Original article

Lycopene - tomato's secret weapon against oxidative stress

Sarkar PD[1], Sahu A[2], Gupta T[3]

Abstract

Back ground: Lycopene, 40 carbon acyclic carotenoid containing 1 1 conjugated double bonds, is a phytochemical found in tomatoes and other red fruits. Oxygen derived free radicals are the most reactive species and as an antioxidant lycopene has a singlet oxygen quenching ability twice as high as that of ?-carotene and 10 times higher that of ?-tocoferol, lycopene participate in a host of chemical reactions to protect critical cellular biomolecules including lipid, proteins and DNA. ***Materials and Methods:*** The present study include 30 subjects having oxidative stress, age between 40-60 years, nonsmoker, with no history of chronic systemic illness and no medication were taken as patients.30 patients matched healthy subjects were taken as control. All subjects were selected from outpatient department of NSCB Medical College Jabalpur M.P. After estimation of base line antioxidant enzyme and vitamins, we supplement 180 gm of tomato (products like soup, paste. ketchup) contain 12 mg of lycopene to the patient group. After 60 days of lycopene supplementation oxidative stress biomarkers like SOD, GPX, GR, GSH, lipid peroxidation product MDA and other antioxidant vitamins A, vitamin C, vitamin E were estimated in patient's blood sample. ***Results:*** The main result of the study revealed that lipid per oxidation product MDA was found to be decreased significantly but after lycopene supplementation levels were improved. The results of SOD , GPX, GR, GSH,Vitamin A ,Vitamin E and Vitamin C were significantly increased after lycopene supplementation, it indicates the improved antioxidant profile after the supplementation of lycopene. ***Conclusion:*** There was a significant decrease in oxidative stress after the supplementation of lycopene therefore the study suggest that body's internal production of antioxidant is not enough to neutralize all free radicals, so increased dietary intake of antioxidant lycopene in the form of tomato products is beneficial, which is easily available in developing country like India.

Key Words: Oxidative stress, Lycopene, MDA, GSH, SOD, Vitamin C, VitaminE

Introduction

Oxidative stress represents an imbalance between the production of reactive oxygen species and a biological system's ability to readily detoxify the reactive intermediates or to repair the resulting damage. Oxidative damage results in Heart disease, Cancer , Diabetes, Osteoporosis, Male infertility, Alzheimer's disease and ageing.[1,2,3,4,5.]

Lycopene, 40 carbon acyclic carotenoid containing 11 conjugated double bonds, is a phytochemical found in tomatoes and other red fruits. Best sources of lycopene are pasteurized tomato products. Lycopene configuration enables it to inactivate free radical. Oxygen derived free radicals are the most reactive species and as an antioxidant lycopene has a singlet oxygen quenching ability twice as high as that of ?-carotene and 10 times higher that of ?-tocoferol,6 lycopene participate in a host of chemical reactions to protect critical cellular biomolecules including lipid, proteins and DNA.[7,8,9]

Lycopene from processed tomato productsappears to be more bioavailable than from raw tomatoes[10.]Comparative bioavailability of lycopene from different tomatoproducts such as paste, juice, ketchup, sauce and soup are notknown but lycopene from tomato paste was shown to be morebioavailable than from fresh tomatoes1 1. Dietary lipids and heat treatment make lycopene more bioavailable, thus after processing release of lycopenefrom the food matrix, in presence of dietarylipids and heat-induced isomerization from all trans to cisconformation enhance lycopene bioavailability [7,12]. It ishowever not clear if cis-isomers are biologically more effectivethan trans-isomers. Bioavailability of lycopene is also depends on dose and presence of other carotenoids such as ß-carotene [13.]

The genesis of present study is to investigate the concentration of antioxidant vitamins, enzymes and it is to be seen whether the antioxidant lycopene supplementation help to alleviate the oxidative stress.

1. Purnima Dey Sarkar, Professor and Head, Department of Biochemistry, MGM Medical College, Indore, M P, India.
2. Dr Ashok Sahu, Assistant professor,
3. *Trapti Gupta, Assistant professor,
Department of Biochemistry, NSCB Medical College, Jabalpur, M P, India.

***Corresponds to:** Trapti Gupta, Department of Biochemistry, NSCB Medical College, Jabalpur, M P, India.
Email: traptigupta_3@rediffmail.com.

Materials and Methods

The present study include 30 subjects having oxidative stress, age between 40-60 years, nonsmokers, with no history of chronic systemic illness and medication were taken as patients.30 patients matched healthy subjects were taken as control. All subjects were selected from outpatient department of NSCB Medical College Jabalpur M.P . After estimation of base line antioxidant enzymes and vitamins, we supplement 180 gm of tomato (products like soup, paste. ketchup) contain 12 mg of lycopene to the patient group. All the parameters of oxidative stress biomarkers like SOD, GPX, GR, GSH, lipid peroxidation product MDA and other antioxidants vitamin A, vitamin C, vitamin E were measured at the time of enrollment for all subjects, but patient group were again reassessed for the same parameters after follow up of 60 days lycopene supplementation period. Patients already on antioxidant supplementation at the time of enrollment were excluded.

After overnight 12 hours fasting, basal sample (10 ml whole blood) was collected, under aseptic conditions, from both the control and study groups. Samples were collected and analyzed for biochemical markers within 3 hours of sample collection by the following methodologies:

MDA(TBARS)14, SOD by Mishra and fridovich15 and Erythrocyte reduced glutathione (GSH) by Beutler et al16, GPX by Paglia, D.E. et al17 GR by Carlberg I18 , Vitamin-E (alpha tocopherol, Quaife et al, 1949;Baker and Frank, 1968) Vitamin-C (Ascorbic Acid) (Evelyn and Malloy ,1938.) Vitamin-A (Retinol) (Bessey et al. 1946; Karmarkar and Raja Gopal 1952)

Statistical analysis was performed using 14.3 SPSS software, which involves paired and unpaired t-tests. Mean values and SD were calculated for each group and were compared between 2 groups. The 0.05 as point of minimal statistical significance.

Results

The main result of the study revealed that lipid per oxidation product MDA was found to be decreased significantly, baseline level were 6.54±0.67 and after lycopene supplementation levels were 3.73±0.72 ($p<0.001$). Like MDA improvement from oxidative stress for other antioxidant enzymes and vitamins levels was found after 60 days lycopene supplementation. The results were, SOD 5.88±0.71 ($p<0.02$), GPX (73.36±7.59, $p<0.001$), GR (55.1±6.1 1, $p<0.001$), GSH (9.27±0.83, $p<0.001$), Vitamin A (43.16±11.04, $p<0.001$), Vitamin E (1.21±0.42, $p<0.001$) and Vitamin C (0.78±0.35, $p<0.001$).Result of present study directly indicates the improved antioxidant profile after the supplementation of lycopene.

Discussion

In our study we include Vitamin E, vitamin A,vitamin C, malondialdehyde (MDA) reduced glutathione (GSH) glutathione peroxidase (GPx), glutathione reductase (GR) and superoxide dismutase (SOD). Antioxidant defense mechanisms involve both enzymatic and nonenzymatic strategies.

Oxidative stress result in excessive free radicals leading to increased lipid peroxidation, as indicated by significant increase in the levels of Malondialdehyde (MDA,a marker of lipid peroxidation). Apart from this, there is a significant decrease in the antioxidant status of the body, reflected by low levels of reduced glutathione (GSH) glutathione peroxidase (GPx), glutathione reductase (GR) and superoxide dismutase (SOD).

In present study serum MDA is significantly increase in patients suffering from oxidative stress as compared to control it is in accordance to previous findings that in oxidative stress Reactive oxygen species degrade polyunsaturated lipids, forming malondialdehyde. This compound is a reactive aldehyde and is one of the many reactive electrophile species that cause toxic stress in cells and form covalent protein adducts which are referred to as advanced lipoxidation end products (ALE), in analogy to advanced glycation end-products (AGE). The production of this aldehyde is used as a biomarker to measure the level of oxidative stress in an or ganism.19,20 Serum SOD activity is significantly decrease in patient group as compare to control simply stated, SOD outcompetes damaging reactions of superoxide, thus protecting the cell from superoxide toxicity.21

Glutathione peroxidase (GPx) and reductase (GR) are two enzymes, GSH is the substrate for them, are found in the cytoplasm, mitochondria, and nucleus. We found significant decrease in GPX,GSH,GR in patients group because Glutathione peroxidase (GPX) metabolizes hydrogen peroxide to water by using reduced glutathione (GSH) as a hydrogen donor.22,23 Glutathione disulfide is recycled back to glutathione by glutathione reductase (GR) using the cofactor NADPH generated by glucose 6- phosphate dehydrogenase. Yu24reported that reduced glutathione is an ef fective reductant and plays an important role in a variety of detoxification processes. The enzyme glutathione reductase plays a pivotal role in replenishing and maintaining optimum con-

centrations of reduced glutathione in biological systems.

Antioxidant Vitamins work with the synergy of these antioxidant enzyme, Vitamin E and vitamin A are most important chain breaking antioxidants and they protect polyunsaturated fatty acids from peroxidative damage by donating hydrogen to the lipid peroxyl radical.25,26 Because of the lipophilic property of the tocopherol, it is the major free radical chain terminator in the lipophilic environment. Vitamin C act as a reducing and antioxidant agent directly reacts with superoxides, hydroxyl radicals, and various lipid hydroperoxides. In addition it can also restore the antioxidant properties of oxidised vitamin E.27, 28

The present study reveals decreased levels of glutathiones(GPX,GR,GSH), vitamin E, vitamin C and vitamin A. This may be due to increased lipid peroxidation in patients group.

The oxidative stress was drastically reduced and antioxidant status was improved by supplementation of lycopene. As an antioxidant lycopene has a singlet oxygen quenching ability twice as high as that of ?-carotene and 10 times higher that of ?-tocoferol,6 lycopene participate in a host of chemical reactions to protect critical cellular biomolecules including lipid, proteins and DNA.7,8,9 lycopene create first line of defence against free radicals so it protect all the antioxidant enzyme and vitamins from oxidative damage thus there is improvement in the levels of all antioxidants after lycopene supplementation.

Conclusion

Our study shows a significant increase in the lipid peroxidation as oxidative stress advances, which is associated with decreased antioxidant levels.There was a significant decrease in oxidative stress after the supplementation of lycopene therefore the study suggest that body's internal production of antioxidant is not enough to neutralize all free radicals, so increased dietary intake of antioxidant lycopene in the form of tomato products is easily available in developing country like India, beneficial and may prevent further complications related with OS.

Tables

Table:-1 levels of antioxidant vitamins and enzymes in patient group and control

Parameters	Healthy subject	Study subject
Vit A µg/dl	52.36±9.17	18.7± 5.7**
Vit E mg/dl	1.15±0.40	0.36±0.18**
Vit C mg/dl	0.95±0.32	0.27 ± 0.12^{NS}
MDA nmol/ml	6.67±0.54	6.5±0.67*
SOD Units/ml	5.51±0.67	3.2±0.72**
GPX Unit/gHb	64.14±7.71	48.3±5.4**
GR Unit/L	54.83±6.83	40.9±5.7**
GSH Unit/gHb	8.73±0.68	8.11 ± 1.07^{NS}

***** highly significant * significantNS not significant***

Table:-2 showing level of Significance of antioxidant enzymes and vitamins before and after lycopene supplementationin patient group.

Parameters	Baseline levels	After Supplementation
Vit A µg/dl	18.7± 5.7	53.16±11.04**
Vit E mg/dl	0.36±0.18	1.21±0.42**
Vit C mg/dl	0.27±0.12	0.78±0.35**
MDA nmol/ml	6.5±0.67	3.73±0.72**
SOD Units/ml	3.2±0.72	5.88±0.71*
GPX Unit/gHb	48.3±5.4	73.36±7.59**
GR Unit/L	40.9±5.7	55.1±6.11**
GSH Unit/gHb	8.11±1.07	9.27±0.13**

***** highly significant * significant***

Figures

Chart:-1 Levels of Vitamins and Antioxidants before and after Lycopene supplementation

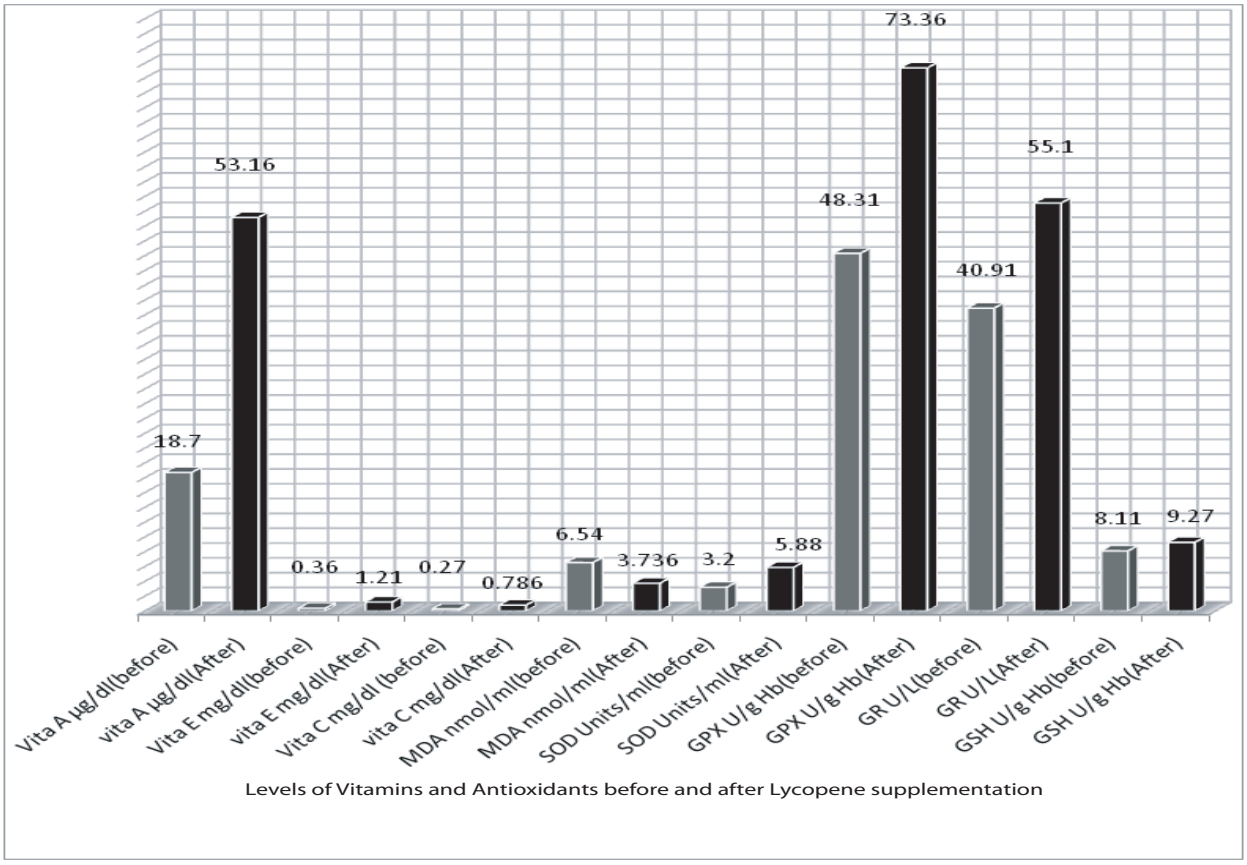
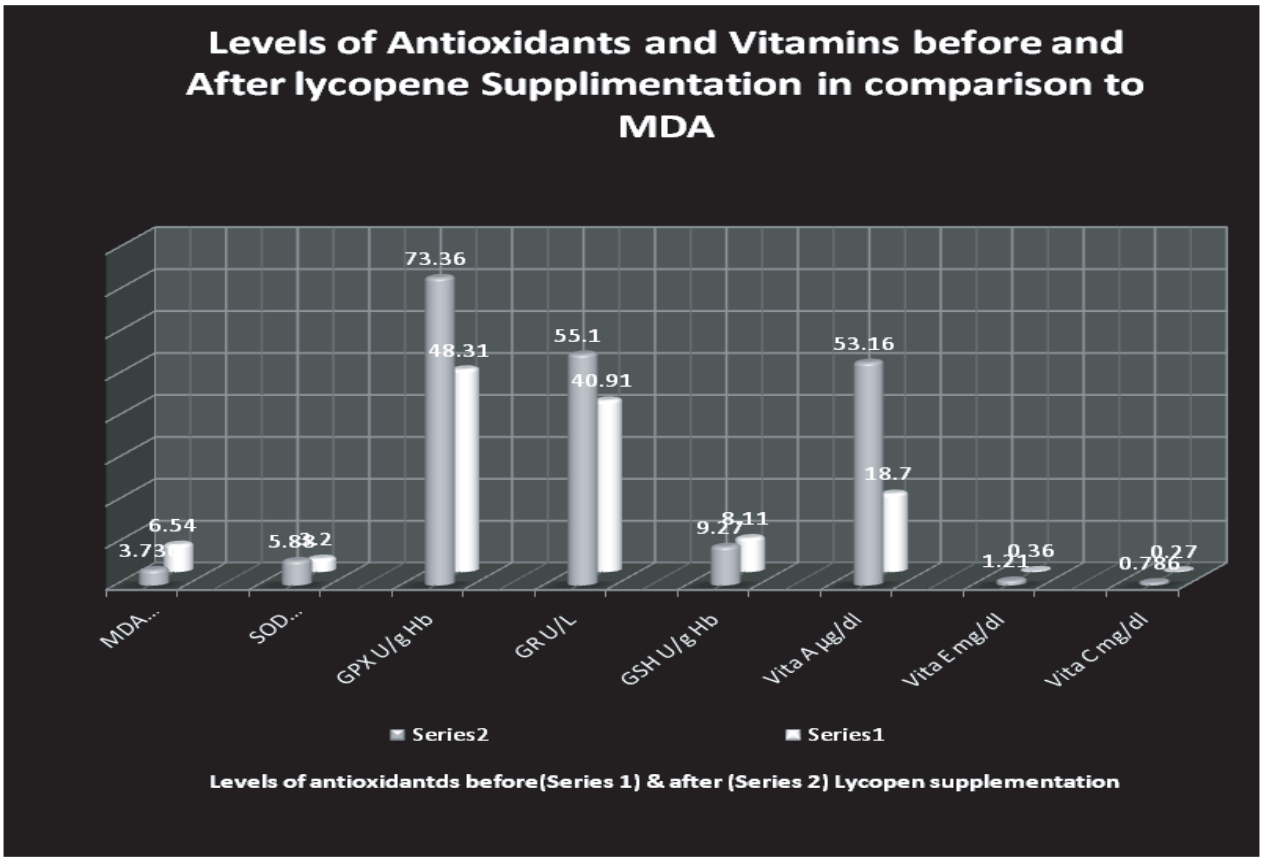


Chart:2 Levels of Antioxidants and Vitamins before and After lycopene Supplementation in comparison to MDA



Referance

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