Influence of the Reaction Conditions on the Antimutagenic Effect of Maillard Reaction Products Derived from Xylose and Lysine

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The antimutagenicity of Maillard reaction products (MRPs) was investigated by refluxing D-xylose and L-lysine under various reaction conditions. The mutagenicity of 2-amino-3-methylimidazo[4,5-*f*]quinoline (IQ) to *Salmonella typhimurium* TA98 was reduced by all MRPs, whereas 4-nitroquinoline *N*-oxide was not affected except for the MRP obtained from xylose–lysine molar ratio 1:1 at pH 11.0 for 10 h. Higher antimutagenic effect was observed in MRPs prepared at an alkaline pH (9.0 and 11.0), at lower xylose–lysine molar ratios (1:2 and 1:3), or for 5 h. For all 27 MRPs prepared, only 3 combinations, including molar ratio 1:2 at pH 9.0 for 10 h and molar ratio 1:1 at pH 9.0 for 15 h and at pH 11.0 for 10 h, exhibited over 70% inhibitory effect on mutagenicity of IQ to both TA98 and TA100 strains.

INTRODUCTION

The Maillard reaction or the nonenzymatic browning reaction is a reaction between amino and carbonyl compounds that occurs in foods during storage, preparation, or processing. This reaction has been studied from various aspects including chemical, technological, physiological, and toxicological, and numerous reviews are available (Monnier, 1989; O'Brien and Morrissey, 1989; Ames, 1990). Recently, research on the Maillard reaction has focused on new areas; one aspects is the antimutagenicity of Maillard reaction products (MRPs) from amino acids and sugars (Namiki, 1988). Although it is indicated that MRPs in food might have an antimutagenicity property, the basic knowledge and research data concerning this aspect are still in lacking. Food contains various amino acids and sugars; the building of basic antimutagenic data in each single model system of one sugar to one amino acid should assist us to realize the complex system in food.

The antimutagenicity of MRPs has been studied by some researchers in the lysine–glucose system, the glycine–glucose system, and the glycine–sucrose system (Chan et al., 1979; Kato et al., 1985; Kim et al., 1986; Yamaguchi and Iki, 1986). Kong et al. (1989) also studied the antimutagenicity of amino–carbonyl mixtures of phenylalanine or cysteine and glucose or fructose in the presence of malic acid. In our previous study (Yen et al., 1992), the antimutagenicity of 12 MRPs prepared from 4 amino acids (glycine, L-lysine monohydrochloride, tryptophan, and L-arginine monohydrochloride) and 3 sugars (glucose, xylose, and fructose) was investigated. The results showed that MRPs obtained from xylose and lysine have a stronger antimutagenic effect against the mutagenicity of 2-amino-3-methylimidazo[4,5-*f*]quinoline (IQ), 2-amino-6-methyldipyrido[1,2-*a*:3′,2′-*d*]imidazole (Glu-P-1), and 3-amino-1,4-dimethyl-5*H*-pyrido[4,3-*b*]indole (Trp-P-1) toward *Samonella typhimurium* TA98, and the antimutagenic effect of MRPs was also correlated with their antioxidative activity and reducing power. Since the formation of Maillard reaction products was affected by the reaction conditions (Reynolds, 1963; Obretenov and Kuntcheva, 1990), the antimutagenic effect of xylose–lysine MRPs may be also influenced by reaction conditions.

The objectives of this study were to determine the influence of pH, time, and molar ratio of reactants on the antimutagenic effect of Maillard reaction products prepared from xylose and lysine and to find the optimum reaction condition for preparation of antimutagenic MRPs for further purification and identification of antimutagenic component(s).

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MATERIALS AND METHODS

Materials. D-Xylose, L-lysine monohydrochloride, and 4-nitroquinoline *N*-oxide (NQNO) were obtained from Sigma Chemical Co. (St. Louis, MO). 2-Amino-3-methylimidazo[4,5-*f*]-quinoline (IQ) was purchased from Wako Pure Chemical Co. (Tokyo).

Preparation of Maillard Reaction Products (MRPs) with Various Reaction Conditions. The MRPs were prepared by refluxing D-xylose and L-lysine monohydrochloride at 100 °C in an oil bath. Three factors including initial pH, molar ratio of reactants, and heating time were selected for defining factor levels (Giovanni, 1983). To determine the effects of pH, heating time, and molar ratio of reactants on mutagenic activity of IQ and NQNO and to define the range of factor levels, a series of MRPs were prepared under various combinations by changing one factor of reaction conditions, respectively. To study the effect of initial pH, the MRPs were prepared by dissolving 1.0 M xylose and 1.0 M lysine in 0.1 M potassium phosphate buffer with five different pH values (3, 5, 7, 9, 11, and 13) and refluxed at 100 °C for 10 h. To study the effect of reaction time, the MRPs were prepared by dissolving 1.0 M xylose and 1.0 M lysine in 0.1 M potassium phosphate buffer (pH 7.0) and refluxed at 100 °C for 0, 5, 10, 15, and 20 h, respectively. To study the effect of molar ratio of reactants, the MRPs were prepared by dissolving different xylose/lysine molar ratios (1.0/3.0, 1.0/2.0, 1.0/1.0, and 2.0/1.0) in 0.1 M potassium phosphate buffer (pH 7.0) and refluxed at 100 °C for 10 h. All of the MRPs were diluted properly and assayed for their toxicity and mutagenicity toward *S. typhimurium* TA98. The dose of MRPs with no toxicity and mutagenicity was used for the antimutagenic assay.

Optimization of Reaction Conditions. To select the optimum combination of reaction conditions under which the most highly antimutagenic MRPs were formed, we selected 27 combinations of reaction conditions through defining factor levels in the above section. Three initial pH values, 7.0, 9.0, and 11.0, were used. For each pH, three different xylose–lysine molar ratios (2.0/1.0, 1.0/1.0, and 1.0/2.0) were selected; therefore, nine different reaction mixtures were obtained. Each reaction mixture (25 mL) was refluxed at 100 °C in a 100-mL round flask for three different heating times (0, 5, and 10 h). All samples were freeze-dried, and the mutagenicity and antimutagenicity were determined. The dose of mutagen (IQ) used was 0.1 μg/plate.

Mutagenicity and Toxicity Assay. The mutagenicity of MRPs was determined according to the Ames test with a 20-min

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preincubation at 37 °C (Maron and Ames, 1983). The histidine-requiring strains of *S. typhimurium* TA98 and TA100 were kindly supplied by Dr. B. N. Ames (UC, Berkeley). The S9 mix (Organ Teknika Co.) was prepared from Sprague-Dawley male rats treated with Aroclor 1254 according to the method of Ames et al. (1975). Diluted MRPs (0.1 mL) were added to 0.1 mL of overnight-cultured *S. typhimurium* TA98 or TA100 and 0.5 mL of S9 mix or 0.1 M phosphate buffer in place of S9 mix. The entire mixture was preincubated at 37 °C for 20 min before 2 mL of molten top agar was added, and then the mixture was poured on an minimum agar plate. The His^+ revertant colonies were counted after incubating at 37 °C for 48 h. Each assay was performed in triplicate, and the data presented are the means of at least two experiments. The mutagenicity was expressed as the number of revertant colonies per plate at a given concentration of each MRP. In this mutagenicity testing, the result was recognized as positive when the number exceeded twice the number of spontaneous revertants (Ames et al., 1975). To examine the toxic effect of MRPs to TA98, the mixtures after preincubation were diluted with phosphate buffer, and the diluted mixtures were poured into nutrient-rich agar plates. The plates were incubated at 37 °C for 2 days, and the number colonies was counted.

Antimutagenicity Assay. The antimutagenic effect of each MRP was assayed according to the Ames method except for the addition of mutagen before preincubation. The mutagens used were NQNO (0.1 μg/plate), a direct-acting mutagen, and IQ (0.01 μg/plate), which requires S9 mix for metabolic activation. Mutagen (0.1 mL) was added to the mixture of strain and MRP with S9 mix for IQ or with 0.1 M phosphate buffer (pH 7.4) for NQNO. The mutagenicity of each mutagen in the absence of MRPs (control) was defined as 100%. A lower percentage of revertants relative to the control indicates the strong antimutagenicity of MRP (Francis et al., 1989).

Statistical Analysis. The interaction between the treatments and the comparison of the means obtained for each group were calculated as described by Duncan (1955). Statistical differences at $p < 0.05$ were considered to be significant.

RESULTS AND DISCUSSION

Mutagenicity and Toxicity of Maillard Reaction Products Prepared from Xylose and Lysine. The mutagenicity and toxicity of MRPs prepared from xylose and lysine under various reaction conditions toward *S. typhimurium* TA98 were evaluated. For the dose less than 5 mg/plate, no mutagenicity or toxicity was found in any of the MRPs either with or without S9 mixture (data not shown). For the dose greater than 5 mg/plate, mutagenicity occurred under some reaction conditions such as xylose–lysine molar ratio 1:2 at pH 7.0 for 10 h (10 mg/plate), or toxicity was found in molar ratio 1:1 at pH 9.0 for 10 h (20 mg/plate). If mutagenicity or toxicity occurred in MRPs, the results of the antimutagenicity assay thereafter would be influenced and confused due to the increase or decrease in numbers of revertants of *S. typhimurium* TA98. Therefore, the dose of 5 mg/plate was selected for the antimutagenicity assay.

Effects of Reaction Conditions of Xylose–Lysine MRPs on the Mutagenicity of IQ and NQNO. The effects of initial pH, heating time, and molar ratio of reactants on the mutagenicity of mutagens IQ and NQNO toward *S. typhimurium* TA98 are shown in Table I. In general, the mutagenicity of IQ was reduced by all xylose–lysine MRPs, whereas the mutagenicity of NQNO was not affected except for the MRP of xylose–lysine prepared with molar ratio 1:1 at pH 11.0 for 10 h. Furthermore, some MRPs exhibited an enhancing effect on the mutagenicity of NQNO. The antimutagenic compounds in MRPs are still not completely understood at the present time. Some researchers suggested the antimutagenicity of MRPs may be due partially to the reactive substances in melanoidin which could scavenge the free radical,

Table I. Effect of Xylose–Lysine Maillard Reaction Products (MRPs) with Various Reaction Conditions on the Mutagenicity of IQ and NQNO toward *S. typhimurium* TA98

reaction conditions	IQ, 0.01 μg/plate	NQNO, 0.1 μg/plate
initial pH[a]		
3	167 ± 10 (11.0)[b]	220 ± 20 (117.0)
5	247 ± 20 (16.3)	260 ± 15 (138.3)
7	310 ± 21 (20.4)	272 ± 25 (144.7)
9	138 ± 7 (9.8)	280 ± 26 (148.9)
11	167 ± 5 (11.0)	90 ± 7 (47.9)
13	513 ± 23 (33.8)	225 ± 9 (119.7)
reaction time[c]		
0 h	1505 ± 105 (99.0)*	205 ± 21 (109.0)*
5 h	140 ± 11 (9.2)	256 ± 16 (136.2)
10 h	310 ± 15 (20.4)	272 ± 22 (144.7)
15 h	403 ± 30 (26.5)	280 ± 6 (148.9)
20 h	367 ± 32 (24.1)	294 ± 10 (156.4)
molar ratio[d]		
1.0/3.0	176 ± 2 (11.6)	162 ± 5 (86.2)*
1.0/2.0	125 ± 4 (8.2)	108 ± 6 (57.4)
1.0/1.0	310 ± 8 (20.4)	272 ± 15 (144.7)
2.0/1.0	235 ± 10 (15.5)	302 ± 25 (160.6)
control	1520 ± 90 (100.0)	188 ± 17 (100.0)
spontaneous revertants	37 ± 3	25 ± 4

[a] Samples were prepared by refluxing 1.0 M xylose and 1.0 M lysine in 0.1 M potassium phosphate buffer with different pH values at 100 °C for 10 h. [b] His^+ revertants/plate (percentage relative to control value). Mutagens were preincubated with and without MRPs (5.0 mg) at 37 °C for 20 min. Control plates were with mutagen but without MRP. Spontaneous revertants were obtained without MRP and mutagen. Data are means ± SD of six plates. Those marked with asterisks show no significant differences compared with the corresponding control value ($p < 0.05$). [c] Samples were prepared by refluxing 1.0 M xylose and 1.0 M lysine at 100 °C and pH 7.0. [d] Molar ratio: moles of xylose/moles of lysine. Samples were prepared by refluxing xylose–lysine mixture with different molar ratios at 100 °C and pH 7.0.

inactivate the mutagen, or inhibit enzyme activity of the S9 mixture (Kim et al., 1986; Hayase et al., 1989). In this study, the MRPs inhibited the activity of indirect-acting mutagen IQ and failed to inhibit that of direct-acting mutagen NQNO to *S. typhimurium* TA98. This result indicated that the antimutagenicity of MRPs derived from xylose and lysine may result from inhibition of the formation of mutagen activating from promutagen or affecting the metabolic activation by the S9 fraction of rat liver to a reactive *N*-hydroxy metabolite of IQ. Preincubation of MRPs with IQ and S9 mixture at 37 °C for 20 min may induce the MRPs to react with IQ and/or S9 mixture, which leads to inhibition of the mutagenicity of IQ. IQ is a heat-induced mutagen which has been proven to be carcinogenic in animal experiments (Matsukura et al., 1981; Ohgaki et al., 1984) and shown to be the main mutagenic heterocyclic amine in heating foods (Nagao et al., 1983). On the other hand, free amino groups in a molecule of IQ play an important role in the expression of mutagenic activity (Okamoto et al., 1981). Grivas and Jagerstad (1984) showed that both the imidazole ring and its 2-amino group are required for the high mutagenicity of the IQ compounds. Likewise, the 3-methyl group was associated with the mutagenicity of IQ compounds (Jagerstad and Grivas, 1985). Kim et al. (1986) suggested the inhibition of IQ by melanoidins prepared from D-glucose and glycine was due to blocking or modification of a free amino group of IQ. For the antimutagenicity of MRPs prepared from xylose and lysine, we suggested the modification of the 3-methyl group of IQ could be another explanation in addition to the blocking or modification of the 2-amino group of the IQ molecule. However, further study is needed to confirm this statement. The muta-

Table II. Effect of Xylose–Lysine Maillard Reaction Products (MRPs) Prepared with 27 Reaction Combinations on the Mutagenicity of IQ toward *S. typhimurium* TA98

initial pH	molar ratio[a]	reaction time, h 5	10	15
7	1.0/2.0	1095 ± 14 (48.9)[b]	1020 ± 10 (45.6)	545 ± 15 (24.4)
	1.0/1.0	1044 ± 87 (46.7)	834 ± 77 (37.3)	151 ± 13 (6.8)
	2.0/1.0	1316 ± 18 (58.8)	1038 ± 102 (46.4)	278 ± 31 (12.4)
9	1.0/2.0	623 ± 12 (27.8)	668 ± 38 (29.9)	697 ± 1 (31.2)
	1.0/1.0	1259 ± 41 (56.3)	810 ± 26 (36.2)	114 ± 10 (5.1)
	2.0/1.0	1534 ± 20 (68.6)	1700 ± 8 (76.0)	1702 ± 27 (76.1)
11	1.0/2.0	774 ± 70 (34.6)	617 ± 17 (27.6)	792 ± 14 (35.4)
	1.0/1.0	1656 ± 25 (74.0)	331 ± 11 (14.8)	732 ± 27 (77.4)
	2.0/1.0	1432 ± 56 (64.0)	1977 ± 129 (88.4)	1910 ± 181 (85.4)
control		2237 ± 31 (100.0)	2237 ± 31 (100.0)	2237 ± 31 (100.0)
spontaneous revertants		37 ± 3	37 ± 3	37 ± 3

[a] Molar ratio: moles of xylose/moles of lysine. [b] His^+ revertants/plate (percentage relative to control value). IQ (0.1 μg/plate) was preincubated with or without MRPs (5.0 mg) at 37 °C for 20 min. Control plates were with mutagen but without MRPs. Spontaneous revertants were obtained without MRPs and mutagen. Data are means ± SD of six plates. All values show significant differences compared with control value ($p < 0.05$).

Table III. Effect of Xylose–Lysine Maillard Reaction Products (MRPs) Prepared with 27 Reaction Combinations on the Mutagenicity of IQ toward *S. typhimurium* TA100

initial pH	molar ratio[a]	reaction time, h 5	10	15
7	1.0/2.0	578 ± 14 (54.0)[b]	494 ± 8 (46.2)	535 ± 35 (50.0)
	1.0/1.0	292 ± 10 (27.3)	378 ± 10 (35.3)	518 ± 14 (48.4)
	2.0/1.0	281 ± (26.3)	450 ± 10 (42.1)	562 ± 16 (52.5)
9	1.0/2.0	325 ± 6 (30.4)	260 ± 8 (24.3)	455 ± 14 (42.5)
	1.0/1.0	247 ± 11 (23.0)	228 ± 20 (21.3)	256 ± 18 (23.9)
	2.0/1.0	1127 ± 13 (105.3)	695 ± 5 (65.0)	1457 ± 74 (136.2)
11	1.0/2.0	596 ± 43 (55.7)	413 ± 60 (38.6)	447 ± 11 (41.8)
	1.0/1.0	219 ± 16 (20.5)	213 ± 12 (19.9)	225 ± 44 (21.0)
	2.0/1.0	1893 ± 48 (176.9)	1160 ± 10 (109.3)	805 ± 17 (75.2)
control		1070 ± 10 (100.0)	1070 ± 10 (100.0)	1070 ± 10 (100.0)
spontaneous revertants		149 ± 20	149 ± 20	149 ± 20

[a,b] Descriptions are the same as in Table II.

genicity of heat-induced mutagens once caused remarkable concern about their actual involvement in carcinogenesis, but it seems gradually to be less serious than first thought due to their own weak carcinogenicity, their inactivation by other food components, and their low levels observed in actual food. Since the antimutagenicity of MRPs is observed in some amino acid and sugar systems, the actual role of heat-induced mutagens in carcinogenesis should be taken into account with regard to both food preparation and intake.

The effect of each reaction condition for xylose–lysine MRPs on the mutagenicity of IQ is discussed below. For the initial pH of reaction mixture, the MRPs prepared at pH 9.0 and 11.0 showed greater antimutagenicity and inhibited 90.2 and 89.0% of activity of IQ toward *S. typhimurium* TA98, respectively, but no significant difference was found in the antimutagenicity of these two combinations ($p < 0.05$). In addition, there was observed a marked decrease in antimutagenicity of MRPs prepared at pH 7.0 or 13.0. The greater antimutagenic effect in MRPs of xylose–lysine was prepared with molar ratio 1:1 at pH 7.0 within 10 h, and the greatest effect was found at 5 h. The antimutagenic effect of MRPs decreased with increasing of heating time over 10 h. For the molar ratios, it is evident that the greatest antimutagenic MRPs occurred in xylose–lysine with molar ratios 1:2 and 1:3 (88.4 and 91.8%), but no significant difference was found in the antimutagenicity of these two combinations ($p < 0.05$). However, the antimutagenic effect was over 75% for all of the samples.

Optimization of Reaction Conditions. A narrower range of level of each reaction condition was selected through defining levels of factors in Table I. The mutagenicity of all 27 MRPs toward *S. typhimurium* TA98 and TA100 was assayed by the Ames test. For the dose of 5 mg/plate, no mutagenicity and toxicity were found in all of the MRPs either with or without S9 mixture (data not shown). The inhibitory effect of all 27 MRPs on the mutagenicity of IQ toward *S. typhimurium* TA98 and TA100 is shown in Tables II and III, respectively. All of the xylose–lysine MRPs inhibited the mutagenicity of IQ toward *S. typhimurium* TA98 and TA100, but the degree of antimutagenic effect on IQ varied with test strains and reaction conditions for preparation of MRPs. For *S. typhimurium* TA98, combinations, including xylose–lysine molar ratio 1:2 at pH 7.0 for 15 h, at pH 9.0 for 5 and 10 h, and at pH 11.0 for 10 h, molar ratio 1:1 at pH 7.0 for 15 h, at pH 9.0 for 15 h, and at pH 11.0 for 10 h, and molar ratio 2:1 at pH 7.0 for 15 h, showed over 70% antimutagenicity to IQ. For strain TA100, nine combinations, including xylose–lysine molar ratio 1:2 at pH 9.0 for 10 h and molar ratio 1:1 at pH 7.0 for 5 h and at pH 9.0 and 11.0 for 5, 10, and 15 h, showed over 70% inhibitory effect of IQ. Comparing the results from both test strains showed that only three combinations, including xylose–lysine molar ratio 1:2 at pH 9.0 for 10 h and molar ratio 1:1 at pH 9.0 for 15 h and at pH 11.0 for 10 h, exhibited over 70% inhibitory effect to IQ in *S. typhimurium* TA98 and TA100. These three combinations for preparation of MRPs with greater antimutagenic effect occurred at an alkaline pH or lower xylose–lysine molar ratio. On the other hand, for the mutagenicity test, strain TA98 detected various frameshift mutagens but TA100 detected mutagens that cause base-pair substitutions (Maron and Ames, 1983). IQ induced both types of mutation mentioned (Matsukura et al., 1981; Ohgaki et al., 1984). This result indicates that

the antimutagenic compound(s) in xylose–lysine MRPs had properties of inhibition of both frameshift and base-pair mutation of IQ. However, the antimutagenic compound(s) in xylose–lysine MRPs may be complex and not a single compound because there is no clear correlation in the antimutagenicity of xylose–lysine MRPs on IQ by TA98 and TA100 from the above results ($r = 0.46431$, $n = 27$, $p < 0.05$).

In conclusion, the mutagenicity of IQ was reduced by all xylose–lysine MRPs, whereas the mutagenicity of NQNO was not affected, except one combination, and enhanced by some combinations. The antimutagenicity of MRPs may be due partially to the reactive substances in melanoidin which could scavenge the free radical, inactivate the mutagen, or inhibit the enzyme activity of S9 mixture. Three reaction condition combinations, including xylose–lysine molar ratio 1:2 at pH 9.0 for 10 h and molar ratio 1:1 at pH 9.0 for 15 h and at pH 11.0 for 10 h, exhibited over 70% inhibitory effect to IQ in *S. typhimurium* TA98 and TA100.

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LITERATURE CITED

Ames, B. N.; MacCann, J.; Yamasaki, E. Methods for detecting carcinogen and mutagens with the Salmonella/microsome mutagenicity test. *Mutat. Res.* **1975**, *31*, 347–364.

Ames, J. M. Control of the Maillard reaction in food system. *Trends Food Sci. Technol.* **1990**, *1*, 150–154.

Chan, R. I. M.; Stich, H. F.; Rosin, M. P.; Powrie, W. D. Antimutagenetic activity of browning reaction products. *Cancer Lett.* **1979**, *15*, 27–33.

Denely, J. P. Maillard reaction: Nonenzymatic browning in food system with special reference to the development of flavor. *Adv. Food Res.* **1985**, *30*, 77–138.

Duncan, D. B. Multiple range and multiple F test. *Biometrics* **1955**, *11*, 1–42.

Francis, A. R.; Shetty, T. K.; Bhattacharya, R. K. Modifying role of dietary factors on the mutagenicity of aflatoxin B1 in vitro effect of plant flavonoids. *Mutat. Res.* **1983**, *222*, 393–401.

Giovanni, M. Response surface methodology and product optimization. *Food Technol.* **1983**, *37*, 41–83.

Grivas, S.; Jagerstad, M. Mutagenicity of some synthetic quinolines and quinoxalines related to IQ, MeIQ, or MeIQx in Ames test. *Mutat. Res.* **1984**, *137*, 29–35.

Hayase, F.; Hirashima, S.; Okamoto, G.; Kato, H. Scavenging of active oxygen by melanoidins. *Agric. Biol. Chem.* **1989**, *53*, 3383–3385.

Jagerstad, M.; Grivas, S. The synthesis and mutagenicity of the 3-ethyl analogues of the potent mutagens IQ, MeIQ, MeIQx and its 3,7-dimethyl isomer. *Mutat. Res.* **1985**, *144*, 131–138.

Kato, H.; Kim, S. B.; Hayase, F.; Chuyen, N. V. Desmutagenicity of melanoidins against mutagenic pyrolysates. *Agric. Biol. Chem.* **1985**, *53*, 3383–3385.

Kim, S. B.; Hayase, F.; Kato, H. Desmutagenic effect of melanoidins against amino acid and protein pyrolysates. *Dev. Food Sci.* **1986**, *13*, 383–392.

Kong, Z. L.; Shinohara, K.; Mitsuiki, M.; Murakami, H.; Omura, H. Desmutagenicity of furan compounds towards some mutagens. *Agric. Biol. Chem.* **1989**, *53*, 2073–2079.

Maron, D. M.; Ames, B. N. Revised methods for the Salmonella mutagenicity test. *Mutat. Res.* **1983**, *113*, 173–215.

Matsukura, N.; Kawachi, T.; Morino, K.; Ohgaki, H.; Sugimura, T.; Takayama, S. Carcinogenicity in mice of mutagenic compounds from a tryptophan pyrolyzate. *Science* **1981**, *213*, 346–347.

Monnier, V. M. Toward a Maillard reaction theory of aging. In *The Maillard Reaction in Aging, Diabetes and Nutrition*; Baynes, J. W., Monnier, V. M., Eds.; Liss: New York, 1989; pp 1–12.

Nagao, M.; Sato, S.; Sugimura, T. Mutagens produced by heating foods. In *The Maillard Reaction in Food and Nutrition*; Waller, G. R., Feather, M. S., Eds.; ACS Symposium Series 215; American Chemical Society: Washington, DC, 1983; pp 521–536.

Namiki, M. Chemistry of Maillard reactions: Recent studies on the browning reaction mechanism and the development of antioxidants and mutagens. *Adv. Food Res.* **1988**, *32*, 115–184.

Obretenov, J. D.; Kuntcheva, M. J. Influence of the reaction conditions on the formation of nondialyzable melanoidines from D-glucose and L-amino acids. *J. Food Process. Preserv.* **1990**, *14*, 309–324.

O'Brien, J.; Morrissey, P. A. Nutritional and toxicological aspects of the Maillard browning reaction in foods. *Crit. Rev. Food Sci. Nutr.* **1989**, *28*, 211–248.

Ohgaki, H.; Kusama, K.; Matsukura, N.; Morino, K.; Hasegawa, H.; Sato, S.; Takayama, S.; Sugimura, T. Carcinogenicity in mice of a mutagenic compound, 2-amino-3-methylimidazo (4,5-f) quinoline, from broiled sardine, cooked beef and beef extract. *Carcinogenesis* **1984**, *5*, 921–924.

Okamoto, T.; Shudo, K.; Hashimoto, Y.; Kosuge, T.; Sugimura, T.; Nishimura, S. Identification of a reactive metabolite of the mutagen, 2-amino-3-methylimidazo (4,5-f) quinoline. *Chem. Pharm. Bull.* **1981**, *29*, 590–593.

Reynolds, T. M. Chemistry of nonenzymic browning. I. *Adv. Food Res.* **1963**, *12*, 1–52.

Yamaguchi, T.; Iki, M. Inhibitory effect of coffee extract against some mutagens. *Agric. Biol. Chem.* **1986**, *50*, 2983–2988.

Yen, G. C.; Tsai, L. C.; Lii, J. D. Antimutagenic effect of Maillard browning products obtained from amino acids and sugars. *Food Chem. Toxicol.* **1992**, in press.

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