Lycopene Intake Facilitates the Increase of Bone Mineral Density in Growing Female Rats

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Summary Intake of the antioxidant lycopene has been reported to decrease oxidative stress and have beneficial effects on bone health. However, few in vivo studies have addressed these beneficial effects in growing female rodents or young women. The aim of this study was to investigate the effect of lycopene intake on bone metabolism through circulating oxidative stress in growing female rats. Six-week-old Sprague-Dawley female rats were randomly divided into 3 groups according to the lycopene content in their diet: 0, 50, and 100 ppm. The bone mineral density (BMD) of the lumbar spine and the tibial proximal metaphysis increased with lycopene content in a dose-dependent manner; the BMD in 100 ppm group was significantly higher than in the 0 ppm group. The urine deoxypyridinoline concentrations were significantly lower in the 50 and 100 ppm groups than in the 0 ppm group, and the serum bone-type alkaline phosphatase activity was significantly higher in 100 ppm group than in the 0 ppm group. No difference in systemic oxidative stress level was observed; however, the oxidative stress level inversely correlated with the tibial BMD. Our findings suggested that lycopene intake facilitates bone formation and inhibits bone resorption, leading to an increase of BMD in growing female rats.

Key Words lycopene intake, bone mineral density, bone resorption, bone formation, oxidative stress

Maximizing peak bone mass at a young age is important in the primary prevention of osteoporosis (1). The bone is a dynamic organ with well-regulated turnover that is governed by bone resorption by osteoclasts and formation by osteoblasts. Proper balance between bone resorption and formation is crucial for bone integrity (2). It has been reported that reactive oxygen species (ROS), such as hydrogen peroxide and singlet oxygen, are involved in accelerating osteoclast differentiation and bone resorption (3, 4). In addition, an excess of ROS has been shown to inhibit osteoblast differentiation and proliferation (5, 6). Therefore, the elimination of excessive ROS is an effective approach for maintaining bone integrity (7).

Oxidative stress is described by an imbalance between ROS production and the capacity of intravital antioxidant defenses (8). Oxidative stress markers, such as Reactive Oxygen Metabolites-derived compounds (d-ROMs) and malondialdehyde, reflect intravital redox balance, and the assessment of these markers seems to be convenient and reliable with respect to their stability and diversity (9, 10). In addition, the test for d-ROMs evaluates the oxidative stress level by determining the concentration of organic hydroperoxides such as lipid hydroperoxides (11, 12), and has been used as a simple clinical oxidative stress marker in both animal and human serum (13, 14).

The intake of antioxidants is an effective way to eliminate excessive ROS. Lycopene, a carotenoid found mainly in tomatoes and tomato products, is a potent antioxidant whose singlet-oxygen-scavenging capacity is 100 times greater than that of α-tocopherol, a well-known dietary antioxidant (15). Mackinnon et al. showed that lycopene supplementation significantly decreased oxidative stress markers and a bone resorption marker in postmenopausal women (16). Moreover, cellular studies demonstrated that lycopene inhibited the differentiation and ROS production of osteoclasts (17) and stimulated the growth and differentiation of osteoblast-like cells (18). However, the effects of lycopene intake on the bone metabolism of young female subjects, such as growing female rodents or young women, have never been investigated. The maximization of peak bone mass at a young age for prospective skeletal health is essential for the prevention of osteoporosis.

In this study, we investigated the effects of lycopene intake on bone mineral density, bone strength, bone...
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The following procedures were approved by the Animal Experimental Committee of the University of Tsukuba.

Animals and feeding protocols. Twenty-four 6-wk-old female Sprague-Dawley (SD) rats were randomly divided into 3 groups according to the lycopene content in their diet, which was set at 0 (n = 8), 50 (n = 8), or 100 (n = 8) mg/kg (ppm). The 50 ppm dose of lycopene was chosen on the basis of previous studies in rodents (19–21). The higher dose, 100 ppm, was used to potentially obtain more marked effects of lycopene intake. To date, no deleterious effect of continuous lycopene administration has been reported in animal studies that adopted higher lycopene doses than those in the present study. The 50 ppm dose of lycopene was chosen on the basis of previous studies in rodents (19–21). The higher dose, 100 ppm, was used to potentially obtain more marked effects of lycopene intake. To date, no deleterious effect of continuous lycopene administration has been reported in animal studies that adopted higher lycopene doses than those in the present study.

Materials and Methods

Animals and feeding protocols. Twenty-four 6-wk-old female Sprague-Dawley (SD) rats were randomly divided into 3 groups according to the lycopene content in their diet, which was set at 0 (n = 8), 50 (n = 8), or 100 (n = 8) mg/kg (ppm). The 50 ppm dose of lycopene was chosen on the basis of previous studies in rodents (19–21). The higher dose, 100 ppm, was used to potentially obtain more marked effects of lycopene intake. To date, no deleterious effect of continuous lycopene administration has been reported in animal studies that adopted higher lycopene doses than those in the present study (22, 23). The diet composition is described in Table 1. Lycopene was incorporated into the diet as a tomato extract containing 6% lycopene, Lyc-O-Mato 6% was dissolved in cottonseed oil and incorporated into the diet. Lyc-O-Mato 6% (in %): lycopene, 6.00; 

<table>
<thead>
<tr>
<th>Constituents</th>
<th>Control diet (0.3% Ca, 0.3%P)</th>
<th>Lycopene diets (0.3% Ca, 0.3%P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose monohydrate</td>
<td>64.621</td>
<td>64.621</td>
</tr>
<tr>
<td>Casein</td>
<td>18</td>
<td>18</td>
</tr>
<tr>
<td>Cystine</td>
<td>0.2</td>
<td>0.2</td>
</tr>
<tr>
<td>Cottonseed oil</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>CaCO3</td>
<td>0.740</td>
<td>0.740</td>
</tr>
<tr>
<td>KH2PO4</td>
<td>0.501</td>
<td>0.501</td>
</tr>
<tr>
<td>K2HPO4</td>
<td>0.641</td>
<td>0.641</td>
</tr>
<tr>
<td>Roughage</td>
<td>3.0</td>
<td>3.0</td>
</tr>
<tr>
<td>Choline chloride</td>
<td>0.2</td>
<td>0.2</td>
</tr>
<tr>
<td>Water-soluble vitamin mixture</td>
<td>0.1</td>
<td>0.1</td>
</tr>
<tr>
<td>Oil-soluble vitamin mixture</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Ca/P-free salt mix</td>
<td>2</td>
<td>50 or 100</td>
</tr>
</tbody>
</table>

1 The water-soluble vitamin mixture (in %): thiamine, 0.5; riboflavin, 0.5; pyridoxine, 0.5; calcium pantothenate, 2.8; nicotinamide, 2.0; inositol, 20.0; folic acid, 0.02; vitamin B12, 0.002; biotin, 0.01; and glucose monohydrate, 73.7.

2 The rats received a supplement of fat-soluble vitamins in cottonseed oil three times a week which consisted of 70 μg of β-carotene, 105 μg of 2-methyl-1,4-naphthoquinone, 875 μg of α-tocopherol and 525 I.U. of vitamin D3.

Table 1. Compositions of the experimental diets (g/100 g diet).

Lycopene intake would facilitate an increase in bone mass by alleviating oxidative stress in growing female rats.

Serum and tissue sampling. At the end of the experimental period, all rats were fasted overnight. The following day, after anesthesia with diethyl ether, blood samples were taken from the abdominal aorta. The blood samples were centrifuged at 2,500 rpm for 15 min at 4°C to extract serum. Livers were extirpated after blood collection. Immediately after measuring the liver weight, they were frozen with liquid nitrogen. Serum and liver samples were stored at −80°C. The lumbar spine, tibiae and femur of each rat were isolated by dissection, and freed from adjacent soft tissue. The lumbar spine and tibiae were preserved in 70% ethanol.

Lycopene analysis. Serum and hepatic lycopene were determined with slight modification of a previous study (24, 25). Approximately 0.25 mg liver was homogenized in 2 mL absolute ethanol containing 1 g/L butylated hydroxytoluene with a homogenizer (Three-One Motor BL3000, Shinto Scientific Co., Ltd., Tokyo, Japan). The homogenate was saponified by addition of 0.5 mL saturated KOH for 30 min at 70°C. The sample cooled to room temperature was washed with 1 mL distilled water and extracted three times with 3 mL n-hexane. The hexane extract was filled up to 10 mL with n-hexane. One milliliter of the extract was evaporated to dryness under nitrogen at approximately 40°C, dissolved with 50 μL tetrahydrofuran (THF) and supplemented with 150 μL methanol. Finally, 100 μL of the last solution was injected into the high-performance liquid chromatography (HPLC) system. Two milliliters of serum sample was also supplemented with distilled water and extracted with n-hexane. The hexane extract was evaporated to dryness, dissolved and injected into the HPLC system as well as the liver samples. The HPLC system consisted of a DG-980-50 3-Line Degasser, LG-980-02 Ternary Gradient Unit, PU-980 Intelligent HPLC pump and UV-970.
Lycopene Intake and Bone or Oxidative Stress

Table 2. Body weight, food intake, food efficiency, and liver lycopene content.

<table>
<thead>
<tr>
<th>Lycopene content (ppm in diet)</th>
<th>0</th>
<th>50</th>
<th>100</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>8</td>
<td>8</td>
<td>8</td>
</tr>
<tr>
<td>Final body weight (g)</td>
<td>293.88±5.06</td>
<td>296.75±8.85</td>
<td>319.0±10.3</td>
</tr>
<tr>
<td>Body weight gain (g/d)</td>
<td>2.30±0.12</td>
<td>2.31±0.13</td>
<td>2.70±0.2</td>
</tr>
<tr>
<td>Food intake (g/d)</td>
<td>15.15±0.56</td>
<td>15.92±0.74</td>
<td>16.80±0.6</td>
</tr>
<tr>
<td>Food efficiency</td>
<td>0.15±0.01</td>
<td>0.15±0.01</td>
<td>0.16±0.01</td>
</tr>
<tr>
<td>Liver lycopene content (×10⁻² μmol/g tissue)</td>
<td>N.D.²</td>
<td>1.99±0.14</td>
<td>2.85±0.16</td>
</tr>
</tbody>
</table>

¹ Food efficiency was calculated as body weight gain (g/d)/food intake (g/d).
² N.D. means not detectable.
Values were expressed as mean±standard error.
³ N.D. means not detectable.
⁴ p<0.01 compared with 50 ppm group by t-test.

Intelligent UV/VIS detector (JASCO Corporation, Tokyo, Japan). The separation was performed using a methyl-sil RP-18 GP column (Φ 4.0×250 mm; Kanto Kagaku, Tokyo, Japan) with methanol/THF (75 : 25, v/v) as mobile phase at a flow rate 1.0 mL/min. The external standard of lycopene (Sigma Chemical Co., St. Louis, MO) was used as a reference.

Measurement of BMD. The BMD values for the third to sixth lumbar (L3–L6) spine and the whole tibiae were measured by dual-energy X-ray absorptiometry (DXA; Aloka DCS-600R, Hitachi Aloka Medical Ltd., Tokyo, Japan). Analysis of tibial BMD was carried out as previously reported [26]. Briefly, the proximal one-fifth of the tibia, including the epimetaphyseal region representing the cancellous sites, and middle two-fifth of the tibia representing the cortical diaphyseal region, were used.

Femoral mechanical breaking test. The femoral bone strength at the middle diaphysis was tested by measuring the mechanical strength, with an Iio DYN-1255 instrument as previously reported [27]. The force necessary to produce a break at the center of the femur was measured under the following conditions: the sample space was 1.0 cm, the plunger speed was 100.0 mm/min, the load range was 50.0 kg, and the chart speed was 120.0 cm/min.

Urinary deoxypyridinoline (Dpd) excretion. On the 62nd and 63rd day from the start of the experimental period (2 and 3 d before dissection), urine samples were collected overnight under acidic conditions using 2 mL of 2 N hydrochloric acid. All samples were centrifuged at 2,500 rpm for 15 min at 4˚C to eliminate refuse. The supernatants were used for analysis. Commercially purchased enzyme immunoassay (EIA) kits (Osteolinks-DPD, DS Pharma Biomedical Co., Ltd., Osaka, Japan) were used to measure the bone resorption marker, urine Dpd concentration [28]. The procedure was performed according to the manufacturer’s instructions.

Serum bone-type alkaline phosphatase (Bone ALP) activity. The bone formation marker, serum Bone ALP activity was measured by a modified Lowry method as previously reported [29]. Serum samples were heated for 10 min at 56˚C so as to selectively deactivate Bone ALP, or left intact. The release of p-nitrophenol from 10 mm p-nitrophenyl phosphate (p-NPP) in 0.1 M Tris (2-amino-2- methyl-1-propanol)-HCl buffer (pH 10.0) containing 5 mm MgCl₂·6H₂O was measured at 37˚C. The reaction was stopped after 30 min with 1 N NaOH, and the absorbance was determined at 420 nm. The ALP activity was expressed in U, where one unit represents 1 μmol of p-NPP hydrolyzed per minute. The Bone ALP activity was calculated by subtracting heated serum ALP activity from intact serum ALP activity.

Serum oxidative stress level and antioxidative potency. Serum oxidative stress level was determined performing the Reactive Oxygen Metabolites-derived compounds (d-ROMs) test. A free radical analysis system (FRAS) 4 (Health & Diagnostics Ltd., Parma, Italy) and d-ROM test kits (Diacron s.r.l., Grosseto, Italy) were used. The procedure was performed according to the manufacturer’s instructions. The values were expressed in an arbitrary unit, U.CARR, where 1 U.CARR was equivalent to 0.08 mg/100 mL H₂O₂. The antioxidative potency was assessed by performing the Biological Antioxidant Potential (BAP) test which measured the capacity of the serum to reduce ferric ions to ferrous ions. FRAS4 and BAP test kits (Diacron s.r.l.) were used. The procedure was performed according to the manufacturer’s instructions. The values were expressed in μmol ferrous ions/liter of sample. By calculating the BAP/d-ROMs ratio, serum redox balance was also evaluated.

Statistical analysis. Data were expressed as mean±standard error of the mean. Within all groups, data were analyzed by one-way analysis of variance (ANOVA) followed by the Tukey-Kramer test for multiple comparisons. A trend test was performed with the Jonckheere-Terpstra test. A t-test was used to compare the values of liver lycopene content between the 50 and 100 ppm groups. Pearson’s correlation analysis was used to examine the correlation between oxidative stress indices and bone mass, bone strength and bone turnover markers. A significance level of p<0.05 was used for all comparisons and trends. SPSS Statistical Packages (SPSS Inc., Chicago, USA) was used for all statistical analysis.

RESULTS

There were no differences in initial body weight among the groups (0 ppm, 153.00±1.71 g; 50 ppm, 153.13±2.28 g; 100 ppm, 152.88±1.98 g). Lycopene
intake did not significantly affect the final body weight, body weight gain, food intake, or food efficiency (Table 2). No degeneration or hypertrophy of internal organs, muscle, or bone was observed as a result of continuous high-dose lycopene intake.

Serum lycopene levels were undetectable by the analytical method used in this study. Lycopene was not detected in the livers of the 0 ppm group, but could be measured in the 50 and 100 ppm groups. The liver lycopene content of the 100 ppm group was significantly higher than that of the 50 ppm group (Table 2, $p<0.01$).

The BMD of the lumbar spine and the tibial proximal metaphysis were significantly higher in the 100 ppm group than in the 0 ppm group (Fig. 1A, $p<0.05$; Fig. 1B, $p<0.01$). The tibial proximal metaphyseal BMD in the 100 ppm group was also significantly higher than that in the 50 ppm group (Fig. 1B, $p<0.05$). In addition, both BMD values increased in a lycopene dose-dependent manner (Fig. 1A, $p$ for trends $= 0.014$; Fig. 1B, $p$ for trends $= 0.002$). No significant differences or trends in the BMD of the tibial diaphysis were observed among the groups (Fig. 1C). However, the tibial diaphyseal BMD increased similarly to the BMD of the lumbar spine and tibial proximal metaphysis (0 ppm, $119.6\pm 0.9$ mg/cm$^2$; 50 ppm, $120.3\pm 1.6$ mg/cm$^2$; 100 ppm, $121.7\pm 1.2$ mg/cm$^2$).

Table 3. Bone strength and bone turnover markers.

<table>
<thead>
<tr>
<th>Lycopene content (ppm in diet)</th>
<th>0</th>
<th>50</th>
<th>100</th>
<th>$p$ for trends</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bone strength indices</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Femoral breaking force (×10^6 dyn)</td>
<td>20.41±0.48</td>
<td>21.19±0.40</td>
<td>21.05±0.29</td>
<td>0.180</td>
</tr>
<tr>
<td>Femoral breaking energy (×10^5 erg)</td>
<td>12.08±1.12</td>
<td>12.79±0.88</td>
<td>13.99±1.24</td>
<td>0.266</td>
</tr>
<tr>
<td>Bone turnover markers</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urinary Dpd excretion (nmol/mg creatinine)</td>
<td>0.34±0.04</td>
<td>0.19±0.03**</td>
<td>0.20±0.03**</td>
<td>0.013</td>
</tr>
<tr>
<td>Serum bone ALP (mU)</td>
<td>35.79±2.15</td>
<td>44.95±4.61</td>
<td>48.65±4.11*</td>
<td>0.036</td>
</tr>
</tbody>
</table>

Values are expressed as mean±SE. Bone strength indices, $n=16$ in each group; bone turnover markers, $n=8$ in each group.

Breaking force and energy represented the bone architectural function indicating mechanical properties of the femur. Urinary Dpd excretion corrected by urinary creatinine excretion. Serum bone ALP activity was described for mU as mmol per minutes.

* $p<0.05$, ** $p<0.01$ compared with 0 ppm group. Trend test was performed with the Jonckheere-Terpstra test.
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There were no differences in femoral breaking force and energy among the groups (Table 3).

Urinary Dpd excretion, a bone resorption marker, was significantly lower in the 50 and 100 ppm groups than in the 0 ppm group (Table 3, p<0.01). In addition, urinary Dpd excretion decreased in a lycopene-dose-dependent manner (Table 3, p for trends=0.013). The serum bone ALP activity, a marker of bone formation, was significantly higher in the 100 ppm group than in the 0 ppm group (Table 3, p<0.05). In addition, the serum bone ALP activity increased in a lycopene-dose-dependent manner (Table 3, p for trends=0.036). No significant differences between the 50 and 100 ppm groups were observed in either marker.

There was no significant difference in the serum d-ROMs level, BAP, or BAP/d-ROMs ratio among the groups (Fig. 2). However, the serum d-ROMs level inversely correlated with the BMDs of the tibial proximal metaphysis and tibial diaphysis (Fig. 3A, r = -0.341, p<0.05; Fig. 3B, r = -0.304, p<0.05). In addition, serum d-ROMs levels trended to inversely correlate with lumbar spine BMD (r = -0.435, p=0.071).

DISCUSSION

In the present study, we investigated the effect of lycopene intake on bone metabolism throughout circulating oxidative stress in growing female rats. Our data demonstrated that lycopene intake significantly facilitated bone formation, suppressed bone resorption, and increased BMD in growing female rats. However, circulating oxidative stress was not altered by lycopene intake in this study.

The intake of 100 ppm lycopene promoted an increase of cancellous BMD in growing female rats. The lumbar spine and tibial proximal metaphysis whose BMD significantly increased in this study are composed mainly of cancellous bone. A previous study showed that lycopene supplementation significantly decreased the bone resorption marker in postmenopausal women (16). In adult ovariectomized rats, lycopene administration groups showed significantly lower levels of bone resorption markers and higher values of femur BMD, compared with a non-treated group (22). Rao et al. demonstrated that lycopene inhibited the differentiation and mineral resorption activity of osteoclasts (17). We also demonstrated that lycopene intake significantly decreased urinary Dpd excretion, which is a bone resorption marker. Additionally, a cellular study demonstrated that lycopene stimulated cell proliferation and alkaline phosphatase activities of osteoblast-like cells (18). In this study, 100 ppm lycopene diet intake...
significantly increased serum bone ALP activity, which is a bone formation marker. Taken together, these findings suggest that the suppression of bone resorption and facilitation of bone formation contributed to the significant increase in cancellous BMD observed in the 100 ppm lycopene group.

On the other hand, the cortical BMD and bone strength, which were evaluated in the diaphyses of the tibia and femur, respectively, did not differ among the groups. Cancellous bone has been suggested to have more active turnover than cortical bone (30, 31). Based on our bone metabolic marker data, it is possible that lycopene intake somewhat affected bone metabolism through the activity of osteoclasts and osteoblasts. Taken together, the effect of lycopene intake was exhibited by the increased BMD of cancellous bone, which is the site of active turnover by osteoclasts and osteoblasts, rather than cortical bone. Besides, bone strength was measured at the middle of femoral diaphysis, which consists mainly of cortical bone. Thus, our data suggest that lycopene intake exerted its local effect on cancellous bone rather than on cortical bone. Additionally, our results indicated that the continuous 100 ppm lycopene intake was the effective dose for accelerating the increase in cancellous BMD in growing female rats.

Systemic oxidative stress was not significantly alleviated by lycopene intake, whereas lycopene intake markedly suppressed bone resorption and promoted bone formation. The singlet oxygen quenching activity of carotenoids, such as lycopene, which depends on their conjugated double bonds, contributes to the prevention of lipid peroxidation (32). Lycopene has 11 conjugated double bonds and has the most efficient quenching activity among biological carotenoids (15). Previous studies reported that elevated serum lipid peroxide levels induced by 2,7-dimethyl(α)benzanthracene in SD female rats were significantly reduced by a diet supplemented with approximately 50 ppm lycopene for 90 or 120 d, compared with a non-treated group (33, 34). In the present study, serum lycopene concentrations in the lycopene intake groups were undetectable by the analytical methods used. However, previous studies have shown that serum lycopene was detected only in lycopene-administered rodents and the lycopene levels in their serum and organ tissues increased in a dose-dependent manner (23, 35). This suggests that lycopene also existed at low levels in the serum and increased in a dose-dependent manner in our study. It is possible that the supplementation period and the total amount of lycopene consumed in this study were inadequate to attenuate systemic oxidative stress, as evidenced by the d-ROM levels. Regarding the application to human use, further investigation examining longer supplementation periods, but not higher doses, is necessary to achieve more substantial effects of lycopene on bone metabolism and oxidative stress.

Although there were no significant differences in oxidative stress levels among the groups, we observed weak inverse correlations between the systemic oxidative stress level and tibial BMD values. This suggests that systemic oxidative stress was related to bone metabolism under the condition of lycopene intake. On the other hand, it has been shown that local oxidative stress accelerated bone resorption and inhibited osteoblast activity (3, 6). Oxidative stress has also been demonstrated to increase advanced glycation end products (AGEs) cross-linking within bone collagen fibers, which inhibits mineralization and decreases bone elastic strength (36). Hence, an investigation of local oxidative stress in vivo, such as oxidative stress in bone tissue, is required to reveal a more definitive relationship between oxidative stress and bone metabolism.

Besides its potent antioxidant capacity, lycopene has also been reported to induce direct intercellular gap junctional communication and to regulate cell proliferation and differentiation (37). The intracellular gap junctional communication among osteocytes, osteoblasts, and osteoclasts plays crucial roles in bone remodeling (38). Previous cellular studies have shown that lycopene inhibited osteoclast differentiation and activation, and facilitated osteoblast differentiation and proliferation (17, 18). Thus, it is possible that lycopene acts directly on bone metabolism without mediating the oxidative stress pathway. Additional research is required to confirm the mechanism by which lycopene facilitates the increase in BMD.

In conclusion, the present study indicated that lycopene intake facilitated bone formation and inhibited bone resorption, which contributed to an increase in the BMD of growing female rats. Further investigation is required to confirm the effect of lycopene intake on oxidative stress in focal tissues, such as bone tissue. We believe that our study provides novel insights into the utilization of lycopene as an antioxidant to promote skeletal health and in the primary prevention of osteoporosis.

Acknowledgments

The authors would like to thank Kyoritsu Bussan Co., Ltd., Tokyo, Japan, for supplying the lycopene samples.

REFERENCES

6) Bai XC, Lu D, Bai J, Zheng H, Ke ZY, Li XM, Luo SQ.
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