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PROTECTIVE EFFECT OF OCIMUM SANCTUM ON GENTAMICIN INDUCED NEPHROTOXICITY RATS.

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ABSTRACT

The present study deals with nephrotoxicity in humans and we can use ocimum sanctum plants aqueous leaf extract as nephron protective in kidneys. The purpose of pharmaceuticals research is to develop new drugs. The present research work done on gentamicin induced nephrotoxicity rats by doing experimentation. Aminoglycoside antibiotics including gentamicin are widely used in the treatment of gram-negative infections. However the major complication of the use of these drugs is nephrotoxicity, accounting for 10-15% of all cases of acute renal failure. The nephrotoxicity of gentamicin is well established in man & experimental animals. Gentamicin induced nephrotoxicity was ameliorated by various mechanisms among which oxidant mechanism was chosen by us to proceed in experimentation. The experimentation follows by various steps in nephrotoxicity rats and by the plant's leaves extract of ocimum sanctum is induced in rats and the resulting the disease can be controlled and various factors are shown by comparing creatinine levels and factors required to decrease the nephrotoxicity occurred by using antibiotics.

Keywords: *Ocimumsanctum, Gentamicin, Nephrotoxicity*

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INTRODUCTION

Ocimum sanctum[1-8] used in the treatment of arthritis, asthma, bronchitis, common cold, diabetes, fever, influenza, peptic ulcer and rheumatism. Tulasi is also known as "the elixir of life" since it promotes longevity. Treatment of earache, epilepsy, heart disease, malaria, sinusitis, snake bites, stomach ache and vomiting.The leaves of Ocimum contain 0.7% volatile oil comprising about 71% eugenol and 20% methyl eugenol. Eugenol and iso-eugenol by virtue of their antioxidant property play a vital role in relieving the Gentamicin induced nephrotoxicity in rats[9-12].

Nephrotoxicity occurs when your body is exposed to a drug or toxin that causes damage to your kidneys also can be referred to as renal toxicity.

Major complication in the use of Aminoglycoside antibiotics like Gentamicin is Nephrotoxicity.

Step 1: Transport of the drug into proximal tubular cells where they become concentrated & where they exert their toxic influence.

Step 2: Interaction of these agents with one or more intracellular metabolic processes depressing the renal function.

Gentamicin being a cationic drug binds to the anionic phospho-inositides located on the apical membrane.It is followed by pinocytosis of the drug-receptor complex to a secondary lysosome.Within the lysosome, gentamicin interferes with the catabolism of receptor by directly inhibiting phospholipase C. This leads to the accumulation of phosphotidyl-inositol rich myeloid bodies within lysosomes leading to phospholipidosis. An intricate system has evolved in respiring cells to prevent ROS causing injury. Antioxidants have ability to scavenge free radicals[13] & to synergistic effects of other antioxidant.

Material and methods:

Chemicals / Drugs: Gentamicin injection, Ocimum sanctum leaf powder. The experimental protocol has been approved by the Institutional Animal Ethics Committee and by the Animal Regulatory Body of the Government (Regd. No. 769/2011/CPCSEA)

Experimental Animals: Wistar Albino rats

Experimental designs: Animals were divided into two groups each having six rats and treated accordingly.

Group I - Test group
Group II - Control group

Our experiment was carried out based on the following methods.

- Preparation of Aqueous leaf extract of Ocimum sanctum.
- Procurement of experimental animals.
- Testing of Serum creatinine levels.
- Introduction of Gentamicin to rats and monitoring the Serum creatinine levels.
- Administration of Ocimum sanctum aqueous Leaf extract to GM treated rats

Procedure:

Preparation of Aqueous leaf extract of Ocimum sanctum:

- The plant material procured was kept for drying of the entire moisture content by placing the leavesin the Hot air Oven at 60^{o} C for 7 hours.
- Dried leaves were subjected to grinding andthen to sieving under Sieve no.60 to obtain fine powder.
- The fine powder that is to be extracted, in suitably comminuted form is usually packed in a 'thimble' made of filter paper which is then placed into the wider part of the extractor.
- The vapour raised condensed and fell on the packed drug, percolated and extracted out the active constituents.
- The alternate filling and emptying of the body of the extractor went on continuously till the drug is exhausted.
- This was continued for about 20 cycles until the menstruum in the wider part of extractor became colorless.
- The aqueous extract was eventually obtained after evaporating the excess moisture content from it by placing it over heating mantle and gently heating it for an hour at 30^{o}C.

Procurement of experimental animals:

Healthy Wistar Albino rats of about 120-160 gram weight were procured and warehoused under conditions of controlled temperature in rat cages. The rats were housed in groups at a room temperature of 23 ± 3°C and relative humidity of 53-60%, 12 hours light and 12 hours darkness cycles. They were fed with a standard diet and water ad libitum. The animals were divided as two groups with six rats in each group.

Group-1: Control (3 rats of each gender)
Group-2: Test (3 rats of each gender)

Testing of Serum creatinine levels:

Blood samples were collected from six male rats and six female rats by Orbital sinus method. The serum was obtained after centrifugating the blood in a centrifuge for 20 minutes and 2000 rpm speed. The obtained serum was checked for the creatinine content by performing Serum-Creatinine test involving Jaffe's method. Normal levels of Serum Creatinine [14]are:

Males 0.7 – 1.5 mg%
Females 0.4 – 1.3 mg%

Introduction of Gentamicin to rats and monitoring the Serum creatinine levels:

Gentamicin was injected by intra peritoneal route at the dose of 180 mg/kg/day (as per Robbins et al., 1971) in test group. The Gentamicin used in the

study was a vial which labelled as 80mg/2ml. So the doses were calculated according to the weights of the rats under study.

Rats	Body Weight	Gentamicin Dose
Rat 1	130g	25mg/day
Rat 2	160g	28mg/day
Rat 3	150g	27mg/day
Rat 4	160g	28mg/day
Rat 5	140g	25mg/day
Rat 6	130g	25mg/day

Administration of Ocimum sanctum aqueousLeaf extract to GM treated rats:

Now the rats under test group were administered orally with 100mg/kg daily dose of aqueous leaf extract of Ocimum sanctum.

Rats	Body Weight	Drug Dose
Rat 1	130g	13mg/day
Rat 2	160g	16mg/day
Rat 3	150g	15mg/day
Rat 4	160g	16mg/day
Rat 5	140g	14mg/day
Rat 6	130g	13mg/day

RESULTS &DISCUSSION

The rats under test group were checked for their serum creatinine levels as soon as they were procured. Since the serum creatinine values were in conformity with those of normal values, we confirmed that the rats were suitable and healthy enough to perform the in-vivo study. Next, the rats under the test group which were injected with Gentamicin were observed after every 24 hours for any change in their serum creatinine values **Fig 1& 2.** This was followed by checking the serum creatinine levels of the Ocimum sanctum aqueous extract treated Test rats and they showed the decreasing serum creatinine value which was previously elevated, and retaining to normal values or nearly normal values shown in **Table 1& 2**.

Thus, this study was conducted to establish the nephroprotective activity of plant i.e Ocimum sanctum. The GM in albino rats caused the nephrotoxicity. This nephrotoxic agent caused nephropathy mainly due to their free radical generation in kidney tissues. And the kidney damage was indicated by changes in renal function parameters like creatinine. The other parameters like BUN, and the enzymes suchn as GPx, SOD and can also be confirmed histopathologically.

CONCLUSION

As we gone through the study on treatment of kidney toxicity, we can conclude that herbal plants play a unique role in medicine. There is no synthetic drug which relieves overall insufficiency of kidney. But indigenous plants like Ocimum sanctum (Tulasi) possess tissue rejuvenator property which is anyway unavoidable. To sum up, we conclude that the major complication in use of aminoglycoside antibiotics i.e the Nephrotoxicity can be checked using anti-oxidants like Eugenol that is a main component of Ocimum sanctum. However this finding is clinically important but needs to be explored further to determine the optimum dose and combinations of the extract in showing the renal protective function.

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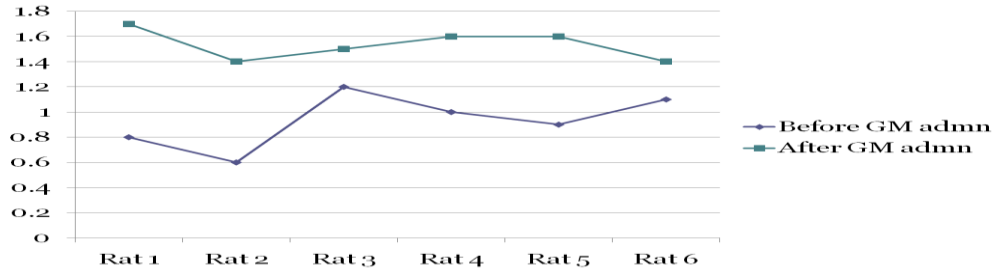

Fig 1: Graph Showing Serum Creatinine Levels

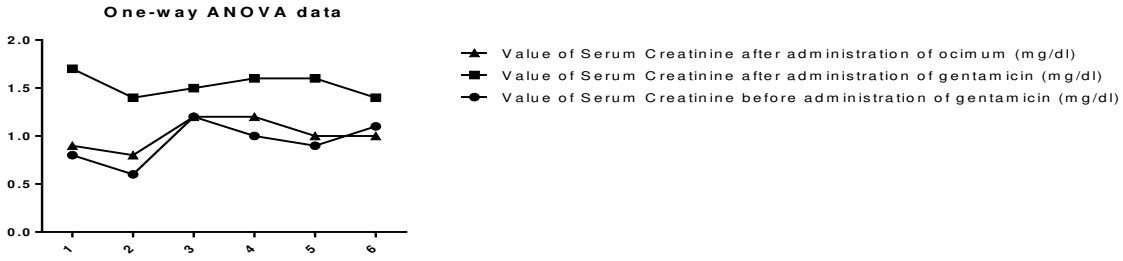

Fig2: Graph Showing Different Values of Serum Creatinine levels

Table 1: Normal Creatinine levels in rats

Rats	Serum Creatinine levels (mg/dl)	Rats	Serum Creatinine levels (mg/dl)
Rat 1(Male)	0.8	Rat 7(Male)	1.2
Rat 2(Female)	0.6	Rat 8(Female)	0.9
Rat 3 (Male)	1.2	Rat 9(Male)	0.9
Rat 4 (Female)	1.0	Rat 10(Female)	0.7
Rat 5 (Male)	0.9	Rat 11(Male)	1.4
Rat 6 (Female)	1.1	Rat 12(Female)	1.2

Table 2: Change In Serum Creatinine levels

Rats	Value of Serum Creatinine before administration of gentamicin (mg/dl)	Value of Serum Creatinine after administration of gentamicin (mg/dl)	Value of Serum Creatinine after administration of ocimum (mg/dl)
Rat 1	0.8	1.7	0.9
Rat 2	0.6	1.4	0.8
Rat 3	1.2	1.5	1.2
Rat 4	1.0	1.6	1.2
Rat 5	0.9	1.6	1.0
Rat 6	1.1	1.4	1.0

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