

EFFECT OF *TERMINALIA ARJUNA* STEM BARK ON ANTIOXIDANT STATUS IN LIVER AND KIDNEY OF ALLOXAN DIABETIC RATS

B. RAGHAVAN* AND S. KRISHNA KUMARI**

*Department of Biochemistry,
P.S.G. College of Arts and Science,
Coimbatore – 641 014

**Department of Biochemistry,
Kongunadu College of Arts and Science,
Coimbatore – 641 029

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Abstract : Free radicals and associated oxidative stress induced by alloxan are implicated in eliciting pathological changes in diabetes mellitus. *Terminalia arjuna* bark, an indigenous plant used in ayurvedic medicine in India, primarily as a cardiogenic is also used in treating diabetes, anemia, tumors and hypertension. The present study examined the effect of ethanolic extract (250 and 500 mg/kg body weight) of *Terminalia arjuna* stem bark in alloxan induced diabetic rats and its lipid peroxidation, enzymatic and nonenzymatic activity was investigated in the liver and kidney tissues. The extract produced significant ($P < 0.05$) reduction in lipid peroxidation (LPO). The effect of oral *T. arjuna* at the dose of 500 mg/kg body weight was more than the 250 mg/kg body weight. The extract also causes a significant ($P < 0.05$) increase in superoxide dismutase, catalase, glutathione peroxidase, glutathione-s-transferase glutathione reductase and glucose-6-phosphate dehydrogenase, reduced glutathione, vitamin A, vitamin C, vitamin E, total sulfhydryl groups (TSH) and non protein sulfhydryl groups (NPSH) in liver and kidney of alloxan induced diabetic rats, which clearly shows, the antioxidant property of *T. arjuna* bark. The result indicates that the extract exhibit the antioxidant activity through correction of oxidative stress and validates the traditional use of this plant in diabetic animals.

Key words : *Terminalia arjuna*
antioxidants

ethanolic extract
alloxan diabetes

INTRODUCTION

Hyperphysiological burden of free radicals causes imbalance in homeostatic phenomena between oxidants and antioxidants in the body. This imbalance leads to oxidative stress that is being suggested as the root cause of ageing and various human diseases like atherosclerosis, stroke, diabetes, cancer and neurodegenerative

diseases, such as Alzheimer's and Parkinsonism (1). Alloxan, which is a chemical used for the induction of diabetes in animals, has been shown to damage pancreatic β -cell by the liberation of oxygen radicals, with a reduction in the antioxidant status (2). Insulin deficiency promotes β -oxidation of fatty acids, which result in the increased formation of hydrogen peroxide (3). The harmful influence of diabetes mellitus on

*Corresponding Author : Email : ragav_psg@yahoo.co.in

metabolism of tissues of various organ is well known. Glucose control plays an important role in the pro-oxidant/antioxidant balance (4). Antioxidants, which can scavenge free radicals against damage and decay, have an important role in biological system and may be helpful in the prevention of cancer, heart diseases, ageing and diabetes mellitus.

The medicinal plants *Terminalia arjuna* (Roxb, Wight Arn) is a large evergreen tree with butterressed trunk. It belongs to *Combretaceae* family, is an important cardiogenic plant described in the Ayurveda (5). Recently the antioxidant activity of the chloroform extract of *T. arjuna* in diabetic rats have been reported (6). In this study we have investigated the antioxidant potential (enzymatic and nonenzymatic) of ethanolic extract (50%) of *T. arjuna* stem bark on liver and kidney of alloxan induced diabetic and control rats.

METHODS

Plant material and preparation of 50% ethanolic extract

The wet *Terminalia arjuna* bark were collected from Siruvani coast of Agali in Kerala during September 2003 and were carefully identified and certified by Botanical Survey of India (BSI), Coimbatore. Ethanolic (50%) extract was prepared according to the traditional system of medicine. The shade dried and coarsely powdered stem bark (1 kg) was extracted with 50% ethanol (1.5 l) in the cold for 72 hours. The extract was filtered and distilled on water bath, a reddish brown syrupy mass was obtained and it was finally dried at low

temperature under reduced pressure in a rotary evaporator (microwave oven). A crude residue (75 g) was obtained giving a yield of 7.5%. When needed, the crude extract was suspended in distilled water and used in the study.

Animals

Male albino rats of Wistar strain weighing about 150–200 g obtained from the Medical College of Trichur (Kerala) were used for the study. They were fed a standard rat pellet diet (Sai Durga feeds, Bangalore) and water ad-libitum and maintained under standard laboratory condition (Temperature 24–28°C, relative humidity 60–70%). Animal described as fasted were deprived of food for 16 h but had free access to water. Ethical clearance for the handling of experimental animals was obtained from the committee constituted for the purpose. (CPCSEANO: 659/02/a).

Chemicals

All purified enzymes, coenzymes, substrates and standards were purchased from Sigma Chemicals Company USA. All other chemicals used were of analytical grade, and purchased from SD Fine, Qualigens and Himedia, India.

Alloxan induced diabetes

Diabetes was induced by a single ip injection of 120 mg/kg of alloxan monohydrate, in sterile saline (7). After 72 hours of alloxan injection, the diabetic rats (glucose level >250 mg/dl) were used for the study (8).

Experimental set up

The animals were divided into 6 groups of 6 each. Group I served as normal healthy control. Group II (untreated diabetic control). Group III diabetic rats given *T. arjuna* bark extract (250 mg/kg PO). Group IV diabetic rats given *T. arjuna* bark extract (500 mg/kg PO). Group V control rat given *T. arjuna* bark extract (250 mg/kg PO). Group VI control rats given *T. arjuna* bark extract (500 mg/kg PO). The extract was administered for the period of 30 days.

Collection of blood, liver and kidney

After the experimental regimen, the animals were sacrificed by cervical dislocation under mild chloroform anesthesia. Blood was collected on decapitation and serum was separated by centrifugation (for 20 min at 2000 rpm). The liver and kidney were excised immediately and thoroughly washed in ice - cold saline. The serum and tissues collected were used for biochemical estimation.

Estimation of biochemical parameters

Serum glucose was measured by GOD/POD method (9), the content of lipid peroxidation (LPO) (10), Enzymatic antioxidants such as superoxide dismutase (SOD) (11), catalase (CAT) (12), glutathione peroxidase (GPx) (13) glutathione reductase (GR) (13), glutathione-s-transferase (GST) (14) and glucose-6-phosphate dehydrogenase (G6PD) (15) and non enzymatic antioxidants, glutathione (GSH) (16), β -carotene (Vit A) (17) ascorbic acid (Vit C) (18), α -tocopherol (Vit E) (19), thiol such as total sulfhydryl

groups (TSH) (20) and non protein sulfhydryl groups (NPSH) (20) were estimated in liver and kidney of experimental groups, tissue protein content was estimated by the method of Lowry et al (21).

Statistical evaluation

Statistical evaluation was done using one-way analysis of variance (ANOVA) followed by Duncan's Multiple Range Test (DMRT). Statistical significance was set at ($P < 0.05$).

RESULTS**Serum glucose**

The levels of glucose in serum of alloxan induced diabetic rats were significantly ($P < 0.05$) elevated as compared with control rats. Oral administration of *T. arjuna* (250 and 500 mg/kg body weight) to diabetic rats for 30 days caused significant reduction in serum glucose level/values. (Table I).

Lipid peroxide concentration

In liver and kidney lipid peroxidation (LPO) level were elevated significantly ($P < 0.05$) in diabetic rats as compared to normal rats. Administration of *T. arjuna* bark extract for 30 days lowered the elevated values to near normal (Table II).

Activity of anti-oxidant enzymes

The activities of enzymatic antioxidants such as SOD, CAT, GPx, GST, GR and G6PD in liver and kidney of diabetic rats were

TABLE I: Effect of *Terminalia arjuna* stem bark on serum glucose, of control and experimental rats.

| Parameters | Group I (Control) | Group II (Diabetic) | Group III (Diabetic+TA 250 mg/kg) | Group IV (Diabetic+TA 500 mg/kg) | Group V (Control+TA 250 mg/kg) | Group VI (Control+TA 500 mg/kg) |
|-----------------|----------------------|------------------------|---|--|--------------------------------------|---------------------------------------|
| Serum | | | | | | |
| Glucose (mg/dl) | 98.33±02.66 | 302.97±22.35a* | 125.60±24.73b* | 82.50±04.72cf* | 106.67±0.625d ^{ns} | 113.17±14.25e ^{ns} |

Values are expressed as Mean±SD (n=6)

Statistical comparison :

a : Group I and Group II

b : Group II and Group III

c : Group II and Group IV

d : Group I and Group V

e : Group I and Group VI

f : Group III and Group IV

*P<0.05 ns- non significant.

TABLE II: Effect of *Terminalia arjuna* on LPO level in the liver and kidney of control and experimental rats.

| Parameters | Group I (Control) | Group II (Diabetic) | Group III (Diabetic+TA 250 mg/kg) | Group IV (Diabetic+TA 500 mg/kg) | Group V (Control+TA 250 mg/kg) | Group VI (Control+TA 500 mg/kg) |
|---------------|----------------------|------------------------|---|--|--------------------------------------|---------------------------------------|
| Liver | | | | | | |
| # LPO | 0.20±0.02 | 1.87±0.14a* | 0.12±0.02b* | 0.21±0.05cf* | 0.14±0.02d ^{ns} | 0.25±0.01e ^{ns} |
| Kidney | | | | | | |
| # LPO | 0.42±0.01 | 1.58±0.04a* | 0.26±0.01* | 0.34±0.01cf* | 0.24±0.01d ^{ns} | 0.38±0.07e ^{ns} |

Values are expressed as Mean±SD (n=6)

Statistical comparison :

a : Group I and Group II

b : Group II and Group III

c : Group II and Group IV

d : Group I and Group V

e : Group I and Group VI

f : Group III and Group IV

*P<0.05 ns- non significant.

Units :

: nM of MDA formed/100 g tissue

significantly (P<0.05) reduced as compared to control rats. Oral administration of *T. arjuna* (250 and 500 mg/kg body weight) for 30 days nearly normalized the activities of these enzymes (Table III and IV).

The content of non-enzymatic anti-oxidants

The levels of non-enzymatic antioxidants viz., glutathione (GSH), β -carotene (Vit A), α -tocopherol (Vit E), ascorbic acid (Vit C) and thiol groups such as total sulfhydryl groups (TSH) and non-protein sulf-hydryl

groups (NPSH) in liver and kidney of diabetic rats were significantly reduced in diabetic rats, when compared with control rats. Oral administration of *T. arjuna* (250 and 500 mg/kg body weight) to diabetic rats for 30 days significantly (P<0.05) reversed their values to normal (Table V and VI).

The control rats treated with *T. arjuna* (250 and 500 mg/kg body weight) did not produce any significant alteration in serum and tissue parameter when compared with control animals.

TABLE III: Effect of *Terminalia arjuna* on enzymatic antioxidants in the liver of control and experimental rats.

| Parameters | Group I (Control) | Group II (Diabetic) | Group III (Diabetic+TA 250 mg/kg) | Group IV (Diabetic+TA 500 mg/kg) | Group V (Control+TA 250 mg/kg) | Group VI (Control+TA 500 mg/kg) |
|------------|----------------------|------------------------|---|--|--------------------------------------|---------------------------------------|
| (1) SOD | 11.99±0.64 | 7.16±0.23* | 10.47±0.58b* | 11.76±0.54cf* | 11.12±0.84d ^{ns} | 11.12±0.64e ^{ns} |
| (2) CAT | 6.11±0.67 | 2.56±0.29a* | 4.35±1.31b* | 5.30±0.52cf* | 5.78±0.55d ^{ns} | 5.55±0.24e ^{ns} |
| (3) GPX | 5.98±0.07 | 3.82±0.39a* | 5.50±0.16b* | 6.22±0.14cf* | 5.83±0.10d ^{ns} | 6.40±0.08e ^{ns} |
| (4) GST | 8.42±0.28 | 4.14±0.16a* | 7.03±0.08b* | 6.32±0.08cf* | 8.98±0.92d ^{ns} | 8.69±0.29e ^{ns} |
| (5) GR | 14.33±0.76 | 5.52±0.35a* | 12.77±0.44b* | 13.91±0.77cf* | 14.05±0.09d ^{ns} | 14.18±1.33e ^{ns} |
| (6) G6PD | 3.67±0.26 | 1.88±0.18a* | 4.31±0.16b* | 3.84±0.25cf* | 3.48±0.09d ^{ns} | 3.50±0.41e ^{ns} |

Values are expressed as Mean±SD (n=6)

Statistical comparison :

a : Group I and Group II

b : Group II and Group III

c : Group II and Group IV

d : Group I and Group V

e : Group I and Group VI

f : Group III and Group VI

*P<0.05 ns- non significant.

Units :

(1) : 50% inhibition of nitrite/min/mg protein

(2) : nmoles of H₂O₂ decomposed/min/mg protein

(3) : µg of GSH consumed/min/mg protein

(4) : µmoles of CDNB-GSH conjugate formed/min/mg protein

(5) : µmoles of GSH utilised/min/mg protein

(6) : 0.010D/min/mg protein

TABLE IV: Effect of *Terminalia arjuna* on enzymatic antioxidants in the kidney of control and experimental rats.

| Parameters | Group I (Control) | Group II (Diabetic) | Group III (Diabetic+TA 250 mg/kg) | Group IV (Diabetic+TA 500 mg/kg) | Group V (Control+TA 250 mg/kg) | Group VI (Control+TA 500 mg/kg) |
|------------|----------------------|------------------------|---|--|--------------------------------------|---------------------------------------|
| (1) SOD | 7.08±0.50 | 3.84±0.07a* | 5.80±0.89b* | 7.37±0.36cf* | 6.39±0.50d ^{ns} | 6.46±0.634e ^{ns} |
| (2) CAT | 4.75±0.45 | 2.26±0.12a* | 3.96±0.16b* | 4.88±0.08cf* | 4.48±0.50d ^{ns} | 4.41±0.44e ^{ns} |
| (3) GPX | 5.91±0.36 | 2.34±0.37a* | 3.68±0.53b* | 4.80±0.06cf* | 5.65±0.61d ^{ns} | 5.36±0.65e ^{ns} |
| (4) GST | 6.21±0.02 | 1.65±0.19a* | 5.87±0.42b* | 6.39±0.40cf* | 6.30±0.09d ^{ns} | 6.18±0.01e ^{ns} |
| (5) GR | 14.03±0.32 | 8.33±0.07a* | 13.46±0.51b* | 14.19±0.89cf* | 14.02±0.74d ^{ns} | 13.98±0.40e ^{ns} |
| (6) G6PD | 2.91±0.37 | 1.11±0.09a* | 3.17±0.30b* | 2.68±0.12cf* | 2.49±0.24d ^{ns} | 2.69±0.24e ^{ns} |

Values are expressed as Mean±SD (n=6)

Statistical comparison :

a : Group I and Group II

b : Group II and Group III

c : Group II and Group IV

d : Group I and Group V

e : Group I and Group VI

f : Group III and Group IV

*P<0.05 ns- non significant.

Units :

(1) : 50% inhibition of nitrite/min/mg protein

(2) : nmoles of H₂O₂ decomposed/min/mg protein

(3) : µg of GSH consumed/min/mg protein

(4) : µmoles of CDNB-GSH conjugate formed/min/mg protein

(5) : µmoles of GSH utilised/min/mg protein

(6) : 0.010D/min/mg protein

TABLE V: Effects of *Terminalia arjuna* on nonenzymatic antioxidants in the liver of control and experimental rats.

| Parameters | Group I (Control) | Group II (Diabetic) | Group III (Diabetic+TA 250 mg/kg) | Group IV (Diabetic+TA 500 mg/kg) | Group V (Control+TA 250 mg/kg) | Group VI (Control+TA 500 mg/kg) |
|------------|----------------------|------------------------|---|--|--------------------------------------|---------------------------------------|
| (1) Vit A | 15.30±1.75 | 9.69±0.38a* | 17.03±1.53b* | 15.02±1.12cf* | 16.57±1.07d ^{ns} | 15.22±0.67e ^{ns} |
| (2) Vit C | 0.89±0.03 | 0.25±0.01a* | 0.49±0.03b* | 0.89±0.04cf* | 0.75±0.06d ^{ns} | 0.91±0.07e ^{ns} |
| (3) Vit E | 6.18±0.40 | 3.43±0.25a* | 6.67±0.48b* | 7.93±0.46cf* | 6.34±0.43d ^{ns} | 6.41±0.33e ^{ns} |
| (4) GSH | 6.12±0.15 | 2.96±0.12a* | 6.35±0.24b* | 6.78±0.15cf* | 6.17±0.21d ^{ns} | 6.13±0.29e ^{ns} |
| (5) TSH | 6.18±0.41 | 3.78±0.22a* | 6.98±0.14b* | 7.48±0.21cf* | 6.21±0.22d ^{ns} | 6.50±0.36e ^{ns} |
| (6) NPSH | 1.05±0.08 | 0.69±0.03a* | 0.98±0.05b* | 1.07±0.05cf* | 1.08±0.03d ^{ns} | 1.08±0.04e ^{ns} |

Values are expressed as Mean±SD (n=6)

Statistical comparison :

a : Group I and Group II

d : Group I and Group V

b : Group II and Group III

e : Group I and Group VI

c : Group II and Group IV

f : Group III and Group IV

*P<0.05 ns- non significant.

Units :

(1) : µg/mg protein

(2) : µg/mg protein

(3) : µg/mg protein

(4) : µg/mg protein

(5) : µg/mg protein

(6) : µg/mg protein

TABLE VI: Effect of *Terminalia arjuna* on nonenzymatic antioxidants in the kidney of control and experimental rats.

| Parameters | Group I (Control) | Group II (Diabetic) | Group III (Diabetic+TA 250 mg/kg) | Group IV (Diabetic+TA 500 mg/kg) | Group V (Control+TA 250 mg/kg) | Group VI (Control+TA 500 mg/kg) |
|------------|----------------------|------------------------|---|--|--------------------------------------|---------------------------------------|
| (1) Vit A | 10.82±0.50 | 4.61±0.62a* | 8.79±0.30b* | 9.66±0.35cf* | 10.74±0.63d ^{ns} | 10.39±0.34e ^{ns} |
| (2) Vit C | 1.28±0.06 | 0.17±0.01a* | 0.43±0.10b* | 1.16±0.01cf* | 1.24±0.04d ^{ns} | 1.33±0.02e ^{ns} |
| (3) Vit E | 4.49±0.44 | 2.27±0.31a* | 7.22±0.49b* | 5.35±0.35cf* | 4.51±0.44d ^{ns} | 4.90±0.13e ^{ns} |
| (4) GSH | 4.43±0.19 | 2.07±0.09a* | 4.07±0.16b* | 5.15±0.39cf* | 4.40±0.74d ^{ns} | 4.33±0.27e ^{ns} |
| (5) TSH | 4.61±0.24 | 2.52±0.31a* | 3.95±0.06b* | 4.54±0.31cf* | 4.57±0.54d ^{ns} | 4.57±0.43e ^{ns} |
| (6) NPSH | 1.65±0.07 | 0.92±0.06a* | 1.43±0.10b* | 1.57±0.09cf* | 1.73±0.54d ^{ns} | 1.62±0.16e ^{ns} |

Values are expressed as Mean±SD (n=6)

Statistical comparison :

a : Group I and Group II

d : Group I and Group V

b : Group II and Group III

e : Group I and Group VI

c : Group II and Group IV

f : Group III and Group IV

*P<0.05 ns- non significant.

Units :

(1) : µg/mg protein

(2) : µg/mg protein

(3) : µg/mg protein

(4) : µg/mg protein

(5) : µg/mg protein

(6) : µg/mg protein

DISCUSSION

Our findings reveal that the significant decrease of serum glucose level in extract treated diabetic rats. Lipid peroxidation (LPO) is the process whereby oxygen interacts polyunsaturated fatty acids. When this process occurs in biological membrane, gross alteration of structural, organizational and enzyme function may result. Further more, lipid peroxide mediated damage has been observed in the development of type 1 and type 2 diabetes mellitus (22).

In the present study, we have observed an increased level of LPO in liver and kidney of alloxan induced diabetic rats. The reduction of two electrons from alloxan gives dialuric acid, which undergoes oxidation and leads to generation of $O_2^{\cdot-}$, H_2O_2 and OH^{\cdot} . Dialuric acid has been observed to stimulate lipid peroxidation *in vitro* (4). In this context a marked increase in LPO in liver and kidney of diabetic animals, were reported by Annamali (23), and Venkataswaran (24). Our results show that, oral administration *Terminalia arjuna* bark extract (at a doses of 250 and 500 mg/kg body weight) significantly ($P < 0.05$) decreased the level of LPO. This indicates that *T. arjuna* bark extract may scavenge or inhibit the free radical formation and effectively prevent the liver and kidney damage.

Reduced activities of SOD and CAT in liver and kidney tissues have been observed in diabetes rats, and this activity may result in a number of deleterious effects due to accumulation of superoxide radicals ($O_2^{\cdot-}$) and hydrogen peroxide (H_2O_2) (4). Administration of *T. arjuna* bark extract increases the activities of SOD and CAT in

diabetic rats. The result of the SOD and CAT activity clearly shows that *T. arjuna* contains a free radical scavenging activity, which could exert a beneficial action against pathological alteration caused by the presence of $O_2^{\cdot-}$ and OH^{\cdot} . This action could involve mechanism related to scavenging activity.

The decrease in the activities of these (GPx, GST, GR) enzymes result in the involvement of deleterious oxidative changes and also insufficient availability of GSH. The present study observed the depleted levels of GPx, GST and GR in alloxan induced diabetic rats and elevation of GPx, GST and GR after treatment with *Terminalia arjuna* bark extract. Our study corroborates the study of Manonmani et al., (6) who have indicated the protective effect of *T. arjuna* and its potential to elevate the antioxidant status of chloroform extract in heart and liver of alloxan rats.

G6PD (glucose-6-phosphate dehydrogenase), a pentose phosphate pathway enzyme, is considered as a supporter of primary antioxidant enzymes through production of cellular NADPH, decrease in activity of G6PD in liver and kidney of diabetic rats, may be due to inhibition of protein synthesis and accelerated proteolysis and structural disintegration (25). However, the activity of G6PD was significantly ($P < 0.05$) increased by *Terminalia arjuna* bark extract treatment indicating improvement in glucose utilization by pentose phosphate pathway.

Hyperglycemia can increase oxidative stress and change the redox potential of glutathione (26). Decreased level of GSH in liver and kidney of diabetic rats may

increase their susceptibility to oxidative injury (27). Reduction of oxidised form of glutathione requires NADPH, as a cofactor and enzyme glutathione reductase. The reduced availability of NADPH, which could be either due to reduced synthesis or increased metabolism of NADPH through some other pathway, could be also responsible for low levels of reduced glutathione in alloxan diabetic rats as compared to control rats (28). Other workers have also reported, decreased level of liver and kidney GSH in alloxan induced diabetic rats (29, 30). Administration of *Terminalia arjuna* bark extract (250 and 500 mg/kg) increases the content of GSH in liver and kidney of diabetic rats, may be due to less production of ROS.

Vitamin A acts as a powerful, free radical scavenger (Singlet oxygen) and chain breaking antioxidant (31). The function of vit A as radical scavenging antioxidants, can protect the cells from oxidative damage (32). It probably assists vit E in inhibition of lipid peroxidation by recycling the vit E (33). Decreased level of vit A in liver and kidney of diabetic rats may be due to more of oxygen radicals in tissues in alloxan diabetic animals. Administration of *T. arjuna* bark extract (250 and 500 mg/kg body weight) brought back the decreased level to normal level. This might have been possible due to regeneration of vit A from its radical.

Vitamin C is an excellent hydrophilic antioxidant, it readily scavenges ROS and peroxy radical (34, 35). Also act as a co-antioxidant by regenerating the vit A, E and GSH from radicals (36). We have observed a decreased level of vit C in liver and kidney of diabetic rats. This decrease level could be

due to the increased utilization of vit-C in deactivation of the increased level of reactive oxygen species or to decrease in the GSH level. Since, the GSH is required for the recycling of vit C (37, 38). Administration of *T. arjuna* bark extract improve the level of vit-C in liver and kidney of diabetic rats, may be expected to enhance the GSH level or stimulation of the system to recycle the dehydro ascorbic acid back to ascorbic acid.

The decreased level of vit E found in liver and kidney of diabetic rats as compared with control rats could be due to the increased oxidative stress, which accompanies the decrease in the level of antioxidant and may be related to the causation of diabetes mellitus (23). Low level of vit E observed in alloxan diabetic rats compared to normal controls suggests decreased regeneration of vit E from its radical. Regeneration of vit E requires ascorbic acid, an aqueous phase antioxidant, which requires GSH (28). Since vit C and E are synergistic antioxidants administration of *T. arjuna* bark extract improve the vit E level in liver and kidney of diabetic rats.

Total sulfhydryl (TSH) and nonprotein sulfhydryl (NPSH) group level decreases in the liver and kidney of diabetic rats. This is presumed to be due to oxidation of essential thiols (39). The nonprotein sulfhydryl group is predominantly contributed by cysteine in glutathione and some minor thiols. Liver plays a major role in glutathione homeostasis and is the main export organ for glutathione (40). Administration of *T. arjuna* bark extract restore the decreased level of TSH and NPSH in liver and kidney of diabetic rats, is possibly due to increased glutathione export from muscles into circulation.

It has been well documented that *T. arjuna* bark extract contains acids (arjunic acid, terminic acid, glycosides, tannins, saponins, flavones etc.) may provide antioxidant activity, which may be attributed to its protective action on lipid peroxidation and to the enhancing effect on cellular antioxidant defense. In conclusions, the glucose lowering activity observed in the

diabetic animals may be due to the stimulation of the β - cells of the pancreatic islets, we strongly report the antioxidant effect of *T. arjuna* in normal and alloxan treated animals. It has been found that only 500 mg/kg of *T. arjuna* extract (ethanolic) exhibited significant antioxidant effect hence thereby *T. arjuna* may alter the renal and hepatic protection against oxidative damage by diabetes.

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