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ANTIOXIDANT ACTIVITY OF CYATHULA PROSTRATE, IPOMEA OBSCURA AND MARSILEA QUADRIFOLIA IN NEPHROTOXICITY INDUCED MALE ALBINO RATS.

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ABSTRACT

This present study deals with the anti oxidant activity in Cyathula prostratae (whole part), Ipomea obscura (leaves), Marsilea quadrifolia (leaves). The selected plant was collected, shade dried and made into powder. Anti oxidant activity was evaluated in gentamicin induced rats. From these results it can be understood that plant crude showing its pharmacological action on nephrotoxic rats after gentamicin administration. This is exactly what the action that is being observed from the drug induced group which also shown its action in the plants treated group. From these results it can be understood that the plant powder has antioxidant activity against gentamicin nephrotoxic induced rats.

KEYWORDS: antioxidant, ROS, gentamicin, nephrotoxicity, LPO, SOD, Gpx.

INTRODUCTION

Antioxidants compounds are exogenous or endogenous in nature which either prevent the generation of toxic oxidants, intercept any that are generated and inactivate them and thereby block the chain propagation reaction produced by these oxidants.[1,2] Reactive oxygen species (ROS) are an entire class of highly reactive molecules derived from the metabolism of oxygen. ROS, including superoxide radicals, hydroxyl radicals, and hydrogen peroxide,are often generated as byproducts of biological reactions or from exogenous factors. In vivo, some of these ROS play positive roles in cell physiology; however, they may also cause great damage to cell membranes and DNA, inducing oxidation that causes membrane lipid

peroxidation, decreased membrane fluidity, and DNA mutations leading to cancer, degenerative, and other diseases.[4-6]

Drug-induced nephrotoxicity is an important cause of renal failure. Aminoglycosides throughout the endocytic pathway are taken up into the epithelial cells of the renal proximal tubules and stay there for a long time, which leads to nephrotoxicity. Acidic phospholipids, broadly distributed in the plasma membranes in various tissues, were considered to be the binding site of aminoglycosides in brush-border membrane of proximal tubular cells.[7, 8] Hydroxyl radicals play a role in the pathogenesis of gentamicin nephrotoxicity, gentamicin can induce suppression of Na(+)-K(+)-ATPase activity and DNA synthesis in rats proximal tubules leading to renal injury; this injury may be relevant to reactive oxygen metabolites generated by gentamicin. Renal cortical mitochondria is the source of reactive oxygen metabolites, which induces renal injury.[9]

The incidence of renal dysfunction following aminoglycoside administration was detected by many workers.[10, 11] Gentamicin is aminoglycoside broadspectrum antibiotic used against pathogenic gram negative and positive bacteria.[12] Its administration into rats induced impairment of renal function through liberation of oxygen free radical.[13,14] These changes reflected the severity of renal insufficiency which occurred in association with the sudden fall in glomerular filtration rate because of the majority of administrated GM enters specifically the proximal tubular epithelial cells, binds to anionic phospholipids in the target cells inducing abnormalities in the function and metabolism of multiple intracellular membranes and organelles then developed injury in the proximal tubular epithelial cells of kidney that caused acute renal failure.[15]

The World Health Organization has defined traditional medicine as comprising therapeutic practices that have been in existence for hundreds of years.[16] The traditional preparations comprise medicinal plants, minerals and organic matter. Herbal drugs constitute only those traditional medicines which primarily use medicinal plant preparations for therapy.[17] Siddha medicine is essentially promotive and preventive in therapeutic approach.

Today popularity of complementary medicine has increased, Worldwide. Herbal remedies have been developed by traditional knowledge of herbs, which is a ray of hope for kidney failure patients. A number of herbs, traditionally used are *Tribulus terrestris, Marsilea*

quadrifolia, Ipomea obscura, cyathula prostate, Hybanthus enneaspermus, Clitoria ternatea, Hygrophila auriculata etc.

MATERIALS AND METHODS

Plant Material

Fresh plant sample *Cyathula prostrate* (whole part), *Ipomea obscura* (leaves) and *Marsilea quadrifolia* (leaves) were collected from various parts of Thanjavur district. The whole plant and plant parts for medicinal use were washed, shade dried, powdered. Crude powder of these plants were given to the experimental rats at the dose of 100mg/100g body weight.

Experimental Methods

Male albino rats of 8 -10 weeks of age weighing between 100 and 120g were used for the study. The animals were housed in polypropylene cages. Animals were divided into five groups of three animals. The animals were acclimatized for a week under laboratory conditions. All experiments were performed according to the norms of the local ethical committee.

Experimental animals were distributed randomly, in five groups, containing three animals each. The first group followed by normal animals provided with usual rat feed and water *adlibitum.* Gentamicin (40mg/kg.b.wt) induced to the animals provided with normal rat feed and water act as the second group. Third, fourth and fifth group animals were treated with normal rat feed, water, gentamicin and crude powder of *Cyathula prostrate* (CP), *Ipomea obscura* (IO) and *Marsilea quadrifolia* (MQ) given separately according to the body weight and the drug followed by it. At the end of treatment, animals were fasted overnight, anaesthetized with ether the kidney tissue and blood serum was collected for biochemical analysis.

Biochemical Parameters: After the collection of the tissues sample of the kidney, the antioxidant assay like Lipid peroxidase, reduced glutathione, glutathione peroxidase and super oxide dismutase activity was studied by different methods. Mean values standard were calculated and for all the values carried out.[22]

RESULTS AND DISCUSSION

Tissue lipid peroxidation was estimated by the thiobarbutyric method. The byproducts of lipid peroxidation (Aldehyde especially malonic dialdehyde) formed by degradation of

hydroperoxide react with thiobarbituric acid forming pink coloured trimethine complex which was measured spectrophotometrically at 530nm.[18] After the treatment with crude powder of the medicinal plants were CP, IO and MQ at the dose of 100mg/g.bwt, the tissue Lipid peroxidation level was reduced. The result of this study shows that gentamicin produced nephrotoxicity was evidenced by increasing in lipid peroxidation products suggesting the involvement of oxidative stress and suggestive of tubular damage. The drug treated groups exert a protection against oxidative stress and tubular damage against gentamicin induced nephrotoxicity.

Reduced glutathione was determined according to the method of Ellman.[22, 23] This method is based on the development of yellow colour when 5.5'- dithionitrobenzoic acid is added to compounds containing sulphydryl group. The yellow colour developed was read at 412nm. After the treatment with crude powder of the medicinal plants were CP, IO and MQ at the dose of 100mg/g.bwt the reduced glutathione on tissue level was increased to 6.01 µg/mg protein, 6.46 µg/mg protein, 6.91 µg/mg protein and the results were compared with the normal and gentamicin induced rats.

The activity of mitochondrial glutathione peroxidase was assayed by the method of Rotruck *et al.*[19] In this experimental study normal animals show 2.36U/mg protein, as the normal level of glutathione peroxide on tissue. After the induction of nephrotoxicity with gentamicin (40mg/kg) in nephrotoxic animals, it was found that there was decreased by 1.60 U/mg protein than the normal level. After the treatment with crude powder of the medicinal plants were CP, IO and MQ the glutathione peroxide on tissue level was increased.

The method involves gentamicin of superoxidase radical of riboflavin and its detection by nitrite formation from hydroxylamine hydrochloric acid. Nitrite reacts with sulphuric acid to produce diazonium compound which subsequently reacts with naphthylamine to produce a red an ozo compound whose absorbance is measured at 543nm.The medicinal plants CP, IO and MQ shows increased value on super oxide dismutase in the serum sample of gentamicin induced nephrotoxic rats.

There was an decreased activity of lipid peroxidase and increased activity in Reduced Glutathione, glutathione peroxide and Super oxide dismutase and activated with produced free radicals and involvement of oxidation stress and finally damage to the proximal tubule. Lipid peroxidation is an initial event in the GM induced nephrotoxicity injury cascade.[20, 21]

The drug administration for 30 days was able to treat and protect the proximal tubular damage against gentamicin induced nephrotoxicity, by the activation of antioxidant enzymes.

Table: Antioxidant Activity of Cp, Io and Mq Crude Powder on Normal and Nephrotoxic Rats

Group	Dose	LPO nmolesMDA/mg	GSH µg/mg protein	SOD Mole/O_2decompose /min/100mg protein	GPx U/mg protein
Normal	Isosaline	2.36 ±1.41	9.6±5.76	3.3±0.99	2.36±0.16
Gentamicin treated	40mg/kg	3.46 ±1.38	5.7±3.99	1.2±0.24	1.60±0.11
CP+Gentamicin	100mg/kg	2.87±2.29	5.91±2.95	1.77±1.23	1.86±0.12
IO+Gentamicin	100mg/kg	1.69±1.01	7.82±5.47	1.92±1.72	1.94±0.13
MQ+Gentamicin	100mg/kg	1.98±1.78	6.76±4.73	1.96±1.76	2.1±0.14

CONCLUSION

The crude powder of the plant *Cyathula prostratae* L.Blume, *Ipomea obscura* Linn *and Marsilea quadrifolia Linn has* antioxidant and nephroprotective activity against the gentamicin induced nephrotoxic rats. Further studies, are needed to identify the phytoconstituents of the plants that may be responsible for the nephroprotective activity.

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