandin D2 synthase, which is a member of the glutathione transferases, catalyzing the isomerization of prostaglandin H2 to prostaglandin D2. This is a mediator of allergy and inflammation responses and hence could be of therapeutic importance in the treatment of allergy and asthma (Mazari *et al.,* 2015). Furthermore, it was found in other studies that even small doses of azo-dyes absorbed from tattoos were recently suggested to trigger immune responses of the body (Baumler, 2015).

CONCLUSION

Food additives ensure that food can be delivered around the world maintaining its quality and safety, without losses in an evergrowing competitive market. Their role is becoming more and more important with the increase in consumption of highly processed food due to changing lifestyles of modern citizens. Nevertheless the food additives should be used judiciously according to the legal requirements.

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