Possible Mechanisms of Antimutagenic Effect of Maillard Reaction Products Prepared from Xylose and Lysine

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Possible mechanisms of antimutagenicity of Maillard reaction products (MRPs) prepared by heating xylose and lysine (molar ratio 1:2) at pH 9.0 and 100 °C for 1 h were investigated using a *Salmonella*/microsome assay. The mutagenicity of 2-amino-3-methylimidazo[4,5-*f*]quinoline (IQ) was markedly reduced by the addition of xylose–lysine MRPs toward *Salmonella typhimurium* TA98 and TA100, whereas the mutagenicity of 4-nitroquinoline *N*-oxide was not inhibited. The xylose–lysine MRPs exhibited no inhibitory activity to IQ on the bioantimutagenic assay; this result indicated that the antimutagenic effect of xylose–lysine MRPs is a desmutagenic action, not by modification of DNA repair processes in the bacterium cell. According to further study to elucidate the antimutagenic mechanisms of action, xylose–lysine MRPs reduced the mutagenicity of IQ by interaction with proximate metabolites of IQ, not by direct inhibition of hepatic microsomal activation. The mutagenicity of IQ was decreased by increasing reaction periods between xylose–lysine MRPs and IQ metabolites, but with neither S9 mixture, intact IQ, or DNA. In conclusion, the antimutagenic effects of xylose–lysine MRPs to IQ might be due to interaction with proximate metabolites of IQ to form inactive adducts.

INTRODUCTION

The Maillard reaction, between carbonyl and amino compounds, is an important reaction that occurs in foods during processing and storage. Numerous reviews of this reaction from various aspects of foods are available (Namiki, 1988; Monnier, 1989; O'Brien and Morrissey, 1989). Amino acids and sugars were used to study the antimutagenicity of Maillard reaction products (MRPs) in model systems (Chan et al., 1979; Kato et al., 1985; Yamaguchi, and Iki, 1986; Kong et al., 1989; Yen et al., 1992). Antimutagenic compounds in MRPs remain incompletely understood. The antimutagenic activity of MRPs may be due partially to reactive substances in melanoidin that scavenge free radicals, inactivate the mutagen, or inhibit enzyme activity of the S9 mixture (Kim et al., 1986; Hayase et al., 1989). We (Yen et al., 1992; Yen and Lii, 1992b) demonstrated the antimutagenic effect of MRPs to correlate well with their antioxidative activity and reducing power.

Antimutagens are classified into desmutagens and bioantimutagens according to modes of action (Kada et al., 1985). The former inactivates mutagens by chemical or enzymatical modifications, whereas the latter suppresses the process of mutagenesis (mutation fixation) after DNA is damaged by mutagens. Yen and Tsai (1993) indicated that the inhibitory effect of glucose–tryptophan MRPs is due to a desmutagenic effect, not a bioantimutagenic effect. The role of MRPs in the inhibition of mutagenicity induced by mutagens at the microsomal activation step, by direct interaction with proximate metabolites of mutagens, or by modification of DNA metabolism remains unclear.

The objective of this study was to investigate the possible mechanisms of antimutagenicity of Maillard reaction products prepared from xylose and lysine.

MATERIALS AND METHODS

Materials. D-Xylose, L-lysine monohydrochloride, and 7,8-benzoflavone 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). All other reagents used were of guaranteed grade.

Preparation of Xylose–Lysine Maillard Reaction Products (XL MRPs). The XL MRPs was prepared by dissolving D-xylose (0.1 mol) and L-lysine monohydrochloride (0.2 mol) in potassium phosphate buffer (0.1 M, pH 9.0), adjusted to 100 mL, and then refluxed in an oil bath at 100 °C for 1 h. After reaction, the XL MRPs were freeze-dried and stored at −20 °C until use.

Assay for Antimutagenic Effects. The antimutagenic effect of XL MRPs was examined according to the Ames method (Maron and Ames, 1983). *Salmonella typhimurium* TA98 and TA100 were supplied by Professor B. N. Ames (University of California, Berkeley, CA). The S9 mix was prepared from Sprague-Dawley male rats treated with Aroclor 1254 (Organ Teknika Co., Switzerland). The mutagens used were the direct-acting mutagen 4-nitroquinoline *N*-oxide (NQNO) (1 μg/plate for TA98 and 0.1 μg/plate for TA100) and IQ (0.1 μg/plate for TA98 and 0.5 μg/plate for TA100), which requires the S9 mix for metabolic activation. Mutagen (0.1 mL) was added to the mixture cultured overnight of *S. typhimurium* TA98 or TA100 (0.1 mL), XL MRPs (0–5 mg), and S9 mix (0.5 mL). The entire mixture was preincubated at 37 °C for 20 min before molten top agar (2 mL) was added; the mixture was poured onto a minimal agar plate. The His+ revertant colonies were counted after incubation 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 dosage of XL MRPs (<5 mg/plate) exhibited no mutagenicity and no lethal effect to the bacteria. The mutagenicity of each mutagen in the absence of the Maillard reaction product was expressed as 100. A smaller percentage of revertants of samples to the revertants of control indicates stronger antimutagenicity of sample (Francis et al., 1989).

Bioantimutagenicity Assay. The bioantimutagenicity test was conducted as described by Sato et al. (1987). *S. typhimurium* TA98 and TA100 were cultured overnight. A bacterial suspension (5 mL) was washed twice by means of centrifugation with a cold $^1/_{15}$ M phosphate buffer (PB) at pH 7.0 and resuspended in cold PB (4 mL). To this bacterial suspension (3 mL) were added 5 μg of IQ/0.5 mL for TA98, 50 μg of IQ/0.5 mL for TA100, and S9 mix (3 mL), and the mixture was incubated at 37 °C for 1 h with slow shaking. The treated bacteria were washed twice with centrifugation with cold PB and resuspended in cold PB. The Ames tests were performed with or without XL MRPs on the treated bacteria. The amount of XL MRPs was 2.0 mg/plate.

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0021-8561/94/1442-0133$04.50/0

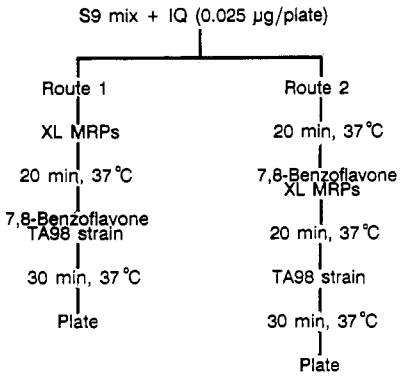

Figure 1. Effect of xylose–lysine Maillard reaction products (XL MRPs) on the hepatic microsomal activation of IQ.

Another volume (1 mL) of the bacterial suspension was used to determine spontaneous mutation.

Effect of XL MRPs on the Hepatic Microsomal Activation of IQ. The two experimental protocols to study the effects of XL MRPs on the hepatic microsomal activation of IQ were designed by Alldrick and Rowland (1988) and adapted to our optimal assay conditions (Figure 1). In the first experiment, IQ (0.025 μg/plate), S9 mix (0.5 mL), and XL MRPs (0.5–4 mg/plate) were incubated together at 37 °C for 20 min. Overnight-cultured TA98 (0.1 mL) and 7,8-benzoflavone (10 μg/plate) were added to the reaction mixture, and the assay was performed as described for the antimutagenicity test (Figure 1, route 1). In the second experiment, the procedure was slightly modified. IQ and S9 mix were incubated together for 20 min; XL MRPs and 7,8-benzoflavone were then added, and the mixture was incubated for another 20 min. Finally, overnight-cultured TA98 (0.1 mL) was added to the reaction mixture and the assay was performed as before (Figure 1, route 2).

Effects of XL MRPs on the Hepatic Microsomal Enzyme, IQ, IQ Metabolites, and *S. typhimurium* Strain TA98. To evaluate the effects of XL MRPs on the S9 mix, IQ, IQ metabolites, and strain TA98, we performed experiments according to the methods of Gichner et al. (1987) and Aryton et al. (1992) by reaction of XL MRPs with the above factors. To investigate the effect of XL MRPs on the S9 mix, XL MRPs (0.1 mL, 2 mg/plate) and S9 mix (5 mL) were preincubated together at 37 °C for 0, 10, 20, or 40 min. Overnight-cultured TA98 (0.1 mL) and IQ (0.1 mL, 0.1 μg/plate) were then added, and the mixture was incubated at 37 °C for another 20 min; the assay was performed as before. To examine the effect of XL MRPs on the intact IQ, XL MRPs (0.1 mL, 2 mg/plate) and IQ (0.1 mL, 0.1 μg/plate) were incubated together at 37 °C for 0, 10, 20, or 40 min. Overnight-cultured TA98 (0.1 mL) and S9 mix (0.5 mL) were then added, and the mixture was incubated at 37 °C for another 20 min; the assay was performed as before. To study the effect of XL MRPs on IQ metabolites, S9 mix (5 mL) and IQ (0.1 mL, 0.1 μg/plate) were preincubated together at 37 °C for 20 min. XL MRPs (0.1 mL, 2 mg/plate) was then added, and the mixture was incubated for 0, 10, 20, or 40 min. Finally, overnight-cultured TA98 (0.1 mL) was added, and the mixture was incubated at 37 °C for another 20 min; then the assay was performed as before. To discover the effect of XL MRPs on strain TA98, overnight-cultured TA98 (5 mL) and XL MRPs (5 mL) were incubated together at 37 °C for 1 h. The bacteria were washed three times with nutrient broth with centrifugation (6000 rpm, 20 °C, 10 min). Finally, treated TA98 (0.1 mL), IQ (0.1 mL, 0.1 μg/plate), and S9 mix (0.5 mL) were incubated together at 37 °C for another 20 min, and then the assay was performed as before.

Statistical Analysis. The correlation between antimutagenicity and the characteristics of the Maillard reaction product was calculated according to Duncan's multiple range test (Duncan, 1955).

RESULTS AND DISCUSSION

Antimutagenic Effect of XL MRPs. The mutagenicity of XL MRPs was evaluated in the preliminary tests. No mutagenicity was found for XL MRPs in a dosage less than 5 mg/plate toward *S. typhimurium* TA98 and TA 100 either with or without S9 mix; as a result, the revertants of the sample were less than twice that of spontaneous revertants (data not shown). This dosage was therefore used for further study of antimutagenicity of XL MRPs. Two mutagens, direct-acting mutagen NQNO and indirect-acting mutagen IQ, were used to evaluate the antimutagenic activity of XL MRPs; the results are shown in Table 1. No antimutagenic activity was found for XL MRPs to NQNO in *S. typhimurium* TA98 and TA100 without S9 mix at the dosage of 0.5–5 mg/plate. However, the mutagenicity of NQNO was enhanced by increasing concentration of XL MRPs toward *S. typhimurium* TA100. The mutagenicity of IQ toward both TA98 and TA100 with S9 mix was decreased with increasing concentration of XL MRPs. The inhibitory effect of XL MRPs on the mutagenicity of IQ toward TA98 was stronger than that toward TA100. The antimutagenic activity of XL MRPs to IQ was slightly weaker than that reported by Yen and Lii (1992a); this result might be due to the heating period of preparation of XL MRPs that was only 1 h in this work.

Bioantimutagenic Effect of XL MRPs. The bioantimutagenic effect of XL MRPs on the mutagenicity of IQ is shown in Table 2. The results indicate that the mutagenicity of IQ to TA98 and TA100 was not decreased by XL MRPs in the bioantimutagenic test. This result is similar to that reported by Yen and Tsai (1993), which indicated that the inhibitory mechanism of glucose–tryptophan MRPs was due to a desmutagenic effect, not a bioantimutagenic effect. Hence, the XL MRPs may directly inactivate mutagen or metabolic enzyme to inhibit mutagenicity before the DNA reacted with mutagen. The DNA was not repaired by treatment with XL MRPs when it was damaged by IQ. The antimutagenicity of XL MRPs on IQ is the desmutagenic effect, not the bioantimutagenic effect. The desmutagenic effect of XL MRPs might be due to inactivation of hepatic microsomal enzymes, or chemical modification of mutagen metabolites, or modification of DNA, etc. Further study was conducted to clarify these points.

Effect of XL MRPs on the Hepatic Microsomal Activation of IQ. To investigate at what level XL MRPs inhibit IQ mutagenicity (e.g., at the microsomal activation level or by direct interaction with proximate metabolites of IQ), we performed experiments as described in Figure 1 modified from the study of Alldrick and Rowland (1988). 7,8-Benzoflavone was added to the preincubated mixture of S9 mix, IQ, and XL MRPs to show the effect of microsomal activation (Figure 1, route 1). Adding XL MRPs and 7,8-benzoflavone together after preincubation of S9 mix with IQ (Figure 1, route 2) demonstrated the direct interaction of XL MRPs with the proximate metabolites of IQ.

Because 7,8-benzoflavone can inactivate cytochrome P-450 in S9 mix and inhibit mutagenicity of IQ (Kato and Yamazoe, 1987), we used it to inactivate the S9 mix. At the beginning, the concentration of 7,8-benzoflavone for inactivation of S9 activity was evaluated; the results appear in Table 3. About 95% of mutagenicity of IQ was inhibited by 7,8-benzoflavone at the concentration 5–20 μg/plate, and no toxicity was found at the concentration 20 μg/plate. Thus, 7,8-benzoflavone at the concentration 10 μg/plate was used in the test.

The inhibitory effect of XL MRPs on the mutagenicity of IQ through these two routes is shown in Table 4. In general, there are similar inhibitory effects for XL MRPs on IQ through these two routes ($P > 0.05$). Thus, we predict

Table 1. Effect of Xylose–Lysine Maillard Reaction Products (XL MRPs) on the Mutagenicity of NQNO and IQ toward *S. typhimurium* TA98 and TA100

XL MRPs[a] (mg/plate)	NQNO		IQ	
	TA98	TA100	TA98	TA100
0.5	646 ± 16 (110.8)[b]	970 ± 19 (94.7)	2911 ± 63 (86.2)*	1308 ± 69 (101.6)
1	628 ± 53 (107.7)	910 ± 56 (88.9)	2868 ± 24 (84.9)*	1257 ± 107 (97.6)
2	570 ± 40 (97.8)	1140 ± 37 (111.3)	2288 ± 84 (67.7)*	1006 ± 95 (78.1)*
4	562 ± 30 (96.5)	1200 ± 24 (117.1)*	1848 ± 53 (54.7)*	943 ± 38 (73.2)*
5	580 ± 35 (99.6)	1423 ± 46 (138.9)*	1127 ± 48 (33.4)*	910 ± 8 (70.7)*
control	583 ± 17 (100.0)	1021 ± 63 (100.0)	3376 ± 123 (100.0)	1287 ± 147 (100.0)
spontaneous revertants	38 ± 6	151 ± 18	52 ± 5	179 ± 12

[a] Samples were prepared by refluxing 1.0 M xylose and 2.0 M lysine at pH 9.0 and 100 °C for 1 h. [b] His+ revertants/plate (percentage relative to control value). NQNO (1 μg/plate for TA98; 0.1 μg/plate for TA100) and IQ (0.1 μg/plate for TA98; 0.5 μg/plate for TA100) were preincubated with XL MRPs 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 three plates. Those marked with asterisks show significant differences compared with the corresponding control value ($P < 0.05$).

Table 2. Bioantimutagenic Effect of Xylose–Lysine Maillard Reaction Products (XL MRPs) on IQ Activation to *S. typhimurium* TA98 and TA100 in the Presence of S9 Mix

IQ (μg/plate)	XL MRPs[a] (mg/plate)	His+ revertants/plate[b]	
		TA98	TA100
10	0	1382 ± 55 (100.0)A[c]	
10	2	1489 ± 48 (107.6)A	
50	0		488 ± 22 (100.0)A
50	2		416 ± 28 (85.2)A
spontaneous revertants		43 ± 6	193 ± 5

[a] Samples were prepared by refluxing 1.0 M xylose and 2.0 M lysine at pH 9.0 and 100 °C for 1 h. [b] Spontaneous revertants were obtained without IQ and MRPs. Data are means ± SD of three plates. Values in parentheses are percentages relative to control value (100%). [c] Values in a column with the same upper case letters are not significantly different ($P > 0.05$).

Table 3. Effect of Concentration of 7,8-Benzoflavone on the Hepatic Metabolic Activation of IQ

7,8-benzoflavone (μg/plate)	His+ revertants/plate[a] TA98
0	1367 ± 110 (100.0)[b]
5	78 ± 17 (5.7)
10	74 ± 10 (5.4)
15	80 ± 16 (5.8)
20	69 ± 1 (5.0)
spontaneous revertants	39 ± 2

[a] Experiment conditions: IQ (0.025 μg/plate); S9 mix (0.5 mL); *S. typhimurium* TA98 (0.1 mL); preincubation time, 20 min. Spontaneous revertants were determined without IQ and 7,8-benzoflavone. Values are means ± SD of three plates. [b] Values in parentheses are percentages relative to control value (100%).

that the antimutagenic activity of XL MRPs on IQ was not due to inactivation of the S9 mix. Alldrick and Rowland (1988) indicated that the antimutagenicity of caffeine was due to inactivation of S9 mix, as the inhibitory effect was found only in route 1, not in route 2. However, XL MRPs probably interact directly with proximate metabolites of IQ, as the result indicated that XL MRPs added after preincubation of IQ with S9 mix decreased the mutagenicity of IQ (route 2).

Effects of XL MRPs on the Hepatic Microsomal Enzymes, IQ, IQ Metabolites, and *Salmonella typhimurium* Strain. To elucidate the actual desmutagenic effect of XL MRPs, we preincubated XL MRPs with S9 mix, intact IQ, IQ metabolites, and *S. typhimurium* strain for various periods. Table 5 shows the inhibitory effect of XL MRPs on the mutagenicity of IQ by preincubation with S9 mix for various periods. In the control group, the mutagenicity of IQ was increased with increasing preincubation period with S9 mix up to 20 min. When the S9

Table 4. Effect of Xylose–Lysine Maillard Reaction Products (XL MRPs) on the Hepatic Metabolic Activation of IQ

XL MRPs[a] (mg/plate)	His+ revertants/plate[b]	
	route 1	route 2
control	1178 ± 204 (100.0)A[c]	1085 ± 65 (100.0)A
0.5	949 ± 53 (80.5)A	943 ± 92 (86.9)A
2	772 ± 49 (65.5)A	527 ± 52 (48.5)A
4	234 ± 30 (19.8)A	252 ± 38 (23.2)A

[a] Samples were prepared by refluxing 1.0 M xylose and 2.0 M lysine at pH 9.0 and 100 °C for 1 h. [b] Experiments are performed according to Figure 1. Control plates were with IQ but without MRPs. Spontaneous revertants were determined without IQ and MRPs. Data are means ± SD of three plates. Values in parentheses are percentage relative to control value (100%). [c] Values in a row with the same upper case letters are not significantly different ($P > 0.05$).

Table 5. Effect of Preincubation of S9 Mix with Xylose–Lysine Maillard Reaction Products (XL MRPs)[a] for Various Periods on the Mutagenicity of IQ

incubation time[b] (min)	His+ revertants/plate[c]		% of control
	control	XL MRPs	
0	1421 ± 95A[d]	579 ± 87A	40.7A
10	1832 ± 140B	731 ± 84B	39.9A
20	2482 ± 155C	955 ± 41B	38.4A
40	2658 ± 11C	1063 ± 43B	39.9A
spontaneous revertants	40 ± 2	40 ± 2	

[a] Samples were prepared by refluxing 1.0 M xylose and 2.0 M lysine at pH 9.0 and 100 °C for 1 h. [b] The XL MRPs (2 mg/plate) were preincubated with S9 mix at 37 °C for various periods and then mixed with IQ (0.1 μg/plate) and *S. typhimurium* TA98 and incubated at 37 °C for an additional 20 min. [c] Results are presented as means ± SD for three plates. The number of IQ-induced revertants in the absence of XL MRPs (control group) was expressed as 100%. [d] Values in a column with different upper case letters are significantly different ($P < 0.05$).

mix was preincubated with XL MRPs for 0–40 min, the inhibitory effect of XL MRPs on the mutagenicity IQ was about 60%; it was not increased with the preincubation period. If XL MRPs inhibited the activation of the S9 mix, the mutagenicity of IQ would decrease with increasing preincubation period. Therefore, according to this result and the data in Table 4, the antimutagenic effect of XL MPRs is confirmed not to be due to inactivation of activity of hepatic microsomal enzymes.

Table 6 shows the inhibitory effect of XL MRPs on the mutagenicity of IQ by preincubation of XL MRPs with IQ for various periods. About 50% of mutagenicity of IQ was decreased by added XL MRPs; however, the inhibitory effect of XL MRPs on the mutagenicity of IQ was not increased with increasing preincubation period of XL MRPs with IQ. Gichner et al. (1987) indicated that the mutagenicity of *N*-methyl-*N'*-nitro-*N*-nitrosoguanidine

Table 6. Effect of Preincubation of IQ with Xylose–Lysine Maillard Reaction Products (XL MRPs)[a] for Various Times on the Mutagenicity of IQ

incubation time[b] (min)	His+ revertants/plate[c] control	His+ revertants/plate[c] XL MRPs	% of control
0	1814 ± 18A[d]	875 ± 128A	48.2A
10	2290 ± 130B	1107 ± 112AB	48.3A
20	2580 ± 193B	1287 ± 167B	49.8A
40	2647 ± 195B	1319 ± 24B	49.8A
spontaneous revertants	40 ± 2	40 ± 2	

[a] Samples were prepared by refluxing 1.0 M xylose and 2.0 M lysine at pH 9.0 and 100 °C for 1 h. [b] The XL MRPs (2 mg/plate) were preincubated with IQ (0.1 μg/plate) at 37 °C for various periods and then mixed with S9 mix and *S. typhimurium* TA98 and incubated at 37 °C for an additional 20 min. [c] Results are presented as means ± SD for three plates. The number of IQ-induced revertants in the absence of XL MRPs (control group) was expressed as 100%. [d] Values in a column with different upper case letters are significantly different ($P < 0.05$).

Table 7. Effect of Xylose–Lysine Maillard Reaction Products (XL MRPs)[a] on the Mutagenicity of IQ Which was Preincubated with S9 Mix for Various Times

incubation time[b] (min)	His+ revertants/plate[c] control	His+ revertants/plate[c] XL MRPs	% of control
0	2690 ± 25A[d]	2348 ± 140A	87.2A
10	2807 ± 107A	2120 ± 144AB	75.5AB
20	3048 ± 26AB	2080 ± 200AB	68.2BC
40	3205 ± 244B	1879 ± 205B	59.1C
spontaneous revertants	40 ± 2	40 ± 2	

[a] Samples were prepared by refluxing 1.0 M xylose and 2.0 M lysine at pH 9.0 and 100 °C for 1 h. [b] The IQ (0.1 μg/plate) was preincubated with S9 mix at 37 °C for various periods and then mixed with XL MRPs and *S. typhimurium* TA98 and incubated at 37 °C for an additional 20 min. [c] Results are presented as means ± SD for three plates. The number of IQ-induced revertants in the absence of XL MRPs (control group) was expressed as 100%. [d] Values in a column with different upper case letters are significantly different ($P < 0.05$).

was reduced by preincubation with *p*-aminobenzoic acid for 0–60 min. If the XL MRPs could interact with or modify IQ, the mutagenicity of IQ would be decreased with increasing preincubation period. Our test clearly indicated that intact IQ did not directly interact with XL MRPs to diminish its mutagenicity.

The inhibitory effect of XL MRPs on the mutagenicity of IQ preincubated with S9 mix for various periods is shown in Table 7. In the control group (without added XL MRPs), the mutagenicity of IQ increased with increasing preincubation period (0–40 min). This result might be due to the fact that the content of IQ metabolites increased with the preincubation period. It also can be found that 22.8–40.9% mutagenicity of IQ metabolites was inhibited following reaction with XL MRPs. The inhibitory effect of XL MRPs on proximate metabolites of IQ was significantly ($P < 0.05$) increased with increasing period of incubation. Therefore, the antimutagenic effect of XL MRPs on IQ is clearly attributed to interaction between XL MRPs and IQ metabolites to form inactivate adducts.

When the bacteria (TA98) were exposed to XL MRPs at various concentrations and the XL MRPs were subsequently removed by washing with fresh nutrient broth before interaction with IQ, no decreased mutagenic response was observed (Table 8). This result indicated that XL MRPs may not interact with DNA in such a way as to protect it from the ultimate mutagen. A possible mechanism of the antimutagenic action of ellagic acid involves direct interaction with DNA or masking the

Table 8. Mutagenicity of IQ to Bacteria Treated with Xylose–Lysine Maillard Reaction Products (XL MRPs)

XL MRPs[a] (mg/plate)	His+ revertants/plate[b]	% of control
0	1533 ± 86	100.0A[c]
0.5	1544 ± 98	100.7A
2.0	1402 ± 85	91.4A
4.0	1508 ± 119	98.3A
spontaneous revertants	39 ± 5	

[a] Samples were prepared by refluxing 1.0 M xylose and 2.0 M lysine at pH 9.0 and 100 °C for 1 h. [b] *S. typhimurium* TA98 and XL MRPs were preincubated at 37 °C for 1 h. The bacteria were then washed three times with nutrient broth and were then mixed with IQ (0.1 μg/plate) and S9 mix at 37 °C for 20 min. Results are presented as means ± SD for three plates. [c] The number of IQ-induced revertants in the absence of XL MRPs (control group) was expressed as 100%. Values in a column with the same upper case letters are not significantly different ($P > 0.05$).

mutagen-binding sites of DNA that result in its protection from mutagens (Teel, 1986).

Conclusions. On the basis of the results of this study, it can be concluded that the antimutagenicity of XL MRPs on IQ is a desmutagenic effect, not a bioantimutagenic effect. The antimutagenic mechanism of XL MRPs on IQ is attributed to the interaction of XL MRPs with proximate IQ metabolites to form inactive adducts, not to inhibition of the activity of hepatic microsomal enzymes, direct reaction with intact IQ, or interaction with DNA.

ACKNOWLEDGMENT

This research work was partially supported by the National Science Council, Republic of China, under Grant NSC 81-0409-B005-515.

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Received for review June 8, 1993. Accepted October 18, 1993.[⊛]

[⊛] Abstract published in *Advance ACS Abstracts,* December 1, 1993.