Chapter 4
Furan

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4.1 Introduction

Furan (C_4H_4O) (CAS No. 110-00-9) is a heterocyclic organic compound, consisting of a five-membered aromatic ring with four carbon atoms and one oxygen (Fig. 4.1). It is an intermediate in the production process of tetrahydrofuran, pyrrole, and thiophene, in the manufacturing of lacquers and resins [1], and for the production of pharmaceuticals, agricultural chemicals (insecticides), and stabilizers [2]. It is a colorless, volatile liquid having a relatively low boiling point of 31.3 °C.

The existence of furan and furan-substituted compounds in foods has been known for quite some time to contribute to the sensory properties of food. It is one of the volatile aroma compounds formed in a number of heated foods through thermal degradation of natural food constituents. On the other hand, the presence of furan in diet is considered as a concern as it is an animal carcinogen and classified as "possibly carcinogen to humans" (Group 2B) by the International Agency for Research on Cancer (IARC) [1, 3, 4]. Due to its toxicity, scientific community and food regulatory agencies have intensely focused on the occurrence, source, formation, and mitigation of furan in foods, and considerable research has been devoted to investigating this volatile food-borne contaminant.

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Fig. 4.1 Chemical structure of furan

4.2 Formation Mechanisms of Furan

Since its discovery, monitoring the formation and level of furan in foods became an essential issue for FDA, which has taken an action first by publishing an analysis method in foods and starting to build a broad database [5]. The database includes different varieties of foods, such as coffee, baby foods (porridge, juice), canned or jarred vegetables, infant formula, meat products, fruit juices, fish, milk products, cereal products, soups, and sauces. The furan levels in these foods range from not detected to 174 μg/kg [5]. The European Food Safety Authority (EFSA) has also started to collect data in EU and published scientific reports in 2009, 2010, and 2011 on the results of the monitoring of furan levels [6–8].

According to the latest report including the data submitted up to the end of 2010 from 20 countries, highest furan levels were found in coffee with the mean values of 45 μg/kg for brewed coffee, 394 μg/kg for instant coffee powder, 1936 μg/kg for roasted ground coffee, 2016 μg/kg for nonspecified coffee, and 3660 for roasted coffee beans [6]. The same report indicated the maximum level of 11,000 μg/kg in roasted coffee bean as the highest among all the food groups.

Elucidating the mechanism of furan formation is an important issue to develop mitigation strategies. Several model studies have been carried out to identify potential precursors and enlighten the formation pathways [9–11]. EFSA report has indicated that foods having high levels of carbohydrates were most likely to form furan [7]. Amino acids and reducing sugars forming Maillard reaction products and lipid oxidation of polyunsaturated fatty acids (PUFAs) or triglycerides, carotenoids, and ascorbic acid are responsible for furan formation. Among them, ascorbic acid and polyunsaturated lipids (such as linoleic and linolenic acid) were reported as the most effective precursors [12]. The US FDA has reported that a variety of carbohydrate/amino acid mixtures or protein model systems (e.g., alanine, cysteine, casein) and vitamins (ascorbic acid, dehydroascorbic acid, thiamin) have been used to produce, isolate, and identify furans in food [5]. The potential routes of furan formation from different components present in food are summarized in Fig. 4.2.

Maga first reported that the primary source of furans in foods is thermal degradation and the rearrangement of carbohydrates such as glucose, lactose, and fructose [3]. Many researchers have further shown that pyrolysis of carbohydrates at extreme temperatures of up to 300 °C formed furan, 2-methylfuran (MF), and further alkylated derivatives [14, 15]. Heyns has revealed that the pyrolysis of several carbohydrates, D-erythrose, D-xylose, D-ribose, D-arabinose, L-sorbose, D-fructose, D-glucurono-6,3-lactone, cellobiose, maltose, lactose, sucrose, raffinose, amylose, amylopectin, and cellulose, at 300–500 °C for a short period of time resulted in the same volatile products including furan.

Formation of furan in model systems has been extensively studied by Perez Locas and Yaylayan [10] using pyrolysis-GC-MS analysis and ^{13}C-labeled sugars, amino acids, and ascorbic acid. The study has revealed that furan could be formed

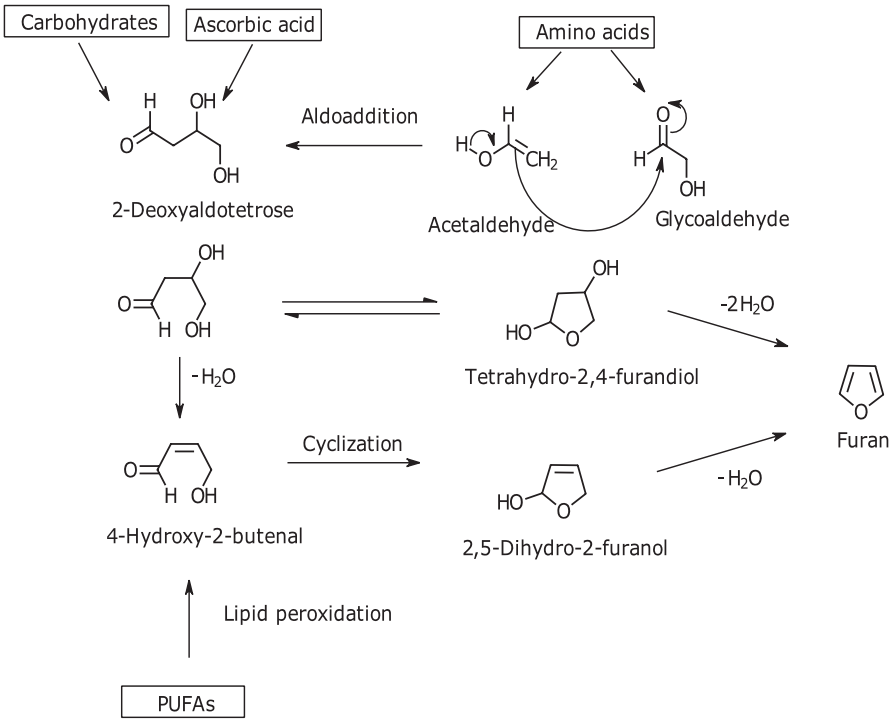

Fig. 4.2 Summary of possible routes for furan formation [2, 10]. (Reused with permission by [13])

from the thermal degradation of certain amino acids such as serine and cysteine, resulting in the formation of two key aldehyde intermediates, acetaldehyde and glycolaldehyde. They could undergo aldol addition forming 2-deoxyaldotetrose, which further reacts to form furan [10]. Hexoses were found to mainly degrade into aldotetrose derivatives to produce the parent furan. Thermal degradation of hexoses leads to the formation of 2-deoxy-3-ketoaldotetrose and 3-deoxyosone, which further react to form furan. Maillard reaction is also responsible for furan formation. The same study has further demonstrated that certain amino acids such as aspartic acid, threonine, and α-alanine require the presence of a sugar to form furan. Another study conducted by Cho and Lee [16] has also demonstrated that when the ribose/serine model system was heated at 90, 121, and 150 °C, it contained higher amounts of furan compared to other Maillard systems tested. The molar ratio of reactants also affected the furan formation from the Maillard model systems. The glucose/serine and glucose/alanine model systems have formed the highest furan at a molar ratio of 0.5:0.5.

Owczarek-Fendor et al. [17] have revealed that the addition of whey proteins into starch-based model food systems enhanced the generation of furan considerably at pH 4 and pH 6 when glucose, fructose, or lactose is present. The opposite trend was observed for sucrose.

Ascorbic acid is one of the important precursors of furan. Pyrolysis of ascorbic acid could generate furan via the formation of the 2-deoxyaldotetrose moiety, a direct precursor of the parent furan. Oxidative degradation of PUFAs forms lipid peroxidation products such as 4-hydroxy-2-butenal, which then undergo cyclization reaction and form furan [10].

Becalski and Seaman [18] have proved furan formation from the decomposition of ascorbic acid and from the oxidation of polyunsaturated fatty acids at elevated temperatures. Kinetic studies have revealed that ascorbic acid oxidation is the critical step in furan formation in tomato paste and pulp during heating [19].

Limacher, Kerler, Conde-Petit, and Blank [9] have investigated the formation of furan from ascorbic acid and related precursors in model systems simulating food preparation conditions such as roasting and pressure cooking. The results have confirmed that ascorbic acid is the major precursor of furan under roasting conditions despite low yield (<1 mol%). Pressure cooking conditions has led much lower furan formation than roasting conditions. However, pH has been found to play an important role in furan formation from ascorbic acid model systems treated with pressure cooking such that furan formation is much higher at pH 4 (57.5 μmol/mol) than pH 7 (3.69 μmol/mol). Finally, the researchers have suggested ascorbic acid as the potential precursor but depending on the pH.

2-Furaldehyde and 2-furoic acid, the degradation products of ascorbic acid and dehydroascorbic acid, have been reported to form furan [9, 20, 21]. 2-Furaldehyde is found to be a furan precursor in both dry and aqueous model systems, where 2-furoic acid is effective only under roasting conditions [9].

It is well known that thermal process is responsible for furan formation. According to the furan survey of FDA, fruit juices contain a certain amount of furan as a result of its thermal treatment as they are rich in ascorbic acid and carbohydrates, the precursors of furan. Not only thermal process but also ionizing radiation as an alternative nonthermal process has been used in fruit juices to ensure inactivated food-borne pathogen. According to the study conducted by Fan [22], both ionizing radiation and thermal treatments induce furan formation in apple and orange juice. Increased radiation dose from 0 to 5 kGy has resulted in increased furan formation. Another study has observed that irradiation induced low ng/g levels of furan only in grape and pineapple among several fresh fruits tested [23]. On the other hand, radiation to 4.5 kGy at 5 °C or to 10 kGy in the frozen state does not significantly induce furan formation in ready-to-eat meat and poultry products [24].

4.3 Occurrence of Furan in Foods

Due to its low boiling point, furan, formed during thermal processing, easily vaporizes. However, this gives rise to concern in canned or jarred foods as furan accumulates in the headspace. Furan levels have been monitored in a broad range of products (roasted coffee, bakery products, baby foods, etc.) and found to be from none detectable to 11,000 μg/kg [7, 25–33] (Table 4.1).

Table 4.1 Furan contents in certain food products

Product category	Furan content (μg/kg or L)		References
	Mean	Maximum	
Coffee, instant	394	2200	[6]
	91.37	145.2	[34]
Coffee, roasted bean	3660	11,000	[6]
Coffee, roasted ground	1936	6900	[6]
	<100	587	[35]
	89.3	352	[36]
Coffee, roasted ground, decaffeinated	53.1	121	[36]
Coffee, not specified	2016	6588	[6]
Coffee brew	42–45	360	[6]
	51.34	74.3	[34]
Baby foods, cereal	23–25	96	[6]
	5.15	8.6	[37]
	4.41	7.2	[34]
	10.9	53.5	[38]
Baby foods, fruits, and vegetables	10–12	66	[6]
	38.8	38.8	[37]
	7.71	13.36	[34]
Baby foods, fruits only	2.5–5.3	58	[6]
	1.6	2.7	[39]
	5.79	12.2	[37]
	13.6	92.6	[38]
Baby foods, meat, and vegetables	40	169	[6]
	35	64	[39]
	34.6	52.7	[37]
	72.3	224.4	[38]
Baby foods, vegetables only	48–49	233	[6]
	10	29	[39]
	38.83	81.9	[37]
Baby foods, fish-based	49	84	[39]
Baby foods, nonclassified	29–30	215	[6]
	40.7	52.5	[37]
Infant formula	0.2–3.2	2.2–10	[6]
Baked beans	22–24	80	[6]
Beer	3.3–5.2	28	[6]
Cereal product	15–18	168	[6]
Canned fish or meat	17	172	[6]
	26	70	[40]
	25.42	48.5	[34]
Fruit juice	2.2–4.6	90	[6]
Fruit drink	3.69	5.64	[34]

(continued)

Table 4.1 (continued)

Product category	Furan content (μg/kg or L)		References
	Mean	Maximum	
Orange juice	1.18–9.12	27.39	[41]
Fruits	2–6.4	36	[6]
Meat products	13–17	160	[6]
Milk products	5–5.6	80	[6]
Sauces	8.3–11	175	[6]
	1.27–26.07	69.13	[34]
Soups	23–24	225	[6]
Soy sauce	27	78	[6]
	44.32	69.13	[34]
	31.60	215.33	[42]
Vinegar	48.15	68.24	[34]
Vegetable juice	2.9–9	60	[6]
Vegetable	6.9–9.6	74	[6]
Cocoa	9–10	40	[6]
Snacks and crisps	9.6–10	47	[6]
	14.92–79.32	95.64	[34]
Soft drinks	0.8–1.2	4.5	[6, 41]
Soya products	6.7	28	[6]
Sweets	5–6	34	[6]
Tea	1–1.7	3.7	[6]
	68.28	71.58	[34]
Vegetable fats	1.5–1.7	10	[6]
Wine and liquors	1.3	6.5	[6]
	40.44–92.26	112.5	[34]

Among the foods containing furan, coffee has been reported to contain the highest amount of furan, and high consumption of coffee increases the exposure of carcinogenic furan. Baby foods (jarred/in closed containers) also take special attention due to its sensitive consumer group. Therefore, these two food groups are particularly discussed in this chapter.

4.3.1 Coffee

Roasted coffee is the group with the highest furan levels up to 11,000 μg/kg. Coffee preparation involves different steps starting from roasting the green beans, following grinding and brewing. These steps affect the final concentration of furan in coffee brew.

Roasting occurs at higher temperatures than most other thermal processes, which causes the formation of furan in addition to other certain thermal process contaminants [43]. Roasting degree plays an important role in the final furan content of

coffee bean. Guenther, Hoenicke, Biesterveld, Gerhard-Rieben, and Lantz [25] have reported that the formation of furan during roasting is dependent on roasting conditions and is, therefore, directly linked to achieving targeted flavor profiles. They have also found that furan formation has not significantly varied for different green coffee types, which has been previously reported by other researchers [35]. But, in another study, higher concentrations in *Coffea canephora* (robusta) than *Coffea arabica* species have been reported [44].

Although roasted coffee bean contains certain amount of furan, the steps prior to coffee consumption cause furan loss due to its high volatility and low solubility in water. Only approximately 10% of the initially generated furan during roasting is estimated to get into the cup of coffee for consumption [25].

As a first step of coffee preparation, grinding causes significant loss of volatile aroma compounds as well as furan due to the opening of the cell structures. Smaller mean particle size has been related to increased furan losses, such that around 40% of furan loss occurs at the typical European drip filter grind sizes (350–500 mm) [25]. Degassing process, which is applied to vacuum-packed roasted or ground coffee to remove CO_2 formed during roasting, also decreased the furan content by approximately 20%. In packed coffee, furan loss does not occur during the first 3 months of shelf life [25]. Zoller, Sager, and Reinhard [27] have assumed that more than 50% of the initial amount of furan is preserved until use, if the coffee beans and the soluble coffee are stored more or less airtight or aroma-tight. Different researchers have found out that the initial furan content of coffee powder and the type of brewing greatly affect the furan content of coffee brew [25, 27, 45]. In the brewing step, the type of preparation and brew recipe play an important role on the final amount of furan in the cup. Furan losses in various brewing techniques, such as drip filtering, fully automated machines, machines using coffee pads or capsules, are different. Among these brewing techniques, espresso-type coffee contains the highest concentration, while filter coffee contains the lowest.

Filtered coffee continues losing furan during the time the pot was held warm [27]. A study conducted by Zoller, Sager, and Reinhard [27] has shown that most of the furan (29%) is extracted with the first 65 mL when espresso is brewed with a semiautomatic machine and further 65 mL extract increases the furan extraction only to 32% with a high variation. Goldmann et al. [46] have reported that furan concentration steadily decreases due to the exposure of brew to the atmosphere. Another study has confirmed the furan loss as 50% after 1 h of brewing [27]. Soluble coffee brews have lower concentration of furan (0.91 mg/kg), while brew produced with automatic coffee machines has the highest [45, 47]. Closed systems, e.g. automatic machines, could keep furan from moving away, which leads to higher furan content in those systems. In addition, a high ratio of coffee powder to water could obviously transfer higher amounts of furan to brew.

Mesías and Morales [48] have investigated the amount of furan removed from the coffee beverage by volatilization during consumption time. Among different scenarios tested, maximum furan loss (97%) occurred when the brew is kept in a sealed thermo for 8 hours. Furthermore, placing the brew on one side at room temperature for 5 min alone or after 30 s of stirring (simulating sugar-added brew) is the

most common behavior, which causes 74% and 64% furan loss, respectively. Becalski, Halldorson, Hayward, and Roscoe [36] found 50% loss of furan in coffee brew at 30 min that was stored in the pot followed by storing in the cup.

Overall, these studies highlight the need for a careful evaluation of the dietary exposure to furan by consuming coffee. Despite the fact that furan loss is inevitable upon drinking the brew, Arisseto, Vicente, Ueno, Tfouni, and Toledo [44] have claimed that the remaining levels of furan in the beverages should be carefully evaluated and it might be still relevant to furan exposure due to the high consumption of coffee.

4.3.2 Baby Foods and Foods in Closed Containers

It is a fact that furan is volatile and could easily move away from certain food systems. However, foods processed in closed containers could contain volatilized furan in the headspace [33, 46]. Among these foods, baby foods have received considerable critical attention due to high sensitivity of babies to carcinogens and the larger amount of the foods consumed by this consumer group (relative to body weight) [49].

According to FDA report, infant formula products (N = 31) contain furan about 8–10 μg/kg, while EFSA report has indicated that baby food and infant formulae (N = 1628) contain furan (median) in the range of 0–38 μg/kg [5, 7].

A very recent survey has been conducted in the Spanish market to determine the furan concentration in commercial baby foods [39]. Researchers have detected the lowest furan concentration in infant formula (up to 0.33 μg/L) and cereal-based baby food (0.15–2.1 μg/kg), while baby food containing meat (7.9–61 μg/kg) and fish (19–84 μg/kg) showed the highest concentrations. Another study performed with a total of 35 infant food samples from Chinese market has not reported detectable amount of furan in some baby rice and infant formula samples, but muddy flesh samples contained 86.9 μg/kg as the highest [34].

As indicated in EFSA report, researchers have found that baby foods containing vegetables (48.0–49.0 μg/kg) or vegetable and meat mixtures (40 μg/kg) have higher furan levels than baby foods containing fruit (2.5–5.3 μg/kg) only, meat only, or meat and starches [6, 50]. Similar results were published by other researchers in a more recent study; vegetables and/or meat-based baby foods contain mean furan concentration of 72.3 μg/kg, while lesser amount has been reported in fruit-based (13.6 μg/kg) and cereal-based (10.0 μg/kg) baby foods [38]. Unlike commercially jarred baby foods, freshly home-prepared baby foods contained furan concentration below the limit of detection (0.20 μg/kg) [51]. The reason could be attributed to the different thermal processes, such that home-cooking occurs in open containers causing furan to be removed [50]. Another study, testing the furan levels in reheated retail canned or jarred foods including baby foods, has demonstrated an increase in furan when the food is closed during heating due to there being no loss by evaporation, leading to accumulation; however, heating the samples in open vials has caused very little furan accumulation [33]. Similarly, Roberts et al. [52] have determined various domestic

cooking regimes, such as cooking in saucepan or in a microwave oven, which affects the final concentration of furan in complete ready-to-eat meals (convenience foods) packed in cans or plastic trays and soups and sauces packed in cans, cartons, or jars. In general, heating leads to a decrease in most canned and jarred foods, while decrease is much when heated in a saucepan rather than microwave. Simulated domestic cooking conditions have indicated that the levels of furan also decrease slightly when foods are left to stand on plates due to their volatility.

4.3.3 Other Foods

Other foods, e.g., potato chips (16 μg/kg), crackers and crisp breads (12 μg/kg), and toasted breads (18 μg/kg) have also been reported to contain furan although they have not been processed in closed jars [25, 27, 53]. Lower amount of furan was also detected in cocoa (9–10 μg/kg), soya products (6.7 μg/kg), sweets (5–6 μg/kg), tea (1.0–1.7 μg/kg), vegetable fats (1.5–1.7 μg/kg), and wine and liquors (1.3 μg/kg) [6]. Roasted hazelnut has also been declared to contain certain amounts of furan due to the thermal process it undergoes [54]. In fact, increasing roasting temperatures from 100 to 150 °C has led to an increasing furan content of hazelnuts from 4 μg/kg to about 450 μg/kg.

4.3.4 Analysis Methods

FDA has published the first quantitative method for furan in foods [55]. This method defines the basic steps of the analysis, sample preparation using headspace (HS) sampling, addition of d_4-furan in sealed HS vials, incubation, and gas chromatography-mass spectrometry analysis. Prior to incubation, sample preparation was advised to be under cold conditions in order to eliminate the loss of furan.

The low boiling point of furan presents a challenge in handling it for analysis. Especially, sample preparation should be performed carefully to attain accurate results. Solid samples may need to be carefully homogenized before putting an appropriate amount to the headspace vial, while liquid samples can be directly transformed. Refrigerated or cryogenic conditions are necessary throughout the homogenization, such that a chilled blender is used to homogenize the prechilled sample placed in an ice bath [56]. Becalski et al. [57] have reported an increased furan loss with prolonged blending time. However, approximately 10% loss in spiked furan occurs when moderate-speed homogenization is used for 1 min.

Generally, headspace sampling is a sample preparation method enabling analysis of volatile analytes that are in the gaseous or vapor phase, either injected directly (HS) or interacted, and mostly equilibrated with a polymeric material [58]. Headspace sampling techniques, e.g., directly from the headspace in gaseous phase or solid phase microextraction (SPME), are well-established techniques for furan analysis.

Both HS and SPME methods should ensure that the present furan is removed from the food matrix. For this purpose, incubation is carried out before analysis. Different factors, such as time, temperature, and the nature of the sample, affect the efficiency of incubation [53]. A homogenized sample is mixed with water, if necessary, to ensure that the analyte is mobile [57]. Due to the decreased solubility of furan in a salt-saturated aqueous phase, sodium chloride or sodium sulfate may be added to the vial [46, 57].

According to the study investigating the effect of heating temperature on incubation efficiency, increasing the incubation temperature in aqueous solutions from 30 to 50 °C increased detected furan by 50% [57]. On the other hand, extra formation of furan at higher temperatures during incubation could cause overestimation [53, 59]. Analyses of first results from FDA were carried out at an incubation temperature of 80 °C [55]. FDA then decreases the incubation temperature to 60 °C to prevent low, ng/g, levels of furan formation that can occur during the analysis of a few relatively high-fat foods [60]. Interestingly, Şenyuva and Gökmen [59] have found continuous furan formation during headspace equilibration at 40 and 70 °C in unprocessed food samples, such as green coffee, freshly squeezed tomato, and orange juice. Therefore, matrix-matched calibration for each particular food matrix is highly recommended.

Several studies have reported methods comprising SPME for furan extraction from different food matrices and model systems [9, 29, 46, 50, 58, 61–64]. In principle, furan desorbed from the food matrix during incubation is adsorbed onto the fiber of SPME. It provides concentration of volatile analyte onto the fiber. Then, the analyte is desorbed thermally (1–5 min; 90–300 °C) from the fiber into the injection port of GC-MS. Goldmann, Perisset, Scanlan, and Stadler [46] have tested a number of different fiber types, including polyacrylate; Carbowax®/divinylbenzene; polydimethylsiloxane/divinylbenzene; and Carboxen®/polydimethylsiloxane (CAR/PDMS). Their results have revealed that CAR/PDMS shows decisive advantages in terms of sensitivity. However, the desorption temperature of SPME should be carefully selected as researchers have found out that some volatile furan precursors, such as 2-butenal and furfural, adsorbed on CAR-PDMS SPME fiber could form furan during high-temperature desorption leading to overestimation of the furan content of the sample (Fig. 4.3) [65].

Stir bar sorptive extraction (SBSE) technique has been tested as an alternative to static headspace analysis for coffee and jarred baby food samples [66]. In general, results from the SBSE technique using d_4-labeled furan as an internal standard gave results comparable to that of the static headspace (LOD: 2 μg/kg). One advantage of this extraction method has reported that extra furan formation is eliminated during extraction as it is performed at ambient temperature.

HS and SPME are extensively used for furan analysis, and both analysis principles give satisfactory results, if applied correctly according to the proficiency test conducted in EU [67]. On the other hand, SPME method has some other advantages over HS, such as allowing sample concentration and having lower detection limit than HS.

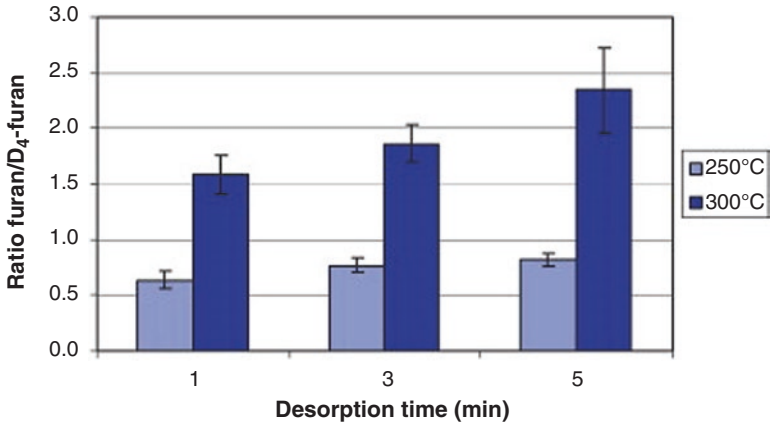

Fig. 4.3 Ratio of furan/d_4-furan (ion 68/ion 72) after SPME-GC–MS analysis of 0.25 mmol of 2-butenal in 1 ml water, spiked with d_4-furan (0.87 μg), as a function of desorption time and temperature. Reused with permission [65]

Quantitative analysis is challenging in headspace sampling when the analyte needs to be emitted from the food matrix. The physical form of the matrix including furan, the standardization and/or normalization of the accumulating polymer(s), and the quantitation approach used have been reported to be important in terms of reliable quantitation [58]. Standard Addition and Stable Isotope Dilution Assay are commonly used as quantifying methods for furan. In 2004, FDA used a static headspace-gas chromatography-mass spectrometry method for the quantification of furan by using the standard addition approach [5, 55]. In 2005, Becalski, Forsyth, Casey, Lau, Pepper, and Seaman [57] have validated a headspace method by using d_4-furan as an internal standard together with an external calibration curve as quantitation approach and attained higher sensitivities and 1 μg/kg limit of quantification. In a previous study, Multiple Headspace Extraction method has been newly proposed for furan quantification and compared with Standard Addition and Stable Isotope Dilution Assay [58]. According to the comparison results, these three techniques have been found to be reliable for furan analysis in combination with HS-SPME-GC-MS.

After FDA has published the first quantitative GC-MS method, researchers started to use this method, but thereafter several papers modifying this method have been published [18, 50, 54, 55, 63, 64]. In these papers, a PLOT (porous layer open tubular), PLOTQ (based on bonded polystyrene-divinylbenzene phase), or an equivalent column for the separation of furan was commonly used. MS was operated in Selected Ion Monitoring (SIM) mode by monitoring major ions at m/z 68, 72 and confirming by monitoring of the ions at m/z 39, 42 for furan and d_4-furan, respectively. The identification of furan is performed by the ratio of m/z 68 compared to its fragment ion at m/z 39.

4.3.5 Toxicity

Furan can pass through biological membranes, and it is rapidly absorbed from the lung or intestine and probably also through the skin due to its low polarity [68]. Rats and mice extensively metabolize after ingestion, whereas human body can be exposed to furan by both ingestion and inhalation while preparing food. Studies with F344 rats using isotopically labeled furan (2,5-^{14}C) have shown that radioactivity has remained in the liver tissues (13%) 24 h post dosing followed by the kidney and gastrointestinal tract (together 1%) [69]. The same study has also demonstrated that elimination of the isotopically labeled furan (80%) occurs mainly by air (40%), followed by feces (22%) and urine (20%) after 24 h of oral administration [69]. Burka, Washburn, and Irwin [69] found out that ingested furan is metabolized to different species in the liver, and these metabolites, including furan itself, react with protein rather than binding to DNA. However, latter studies have revealed that furan is metabolized by cytochrome P-450 to the dialdehyde, *cis*-2-butene-1,4-dial, which can interact directly with DNA [70, 71].

NOAELs based on a 2-year bioassay have been identified for cytotoxicity and hepatocarcinogenicity of 0.5 and 2 mg/kg bw, respectively [72]. It was reported that the margin of exposure for furan indicated a human health concern for a carcinogenic compound that might act via a DNA-reactive genotoxic metabolite [73]. Based on the presently available data, it appears that both genotoxicity and chronic cytotoxicity may contribute to furan-induced tumor formation [2].

4.3.6 Mitigation Strategies

Several attempts have been made to develop mitigation strategies of furan in foods (Fig. 4.4). Due to its carcinogenicity, the ALARA ("as low as reasonably achievable") concept should be applied to furan levels in food. As furan is a consequence of thermal process, one might think to decrease the thermal load applied to food. However, this could not be practical especially for the sealed containers as they undergo pasteurization and sterilization for microbiological safety.

As reviewed by Anese and Suman [74], mitigation of furan formation could be achieved by two conceptually different technological approaches: (a) preventive interventions and (b) removal interventions. Preventive interventions aim to limit the reaction by creating less favorable reaction conditions, while the latter approach aims to decrease the furan content, which is already formed in the food during processing. To prevent furan formation, limiting the precursors in processed foods is not always a viable approach, as furan has not only one precursor.

Ascorbic acid has the highest potential to form furan, followed by polyunsaturated fatty acids, which are both desired food components due to their positive effect on health [53]. However, addition of ascorbic acid to a heat-processed food creates concern with regard to furan formation. In a previous model study, ascorbic acid

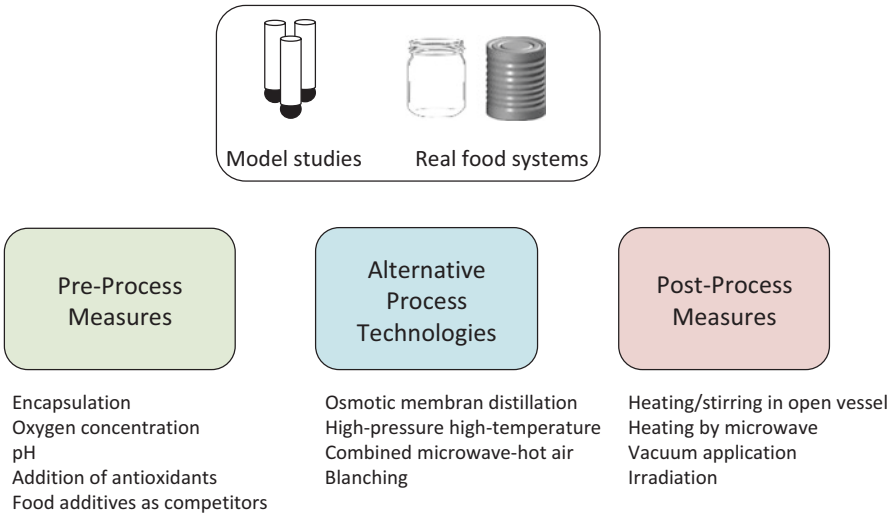

Fig. 4.4 Scheme summarizing the mitigation strategies for furan

was heated in the presence of iron to simulate dry foods containing these ingredients for their nutritional properties [75]. In these model systems, the furan formation rate constant from ascorbic acid increased by 369-fold due to the presence of iron creating oxidizing conditions. At this point, encapsulation may come into prominence as a mitigation strategy. Encapsulation not only preserves the function of ingredient, but also prevents it to react and eventually form furan. Further study has reported that the encapsulation of ascorbic acid by arabic gum and maltodextrin has decreased furan formation up to 57% in model systems containing iron heated at 120 °C ($p < 0.05$) [76].

Reaction conditions, including oxygen concentration, pH, presence of antioxidants, or other certain additives, have been reported to affect the furan formation in model or model food systems. Therefore, researchers have proposed to modify these factors to eliminate furan formation. Palmers et al. [77] have suggested lowering the oxygen concentration or pH prior to thermal processing for furan mitigation in thermally treated plant-based foods.

Becalski and Seaman [18] have shown that the presence of tocopherol acetate and butyl hydroxyanisole (BHA) reduces furan formation from PUFA as much as 70% under pressure cooking conditions. In a very recent study, chlorogenic acid has been found to be the most efficient antioxidant to reduce furan formation in ascorbic acid model systems, while butylated hydroxytoluene (BHT) has shown 92% and 80% reduction of furan in linoleic and linolenic acid model systems, respectively [78]. In soy sauce model systems, BHT and BHA reduced furan by 84% and 56%, respectively [79]. Another study has demonstrated that furan can be reduced in a canned-coffee model system by addition of epicatechin (by 65.3%), epigallocatechin gallate (by 60.0%), catechins (by 44.7%), chlorogenic acid (by 67.0%), ferulic acid (by 57.6%), Trolox (by 50.1%), and caffeic acid (by 48.2%) [80]. Shen et al.

[81] have proposed adding furan formation suppressors such as glutamic acid and/or avoiding from furan forming promoter such as ferric to decrease furan formation from PUFA.

The formation of furan in soy sauce model system was investigated by Kim, Her, Kim, and Lee [79]. The furan content of soy sauce model system has increased by 211% during fermentation up to 30 days after sterilization when compared to the model system without sterilization. The addition of magnesium sulfate and calcium sulfate to soy sauce model system reduced the furan concentration by 36–90% and 27–91%, respectively.

Studies performed on model systems have revealed that furan formation is negatively affected by the presence of additional molecules, which may increase the fragmentation rate of precursors or change the redox status of the reaction system [9]. However, this concept could not be easily extrapolated to food products from simple model systems. Food systems are complex mixtures, and various reactions occur at the same time during heating. These competitive reaction paths lead to significantly lower furan concentration than that obtained in dedicated model systems [9].

Different alternative technologies could be applied to specific food groups to prevent furan formation during processing. For example, tomato paste concentrated using osmotic and membrane distillation systems contains lower amount of furan than that concentrated using conventional thermal evaporation [82]. In the case of vegetable purées, high-pressure high-temperature (HPHT) processing has been suggested as an alternative and successfully applied to reduce furan formation to 1–2 μg/kg purée while ensuring a sterile product [83]. HPHT process has also been proved in sardine in olive oil to achieve reduced furan content such that the furan decreased from 57.9 μg/kg to 16.6 μg/kg by HPHT process when used as an alternative to retort [84]. This process has also been scaled up from lab-scale to the pilot scale [85]. The scale-up has also ensured reduction of furan between 41 and 98% to retorting depending on the food system.

Another technology, combined microwave-hot air for malt roasting was used to mitigate thermal process contaminants, including furan [86]. Combined microwave-hot air reduced furan content in black malt by 23% when compared to conventional process.

Blanching as a pretreatment for potato slices leached out ascorbic acid and reducing sugars, leading to decreased furan concentration by 91% in potato chips; therefore, it is proposed as an alternative unit operation to produce healthier potato chips [87].

Taking the advantage of its volatility, furan could be removed from the food matrix. Based on the evidences from previous researches, EFSA concluded in their report that volatilizing furan by heating and stirring in an open saucepan before consumption has reduced furan levels in canned/jarred foods [6, 27, 33, 52, 88]. However, this technique would be technically difficult for certain foods, for example, for coffee while retaining all the flavor and aroma substances that the consumer demands [53].

Composition of food matrix has an effect on the efficiency of furan volatilization. Van Lancker, Adams, Owczarek, De Meulenaer, and De Kimpe [26] have reported that furan is mainly retained by the lipophilic fraction but not by starch. However, in the case of coffee, defatted coffee and coffee grounds also show the ability to retain furan. Anese et al. [89] have investigated possible vacuum application to remove furan from the food matrix and found that it can effectively be removed from meat sauce, having a high moisture content.

A very recent study has reported that complete elimination of furan via evaporation from baby food samples is not possible even after a long-standing time [39]. Heating promoted diffusion of furan from the food matrix such that if the baby food is heated using a microwave oven or by means of hot water bath, furan content could be decreased by 26% and 42%, respectively. The authors further suggest standing the baby food for 5 min after heating as the furan loss reaches about 50%.

As mentioned in the "Formation" section, irradiation of certain foods could induce furan formation. However, a number of studies indicate that irradiation might be a suitable tool to reduce the furan formation. For example, researchers have revealed that irradiation at doses of 2.5–3.5 kGy that can inactivate 5 log of most common pathogens has significantly reduced the furan levels by 25–40% in all foods studied, e.g., frankfurters, sausages, and infant sweet potatoes [90]. It was confirmed that irradiation reduced furan formation in frankfurters that contained relatively high levels of furan due to previous thermal processing [24]. The composition, particularly the water content, has been declared to be important for the degree of furan reduction in particular foods by irradiation. Although irradiation reduces furan formation in certain foods, it is thought to be unlikely used as the only tool due to its limited effectiveness in most foods, caused nutrient loss, formation of off-odor compounds, and economical aspects [56].

4.3.7 Concluding Remarks

The volatility of furan raises difficulties in handling for analysis. Starting from sampling prior to analysis, the samples should be kept in cold conditions and/or sealed in vials. Headspace sampling, either by direct injection or by using SPME, is a well-established technique for furan analysis, and they are validated and commonly used by researchers. However, using these techniques need additional attention as misapplication could lead to forming extra furan and overestimation.

There are several studies published on the elimination of furan formation in different foods. Different food matrices imply different reaction mediums with numerous variables, such as composition (presence of precursors, i.e., sugars, amino acids, ascorbic acid, PUFA), pH, oxygen concentration, and water content, and might need specific approach. On the other hand, different food products require and undergo relevant thermal process, which ultimately determines the final furan content of food. Eliminating precursors from the food formulation or modifying formulation

or thermal processes may not always be viable approaches, as desired sensory property and/or microbiological safety of the food should be attained at the same time. For example, although coffee contains the highest amount of furan, there is no applicable strategy to be applied without affecting the sensory properties. Or, decreasing the thermal process temperature of canned/jarred foods, particularly baby foods, would not ensure the inactivation of pathogens. Incorporation of certain additives (furan inhibitors) to food products could also yield change in the organoleptic properties. As complex systems, foods may possess more than one potential precursor leading to furan formation through different mechanisms during processing. Mitigation of furan in foods is not an easy task. As reviewed in this chapter, there is no sole method to be applied for controlling furan formation in various kinds of foods. Future studies on developing efficient and applicable strategies are therefore recommended.

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