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*Full Length Research Paper*

# Tomato supplement ameliorates castration-induced oxidative stress in the rat

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**Castration has previously been shown to induce oxidative stress. Previous studies have shown tomato to be a potent anti-oxidant which reduces oxidative stress in many disease conditions. However, the likely role of tomato in ameliorating castration-induced oxidative stress has not been studied and was of interest to us. The present study looked into the effect of tomato supplement on the plasma level of antioxidant enzymes like superoxide dismutase (SOD) and catalase, level of lipid peroxidation rate by estimating the malondialdehyde (MDA) and other parameters like weight gain and blood glucose levels in castrated and sham-operated rats. Castration did not affect weight gain and plasma catalase level; but increased plasma glucose and MDA levels and decreased plasma SOD level. Tomato supplementation reduced weight gain but had no effect on castration-induced hyperglycemia. It also increased plasma SOD and catalase, and decreased plasma MDA level in the castrated rats. These findings suggested that tomato supplementation might have important therapeutic potential as an anti-oxidant during castration and a weight regulator in castrates and non-castrates.**

**Key words:** Anti-oxidant, Blood glucose, Castration, Oxidative stress, Tomato.

## INTRODUCTION

Tomatoes, commonly used in the diet, are a major source of antioxidants and contribute to the daily intake of a significant amount of these molecules. They are consumed fresh or as processed products such as canned tomatoes, sauce, juice ketchup and soup (Lenucci et al., 2006). According to USDA, the average American consumes approximately 18 pounds of fresh tomatoes and 69 pounds of processed tomato products annually (Agriculture statistics, 2003; Lucier et al., 2000) and serve as a convenient way to supply nutrients and various phytochemicals to humans (Wang et al., 2003). Tomato products are excellent sources of potassium; folate; vitamins A, C, and E and fibers (USDA, 2004). It contains a variety of phytochemicals, including lycopene, α- carotene, β-carotene, ϒ-carotene, neurosporene, ζ-carotene, phytofluene, phytoene, lutein and zeaxanthin (Fredrick, 2002). It also contains a variety of polyphenols, such as quercetin, kaempferol, and naringenin, which are thought to have both antioxidant and anticarcinogenic effects (Birt et al., 2001).

Castration has been shown to induce oxidative stress in the acinar epithelium of the rat ventral prostrate, as evidenced from marked increase in 8-hydroxy-2'-deoxyguanosine and 4-hydroxynonenal protein adducts in the regressing epithelium (Tam et al., 2003). Quantification of steady-state mRNA levels of 14 genes involved in the anabolism and catabolism of reactive oxygen species (ROS), showed that castration resulted in dramatic increases of three ROS-generating NAD(P)H oxidases ($N_{OXS}$) including $N_{OX}1$, $gp91^{phox}$ (Nox2) and $N_{OX}4$; significant reductions of key ROS-detoxifying enzymes (superoxide dismutase 2, glutathione peroxidase 1, thioredoxin and peroxiredoxin 5); and unchanged levels of catalase, gluta-

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glutathione reductase, Ɣ-glutamyl transpeptidase and glutathione synthetase (Tam et al., 2003). However, testosterone replacement partially reduced oxidative stress in ventral prostate epithelia of castrated rats, but the level remained higher than in intact rats (Tam et al., 2003). This study shows that testosterone may have antioxidant properties. Results from animal studies collectively illustrate that lycopene supplementation may interfere with androgen activation and thereby potentially have a protective role against oxidative stress (Khachik et al., 2002). Moreover, several antioxidant genes were modulated after castration in rat ventral prostate. Among them, thioredoxin (Holmgren, 1985), peroxiredoxin 5 (Knoops et al., 1999), glutathione peroxidase 1 (Holmgren, 2000), superoxide dimutase 2 (Li et al., 1995) and 15-kDa selenoprotein (Behne and Kyriakopoulos, 2001; Kohrl et al., 2000) are genes functionally related to cellular redox regulation that were down-regulated after castration (Pang et al., 2002). In contrast, other redox related genes such as glutathione reductase (Holmgren, 2000), microsomal glutathione-*S*-transferase (Hayes and Pulford, 1995) and epoxide hydrolase (Nam et al., 1997) were up-regulated after castration (pang et al., 2002).

It was suggested that eating a healthy diet, especially one rich in fruits and vegetables, can help the body in the prevention against oxidative stress (Hanley and Daniel, 1997). Epidemiological evidences strongly suggest that the consumption of tomato and other carotenoid-rich fruits and vegetables is associated with a reduced risk of prostate cancer, and thus the protective health benefits of tomatoes is an active area of prostate cancer research (Etminan et al., 2004; Giovannuci, 1999; 2002; Miller et al., 2002; Van Poppel and Goldbohm, 1995; Ziegler et al., 1996). Diets containing broccoli, tomato, lycopene and a combination of tomato plus broccoli reduced Dunning R-3327H prostate tumor growth rate when compared with the control diet in rats (Canene-Adams et al., 2004).

Epidemiological studies (Etminan et al., 2004), human intervention trials (Chen et al., 2001; Kucuk et al., 2001), and animal cancer models (Boileau et al., 2003; Canine-Adams et al., 2005) indicate that the consumption of whole tomatoes or a variety of tomato components may be more advantageous than lycopene alone. Short-term intake of tomato carotenoids significantly alters androgen status, which may partially be a mechanism by which tomato intake reduces prostate cancer risk.

Short term supplementation of tomatoes in Type-II diabetic patients has been shown to increase antioxidants namely superoxide dismutase (SOD), glutathione reductase (GR), glutathione peroxidase (GSH-Px) and glutathione (GSH); and reduce malondialdehyde (MDA), which is involved in lipid peroxidation (Subhash et al., 2006). Moreover, tomato supplemented diet in patients with coronary heart disease has been shown to significantly improve the levels of serum enzymes involved in antioxidant activities and decreased lipid peroxidation rate (Bose and Agrawal, 2007). Lycopene has recently been shown to enhance docetaxel's effect in castration-resistant prostate cancer associated with insulin-like growth factor 1 receptor (Tang et al., 2011).

Since castration increases oxidative stress due to testosterone deficiency, study on the likely effects of tomatoes in ameliorating the castration-induced oxidative stress was of interest. Because oxidative stress has been implicated in the genesis of hyperglycemia and thus diabetes (Pfaffly, 2001), the present study also investigated the likely hypoglycemic effects of tomatoes in castration-induced oxidative stress in rats.

## MATERIALS AND METHODS

### Animals and experimental design

All necessary protocols were followed to ensure the humane treatment of the animals. Male albino rat (6 weeks of age; n = 24) were purchased from the Institute of Medical Research and Training, University of Ibadan College Hospital, Nigeria and were acclimated to their new environment. The rats were kept under condition of uniform humidity and temperature on a 12-h light-dark cycle. Rats were monitored and weighed daily. Beginning at 7 weeks of age, all rats were provided with normal feed (pelletized growers feed from Bovajay feeds Nig. Ltd, Ogbomosho). At 8 weeks of age, rats were randomly assigned to 4 treatment groups and the average weights of each group were approximately 100 g. Treatment groups were assigned as follows: 1) Sham-operated, tomato-free diet fed (n = 6); 2) Sham-operated, 10% tomato supplement fed (n = 6); 3) Castrated, tomato-free diet fed (n = 6); 4) Castrated, 10% tomato supplement fed (n = 6). At 8 weeks of age, rats were either castrated or sham-operated, and rats were allowed to recover from surgery for 1 day. Castration was performed by scrotal incision after animals were anaesthetized with ketamin. Rats that were switched to dietary treatment of 10% tomato supplement consumed a pelletized diet enriched with 10% freeze-dried tomato powder. The 10% tomato supplement was simply prepared by adding 10 g of tomato powder to every 90 g of the diet. All treatments lasted for six weeks. Rats were sacrificed by cervical dislocation and blood sample was taken via cardiac puncture.

### Sampling protocol

A blood sample was taken, and body weight and blood glucose were measured on a weekly basis. Blood was collected from the heart using 5 ml needle and syringe, and was immediately transferred to another heparinized sample bottles. The blood sample was centrifuged, and plasma was separated and stored at -20°C.

### Determination of SOD, MDA and catalase

Superoxide dismutase activity was determined as previously described (Misra and Fridovish, 1972). MDA was determined as previously described (Ohkawa et al., 1979). Catalase activity was determined as previously described (Dobkin and Glantz, 1958).

### Measurement of blood glucose

Blood glucose was measured with One Touch Basic-plus glucometer using the modified glucose oxidase method (Trinder, 1967). Results of glucose measurement using Glucometer correlate excellently with the result obtained from standard laboratory methods

**Table 1.** Effects of tomato supplement on weight gain and blood glucose level in sham-operated and castrated rats. Values are expressed as Mean ± SEM, (N = 6); *P<0.05.

| | Sham Operated | | Castrated | |
|---|---|---|---|---|
| | **Tomato-free diet** | **10% Tomato supplement diet** | **Tomato-free diet** | **10% Tomato supplement diet** |
| Weight gain (g) | 74.20 ± 8.4 | 57.17±5.2* | 76.55 ± 0.4 | 55.95±4.1* |
| Pre-operation glucose measurement (mg/dl) | 87.2 ± 3.54 | 91.6 ± 5.68 | 84 ± 2.09 | 84.8 ± 7.73 |
| Post-operation glucose measurement (mg/dl) | 66.0 ± 11.37* | 61.8 ± 15.90* | 95.8 ± 2.64* | 92.6 ± 2.80* |

**Table 2.** Effects of tomato supplement on biochemical parameters in sham-operated and castrated rats. Values are expressed as Mean ± SEM, (N = 6); *P<0.05.

| | Sham Operated | | Castrated | |
|---|---|---|---|---|
| | **Tomato-free diet** | **10% Tomato supplement diet** | **Tomato-free diet** | **10% Tomato supplement diet** |
| SOD (IU) | 0.018±0.006 | 0.108±0.019* | 0.003±0.002* | 0.036± 0.004* |
| MDA ($\times 10^{-6}$) (mMol) | 4.54 ± 1.86 | 1.92 ± 1.03* | 6.58 ± 0.28* | 5.50 ± 0.34* |
| Catalase (IU) | 0.04± 0.02 | 0.14± 0.04* | 0.03 ± 0.01 | 0.20 ± 0.06* |

(Ajala et al., 2003; Baig et al., 2007).

#### Statistics

Data were compared among treatments by student's t-test, using SPSS Statistical Software package (SPSS, Chicago) and P value less than 0.05 was set as significance. Values are expressed as mean (±SEM).

## RESULTS

### Effects of tomato diet on the weight gain in sham-operated and castrated rats

The weight gain in the rats fed with tomato-free diet was not significantly different (P>0.05) in both sham-operated and castrated group. There was also no significant difference (P>0.05) in the weight gain in both castrated and sham-operated rats fed with 10% tomato supplement diet. The 10% tomato supplement diet significantly reduced the weight gain in both sham-operated and castrated rats (Table 1).

### Effects of tomato diet on the blood glucose levels in sham-operated and castrated male rats

There are no significant differences (P>0.05) in the pre-operation blood glucose levels in all the groups. The post-operation blood glucose levels in sham-operated groups fed with tomato-free diet or 10% tomato supplement diet are significantly lower (P<0.05) than the corresponding pre-operation blood glucose level. However, the post-operation blood glucose levels in the castrated groups fed with tomato-free diet or 10% tomato supplement diet are significantly higher (P<0.05) than the corresponding pre-operation blood glucose levels (Table 1).

### Effects of tomato diet on the plasma SOD level in sham-operated and castrated male rats

Plasma SOD levels are significantly higher (P<0.05) in the sham-operated groups fed with 10% tomato supplement or tomato-free diet than in the corresponding castrated groups. In both sham-operated and castrated group, the plasma SOD level of the rats fed with 10% tomato supplement diet was significantly higher (P<0.05) than those fed with tomato-free diet (Table 2).

### Effects of tomato diet on the plasma MDA level in sham-operated and castrated male rats

The plasma MDA level of the rats fed with tomato-free diet is significantly higher (P<0.05) in the castrated group than the sham-operated group. The plasma MDA level of the rats fed with 10% tomato supplement diet is significantly lower (P<0.05) in the castrated group than the sham-operated group. The plasma MDA level of the rats fed with 10% tomato supplement diet is not significantly lower (P>0.05) than those fed with tomato-free diet in the sham-operated group but significantly lower (P<0.05) than those fed with tomato-free diet in the castrated group (Table 2).

### Effects of tomato diet on the plasma catalase level in sham-operated and castrated male rats

There is no significant difference (P>0.05) between the plasma catalase level of the rats fed with tomato-free diet

in the castrated and the sham-operated group. There is also no significant difference (P>0.05) between the plasma catalase level of the rats fed with 10% tomato supplement diet in the castrated and the sham-operated group. In both sham-operated and castrated group, the plasma catalase level of the rats fed with 10% tomato supplement diet is significantly higher (P<0.05) than those fed with tomato-free diet (Table 2).

## DISCUSSION

The lack of significant difference in both sham-operated and castrated group fed with tomato-free diet showed that castration had no effect on the weight gain in rats. This finding in the present study is contrary to the previous study of Iliescu et al. (2006) that reported lower body weight in the castrated rat than in the sham-operated rats fed with control diet. The observed lower weight gain in the rats fed with 10% tomato supplement diet than those fed with tomato-free diet in both sham-operated and castrated groups showed that tomato decelerates weight gain. Whether this observation was due to the anti-oxidants or other constituents of tomato is unknown.

The higher blood glucose levels in the castrated groups than in the sham-operated groups fed with tomato-free diet or 10% tomato supplement diet observed in this study show that castration may cause hyperglycemia. This may be similar to the previous findings of Subhash et al. (2007) who reported higher level of oxidative stress in the diabetic patients when compared with non-diabetic patients. Moreover, oxidative stress has been shown to be associated with the generation of diabetes mellitus. So, the observed increase in blood glucose level in the castrated group fed with tomato-free diet may be due to castration-induced oxidative stress. However, tomato did not affect the castration-induced hyperglycemia, suggesting that the anti-oxidant effect of tomato may not be effective in reversing the castration-induced hyperglycemia.

The lower plasma SOD level in the castrated rats than the sham-operated rats fed with tomato-free diet in the present study showed the higher degree of oxidative stress in the castrated group than in the sham-operated group. This is in agreement with the previous study of Tam et al. (2003) who reported a down-regulation in the number of key anti-oxidant enzymes/ROS scavengers like SOD2 among others in the castrated rats. The higher plasma SOD level in the rats fed with 10% tomato supplement than in those fed with tomato-free diet in the sham-operated group in this study showed that tomato is a very effective anti-oxidant. The additional findings in the present study include the ability of tomato to augment the plasma SOD levels of rat fed with 10% tomato supplement diet in the castrated group. This showed that tomato can reverse the castration-induced oxidative stress by increasing the plasma level of anti-oxidant enzymes like SOD.

The higher plasma MDA level in the castrated rats than in the sham-operated rats fed with tomato-free diet in the present study showed that there is higher degree of lipid peroxidation in the castrated group than in the sham-operated group. The insignificant reduction by 10% tomato supplement diet in the plasma MDA level in the sham operated group showed the lack of effect of tomato in the plasma MDA level in rats. Close examination of our data shows similar pattern of effect as in the previous study in healthy human subjects, where lycopene- or tomato-free diets resulted in loss of lycopene and increased lipid oxidation (Rao and Agarwal, 1998), whereas dietary supplementation with lycopene for 1 week increased serum lycopene levels and reduced endogenous levels of oxidation of lipids (Agarwal and Rao, 1998; Rao and Agarwal, 1998). Moreover, the significant reduction by 10% tomato supplement diet in the plasma MDA level in the castrated group showed that tomato potently reduced the lipid peroxidation rate in this group and thus is a potent anti-oxidant.

The lack of significant difference between the plasma catalase level in the castrated and sham-operated rats fed with tomato-free diet showed that castration had no effect on this enzyme. This is also in agreement with the previous study of Tam et al. *(*2003) who reported an unchanged level of catalase transcripts in castrated rats as compared to the control. Also, the higher plasma catalase level of the rats fed with 10% tomato supplement diet than those fed with tomato-free diets in both castrated and the sham-operated group provided further evidence for the anti-oxidant effect of tomato during castration-induced oxidative stress in addition to its anti-oxidant effect in the non-castrated rats.

Intake of tomato and tomato-based food products contributes to the absorption of a wide range of carotenoids in human serum and tissues. The prominent carotenoid in tomatoes is the red pigment lycopene that is also among the major carotenoids found in human serum (Fredrick et al., 2002). Lycopene is one of the most potent antioxidants (Miller et al., 1996). Several studies have indicated that lycopene is an effective antioxidant and free radical scavenger *in vitro* and *in vivo* (Rao and Agarwal, 1998). Lycopene, because of its high number of conjugated double bonds, exhibits higher singlet oxygen quenching ability as compared to β-carotene or α-tocopherol (DiMascio et al., 1989). In *in vitro* systems, lycopene was found to inactivate hydrogen peroxide and nitrogen dioxide (Bohm et al., 1995; Lu et al., 1995). Using pulse radiolysis techniques, Mortensen et al. (1997) demonstrated its ability to scavenge nitrogen dioxide ($NO_2^{\cdot}$), thiyl ($RS^{\cdot}$) and sulphonyl ($RSO_2^{\cdot}$) radicals. Lycopene has been demonstrated to be the most potent antioxidant with the ranking: lycopene > α-tocopherol > α-carotene > β-cryptoxanthin > zeaxanthin = β-carotene > lutein (Stahl et al., 1998). Mixtures of carotenoids like in tomatoes were

more effective than the single compounds. This synergistic effect was most pronounced when lycopene or lutein was present. The superior protection of mixtures may be related to specific positioning of different carotenoids in membranes.

Castrated rats had earlier been shown to have 50 to 100% greater prostate and seminal vescicle carotenoid concentrations than the sham-operated rats provided with the same carotenoid treatments. Carotenoids are antioxidants and are effective singlet oxygen quenchers (Boileau et al., 1999) able to protect the prostate from testosterone-induced oxidative stress through their own subsequent degradation. It was speculated that with castration, testosterone-induced reactive oxygen species were diminished, resulting in less degradation of carotenoids, and thus yielding greater prostate carotenoid accumulations (Campbell et al., 2006). The anti-oxidant ability of tomato during castration may in part be due to the enhanced concentrating power of the tomato carotenoids by the castrates.

In conclusion, the present study supports the previous findings that castration causes oxidative stress. Moreover, it provided strong evidence for the anti-oxidant property of tomato supplement in castration. However, further studies are needed to specify the particular carotenoid(s) or other constituent(s) in tomato that is/are involved in the anti-oxidant function in this condition.

**REFERENCES**


Agarwal S, Rao AV (1998). Tomato lycopene and low density lipoprotein oxidation: a human dietary intervention study. Lipids 33:981–984.

Agriculture Statistics (2003). Statistics of Vegetables and Melons. Chapter IV.

Ajala MO, Oladipo OO, Fasanmade O, Adewole TA (2003). Laboratory assessment of three glucometers. Afr. J. Med. Med. Sci. 32:279-282.

Baig A, Siddiqui I, Jabbar A, Azam SI, Sabir S, Alam S, Ghani F (2007). Comparision between bed side testing of blood glucose by glucometer vs centralized testing in a tertiary care hospital. J. Ayub. Med. Coll. Abbottabad 19(3):25-29.

Behne D, Kyriakopoulos A (2001). Mammalian selenium-containing proteins. Annu. Rev. Nutr. 21:453–473.

Birt DF, Hendrich S, Wang W (2001). Dietary agents in cancer prevention: flavonoids and isoflavonoids. Pharmacol. Ther. 90:157–177.

Bohm F, Tinkler JH, Truscott TG (1995). Carotenoids protect against cell membrane damage by the nitrogen dioxide radical. Nature Med. 1:98–99.

Boileau TWM, Moore AC, Erdman JW Jr. (1999). Carotenoids and Vitamin A. In: Antioxidant Status, Diet, Nutrition, and Health (Papas, A. M., ed.). CRC Press LLC, Boca Raton, FL. pp.133–158.

Bose KSC, Agrawal BK (2007). Effect of lycopene from cooked tomatoes on serum antioxidant enzymes, lipid peroxidation rate and lipid profile in coronary heart disease. Singapore Med. J. 48(5): 415.

Bose KSC, Agrawal BK (2007). Effect of short term supplementation of tomatoes on antioxidant Enzymes and lipid peroxidation in type –II diabetes. Indian J. Clin. Biochem. 22(1):95-98.

Campbell JK, Engelmann NJ, Lila MA, Erdman JW (2007). Phytoene, phytofluene, and lycopene from tomato powder differentially accumulate in tissues of male Fisher 344 rats. Nutr. Res. 27:794–801.

Canene-Adams K, Clinton SK, King JK, Lindshield BL, Wharton C, Jeffery EJ, Erdman JW, (2004). The effect of diets containing tomato, broccoli, lycopene, or finasteride treatment on the growth of Dunning R-3327-H transplantable prostate adenocarcinoma in rats. J. Nutr. 134(suppl.):3535S(abs.).

Chen L, Stacewicz-Sapuntzakis M, Duncan C, Sharifi R, Ghosh L, van Breemen R, Ashton D, Bowen PE (2001). Oxidative DNA damage in prostate cancer patients consuming tomato sauce-based entrees as a whole food intervention. J. Natl. Cancer Inst. 93:1872–1879.

DiMascio P, Kaiser S, Sies H (1989). Lycopene as the most effective biological carotenoid singlet oxygen quencher. Arch. Biochem. Biophys. 274:532–538.

Dobkin GB, Glantz MD (1958). Colometric method for the quantitative determination of plasma Catalase activity. Clin. Chem. 4(4):316-322.

Etminan M, Takkouche B, Caamano-Isorna F (2004). The role of tomato products and lycopene in the prevention of prostate cancer: a metaanalysis of observational studies. Cancer Epidemiol. Biomarkers Prev. 13:340–345.

Giovannucci E (1999). Tomatoes, tomato-based products, lycopene, and cancer: review of the epidemiologic literature. J. Natl. Cancer Inst. 91: 317–331.

Giovannuci E, Rimm EB, Liu Y, Stampfer MJ, Willett WC (2002). A prospective study of tomato products, lycopene, and prostate cancer risk. J. Natl. Cancer Inst. 94:391–398.

Hayes JD, Pulford DJ (1995). The glutathione S-transferase supergene family: regulation of GST and the contribution of the isoenzymes to cancer chemoprotection and drug resistance. Crit. Rev. Biochem. Mol. Biol. 30:445–600.

Holmgren A **(**1985). Thioredoxin. Annu. Rev. Biochem. 54:237–271.

Holmgren A (2000). Antioxidant function of thioredoxin and glutaredoxin systems. Antioxid. Redox. Signal. 2:811–820.

Iliescu R, Cucchiarelli VE, Yanes LL, Iles JW, Reckelhoff JF (2006). Impact of androgen-induced oxidative stress on hypertension in male SHR Am. J. Physiol. Regul. Integr. Comp. Physiol. 292:R731-R735.

Khachik F, Carvalho L, Bernstein PS, Muir GJ, Zhao DY, and Katz NB (2002). Chemistry, distribution, and metabolism of tomato carotenoids and their impact on human health. Exp. Biol. Med. 227:845–851.

Knoops B, Clippe A, Bogard C, Arsalane K, Wattiez R, Hermans C, Duconseille E, Falmagne P, Bernard A (1999). Cloning and characterization of AOEB166, a novel mammalian antioxidant enzyme of the peroxiredoxin family. J. Biol.Chem. 274: 30451–30458.

Kohrl J, Brigelius-Flohe R, Bock A, Gartner R, Meyer O, Flohe L (2000). Selenium in biology: facts and medical perspectives. Biol. Chem. 381:849–864.

Kucuk O, Sarkar FH, Sakr W, Djuric Z, Pollak MN, Khachik F, Li YW, Banerjee M, Grignon D, Bertram JS, Crissman JD, Pontes EJ, Wood DP (2001). Phase II randomized clinical trial of lycopene supplementation before radical prostatectomy. Cancer Epidemiol. Biomarkers Prev. 10: 861–868.

Li Y, Huang TT, Carlson EJ, Melov S, Ursell PC, Olson JL, Noble LJ, Yoshimura MP, Berger C, Chan PH, Wallace DC, Epstein CJ (1995). Dilated cardiomyopathy and neonatal lethality in mutant mice lacking manganese superoxide dismutase. Nat. Genet. 11:376–381.

Lu Y, Etoh H, Watanabe N (1995). A new carotenoid, hydrogen peroxide oxidation products from lycopene. Biosci. Biotech. Biochem. 59:2153–2155.

Lucier G, Lin B, Allshouse J, Kantor L (2000). Factors affecting tomato consumption in the United States. In:Vegetables and Specialties/VGS 282/November 2000.

Miller EC, Giovannucci E, Erdman JW Jr, Bahnson R, Schwartz SJ, Clinton SK (2002). Tomato products, lycopene, and prostate cancer risk. Urol. Clin. North Am. 29:83–93.

Miller NJ, Sampson J, Candeias LP, Bramley PM, Rice-Evans CA (1996). Antioxidant activities of carotenes and xanthophylls. FEBS Lett. 384:240–246.

Misra HP, Fridovish (1972). The role of superoxide anion in the auto-oxidation of epinephrine and a simple assay for SOD. J. Biol. Chem. 247: 3170-3175.

Mortensen A, Skibsted LH (1997). Relative stability of carotenoid radical cations and homologue tocopheroxyl radicals. A real time kinetic

study of antioxidant hierarchy. FEBS Lett. 417:261–266.
Nam SY, Kim JH, Cho CK, Yoo SY, Kim SG (1997). Enhancement of radiation-induced hepatic microsomal epoxide hydrolase gene expression by oltipraz in rats.Radiat. Res. 147:613–620.
Ohkawa H, Ohishi N, Yagi K (1979). Assay of lipid peroxidation in animal tissue by Thiobarbituric reaction. Anal. Biochem. 95:351-358.
Pang S, Dillner K, Wu X, Pousette A, Norstedt G, Flores-Morales A (2002). Gene expression profiling of androgen deficiency predicts a pathway of prostate apoptosis that involves genes related to oxidative stress. Endocrinol. 143:4897-4906.
Pfaffly JR (2001). Review on diabetic complications. Free Radic. Biol. Med. 77: 222.
Rao AV, Agarwal S (1998). Bioavailability and in vivo antioxidant properties of lycopene from tomato products and their possible role in the prevention of cancer. Nutr. Cancer 31:199–203.
Stahl W, Junghans A, de Boer B, Driomina ES, Briviba K, Sies H (1998). Carotenoid mixtures protect multilamellar liposomes against oxidative damage: synergistic effects of lycopene and lutein. FEBS Lett. 427:305–308.
Subhash C, Bose K, Agrawal BK (2006). Effect of lycopene from cooked tomatoes on serum antioxidant enzymes, lipid peroxidation rate, lipid profile and glycated hemoglobin in type II diabetes. Indian J. Nutr. Diet. 43:153-60.
Tam NNC, Ying G, Leung Y, Ho S (2003). Androgenic Regulation of Oxidative Stress in the Rat Prostate. Involvement of NAD(P)H oxidases and antioxidant defense machinery during prostatic involution and regrowth. Am. J. Path. 163(6):2513-2522.
Tang Y, Parmakhtiar B, Simoneau AR, Xie J, Fruehauf J, Lilly M, Zi X (2011). Lycopene enhanced docetaxel's effect in castration-resistant prostate cancer associated with insulin-like growth factor 1 receptor. Neoplasia. 13(2):108-119.
Trinder P (1969): Determination of blood glucose using 4-amino-phenazone as oxygen acceptor J. Clin. Path. 22:246-248.
U.S. Department of Agriculture (2004). Agricultural Research Service [Online]. USDA National Nutrient Database for Standard Reference, Release 16–1. http:// www.nal.usda.gov/fnic/foodcomp [accessed July 28, 2004]. 13.
USDA National Agricultural Statistic Services (2004). Online. http://www.usda.gov/nass/pubs/ agr03/acro03.htm [accessed June 15, 2004]. United States Government Printing Office, Washington, DC.
Van Poppel G, Goldbohm RA (1995). Epidemiologic evidence for β-carotene and cancer prevention. Am. J. Clin. Nutr. 62(Suppl):1393S–1402S.
Wang S, DeGroff VL, Clinton SK (2003). Tomato and soy polyphenols reduce insulin-like growth factor-I-stimulated rat prostate cancer cell proliferation and apoptotic resistance in vitro via inhibition of intracellular signaling pathways involving tyrosine kinase. J. Nutr. 133:2367–2376.
Ziegler RG, Mayne ST, Swanson CA (1996). Nutrition and lung cancer. Cancer Causes Contr. 7:157–177.