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# NEPHROPROTECTIVE ACTIVITY OF FRESH LEAVES JUICE OF *CORIANDRUM SATIVUM* AGAINST RENAL ARTERY LIGATION INDUCED NEPHROPATHY

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## ABSTRACT

**Aim and objectives:** The present was aimed to evaluate the nephroprotective activity of fresh leaves of *Coriandrum sativum* against renal artery ligation induced nephropathy by taking consideration of kidney parameters in serum as well as urine of experimental animals. **Methods:** Blood was collected from retro orbital plexus and urine was collected by using metabolic cages. Kidney parameters like creatinine, uric acid, total protein and potassium were measured in both serum and urine of experimental animals. **Results:** Treatment with fresh leaves juice of *C. sativum* for 28 days has shown a significant decrease in serum creatinine, BUN and potassium levels and increased levels of serum total protein when compared to control group. Treatment with *C. sativum*, has shown a significant increase in urinary creatinine, uric acid and potassium levels and significant decrease in urinary total proteins. **Conclusion:** From the above results we concluded that the fresh leaves juice of *C. sativum* has good anti-oxidant and renoprotective activities.

## I. INTRODUCTION

The people of India are well acquainted with a large number of indigenous medicinal plants than the natives of any other countries. Herbs are the principal form of medicine in India and

they are becoming popular throughout the world.[1] According to WHO report, over 80% of the world population depends on traditional medicine for their primary health care needs.[2]

In spite of the advent of modern high throughput drug discovery and screening techniques, traditional knowledge systems have given clues to the discovery of valuable drugs.[1]

Herbs have used in several domains like medicine, nutrition, flavoring, beverages, fragrances, cosmetics and other industrial purposes and a huge variety of the flora have been extensively evaluated for their antioxidant activities.[3] A part of medicinal herbs is attributed to the antioxidant activities of their constituents including a wide range of polyphenolic compounds and vitamins like A, E and C. Polyphenols are commonly found in plants and they have been reported to have multiple biological effects including antioxidant activity. A wide range of polyphenols from different subgroups are found in various tissues of plants.[4]

Free radicals are chemical species which contains one or more unpaired electrons due to which they are highly unstable and cause damage to the other molecules by extracting electrons from them in order to attain stability. ROS formed *in-vivo*, like superoxide anion, hydroxyl radical and hydrogen peroxide ($H_2O_2$) are highly reactive and potentially damaging transient chemical species. Over the past decade the increasing evidence indicates that the production of ROS contributes the renal damage.[5] The endogenous anti –oxidants, which detoxify the free radicals are depleted during the process of Renal artery ligation. Hence the supply of exogenous anti- oxidants may be beneficial to protect the cells against the renal damage caused by ROS.[5]

Nephropathy is a progressive renal disease caused by damage to the capillaries in the kidney's glomeruli, characterized by decrease in GFR, persistent elevated albuminuria, elevated arterial blood pressure and fluid retention.[5] The major risk factors implicated in the development of nephropathy are hyperglycemia, hyperlipidaemia and hypertension.[4]

Nephropathy is classified into four types, they are; a) Membranous nephropathy, sub epithelial immune deposits are present in between the glomerular basement membrane (GBM) and the podocyte. b) Obstructive nephropathy, obstruction in the urinary tract. c) IgA nephropathy, deposition of the IgA antibody in the glomerulus and d) Chronic analgesic nephritis, a chronic inflammatory change characterized by loss and atrophy of tubules and interstitial fibrosis and inflammation.[6]

The symptoms of nephropathy includes reduced urine output, poor appetite, unexplained itchiness, swelling of feet, puffiness of face & eyes, and shortness of breath, weight loss, nocturnal urination, blood in urea, difficulty in urination, pain in the back or side, foamy or bubbly urine.[7]

The causes of acute renal injury are classified into 3 types. They are pre renal, renal and post renal. Pre renal injury causes includes ischemia, dehydration, severe fall in blood volume due to shock, blood loss or extensive burns, heart failure, cardiogenic shock and anaphylactic shock. They reduce the blood flow to the kidneys. Renal injury causes includes diseases of the kidneys like acute tubular necrosis, toxins and drugs that damage kidneys, hemoglobinuria, myoglobinuria, myeloma light chains, pyelonephritis or acute glomerulonephritis. Post renal injury causes obstruct the urine flow from the kidneys.[8]

The modern medical and surgical procedures for the treatment of renal failure are dialysis, renal transplantation and chemotherapy. Besides the high costs and complexity of the treatments very few patients are able to obtain adequate treatment and kidney disorders place a heavy financial burden on society. A number of extracts of natural products and dietary anti – oxidants have been reported to show protective effects against kidney diseases.

*Coriandrum sativum* (L) is an annual herb with 1-4 feet height, belongs to the family Umbelliferae. The common names are kothimere, dganiya and Chinese parsely. All parts of *C. sativum* are edible; however, its fresh leaves and dried seeds are most frequently used. Its green foliage, containing proteins, vitamins and minerals (like calcium, phosphorus, and iron), fibres and carbohydrates, is used as vegetable, and in salads, while both the leaves and seeds contain Essential Oils, rich in varying components, which provides typical flavour, when added to the food products and acts as preservative.[9] It is a potent anti oxidant plant. When compared with fruits the leaves are rich in anti oxidant property. The plant containing poly phenolic compounds, carotinoids and flavanoids are responsible for its anti oxidant property. Coriander is traditionally used as carminative, stimulant, and anti inflammatory agent. To date, no research investigating the nephro protective effect of fresh leaf juice of *Coriandrum sativum* has been reported.[9]

## 2. MATERIALS AND METHODS

### 2.1. Collection of plant material

The fresh leaves of *Coriandrum sativum* were collected from the supermarket named Mayabazar Megastores, Tirupathi and authentified by Professor B. Sitaram, Department of Dravyaguna (Clinical Pharmacology and Medicinal plants), S.V. Ayurvedic College, Tirupati.

### 2.2. Preparation of coriander fresh leaf juice

A bunch of fresh coriander leaves were cleaned and washed thoroughly in normal water to remove the dirt and any residual harmful pesticides that might be sticking on them and chopped the leaves as small as possible. Put the chopped leaves in a mortar & pestle and ground for 20 minutes. Squeeze the liquid using a muslin cloth and Poured the filtered liquid into a sterilized glass bottle and used for study. The fresh juice was prepared daily just before the administration to the experimental animals.

### 2.3. Dose selection

As the ingredients present in fresh leaf juice of *Coriandrum sativum* had the information indicating that the test material is likely to be nontoxic. Dose of 200mg/kg, *p.o*. of fresh leaf juice of *Coriandrum sativum* was selected for the present study from the review of literature.

### 2.4. Procurement of animals

Healthy male albino rats of wistar strain weighing about 150-200gm were selected for the study and procured from Venkateswara enterprises, Bangalore.

### 2.5. Instruments

Instruments used to carry out the experiment are UV-Visible spectrophotometer (analytical systems, model no: AUV 2060), electronic balance (Shimadzu, Model no: DS-852 J), homogenizer (Ever shine, Model no: 607), auto analyser (Mispa excel, Version: 14e) and cooling centrifuge (Remi, Model no: C-24 BL).

### 2.6. Experimental protocol

#### 2.6.1. Animals

A total of 25 male albino rats weighing 150–200 g were used for the present study. The rats were housed in the Laboratory Animal House, Sri Padmavathi School of Pharmacy, Tirupathi, Andhra Pradesh. The rats were placed in polypropylene cages in an air conditioned

environment and maintained at room temperature of (23 ± 2) ºC with relative humidity (60% ± 10%) under 12 hour dark and light cycle. Rats were given free access to standard pellet diet and water *ad libitum*. All experimental procedures were in compliance with the Animal Ethical Committee and Committee for the Purpose of Control and Supervision of Experiments on animals (CPCSEA) and were approved by University Ethical Committee with an approval number SPSP: 1016/PO/RE/S/06/CPCSEA/2017 /001.

Animals were divided into five groups as Normal control, Preventive control, Preventive treatment, Curative control and Curative treatment, each contain 5 animals and were treated for 28 days as given in the following table.

**Table No 1: Treatment schedule.**

| Group | Name | Treatment | No. of Animals |
|---|---|---|---|
| I | Normal Control | Vehicle (Normal saline 0.9%) | 05 |
| II | Preventive Control | Vehicle for 28days + Renal artery ligation on day 28 | 05 |
| III | Preventive treatment | 200mg/kg of C.S for 28days +Renal artery ligationon day 28 | 05 |
| IV | Curative control | Renal artery ligation on day 1 + vehicle for 28days | 05 |
| V | Curative treatment | Renal artery ligation on day 1+200mg/kg of CS for 28days | 05 |

**2.6.2. Induction of renal ischemia by renal artery ligation**

Male Wistar rats were anesthetized by intramuscular injection of ketamine (90 mg/kg) and xylazine (10 mg/kg). An incision given at just below to the last rib of left side and the left kidney was exposed. Blood supply to the kidney was interrupted by the application of artery clamp around the left renal artery. Ischemia was confirmed by blanching of the kidney. After 45 min, the clamp was removed and reperfusion was confirmed visually. The wound was then closed in two layers with a 4-0 silk suture and the animals were allowed to recover with free access to food and water (Rabb *et al*., 1995; Rabb *et al*., 2000; Savransky *et al*., 2006).

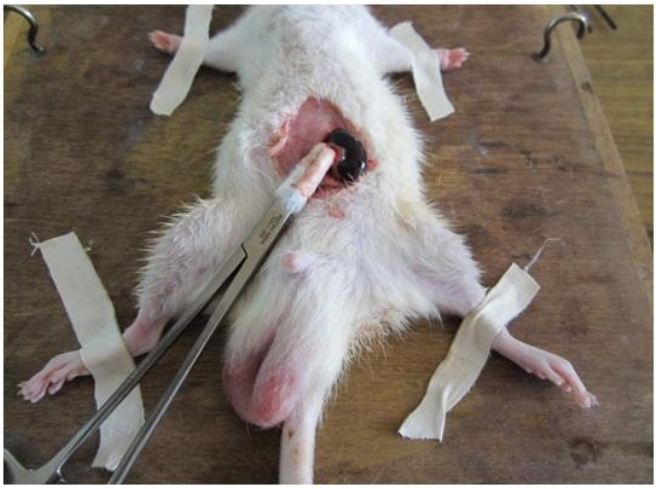

**Fig. 1: Induction of Renal artery ligation (RAL) in experimental rat.**

### 2.7. Collection of blood samples

Blood samples were collected from retro orbital plexus of rats after 72 hrs of RAL in group II and III and at 31st day of RAL in group IV and V in micro-centrifuge tubes. The tubes were kept aside for 1hr at room temperature and serum was isolated by centrifugation at 3000 rpm for 15 min. The clear serum was collected and stored for further biochemical estimations of serum creatinine, blood urea nitrogen (BUN), serum total protein and serum potassium.

### 2.8. Collection of urine samples

Urine samples were collected after 72 hrs of RAL in group II and III and at 31st day of RAL in groups IV and V by housing the rats in individual metabolic cages after oral administration of distilled water (5 ml/animal). After 24hrs the urine was collected and stored. Urine volume, urinary $p^H$, urinary creatinine, uric acid, urinary total protein and urinary potassium were measured.

### 2.9. Kidney samples

At the end of experiment, the rats were sacrificed by decapitation. The kidneys were excised carefully and washed with normal saline. One kidney (kidney that underwent renal clamping) from each group was sliced into two equal halves and one half was homogenised for estimating *in vivo* antioxidant parameters and the other half was put in 10% formalin and used for histopathological studies.

## 3. STATISTICAL ANALYSIS

All the datawas expressed as mean ± S.E.M. Statistical significance between more than two groups was tested using one way ANOVA followed by the Tukey test using computer based fitting program (Prism graph pad,version:5.04). Statistical significance was set at $p<0.05$.

## 4. RESULTS

Acute toxicity studies for fresh leaves juice of the *C.sativum* were not performed as safety was established in earlier studies and no signs of toxicity were reported in literature survey.

For the evaluation of nephroprotective effect against renal artery ligation induced nephropathy, fresh leaves juice of the *C. sativum* was studied at the dose of 200 mg/kg, p.o. as per the earlier studies.

### 4.1. Effect of fresh leaves juice of *C. sativum* (FLJCS) on morphology of kidneys

Pale colored and shrinking kidneys were noticed in preventive and curative control group animals when compared to normal group animals. Kidneys were restored gradually and became into normal morphological features in animals treated with fresh leaves juice of *C. sativum* (Preventive treatment and curative treatment groups).

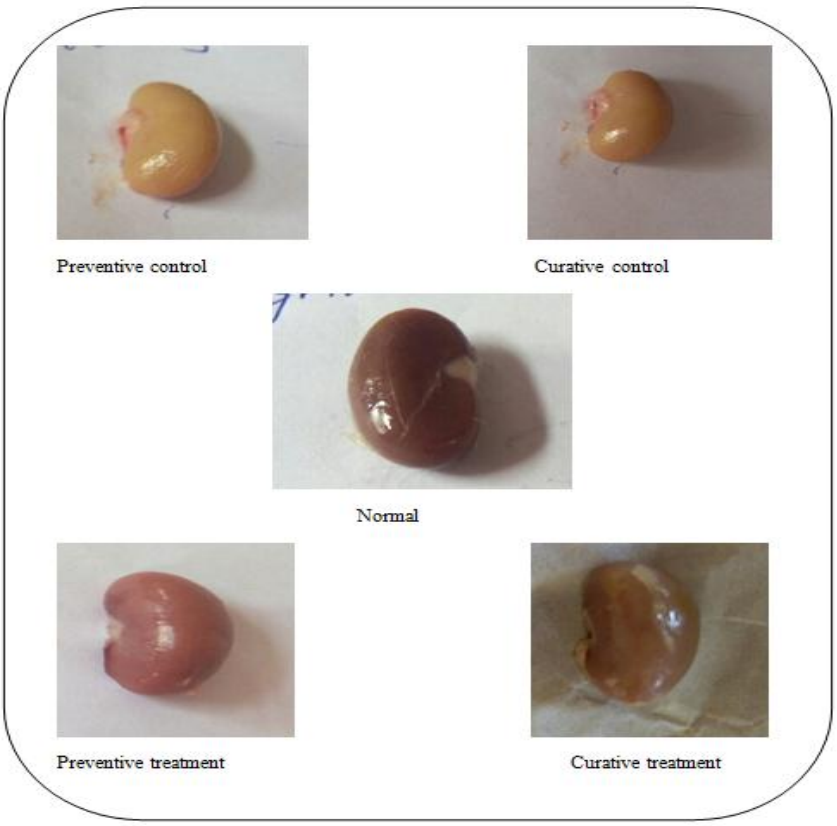


**Fig. 2: Effect of fresh leaves juice of *C. sativum* on morphology of kidneys.**

### 4.2. Effect of fresh leaves juice of *C. sativum* (FLJCS) on serum parameters

Induction of RAL in group II and group IV (preventive control and curative control) had shown a significant increase in serum creatinine, BUN and potassium levels when compared with group I (normal control) indicating that there is a significant deterioration of renal function.

Treatment with fresh leaves juice of *C. sativum* for 28 days in group III (preventive treatment) and group V (curative treatment) has shown a significant decrease in serum creatinine, BUN and potassium levels when compared to group II (preventive control) and group IV (Curative control).

A significant decrease in the serum total protein was noted in group II and IV when compared to group I. A significant increase in the levels of serum total protein was observed in both group III and V when compared to group II and IV indicating that the fresh leaves juice of *C.sativum* reduced the urinary leakage of proteins by ameliorating the renal injury. Values were depicted in table no.2.

**Table No 2. Effect of FLJCS on Serum parameters.**

| S. No | Groups | Creatinine (mg/dl) | BUN (mg/dl) | Total proteins (g/dl) | Potassium (mEq/L) |
|---|---|---|---|---|---|
| I. | Normal | 0.369±0.03 | 9.213±0.13 | 7.452±0.16 | 3.216±0.16 |
| II. | Preventive control | 14.314±0.05*** | 29..34±0.16** | 3.074±0.16*** | 16.85±0.13** |
| III. | Preventive treatment | 0.961±0.05*** | 11.19±0.54** | 5.705±0.26*** | 4.636±0.16** |
| IV. | Curative control | 17.674±0.06*** | 36.79±0.45** | 2.435±0.42*** | 15.23±0.13** |
| V. | Curative treatment | 0.862±0.01*** | 13.64±0.18** | 5.916±0.15*** | 3.876±0.16** |

All values were expressed as Mean ± S.E.M, n=5

*** indicates $p<0.005$ when compared to normal

** indicates $p<0.05$ when compared to control

### 4.3. Effect of fresh leaves juice of *C.sativum* on urinary parameters

Urinary excretion of creatinine, uric acid and potassium was significantly decreased in group II and IV, when compared with the group I indicating the decreased glomerular filtration capacity of kidney due to RAL Treatment with *C. sativum*, has shown a significant increase in urinary creatinine, uric acid and potassium in group III and V.

A significant increase in urinary total protein was noted in group II and IV when compared to group I. A significant decrease in the levels of urinary total proteins was observed in group III and V when compared to group II and IV. Values were expressed in table no.3.

**Table No 3: Effect of FLJCS on urinary parameters.**

| S. No. | Groups | Creatinine (mg/dl) | Uric acid (mg/dl) | Total proteins (g/dl) | Potassium (mEq/L) |
|---|---|---|---|---|---|
| I. | Normal | 1.515±0.43 | 2.544±0.33 | 0.342±0.42*** | 0.830±0.49 |
| II. | Preventive control | 0.154±0.42*** | 1.53±0.82** | 0.582±0.31*** | 0.288±0.12** |
| III. | Preventive treatment | 2.310±0.36*** | 4.820±0.2** | 0.345±0.24*** | 0.550±0.37** |
| IV. | Curative control | 0.188±0.17*** | 1.671±0.6** | 0.647±0.27*** | 0.242±0.62** |
| V. | Curative treatment | 0.656±0.17*** | 5.23±0.62** | 0.354±0.24*** | 0.427±0.18** |

All values were expressed as Mean ± S.E.M, n=5

*** indicates $p<0.005$ when compared to normal

** indicates $p<0.05$ when compared to control

### 4.4. Effect of fresh leaves juice of *C.sativum* on histopathology of rat kidneys

Congestion and mild tubular epithelial cell degeneration was noticed in the histopathology of kidneys of both preventive and curative control animals. Animals treated with *C.Sativum* protected the kidneys.

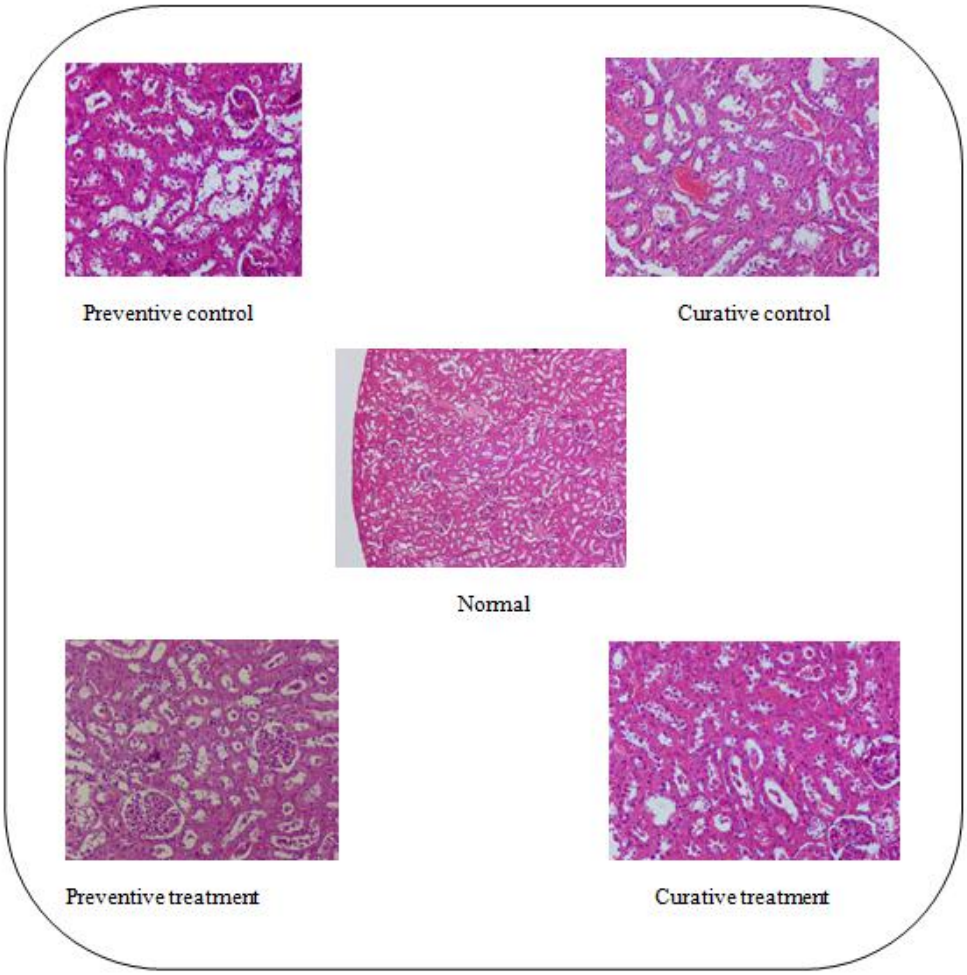


**Fig. 3: Effect of fresh leaves juice of *C. sativum* on histopathology of rat kidneys.**

### 4.5. Effect of fresh leaves juice of *C.sativum* on *in vivo* antioxidant parameters

There was a significant decrease in SOD, catalase and glutathione levels were observed in group II and group IV when compared to group I indicating the excessive production of free radicals. On treatment with *C.Sativum* a significant increase in SOD, catalase, glutathione levels were observed in group III and V. There was a significant increase in the malondialdehyde levels in the control groups (group II and group IV) when compared to the normal group depicting the lipid peroxidation ($p<0.001$). Treatment with *C.Sativum* significantly decreases the malondialdehyde levels in group III and V when compared to the group II and group IV.

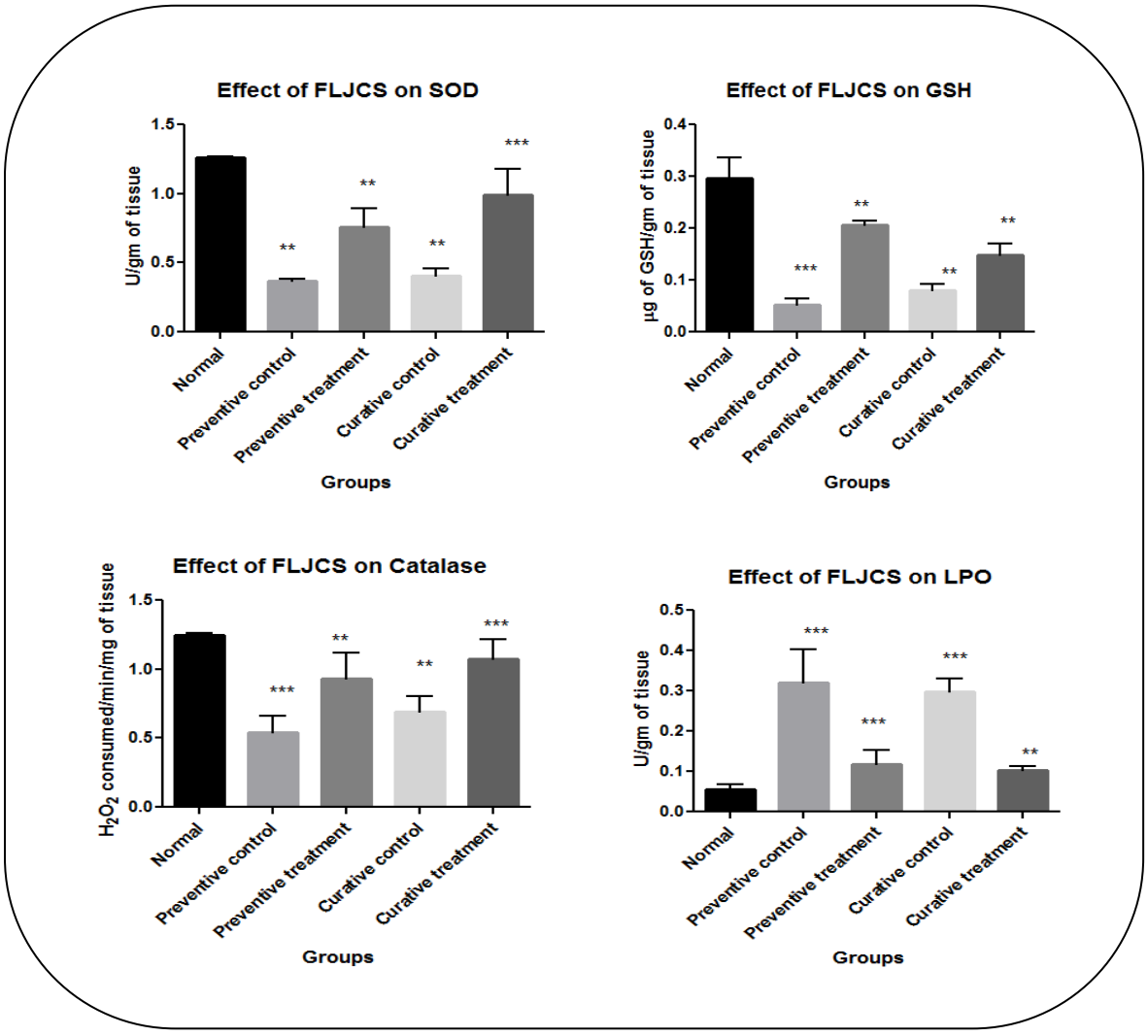


**Fig. 4: Effect of fresh leaves juice of *C. sativum* on Anti-oxidant levels.**

All values were expressed as Mean ± S.E.M and n=5

*** indicates $p<0.001$ when compared with the normal

** indicates $p<0.01$ when compared to control

## 5. CONCLUSION

Rats that underwent renal ischemia followed by reperfusion showed characteristic signs of renal dysfunction and inflammation. Both preventive and curative treatments with fresh leaves juice of *C. sativum* restored the biochemical renal parameters which indicate that fresh leaves juice of *C.sativum* have both preventive and curative nephroprotective effects.

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