chapter five

Food additives

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5.1   Introduction

Food additives are those substances that are intentionally added to food for maintaining or improving its appearance, texture, flavor, and nutritional value, as well as for the prevention of microbial spoilage. This includes any substance intended for use in manufacturing, processing, preparing, packaging, transporting, or keeping food. Evaluation of the safety of the intended use of additives in food is extensively provided for by regulation and legislation.

In compliance with safety requirements, and if no other economic or technically practical means are available, the following may serve as justification for the use of additives in food (according to the Joint FAO/WHO Codex Alimentarius Committee):

(a) preservation of the nutritional value of food. Reduction of the nutritional value of food is justified in the case of consumers with specific dietary needs, and if the food is not an essential component of the diet;
(b) use in special food for consumers with specific dietary needs;
(c) improvement of the stability, the organoleptic properties and the nutritional value of food while its nature is not drastically changed;
(d) use in manufacturing, processing, transport and storage of food, but not with the intention of disguising the use of inferior raw materials, undesirable practices, and techniques.

Five main categories of additives are distinguished:

– texturizing agents: gelling agents, thickeners and emulsifiers;

- colorings;
- flavoring agents: flavors, flavor enhancers and non-nutritive sweeteners;
- preservatives: antioxidants and antimicrobials;
- miscellaneous additives, such as anticaking agents, catalysts, clarifying agents, filter aids, and solvents.

This chapter considers the use of a number of selected food additives in relation to their safety. The use of the majority of the texturizing agents and miscellaneous additives do not pose toxicological risks.

5.2   Use of food additives in relation to their safety

Food additives have been used since prehistoric times to maintain and improve the quality of food products. Smoke, alcohol, vinegar, oils, and spices have been used for more than 10,000 years to preserve foods. These and a small number of other chemicals, such as salts, copper, and chalk, were the major food additives used until the time of the Industrial Revolution. Since then many changes in food manufacturing and food distribution have taken place as a result of urbanization, the decrease in opportunity for individual families to grow their own food, and the increase in the consumer's demand for a broader food assortment and a higher quality of food. Also, food had to be produced on a larger scale. Distribution over long distances involves a longer span of time between production and consumption. Further, food needs to be stored in warehouses and shops, and also at home. In addition, convenience foods require extensive preservation.

Processed food is more perishable than the individual food components themselves. This can be overcome by the use of food additives. Without these, the food choice would be limited, many food products would be prohibitively expensive, and much food would be wasted. Also, food-related poisonings would occur more often. All these factors together have led to an increased use of additives in food, particularly since the 1950s. More than 2500 different chemicals are now in use. Apart from the consumption of salt and sugar, which are also important preservatives, the yearly additive consumption per capita in the early 1960s was estimated to exceed 3 lbs. However, the demand for new, tasty, convenient and nutritious foods continued to increase. In the US, where this development is most pronounced, the additive consumption per capita has increased from 3 to 9 lbs per year. Besides being beneficial, the use of food additives may also involve adverse health effects which can be either indirect or direct. Indirect effects are concerned with unbalanced diets and direct effects with potential toxicity.

The *indirect* health effects of additives are the opposite of some of their beneficial effects. The use of additives has led to a wider food assortment, but also to an increased availability of food with a low nutrient content. This type of food (so-called junk food) can be (and often is) consumed as dietary substitute for more nutritious food. Obviously, educational programs are needed to alert consumers to the need for a balanced diet.

The *direct* effects include short-term as well as long-term toxic effects. Short-term effects of additives are unlikely because of the low levels at which they are applied. On the other hand, hypersensitivity has been attributed to additives, even if they are used at legally acceptable levels. Further, little or no data are available on the health risks from the daily intake of combinations of additives.

Toxicological problems after long-term consumption of additives are not well-documented. There is no conclusive evidence for the relationship between chronic consumption of food additives and the induction of cancer and teratogenic effects in humans. Results of animal studies, however, have suggested that the use of certain additives involves safety problems. Most of these additives are now banned.

Nowadays, food additives undergo extensive toxicological screening before they are admitted for use. However, the majority of additives already in use are believed to be safe for the consumer at the levels applied in food, even though they have not been examined toxicologically. The substances involved are of natural origin and traditionally have been in use since the early days of food processing. Many additives that are used by the consumer in preparing food in the natural matrix, e.g., pectin as thickener, egg yolk as emulsifier, tomato juice as flavor enhancer, and lemon juice as antioxidant, are used in the food industry in a purified form.

The search for new and safer additives to replace debatable ones, and for processing techniques that require fewer additives, continues.

5.2.1 Colorings

Colorings are used to improve the overall attractiveness of food.

Food colors may be of natural as well as synthetic origin. About 50 colors of natural origin and their derivatives are in use, including chlorophylls (green), carotenoids (yellow, orange, and red) and anthocyanins (purple). They have all been toxicologically evaluated. This section deals with synthetic colorings only.

Synthetic colorings are superior to natural pigments in tinctorial strength, brightness, and stability. After the discovery of the first synthetic dye in 1856, a wide variety of colorings became rapidly available. By the end of the 19th century, 80 colorings were in use. In the first decade of this century, most of these substances were prohibited by law on the basis of their composition and purity.

The toxicology of synthetic food colorings was not given any attention until the early 1930s, when 4-dimethylaminoazobenzene was found to be carcinogenic. This dye was used to color butter and margarine yellow, hence its name "butter yellow." Since then other dyes have proved to be toxic and, as a consequence, have been banned from addition to food. Currently, only 9 synthetic colorings are allowed in the US and 11 in the EU. The majority belong to the class of the azo dyes. A few typical examples are discussed below: *amaranth* and *tartrazine*.

Amaranth, (trisodium 1-(4-sulfo-1-naphthylazo)-2-naphthol-3,6-disulfonic acid) has been approved for use as food color in several countries, including the member states of the EC. It is a water-soluble red dye.
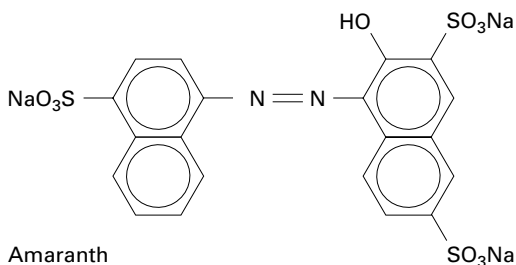
Amaranth

In many long-term studies on carcinogenicity, amaranth has been found to be safe. It is used in food products, such as packaged soup, packaged cake and dessert mix, and canned fruit preserves. In the USA, however, amaranth is no longer in use. The reason for this is the development of tumors in rats fed on a diet containing 3% amaranth.

Tartrazine (5-hydroxyl-1-(*p*-sulfophenyl)-4-(*p*-sulfophenylazo)pyrazole-3-carboxylic acid) is a yellow food coloring.
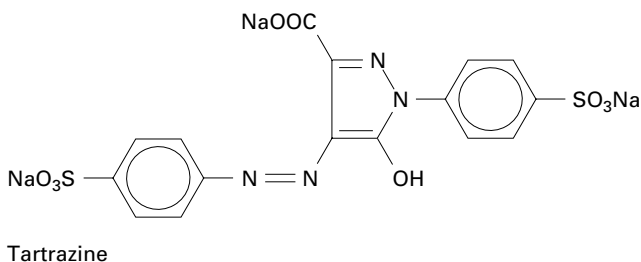
Tartrazine

Tartrazine is widely used in foods, such as the packaged convenience foods mentioned above, smoked fish, chewing gum, sweets, beverages, and canned fruit preserves. The dye has undergone extensive testing, and was found to be harmless in experimental animals. However, various types of allergic reactions are attributed to tartrazine. As little as 0.15 mg can elicit an acute asthmatic attack in sensitive persons. The average daily intake of tartrazine is estimated at 9 mg/kg body weight in the US, while the ADI is 7.5 mg/kg body weight.

5.2.2 Flavoring agents

Flavor has a profound influence on the consumption of food. It imparts that quality to products by which they distinguish themselves. Flavoring agents make up the largest number of food additives. There are three types of flavoring additives: flavorings, flavor enhancers, and (non-nutritive) sweeteners. More than 1500 substances are used as *food flavorings*. The majority are of natural origin or are nature-identical, and do not give rise to concern from a safety point of view. Only a few synthetic substances have been approved as food flavoring. Examples are ethylvanillin, ethylmaltol, and anisylacetone.
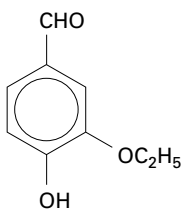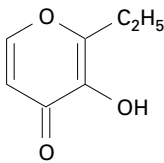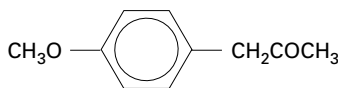

Ethylvanillin   Ethylmaltol   Anisylacetone

Flavor enhancers intensify or modify the flavor of food. They have no taste of their own. They include substances such as monosodium glutamate (MSG) and various nucleotides. These substances are present in Japanese seaweed (traditionally used for seasoning), mushrooms, tomatoes, peas, meat, and cheese. They are often used in soups, sauces and oriental food. No known adverse effects of flavor enhancers have been reported, except for the case of MSG. Humans have been described to be sensitive to food to which MSG had been added. The symptoms include numbness, general weakness, and heart palpitations (see also Part 2, Chapter 2).
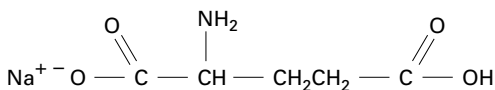

Monosodiumglutamate (MSG)

Sweeteners present the consumer with one of the most important taste sensations. This is reflected by the world production of sugar, which has increased from 8 million tons in 1900 to 70 million tons in 1970. For nutritional and health reasons, however, there is a growing need for sugar substitutes in food that are non-nutritive, i.e., noncaloric, and noncariogenic. Two important noncaloric synthetic sweeteners are saccharin and aspartame.
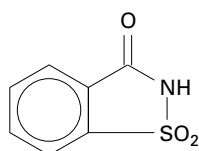
Saccharin
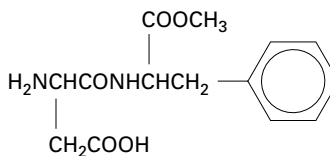
Aspartame

In the US *saccharin* has been used commercially since 1900. It is 300 times sweeter than saccharose and very stable under almost all food processing conditions. Since World War II the consumption of saccharin has steadily increased even though its safety has been questioned repeatedly. Almost 50% of its use is in soft drinks. Individual use as table top sweetener amounts to approximately 20%. The average consumption of saccharin in the US for the whole population has been estimated at 7.1 mg/day per capita, while the intake by the subpopulation of saccharin consumers was 25 mg/day. In Europe, the average intake has been reported to be 15 mg/day.

Since the beginning of its short commercial history, saccharin has been suspected regarding its safety. In 1912 it was prohibited in the US on the basis of acute toxicity tests. However, the ban was lifted during World War I, as sugar became short in supply. After World War II, numerous studies on the toxicity of saccharin were carried out. Up to now, no mutagenicity has been found. However, long-term animal tests showed a higher incidence of bladder cancer. Although it is difficult to extrapolate from experimental animals to the human situation, it appears unlikely that the intake of saccharin at the present average level involves risks of cancer. Therefore, the use of saccharin in food is still approved in the US and in Europe.

Aspartame was discovered in the early 1960s. In the early 1980s, it was admitted in many countries as a sweetener, in addition to saccharin and cyclamate, another synthetic sweetener whose use in food has now been greatly restricted. Aspartame is a dipeptide, consisting of the amino acids phenylalanine and aspartic acid. It is 200 times sweeter than saccharose and is an excellent sweetener for dry products. At high temperature and low pH, aspartame is gradually hydrolyzed, losing its sweetness. It is suitable as table top sweetener, in chewing gum, in soft drinks, dairy products, ice cream, and dessert mixes. Since aspartame is a dipeptide, it is digested and absorbed by the body. However, the amount necessary for a sweet taste is so small that the energy produced is believed to be irrelevant.

Results from toxicity tests suggest that aspartame has no adverse effects on humans even when extreme amounts of 8 mg/kg body weight are taken in. The ADI for aspartame is 40 mg/kg body weight.

The market for sweeteners is still growing and the situation where the ADI for the known sweeteners is reached, is not inconceivable. There is, however, a need for sweeteners that are stable under specific technological conditions and are less controversial than saccharin. Although since the introduction of aspartame the use of saccharin has slowly

declined, aspartame can not replace saccharin completely because of its instability when heated under acidic conditions. Therefore, the search for new sweeteners continues. At present, several non-nutritive sweeteners of natural origin are being investigated. Examples are thaumatin, a macromolecular protein sweetener from an African fruit, 2000 to 3000 times as sweet as saccharose and neohesperidin, present in orange peel, 1500 times as sweet as saccharose. Thaumatin has been admitted in the EU for use in chewing gum and sweets.

5.2.3   Preservatives

Preservatives are added to decrease the degradation rate of foods during processing and storage. They include antioxidants, antimicrobials and antibrowning agents.

5.2.3.1   Antioxidants

Antioxidants primarily prevent or inhibit autoxidation of fatty acids (see also Part I, Chapter 6) in food products and, consequently, the development of rancidity and off-flavor. They are especially useful in preserving dry and frozen foods for long periods of time. The major antioxidants for the protection of dietary fats and oils are phenols. They are either synthetic or natural substances. The synthetic antioxidants include butylated hydroxyanisole (BHA), butylated hydroxytoluene (BHT), *n*-propyl gallate and tertiary-butyl hydroquinone (TBHQ). Important natural food antioxidants are the *tocopherols*. They occur naturally in the majority of fats and oils. The mechanism of the antioxidant action of phenols is shown in Figure 5.1.
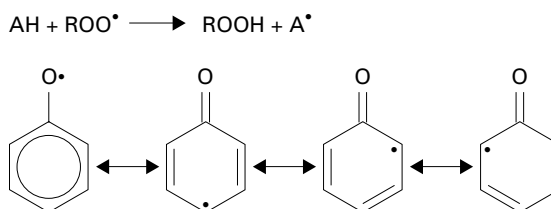

Figure 5.1   Diagrammatic representation of the mechanism underlying the antioxidant action of phenolic antioxidants.

Generally, *BHA* was not believed to be a hazardous substance. However, the results of recent studies in experimental animals suggest that the intake of BHA involves a cancer risk.

The case of *BHT* is more complex. There is evidence that BHT promotes several types of chemical carcinogenesis in a number of experimental animals. Further, liver damage and cytotoxic effects have been found.

Accurate data on the daily intake of BHA and/or BHT by man are not available. Generally, estimates are in the range of 1 to 5 mg/day. Estimated total use in the US of BHA is 143,000 lb/year and of BHT 670,000 lb/year. In the case of *propyl gallate*, no evidence of carcinogenicity, mutagenicity or teratogenicity has been provided. BHA, BHT and propyl gallate are almost universally accepted for use in food since the 1950s.

TBHQ is the most recently developed synthetic food antioxidant. It has been designed especially to protect polyunsaturated oils. In long-term animal feeding tests, no indications of carcinogenicity were obtained. As yet, TBHQ is allowed for use in food in the US and a few other countries, but not in the EU.
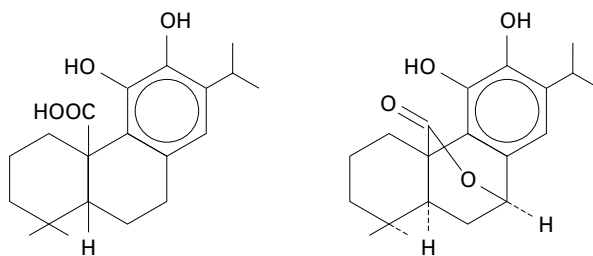
BHA

BHT
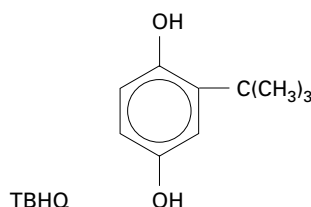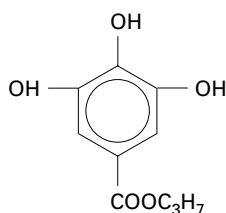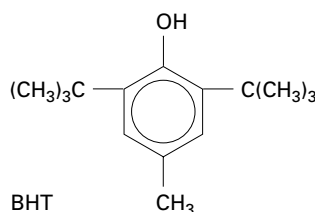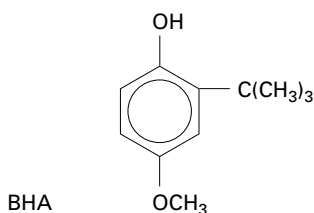
Propyl gallate
(3, 4, 5 – trihydroxybenzoic
acid propyl ester)

TBHQ
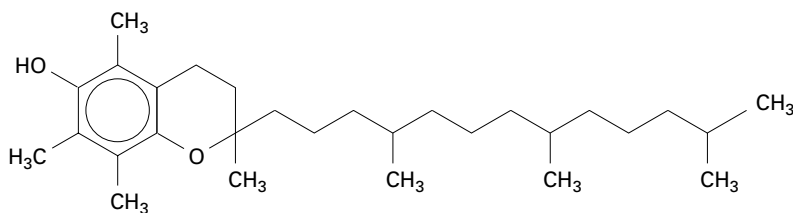
α – Tocopherol (vitamin E)

There are many phenols of natural origin which are strong antioxidants. Sometimes, they are more effective than the major synthetic phenolic antioxidants. At present, *tocopherols* and *rosemary extract* are commercially available.

Antioxidants in rosemary extract

5.2.3.2 *Antimicrobials*

Antimicrobials are used to prevent or inhibit the growth of microorganisms. They play a major role in prolonging the shelf life of foods. Nowadays, consumers expect all foods to be available all year round and to have a fairly long shelf life. In dietary behavior, however, risks from microbial contamination are often overlooked (see Part 1, Chapter 2, Section 2.3.3).

As far as food safety from a microbiological viewpoint is concerned, some advances have been made without calling in the help of additives. These involve the application of certain packaging and processing methods. Nevertheless, the use of chemical antimicrobials is indispensable for safe food handling. Common antimicrobial food additives are

benzoic acid and benzoates, sorbic acid and sorbates, short-chain organic acids (acetic acid, lactic acid, propionic acid, citric acid), parabens (alkyl esters of *p*-hydroxybenzoic acid), sulfite, and nitrite. Most of these substances are believed to be safe for application in food. They are easily excreted and metabolized by both animal and man. An exception should be made for one of them, namely nitrite. The intake of nitrite can lead to the formation of nitrosamines, which are well-known carcinogens.

Nitrite has been used as meat preservative for many centuries. It contributes to the development of the characteristic color and flavor, to the improvement of the texture of meat products, such as bacon, ham, frankfurters, fermented sausages, and canned meats, and also of fish and poultry products. Its antimicrobial effect was not recognized until the late 1920s. The primary aim of using nitrite as an antimicrobial is to prevent germination of the spores of *Clostridium botulinum* and hence the production of the botulinum toxin (see also Chapter 2).

Prolonged ingestion of sodium nitrite has been shown to cause methemoglobinemia, especially in infants. The major adverse effect of nitrite intake is the induction of cancer. In many animal species, this is attributed to the formation of nitrosamines in the reaction of nitrite with secondary amines. Nitrosamine formation can take place in the food itself as well as in the body. The normal acidity of the stomach is ideal for nitrosamine formation.

From a food toxicological point of view, three types of nitrosamines are of importance: dialkyl nitrosamines, acylalkylnitrosamines, and nitrosoguanidines. Cyclic nitrosamines are similar to the dialkyl type. The nitrogen atom becomes part of the heterocyclic ring. Nitrosoguanidines are a special class of highly reactive nitrosamides.
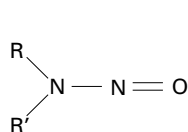
general structure of nitrosamines
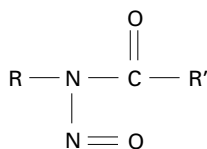
general structure of alkylacylnitrosamines
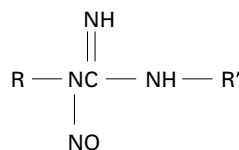
general structure of N – alkyl (R) – N' – alkyl (R') – N – nitrosoguanidines

The hazards due to nitrosamines in food depend strongly on the types and levels of precursors present. Precursors can be endogenous substances, products of food components, and endogenous substances, and also contaminants. Tables 5.1 and 5.2 list nitrosamine precursors and the corresponding nitrosamines that can be formed.

Since many nitrosable substances are formed on degradation of proteins and amino acids, nitrosamine formation cannot always entirely be prevented in food and in the body. One of the most effective inhibitors of nitrosation is ascorbic acid. This vitamin reacts rapidly with nitrite to form nitric oxide and dehydroascorbic acid. In that way, it can inhibit the formation of dimethylnitrosamine by more than 90%. Other inhibitors of nitrosation are gallic acid, sodium sulfite, cysteine, and tannins. Nitrosamine levels in food also depend on the temperature at which food is prepared. Table 5.3 gives some examples of nitrosamine levels in foodstuffs. Cooking can increase the nitrosamine level in food. As can be seen from Table 5.3, frying can increase the nitrosamine level in bacon quite considerably. Up to 135°C, cooking or frying does not result in detectable nitrosamine formation. Above 175°C, however, the nitrosamine levels increase rapidly.

Nitrite addition to fresh meat and food products is still under discussion because of the earlier-mentioned toxicological hazards. Up to now, banning of this additive has been blocked by the food industry. It is stressed that so far no other antimicrobial agent has been

Table 5.1 Nitrosamine precursors, endogenous or formed in food

Compound	Food	Nitrosamine formed
Creatine, creatinine	Meats, meat products, milk, vegetables	Nitrososarcosine (NSA)
Trimethylamine oxide	Fish	Dimethylnitrosamine (DMN)
Trimethylamine	Fish	DMN
Dimethylamine	Fish, meat, and meat products, cheese	DMN
Diethylamine	Cheese	Diethylnitrosamine (DEN)
Sarcosine	Meat and meat products, fish	NSA
Choline, lecithin	Eggs, meat and meat products, soybeans, corn	DMN
Proline, hydroxyproline	Meat and meat products, other foodstuffs	Nitrosoproline and nitrosopyrrolidine (NPyr)
Pyrrolidine	Meat and meat products, paprika	NPyr
Piperidine	Meat and meat products, cheese, black pepper	Nitrosopiperidine (NPip)
Methylguanidine	Beef, fish	Methylnitrosourea
Carnitine	Meat and meat products	DMN
Dipropylamine	Cheese	Di-*n*-propylnitrosamine
Dibutylamine	Cheese	Di-*n*-butylnitrosamine

Table 5.2 Nitrosamine Precursors which Contaminate Foodstuffs

Compound	Chemical class	Nitrosamine derivative
Atrazine	Secondary Amine	N-Nitrosoatrazine
Benzthiazuram	Carbamate	N-Nitrosobenzthiazuram
Carbaryl	Carbamate	Nitrosocarbaryl
Fenuron	Carbamate	DMN
Ferbam	Amide	DMN
Morpholine	Secondary Amine	Nitrosomorpholine
Propoxur	Carbamate	Nitrosopropoxur
Simazine	Secondary Amine	Nitrososimazine
Succinic acid 2,2-dimethyl hydrazide	Amide	DMN
Thiram	Amide	DMN
Ziram	Amide	DMN

Note: See Table 5.1 for abbreviations.

found that can provide protection against *Clostridium botulinum* as effectively as nitrite. In some EU countries (but not in Germany and the UK) and the US, nitrite addition to fresh meat is allowed up to a maximum of 200 ppm.

5.2.3.3 *Antibrowning agents*

Antibrowning agents are chemicals used to prevent browning of food, especially dried fruits and vegetables. Browning of food can occur enzymatically as well as non-enzymatically. The latter is dealt with extensively in Chapter 6. Enzymatic browning is mediated by polyphenol oxidase (PPO). This enzyme becomes available for catalysis upon cell disrupture. PPO contains copper and catalyzes two types of reactions (Figure 5.2):
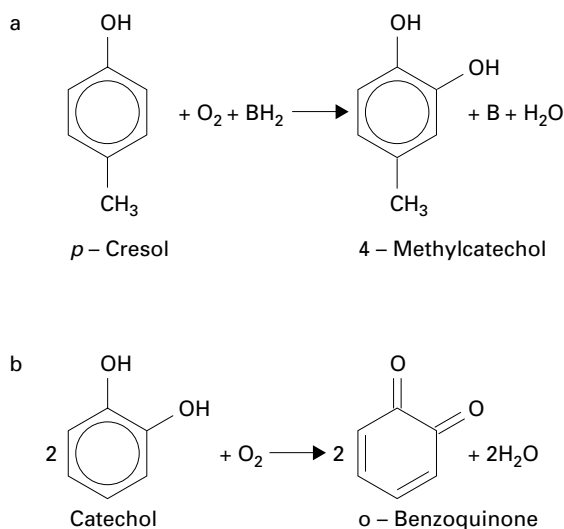
Table 5.3 Nitrosamine levels in food

Food	Nitrosamine	Level (ppb)
Bacon, raw		0
fried	DMN, DEN, NPyr	1–40
	NPip	10–108
	NPyr	11–38
	DMN, NPyr	2–30
Bacon, frying fat	NPyr	10–108
drippings	NPyr	16–39
Luncheon meat	DMN, DEN	1–4
Salami	DMN, DEN	1–4
Danish pork chop	DMN, DEN	1–4
Sausage	DMN	1–3
Sausage, metwurst	NPyr, NPip	13–105
chinese	DMN	0–15
Fish		
raw: sable	DMN	4
salmon	DMN	0
shad	DMN	0
smoked: sable	DMN	4–9
salmon	DMN	0–5
smoked and nitrate- or nitrite-treated:		
salmon, sable, shad	DMN	4–17
salted marine fish	DMN	50–300
smoked and nitrate- or nitrite-treated:	DMN	20–26
Other fish products	DMN	1–9
Fish sauce	DMN	0–2
	NPyr	0–2
Cheese	DMN	1–4
Baby foods	DMN	1–3
Shrimp, dried	DMN	2–10
	NPyr	0–37
Shrimp sauce	DMN	0–10
Squid	NPyr	0–10
	DMN	2–8
	NPyr	0–7
Canned meats (uncooked)	DMN	1–3
Ham and other pork products (uncooked)	DMN	0–5
Beef products (uncooked) (4 days after slaughtering)	DMN	1–2
Wheat flour	DEN	0–10

Note: See Table 5.1 for abbreviations.

  – hydroxylation of monophenols to catechols, i.e., *o*-diphenols;
  – oxidation of catechols to *ortho*-quinones.

    The *ortho*-quinones subsequently undergo a sequence of non-enzymatic reactions to yield brown-black melanin pigments.

    Generally used antibrowning agents are vitamin C, citric acid, and sodium sulfite; the latter is also a well-known antimicrobial agent. Usually, antibrowning agents are not hazardous. Sulfite, however, can cause allergic reactions. It is one of the most widely used food additives. It is cheap and can be used efficiently in a variety of applications. Recently,

a p – Cresol $+ O_2 + BH_2 \longrightarrow$ 4 – Methylcatechol $+ B + H_2O$

b   2 Catechol $+ O_2 \longrightarrow$ 2 o – Benzoquinone $+ 2H_2O$

Figure 5.2   Reactions catalyzed by PPO: (a) hydroxylation; (b) oxidation.

attention has been drawn to the reactions between sulfite and nutrients and other food components. Although sulfite itself is considered to be safe for the majority of consumers, there is hardly any information on the nature and toxic effects of its reaction products.

5.3 Summary

Food additives are intentionally added to food not only to prevent microbial spoilage, but also to maintain stability, organoleptic properties, and the nutritional value of foodstuffs. Evaluation of the safety of food additives is extensively provided for by regulation and legislation.

There are five main categories of additives, namely texturizing agents, colorings, flavoring agents, preservatives, and miscellaneous additives. This chapter treats the use of a number of selected food additives in relation to their safety:

     –   the colorings amaranth and tartrazine;
     –   the flavorings monosodium glutamate and saccharin;
     –   the preservatives BHA, BHT, nitrite, and sulfite.

The majority of the texturizing agents and miscellaneous additives do not pose toxicological hazards.

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