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**Original Article**

# Prevention of liver cirrhosis by green tea supplementation

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**Abstract**

Green tea has most significant effects on human health .Green tea strengthen the immune system by protecting it against oxidants and radicals. Green tea may reduce the risk of many chronic diseases which is showed by several epidemiological studies. This beneficial effect of green tea has been attributed to the presence of high amount of polyphenols which are potent antioxidants. The present study was designed to evaluate the effect of Green tea supplementation on different biochemical parameters in thioacetamide induced cirrhotic rats. For this purpose adult Sprague Dawley rats of male sex were divided into four groups (n=6).Group I remained healthy control rats. Group II, received thioacetamide (at a dose of 200mg/kg b.w twice a week, i.p for 8 weeks).Group III, received thioacetamide (at a dose of 200mg/kg b.w twice a week, i.p for 8 weeks) and green tea (500mg/day, orally for 8 weeks) and Group IV, received green tea (500mg/day,orally for 8 weeks). Biochemical analysis was evaluated by total and direct bilirubin, liver specific enzymes and antioxidant enzymes. Marked increase in total and direct bilirubin and ALT activities was the indicative marker of liver cirrhosis while reduced antioxidants activity (SOD and catalase) and increased MDA level were observed in cirrhotic group. Green tea supplementation markedly reduced total bilirubin and ALT activity and restored the antioxidant enzymes (SOD and catalase ) and MDA level. These results indicate that green tea successively attenuates the thioacetamide induced liver cirrhosis.

**Keywords:** Green tea, Thioacetamide, Liver enzymes, SOD, MDA, Catalase.

## INTRODUCTION

The one of the most popular beverage consumed worldwide is tea. Green tea is taken from plant called Camellia sinensis and consumed in different parts of the world as green, black, or Oolong tea. Among all of these, the consumption of green tea exerts most significant effects on human health (Cabrera et al., 2006). prevention of cancer (Kavanagh et al .,2001), cardiovascular diseases (Sueoka et al., 2001), anti-inflammatory (Dona et al.,2003), antiarthritic (Haqqi et al .,1999), antibacterial (Sudano et al .,2004), antiangiogenic (Sartippour et al., 2002), antioxidative (Osada et al .,2001), antiviral (Weber et al .,2003), neuroprotective (Weinreb et al., 2004), and cholesterol-lowering effects (Raederstorff et al., 2003) have been included in health benefits of consuming green tea (Mckay et al., 2002). Supplementation of green tea, its extracts, and its isolated constituents were also found to be effective in prevention of oxidative stress (Babu et al., 2006) and neurological problems (Unno et al., 2007). Many types of cancer including lung, colon, esophagus, mouth, stomach, small intestine, kidney, pancreas and mammary glands have also been prevented by green tea consumption (Koo et al., 2004). Effect of green tea has also been demonstrated against the influenza virus in its earliest stage and as well as against the Herpes Simplex Virus (Toda et al.,1989;Yama et al., 1997;Weber et al., 2003). Green tea strengthens the immune system action because it protects it against oxidants and radicals. Recent studies suggested that Parkinson's, Alzheimer's disease and other neurodegenerative diseases might be protected by GTPs (Weinreb et al., 2004; Pan et al., 2003).

Green tea contains polyphenols, which include flavanols, flavandiols, flavonoids, and phenolic acids; these compounds may account for up to 30% of the dry weight. Polyphenols of green tea (GTPs) are flavonols, commonly called as catechins.

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Products obtained from green tea are mostly extracts of green tea in liquid and powder form that vary in the proportion of polyphenols (45-90%) and caffeine ( 0.4-10%). The major flavonoids of green tea are a number of catechins which are found in green tea in greater amount than in black and Oolong tea (Vinson 2000). There are four types of catechins mainly find in green tea: epicatechin, epigallocatechin, epicatechin-3-gallate, and EGCG (Sano et al., 2001). Recently green tea has various beneficial effects belong to Catechin, (-)-epigallocatechin-3-gallate (EGCG), is most abundant in tea (Moyers et al., 2004;Higdon et al., 2003). Green tea catechins have an inhibitory effect on Helicobacter pylori infection (Takabayashi et al., 2004; Yee et al., 2002).The positive effect of green tea extract and GTPs observed on the proliferation and activity of bone cells. The progression of liver fibrosis in chronic liver disease is closely related to the proliferation of hepatic stellate cells, and on the proliferation of these cells EGCG has a potential inhibitory effect (Dorchies et al., 2003; Sakata et al .,2004).

Catechins are considered to help protect against cellular damage by contributing along with antioxidant enzymes (superoxide dismutase and catalase) and antioxidant vitamins (vitamins C and E) to the total antioxidant defense system (Abdel-Raheim et al., 2009).Green tea catechins increase total plasma antioxidant activity is shown by in vivo studies (Yokozawa et al., 2002;Skrzydlewska et al., 2002). The activity of superoxide dismutase increases in serum and the expression of catalase in aorta by intake of green tea extracts, these enzymes are implicated in cellular protection against reactive oxygen species (Skrzydlewska et al., 2002; Negishi et al., 2004) . This action is combined with direct action on oxygen species by a decrease in the nitric oxide plasma concentration. Intake of green tea also decreases Malondialdehyde, a marker of oxidative stress (T,Nakagawa et al., 1999). Therefore, the main purpose of this research work was to study the hepatoprotective role of green tea and trace elements in thioacetamide induced liver cirhhosis in experimental rats model.

## MATERIAL AND METHOD

Sprague-Dawley rats (male) weighing 200-250gm were purchased from the animal house of Aga Khan University Hospital, Karachi, Pakistan for the study. Animals were acclimatized to the laboratory conditions before the start of experiment and caged in a quiet temperature controlled animal room (23+4°C). Rats had free access to water and standard rat diet throughout the experimental period except 24 hours prior to decapitation.

**Ethical guidelines:** The experiments were conducted with ethical guideline of internationally accepted principles for laboratory use and care in animal research (Health research extension Act of 1985).

**Study Design:** 24 Male Sprague Dawley rats were randomly divided into four groups, each of six rats. The duration of the study was 8 weeks. Each group received following treatment;
Group I: the control (remain untreated)
Group II: TAA-treated
Group III: TAA+Green tea treated
Group IV: Green tea treated
Group I was the control group and remained untreated and was weighed every week. Group II was the TAA treated group, received thioacetamide at a dose of 200gm/ kg b.w, intraperitoneally, twice a week, for 8 weeks. Group III was the TAA+ Green tea treated group, received thioacetmide at a dose of 200mg/kg b.w, twice a week , for 8 weeks and received green tea 500mg/kg b.w, orally, for 8 weeks daily. Group IV received only green tea at a dose of 500mg/kg b.w, orally for 8 weeks and weighed every week. After 24 hours of last dose of treated groups, rats were decapitated and the blood was collected from the neck wound in the lithium heparin coated tubes. The collected blood was mixed gently and then transferred to centrifuged glass tubes and then centrifuged at 2000 rpm for 20 minutes. Serum was separated and collected in eppindroff tubes and stored at-70°C until analysis. Liver was excised, trimmed of connective tissues, rinsed with saline to eliminate blood contamination dried by blotting with filter paper and weighed. The remaining tissues then kept in freezer at -70°C until analysis.

**Estimation of Serum ALT, total and direct bilirubin:** Plasma ALT, total and direct bilirubin were analyzed using commercially prepared reagent kits from Randox.

**Preparation of post mitochondrial supernatant (PMS):** Liver homogenate was prepared by taking 1g of liver tissue in 10ml of 5mM potassium phosphate buffer (pH 7.8) by using a tissue homogenizer ultra taurax T-25 polytron. The homogenates were centrifuged at 800g for five minutes at 4°C to separate the nuclear debris. The supernatant so obtained was centrifuged at 10,500g for 20 minutes at 4°C to get post mitochondrial supernatant which was used to assay SOD, catalase and MDA.

**Estimation of malondialdehyd (MDA):** The malondialdehyde (MDA) content, a measure of lipid peroxidation, was assayed in the form of thio-barbituric acid reacting substances (TBARS) by the

lipidperoxidation method (Okhawa et al., 1979). Briefly the reaction mixture consisted of 0.2ml of 8.1% sodium dodecyle sulphate, 1.5 ml of 20% acetic acid solution adjusted to pH 3.5 with sodium hydroxide and 1.5 ml of 0.8% aqueous solution of thiobarbituric acid was added to 0.2ml of 10%(w/v) of PMS.The mixture was brought up to 4.0ml with distilled water and heated at 95°C for 60 minutes. After cooling with tap water, 1.0ml distilled water and 5.0ml of the mixture of n-butanol and pyridine (15:1 v/v) was added and centrifuged. The organic layer was taken out and its absorbance was measured at 532 nm on Schimadzu-spectrophotometer UV 120-01 and compared with those obtained from MDA standards.The concentration values were calculated from absorption measurements as standard absorption.

**Estimation of catalase:** Catalase activity was assayed by the method of sinha (Sinha et al., 1979). Briefly the assay mixture was consisted of 1.96ml phosphate buffer (0.01M, pH 7.0), 1.0ml hydrogen peroxide (0.2 M) and 0.04ml PMS (10%w/v) in a final volume of 3.0ml. 2ml dichromate acetic acid reagent was added in 1ml of reaction mixture, boiled for 10 minutes, cooled. Change in absorbance was recorded at 570 nm.

**Estimation of superoxide dismutase (SOD):** Levels of SOD in the cell free supernatant were measured by the method of (Kono et al., 1978). Briefly 1.3ml of solution A (0.1 m EDTA containing 50 mM $Na_2CO_3$,Ph 10.0),0.5ml of solution B (90µmNBT nitrobluetetrazolium dye) and 0.1ml of solution C (0.6%Triton X-100 in solution A),0.1ml of solution D (20mM Hydroxyl amine hydrochloride,pH 6.0) were mixed and the rate of NBT reduction was recorded for one minute at 560 nm.0.1ml of the supernatant was added to the test cuvette as well as reference cuvette, which does not contain solution D. Finally, the percentage inhibition in the rate of reduction of NBT was recorded as described above. One enzyme unit was expressed as inverse of the amount of protein (mg) required in one minute.

**Statistical Analysis:** Results are presented as mean ± SD. Statistical significance and difference from control and test values were evaluated by student's t-test. P-values of *P<0.01 and **P<0.05 were considered significant.

## RESULTS

**Effect of thioacetamide and green tea treatment on liver weight and liver to body weight ratio in control and treated rats:** Increased liver weight and relative liver weight was observed in TAA group after 8 weeks administration of TAA as compare to control (6.11±0.2 P<0.01) (0.04±0.001 P<0.01) (Table 1). Whereas reduction in the liver weight and relative liver weight was observed in TAA+G group as compare to control (5.8 ± 0.15 P<0.01) (0.035±0.001 P<0.01) respectively. An increase in liver weight was observed in Green tea treated rats (6.1±0.34 P<0.01) as compare to control where as relative liver weight was almost normal (0.031±0.001 P<0.01) as compare to control.

**Effect of thioacetamide and Green tea treatment on serum bilirubin, ALP and ALT activity in control and treated rats:** Level of total bilirubin was significantly increased in TAA treated rats( 2.19±0.01 P<0.01) as compare to control, green tea supplementation reduced this elevated level (0.65 ± 0.01 P<0.01) as compare to control. Increased level of direct bilirubin was found in TAA treated rats (3.41 ± 0.2 P<0.01) as compare to control which was reduced almost up to normal level in TAA+ G tea group (1.2±0.02 P<0.01) as compare to control.

Level of serum ALT was markedly increased in TAA treated group (921.3±68.19 P<0.01) as compare to control.. Alanine amino transferase level was significantly decreased in TAA+G group as compare to control (210.82±13.6 P<0.01). Alone Green tea had no significant effect on plasma ALT activity. Gamma glutamyl transferase (GGT) level almost increased in TAA-treated rats as compare to control (08±1.1 P<0.01) and decreased in Green tea treated group as compare to control (0.6±0.3 P<0.01).

**Effect of thioacetamide and green tea treatment on hepatic concentration of MDA in control and treated rats:** Level of MDA was markedly increased in TAA-treated group as compare to control (18.49±4.28 P<0.05).Green tea administration in TAA+G group decreased the concentration of MDA as compare to control (10.6±5.41 P<0.05) while green tea treated group showed a slight increase in MDA level as compare to control (16.7±4.48 P>0.05).

**Effect of thioactamide and green tea treatment on hepatic concentration of superoxide dismutase in control and treated rats:** Table 3 showed a significant decrease in SOD activity in TAA-treated group as compare to control (1657.5±211.7 P>0.05).TAA+G group, after green tea supplementation showed normal levels of SOD activity (1813.3±59.77 P>0.05) as compare to control. SOD activity reduced in green tea treated group (1297.6±873.7 P<0.01) as compare to control.

**Effect of thioactamide and green tea treatment on hepatic concentration of catalase in control and treated rats:** Concentration of catalase was significantly deccreased in TAA-treated group (3.85±0.01 P<0.01) as compare to control. Administration of green tea in TAA+G group significantly reduced catalase level (8.78±0.01 P<0.01) as compare to control. Alone green tea treatment had no effect on catalase (7.1±0.3 P<0.01).

## DISCUSSION

Liver cirrhosis has been reported by administration of thioacetamide (TAA), depending on the period to exposure. Our studies are in agreement with previous reported studies (Balansky et al., 2007). After administration of TAA, TAA is converted into TAA-S-oxide (TASO) by hepatic microsomal cytochrome P450 2E1 (CYP 2E1) then converted to its toxic metabolite thioacetamide S-dioxide (TASO2) (Chilakapati et al., 2005). Its metabolite interferes with the movement of RNA from the nucleus to the cytoplasm which causes membrane injury. Number of hepatocytes reduces as well as a decrease in rate of oxygen consumption and bile volume occurs (Taranalli and Kuppast, 1996). In the assessment of liver damage by TAA, liver marker enzymes (ALT,ALP,GGT) activities and total and direct bilirubin become increased which was observed in thioacetamide treated rats in our study. Increased levels of serum marker enzymes indicate injury of liver tissue. This may due to damaged structural integrity of the liver because they are located in cytoplasmic location and after cellular damage they are released into the circulation (Recknagel et al., 1989). The present study describes the long term administration of thioacetamide resulted in the development of severe liver injury in rats. Dashti reported that thioacetamide administration is easy and reliable for the induction of liver cirrhosis in experimental animal models and Muller reported that resulting disease resembles the human cirrhosis. In our study MDA level is increased in TAA treated rats which is the end product of oxidative stress. Oxidative stress and subsequent lipid peroxidation have been reported to initiate cirrhosis of tissue, the formation of reactive oxygen species (ROS) have been reported in TAA-induced liver diseases, which initiate the per oxidation reaction (Ortega et al., 1997). Lipid per oxidation is a degenerating process in the tissue that arises with production of free radical and the production of end product malondialdehyde (Ali et al., 2001). In our study antioxidant defense system are suppressed in TAA-treated rats. In the cirrhotic liver of animals the loss of hepatocytes were indirectly analyzed by the activity of the antioxidant enzymes (SOD and Catalase) SOD and catalase results were inversely to that of the oxidative stress biomarker, so in the cirrhotic rats the values of SOD and catalase were lower than in the control rats. These result indicated the occurrence of severe damage in the cells of cirrhotic liver. Excess of reactive oxygen species (ROS) is due to imbalance between the rate of ROS production and ROS removal (McMichael, 2007). Green tea contains high concentration of chemicals known as polyphenols which contain the antioxidant activity that significantly reduces changes in cirrhosis. Flavonoids are phenolic compounds that are widely distributed in plants and multiple biological effects have been reported including antioxidant and free radical scavenging abilities (Baek et al., 1996). In present study, green tea supplementation to thioacetamide treated rats resulted in the reversal of altered levelsof bilirubin and ALT, antioxidant enzymes, MDA and in body weight, indicates that green tea successfully attenuates liver cirrhosis in rats.

**Table 1:** Liver weight, liver to body weight ratio in control and treated rats

| Groups | Liver weights | Relative liver weight |
|---|---|---|
| Control | 5.33±0.31* | 0.033±0.001* |
| TAA | 6.11±0.2 * | 0.04±0.001* |
| TAA+G | 5.8±0.15* | 0.035±0.001* |
| Green tea | 6.1±0.31* | 0.031±0.003* |

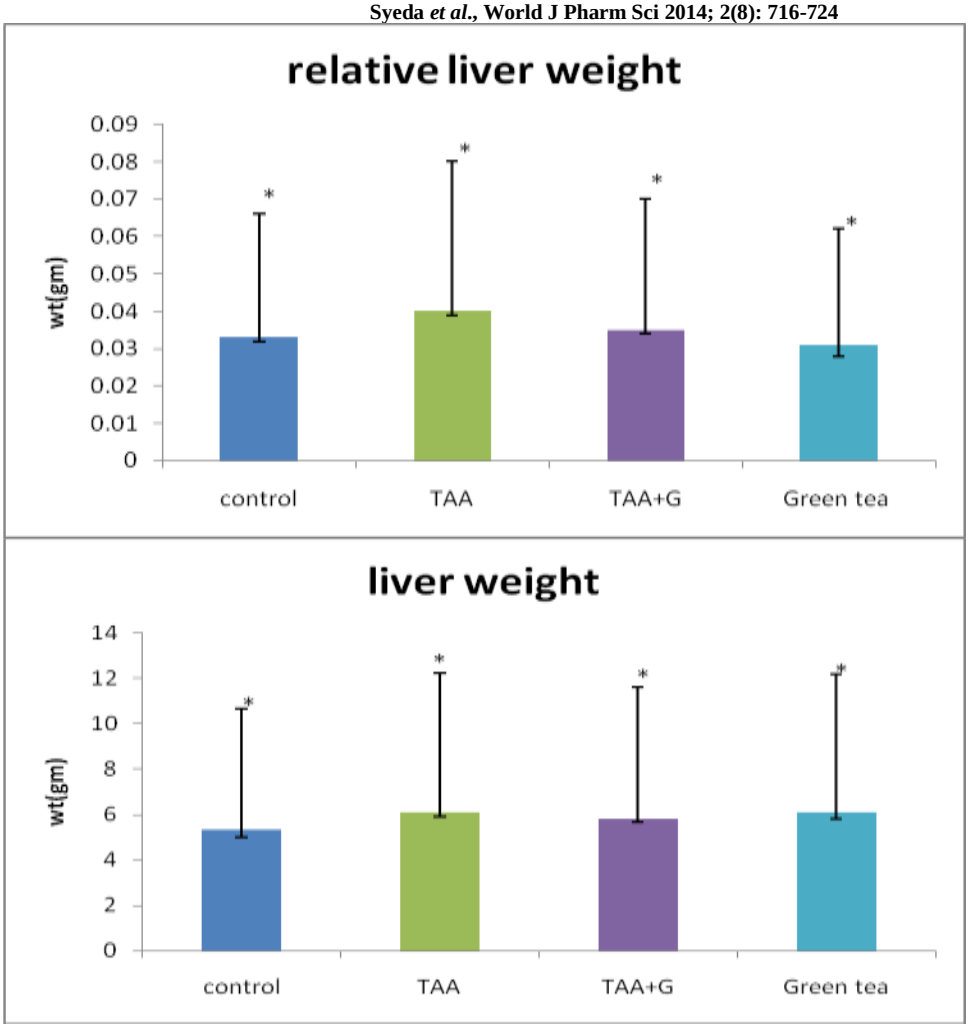
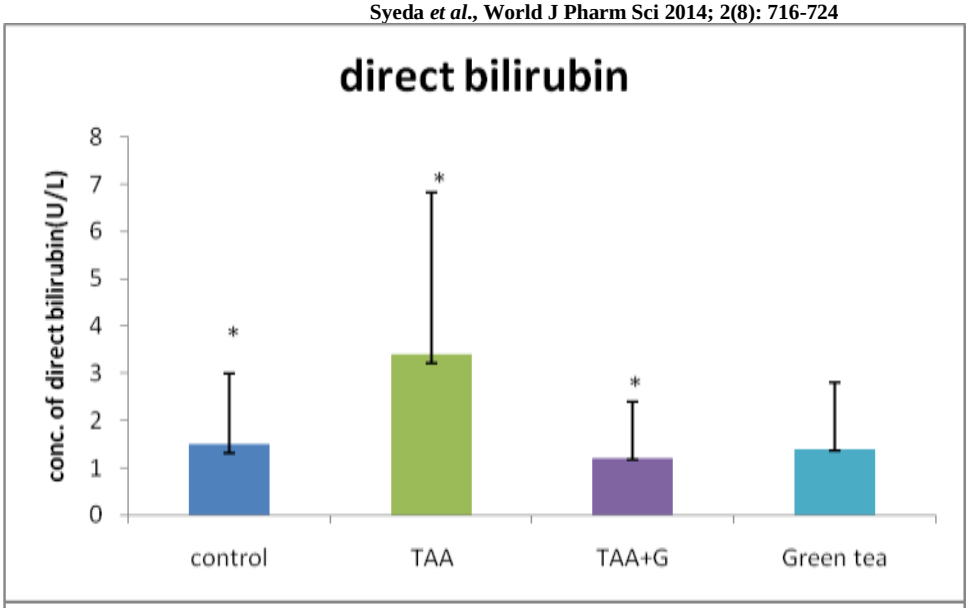
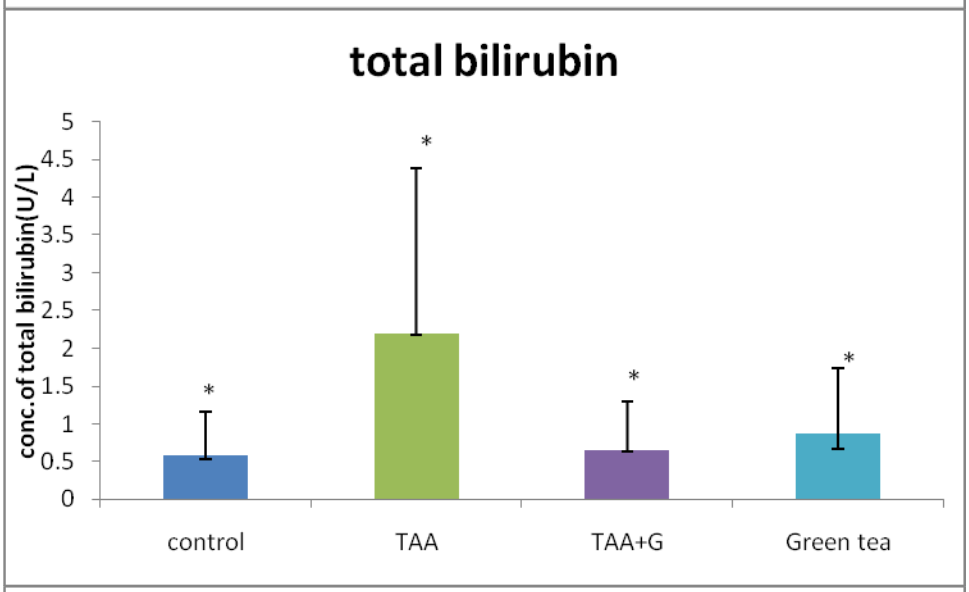
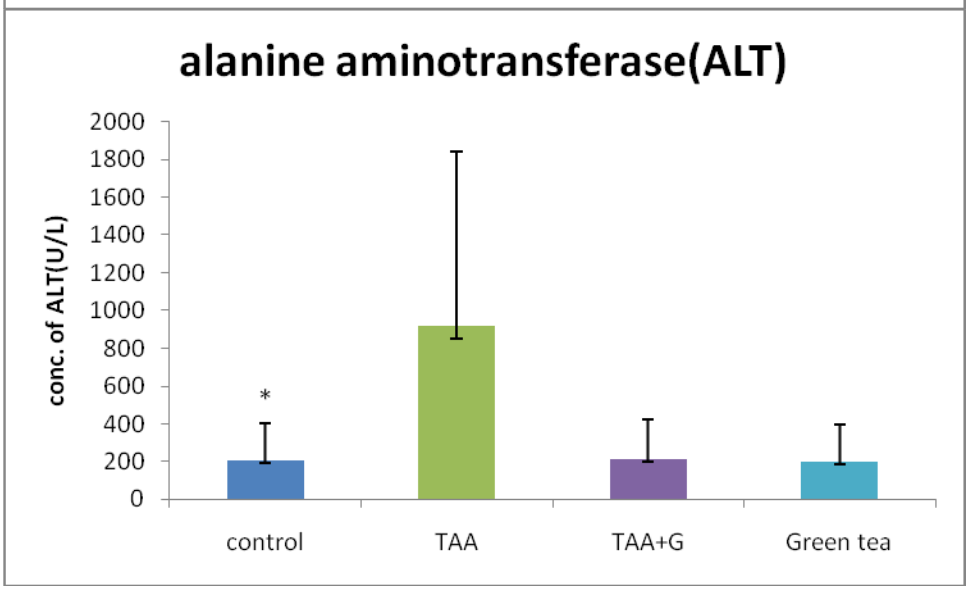


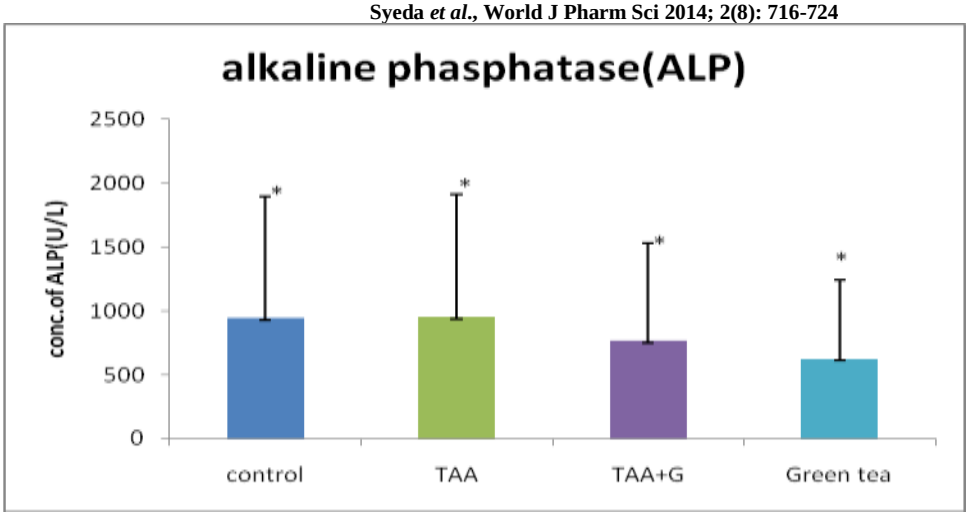

**Table 2:** Effect of thioacetamide and green tea treatment on serum bilirubin, ALT, ALP and GGT in control and treated rats.

| Parameters | Control | TAA | TAA+G | Green tea |
|---|---|---|---|---|
| Total bilirubin (U/L) | 0.58±0.04 * | 2.19±0.01* | 0.65±0.01* | 0.87±0.2* |
| Direct bilirubin(U/L) | 1.50±0.2* | 3.41±0.2* | 1.2±0.02* | 1.4±0.02 |
| Alanine aminotransferase (U/L) | 200.7±11.7* | 921.3±68.19 | 210.82±13.6 | 198±10.1 |
| Alkaline phasphatase (U/L) | 948±21* | 956±23* | 764±12* | 621±10* |
| Gamma Glutamyl transferase (U/L) | 07±1.2* | 08±1.1* | 05±0.6* | 06±0.3* |


direct bilirubin
conc. of direct bilirubin(U/L)
8
7
6
5
4
3
2
1
0
*
*
*
control
TAA
TAA+G
Green tea


total bilirubin
conc.of total bilirubin(U/L)
5
4.5
4
3.5
3
2.5
2
1.5
1
0.5
0
*
*
*
*
control
TAA
TAA+G
Green tea


alanine aminotransferase(ALT)
conc. of ALT(U/L)
2000
1800
1600
1400
1200
1000
800
600
400
200
0
*
control
TAA
TAA+G
Green tea



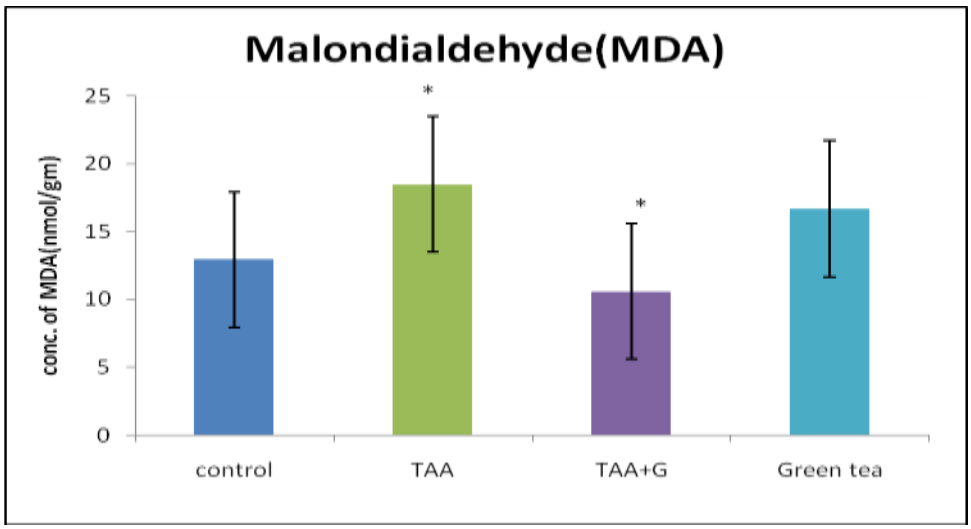
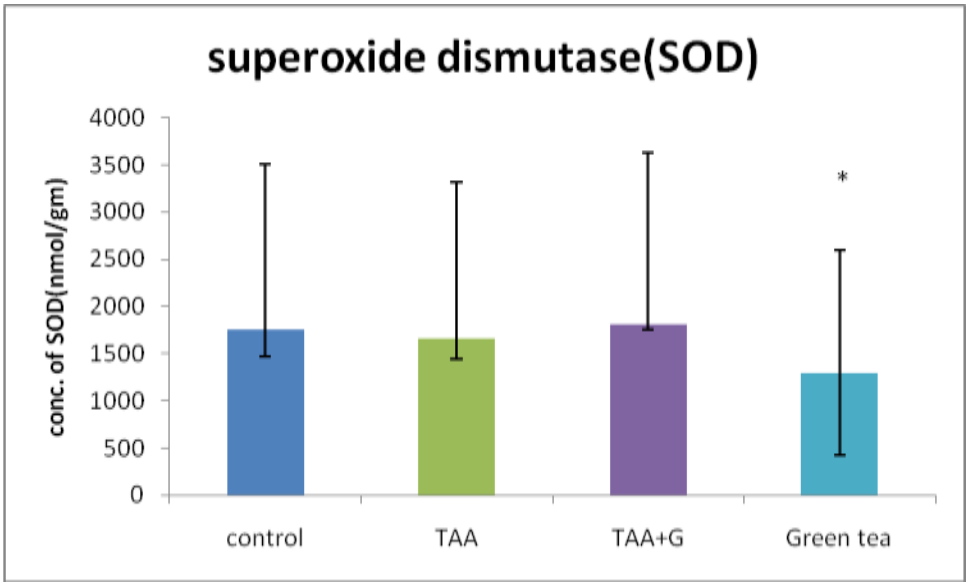
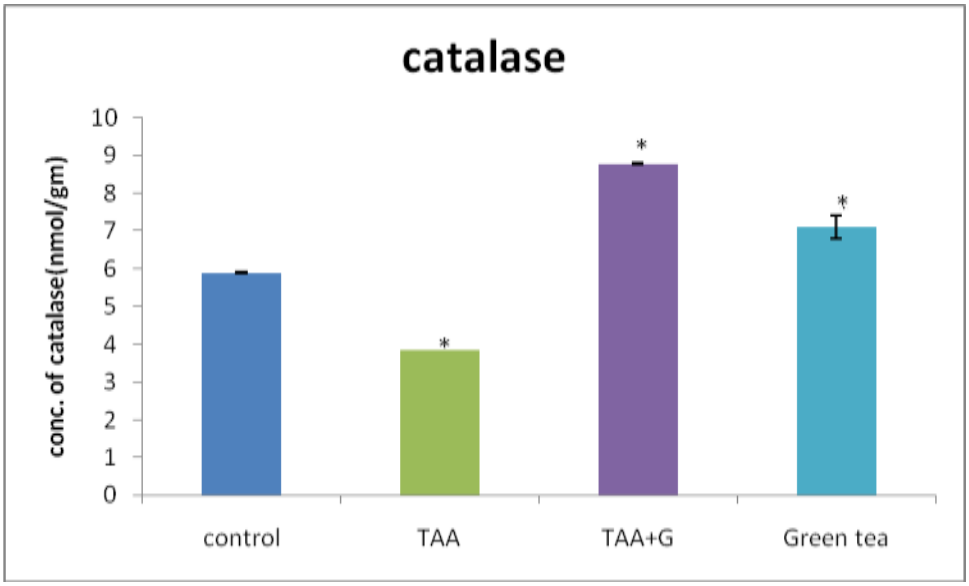




**Table 3:** Effect of thioacetamide and green tea treatment on hepatic concentration of superoxide dismutase, malondialdehyde and catalase

| Parameters | Control | TAA | TAA+G | Green tea |
|---|---|---|---|---|
| SOD nmol/gm | 1754.25±288.4 | 1657.5±211.7 | 1813.3±59.77 | 1297.6±873.7* |
| MDA nmol/gm | 12.96±1.55 | 18.49±4.28* | 10.6±5.41* | 16.7±4.48 |
| Catalase nmol/gm | 5.9±0.02 | 3.85±0.01* | 8.78±0.01 | 7.1±0.3 |




REFERENCES

1. Abdel-Raheim et al. Effect of green tea extract and vitamin C on oxidant or antioxidant. Indian J Clin Biochem. 2009; 24(3):280–287.
2. A.D. Taranalli, I.J. Kuppast. Study of wound healing activity of seeds of Trigonella foenum-graecum in rats. Ind J. Pharm. Sci 1996; 58: 117–119
3. Babu PV et al. Therapeutic effect of green tea extract on oxidative stress in aorta and heart of streptozotocin diabetic rats. Chem Biol Interact. 2006;162:114–120.
4. Cabrera C et al. Beneficial effects of green tea a review. J Am Coll Nutr.2006; 25:79–99.
5. Chilakapati J et al. Saturation toxicokinetics of thioacetamide: role in initiation of liver injury. Drug Metab Dispos 2005; 33(12):1877-1885.
6. Dashti H et al. Thioacetamide and carbon tetrachloride induced liver cirrhosis. Eursurg.Res. 2001; 21:83-91.
7. Dona M et al. Neutrophil restraint by green tea: inhibition of inflammation, associated angiogenesis, and pulmonary fibrosis. J Immunol. 2003; 170:4335–4341.
8. Dorchies OM et al. Anti-fibrotic properties of green tea catechins on mouse muscle cell cultures. Neuromuscul Disord. 2003;13:639
9. Haqqi TM et al. Prevention of collagen-induced arthritis in mice by a polyphenolic fraction from green tea. Proc Natl Acad Sci USA. 1999; 96:4524–4529.
10. Halliwell B, Gutteridge JMC. Free Radicals in Biology and Medicine. Oxford: Clarendon Press 1985;

11. Higdon JV, Frei B. Tea catechins and polyphenols: health effects, metabolism, and antioxidant functions. Crit Rev Food Sci Nutr. 2003; 43:89–143.
12. Kavanagh KT et al. Green tea extracts decrease carcinogen-induced mammary tumor burden in rats and rate of breast cancer cell proliferation in culture. J Cell Biochem. 2001; 82:387–398.
13. Koo MWL, Cho CH. Pharmacological effects of green tea on the gastrointestinal system. Eur J Pharmacol. 2004; 500:177–185.
14. McMichael MA. Oxidative stress, antioxidants, and assessment of oxidative stress in dogs and cats. J Am Vet Med Assoc 2007; 231(5):714-720.
15. McKay DL, Blumberg JB. The role of tea in human health. J Am Coll Nutr. 2002; 21:1–13.
16. Moyers SB, Kumar NB. Green tea polyphenols and cancer chemoprevention: multiple mechanisms and endpoints for phase II trials. Nutr Rev. 2004; 62:204–211.
17. Muller A et al. Thioacetamide-induced cirrhosis-like liver lesions in rats. Usefulness and rehability of this animal model. Exp. Pathol 1988; 34: 229-236.
18. Negishi H et al. Black and green tea polyphenols attenuate blood pressure increases in stroke-prone spontaneously hypertensive rats. J Nutr. 2004; 134:38–42.
19. N.L. Baek et al. Hepatoprotective activity of extracts from stem of Mussaenda erythrophylla lam. Against carbon tetrachloride-induced toxicity in rats 1996;
20. Oretega M.A et al. Hepatotoxic agent thioacetamide induces biochemical and histological alteration in rat small intestine. Dig.Dis.Sci 1997;42(8):1715-1723.
21. Pan TH et al. Potential therapeutic properties of green tea polyphenols in Parkinson's disease. Drugs Aging. 2003; 20:711–721.
22. Raederstorff DG et al. Effect of EGCG on lipid absorption and plasma lipid levels in rats. J Nutr Biochem. 2003; 14:326–332.
23. R. Balansky et al. Potent carcinogenicity of cigarette smoke in mice exposed early in life Carcinogenesis 2007; 10:2236–2243.
24. Recknagel, R.O et al. Mechanisms of carbon tetrachloride toxicity, Pharmacol. Therapeutics 1989; 43: 139-154.
25. Sueoka N et al. A new function of green tea: prevention of lifestyle-related diseases. Ann N Y Acad Sci. 2001; 928: 274–280.
26. Sudano Roccaro A et al. Epigallocatechin-gallate enhances the activity of tetracycline in staphylococci by inhibiting its efflux from bacterial cells. Antimicrob Agents Chemother. 2004; 48:1968–1973.
27. Sartippour MR et al. Green tea inhibits vascular endothelial growth factor (VEGF) induction in human breast cancer cells. J Nutr. 2002; 132:2307–2311.
28. Sano M et al. Simultaneous determination of twelve tea catechins by high-performance liquid chromatography with electrochemical detection. Analyst. 2001; 126:816–820.
29. Sakata R et al. Green tea polyphenols epigallocatechin-3-gallate inhibits platelet-derived growth factor-induced proliferation of human hepatic stellate cell line LI90. J Hepatol. 2004; 40:52–59.
30. Skrzydlewska E et al. Protective effect of green tea against lipid peroxidation in the rat liver, blood serum and the brain. Phytomedicine. 2002; 9:232–238.
31. S. Ali et al. Xanthine oxidase-derived reactive oxygen metabolites contribute to liver necrosis: protection by 4-hydroxypyrazolo [3,4-d]pyrimidine Biochim. Biophys. Acta 2001; 1: 21–30.
32. Takabayashi F et al. Inhibitory effect of green tea catechins in combination with sucralfate on Helicobacter pylori infection in Mongolian gerbils. J Gastroenterol. 2004; 39:61–63.
33. Toda M et al. Antibacterial and bactericidal activities of Japanese green tea. Nippon Saikingaku Zasshi. 1989; 44:669–672.
34. T, Nakagawa T et al. Effects of green tea tannin on cisplatin-induced nephropathy in LLC-PK1 cells and rats. J Pharm Pharmacol. 1999; 51:1325–1331.
35. Unno K et al. Daily consumption of green tea catechin delays memory regression in aged mice. Biogerontology. 2007; 8(2):89–95.
36. Vinson JA. Black and green tea and heart disease: a review. Biofactors. 2000; 13:127–132.
37. Weber JM et al. Inhibition of adenovirus infection and adenain by green tea catechins. Antiviral Res. 2003; 58:167–173.
38. Weinreb O et al. Neurological mechanisms of green tea polyphenols in Alzheimer's and Parkinson's diseases. J Nutr Biochem. 2004; 15:506–516.
39. Yee YK et al. Chinese tea consumption and lower risk of Helicobacter infection. J Gastroenterol Hepatol. 2002; 17:552–555.
40. Yama TS et al. Microbiological activity of whole and fractionated crude extracts of tea (Camellia sinensis), and of tea components. FEMS Microbiol Lett. 1997; 152:169–174.
41. Yokozawa T et al. Antioxidative activity of green tea polyphenol in cholesterol-fed rats. J Agric Food Chem. 2002; 50:3549–3552.