

Antioxidant effects of *Musa paradisiaca* L. in acetaminophen induced hepatic toxicity in albino rats

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ABSTRACT

The improper functioning of the antioxidant defense system of our body results in the damage of macromolecules such as DNA, protein and lipids. This forms the basis of pathology of various diseases. Antioxidants prevent the accumulation of the free radicals and protect the body from diseases. The present study was designed to assess the antioxidant potential of *Musa paradisiaca* L in acetaminophen induced damage. The experimental models were grouped into six groups comprising of six rats each. Group I served as normal control, Group II was induced with acetaminophen at a dose of 2g/kg BW as a single dose. Group III was induced with acetaminophen and orally administered aqueous extract of *Musa paradisiaca* L at a dose of 100mg/Kg BW for 15 days. Group IV was induced with acetaminophen and orally administered aqueous extract of *Musa paradisiaca* L at a dose of 200mg/Kg BW for 15 days. Group V received the aqueous extract of *Musa paradisiaca* L alone at a dose of 200mg/Kg BW for 15 days. Group VI was induced with acetaminophen and administered silymarin at a dose of 25mg/KgBW for 15 days. At the end of the experimental period the animals were sacrificed. Serum and hepatic tissue were used for the study. The following parameters were analysed in the hepatic tissue – Lipid peroxidation (LPO), Superoxide Dismutase (SOD), Reduced Glutathione(GSH) and protein. The serum protein level was also measured. The induction of hepatic damage with acetaminophen resulted in increased lipid peroxidation and reduced scavenging activity of the defense system of the body. On treatment with the aqueous extract of *Musa paradisiaca* L the antioxidant system was activated reducing the lipid peroxidation and accumulation of free radicals, thereby protecting the hepatic tissue from oxidative damage.

INTRODUCTION

The liver is a vital organ with a wide range of functions such as detoxification, protein synthesis and is involved in the biosynthesis of enzymes and other components required for digestion. Mankind is exposed to various foreign chemicals (xenobiotics) – drugs, food additives and pollutants in their day to day life. Acetaminophen, alcohol, ibuprofen, CCl₄, lead and contraceptives are some drugs that cause hepatic injury. Most of these compounds are subjected to chemical alteration in the

human body. The liver plays a major role in this process (Akilavalli *et al*, 2011). This physiological activity of liver results in the generation of highly reactive free radicals, which covalently bonds with membrane lipids causing lipid peroxidation (Radhika *et al*, 2011). Reactive oxygen species (ROS) are generated by many redox processes that normally occur in the metabolism of aerobic cells. ROS include free radicals such as superoxide (O²⁻), hydroxyl radical (.OH), peroxy radical (RO.²) as well as non-radical species such as hydrogen peroxide (H₂O₂). These species are highly reactive and harmful to the cells (Bhuvaneshwari *et al*, 2011). The imbalance between the reactive oxygen species and the antioxidant defense system of our body results in the damage of macromolecules such as DNA, Protein and Lipids.

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This forms the basis of pathology of various diseases (Gupta, 2006). *Musa paradisiaca* L. is a tree like herb widely cultivated in the tropics. Fruits, leaves, peels, roots of the plant have been used in the treatment of dysentery and diarrhoea, in inflammation, antiulcerogenic activity and hypolipidemic activity (Imam and Akter, 2011). It is also used in the treatment of urolithiasis (Weremfo *et al* 2011).

The present study was hence designed to investigate the antioxidant potential of *Musa paradisiaca* L in acetaminophen induced damage in albino rats.

MATERIALS AND METHODS

Collection of Plant Material

The flowers of *Musa paradisiaca* L. were collected in and around Trichy, identified and authenticated with the Flora of Presidency of Madras and confirmed with the voucher specimen deposited at the RAPINAT Herbarium at St. Joseph's College, Trichy.

Preparation of aqueous extract

The flowers were freshly ground and mixed with six times the volume of water and boiled until it reduced to 1/3rd. It was then filtered through a muslin cloth. The residue was re extracted. The filtrate was mixed and evaporated to dryness till it reaches a paste like consistency. The extract was refrigerated until further use.

Experimental models

Wistar strains of Albino rats of both sexes weighing 150-200g were used for the study. Animals were housed in well ventilated cages in the CPCSEA approved animal house. The protocol was approved by the Institutional Animal Ethics committee. They were fed with pelleted rat chow and water *ad libitum*. They were acclimatised to the laboratory conditions for a week before starting the experiment.

Experimental Design

The experimental models were grouped into six groups comprising of six rats each. Group I served as normal control, Group II was induced with acetaminophen at a dose of 2g/kg BW as a single dose. Group III was induced with acetaminophen and orally administered aqueous extract of *Musa paradisiaca* L at a dose of 100mg/Kg BW for 15 days.

Group IV was induced with acetaminophen and orally administered aqueous extract of *Musa paradisiaca* L at a dose of 200mg/Kg BW for 15 days. Group V received the aqueous extract of *Musa paradisiaca* L at a dose of 200mg/Kg BW alone for 15 days. Group VI was induced with acetaminophen and orally administered silymarin at a dose of 25mg/KgBW for 15 days. At the end of the experimental period the animals were sacrificed. Serum and hepatic tissue were used for the study.

The following parameters were analyzed in the hepatic tissue –

Estimation of protein

Aliquots of the suitably diluted serum (0.1ml to 10ml by two serial dilutions) was made up to 1.0ml with water and 4.5ml of alkaline copper reagent was added to all the tubes including blank, containing 1.0ml water and standards containing aliquots of standard BSA and made up to 1ml with water. The tubes were incubated for 10 min at room temperature. 0.5 ml was added to all the tubes and incubated for 20 min at room temperature. The blue colour developed was read at 640nm (Lowry *et al*, 1951).

Estimation of Lipid per oxides

0.1ml of tissue homogenate was mixed with 4 ml of 0.85N H₂SO₄ and mixed gently. 0.5 ml of phosphotungstic acid was added and stirred well. The contents were centrifuged for 10 min. The supernatant was discarded and the sediment mixed with 2.0 ml of N/12 H₂SO₄ and 0.3 ml of 10% phosphotungstic acid. The mixture was centrifuged for 10 min. The sediment was suspended in 4.0 ml of distilled water and 1 ml of TBA reagent. The tubes were kept in a boiling water bath for 1 hr. After cooling 5ml of butanol was added to each tube and the colour extracted in the butanol phase was read at 532 nm (Ohkawa *et al*, 1979).

Assay of Superoxide Dismutase

0.1 ml of tissue homogenate was added to tubes containing 0.75 ml ethanol and 0.15 ml chloroform (chilled in ice) and centrifuged. To 0.5 ml of supernatant added 0.5 ml EDTA solution and 1 ml of buffer. The reaction was initiated by the addition of 0.5ml of epinephrine and the increase in absorbance was measured at 480 nm (Misra and Fridovich, 1972).

Estimation of Reduced Glutathione

One ml of homogenate/blood was precipitated with 1 ml of TCA and the precipitate was removed by centrifugation. To 5ml of the supernatant added 2ml of DTNB and the total volume was made up to 3 ml with phosphate buffer. The absorbance was read at 412 nm (Moron *et al*, 1979).

Statistical Analysis

The values were expressed as mean \pm SEM. The statistical analysis was carried out by one way analysis of variance followed by "t" test. P values <0.05 were considered statistically significant.

RESULTS AND DISCUSSION

The results clearly depicted the oxidative damage caused by acetaminophen induced toxicity. The rats in group II showed a significant increase in lipid peroxidation with a corresponding decrease in the serum and tissue protein and antioxidant activity. On treatment with aqueous extract of *Musa paradisiaca* L the rats showed a noteworthy improvement in the antioxidant status and protein levels with a concurrent decrease in the lipid peroxidation. The serum and tissue protein levels are depicted in Table-1 and the

Table. 1: Level of serum and tissue protein in experimental models .

Groups/Parameter	Group I	Group II	Group III	Group IV	Group V	Group VI
Serum Protein (mg/dl)	7.2 ± 0.82	2.5 ± 0.94*	4.68 ± 1.02	6.9 ± 0.86**	6.97 ± 0.69	7.09 ± 0.77**
Tissue Protein (mg/g wet tissue)	88.25±2.01	41.34±0.56*	61.57±1.09	83.51±0.73**	74.75±1.08	84.75±0.31**

Values are ± SEM (n=6).

* p<0.05 statistically significant when compared to normal control

** p<0.05 statistically significant when compared to disease control

Table. 2: Antioxidant status of the diseased and treated experimental models .

Groups/Parameter	Group I	Group II	Group III	Group IV	Group V	Group VI
LPO(nmoles/mg prot)	1.44±1.09	6.77±0.14*	4.17±0.72	1.62±1.11**	1.51±0.23	1.25±0.97**
SOD (U/mg prot)	2.09±0.94	6.77 ± 0.88*	3.91 ± 0.66**	2.91 ± 0.76	2.65 ± 0.48	2.51 ± 0.22**
GS H(nmoles/min/mg)	2.77 ± 0.11	0.83 ± 0.02*	3.33 ± 0.85	1.33 ± 0.38**	2.34 ± 0.43	2.98 ± 1.13**

Values are ± SEM (n=6).

* p<0.05 statistically significant when compared to normal control

** p<0.05 statistically significant when compared to disease control

antioxidant status in the disease control and the treated groups are shown in Table 2. Overdose of acetaminophen causes a potentially fatal, hepatic necrosis which can be attributed to the formation of a toxic metabolite N-acetyl-p-benzoquinoneimine (NAPQI) by the action of cytochrome P 450 (Lee *et al.*, 1996).

Most protein found in the plasma are synthesized by the hepatocytes and secreted into circulation. A reduction in the protein levels in the serum and hepatic tissue may be a result of possible damage to the hepatocytes induced by the ingested toxins. The serum protein level is a marker of the synthetic function of the liver and a valuable guide to assess the severity of the damage (Nair, 2006). In the present study the level of protein in serum and hepatic tissue increased on treatment with aqueous extract of *Musa paradisiaca* L. The induced activity of cytochrome P450 2E1 results in the production of the toxic metabolite NAPQI which in turn causes an accumulation of reactive oxygen species.

The accumulating oxygen radicals, inhibits glutathione synthesis, producing glutathione loss from the tissue, activating the peroxidation of the lipids in the cell membranes and impairing antioxidant defense systems in the experimental animals (Monika Bhadauria, 2006). Administration of acetaminophen activates cytochrome P450 2E1 which results in the accumulation of lipid peroxides in the tissue. On treatment with the aqueous extract of *Musa paradisiaca* L the antioxidant status of the experimental models improved thereby preventing the accumulation of reactive oxygen species and lipid peroxidation. Glutathione is a protective compound found within the body and functions to remove potentially toxic electrophilic compounds and protects the organ against dysfunction. Studies suggest that an inverse relationship exists between peroxidative decomposition of membrane PUFA and GSH levels (Singh *et al.*, 2003). It is the most abundant tripeptide thiol antioxidant system of our body and plays a multifactorial role in antioxidant defense. It acts as a direct scavenger and as a co substrate for GPx (Hatem *et al.*, 2010). The present study also shows an inverse relationship between peroxidative decomposition of the membrane and the GSH levels. Superoxide dismutase is the most important anti-oxidant enzyme. The antioxidant enzymes SOD, catalase and peroxidases form a mutually helpful group of defense against reactive oxygen

species (Rajesh and Latha, 2004). It prevents the generation of hydroxyl ions and protects the cellular constituents from oxidative damage (Dasa *et al.*, 2007).

The accumulation of the lipid peroxides and the depletion of SOD and GSH, indicate the necessity of these enzymes for the quick removal of the accumulated toxins from the system. On treatment with the aqueous extract of *Musa paradisiaca* L the enzymatic and non enzymatic antioxidant systems were activated preventing the decomposition of the membranes.

CONCLUSION

The present study depicts the efficacy of the plant in activating the antioxidant systems of the animals thereby restoring the normal functioning of the liver. It is clear from the study that the aqueous extract of *Musa paradisiaca* L possesses significant antioxidant potential.

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