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PHARMACOLOGICAL EVALUATION OF SODIUM DIETHYLDITHIOCARBAMATE TRIHYDRATE AS NEPHROPROTECTIVE POTENTIAL IN RATS

Akanksha Sharma, Harikesh Maurya, U. V. S. Sara and Kislaya Mishra *

Hygia Institute of Pharmaceutical Education & Research, Sitapur-Hardoi Bypass Road, Opp. Sahara City Homes, Prabandh Nagar, Lucknow - 226013, Uttar Pradesh, India.

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Correspondence to Author:
Kislaya Mishra

Assistant Professor,
Department of Pharmacology,
Hygia Institute of Pharmaceutical Education & Research, Sitapur-Hardoi Bypass Road, Opp. Sahara City Homes, Prabandh Nagar, Lucknow - 226013, Uttar Pradesh, India.

E-mail: kislayamishra81@gmail.com

ABSTRACT: Objective: The present study was carried out to evaluate the pharmacological evaluation of SDDCT as nephroprotective potential in rats. **Material and Methods:** The current study was designed to evaluate the pharmacological potential of SDDCT in Gentamicin induced nephrotoxicity in rats. The SDDCT found to be useful in suppression of nephrotoxicity. The pharmacological potential was evaluated in gentamicin 100 mg/kg induced nephrotoxicity in rats for seven days through i.p. administration, the effect of SDDCT at a different dose level that is a higher dose (100 mg/kg b.w. p.o.) and lower dose (50 mg/kg b.w. p.o.). Various physical, biochemical, and antioxidant parameters were studied. Gentamicin induced glomerular destruction, accumulation of inflammatory cells, epithelial desquamation and necrosis in parts of medulla was found to reduce in the groups receiving SDDCT along with Gentamicin. SDDCT also normalized Gentamicin induced increase in serum creatinine (0.40 ± 0.15), serum urea (30.33 ± 2.21), serum uric acid (1.80 ± 0.27) and blood urea nitrogen (16.06 ± 1.50) levels. This is also evidenced by histopathological studies. **Result and Discussion:** The nephroprotective activity of SDDCT was determined by comparing diseased group and treatment group with reference and standard group on the basis of improvement in elevated levels of biomarkers such as; BUN, Creatinine, Urea, Uric acid, decrease in level of MDA and increase in level of SOD, catalase and GSH. At last, it was observed that a high dose (100 mg/kg) of SDDCT was more significantly effective as compared to the low dose (50 mg/kg) on the basis of an evaluation of overall biological parameters and histopathological activities.

INTRODUCTION: The kidney performs a variety of work required for the proper functioning of the body. Among them, the important function is regulation of fluid content, maintenance of electrolyte balance, removal of waste product from body, erythropoiesis, and hormone balance [1].

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If the Blood carry's a poisonous substance, if the person administered accidentally or purposely, the organ gets exposed to these mediators. Some poisonous substances affect the nephron part and damage there outer and inner structure leading to a condition of apoptosis [2]. Some poisons substance undergoes various reactions and leading to changes in the structure, further damaging the kidney [3, 4].

Gentamicin is the most important drug used to cure an infection caused by bacteria [5]. Along with having its potency over bacterial infection, it also had an adverse effect over the kidney by damaging the nephron parts or complete destruction of a

kidney when administered at a larger amount. The toxicity of kidney gentamicin basically affects the tubular part of nephron and affects their shape and structure, causing inflammation in the parietal layer of glomeruli or tubules, damaging the cells of the kidney leading to the condition of apoptosis or by destructing the fibrous tissues causing toxicity of kidney [6]. Inside the membrane the Gentamicin gets deposited and leading to formation of harmful oxygen species causes the generation of free radicals and a decrease in antioxidant defense mechanism leads to an increase in oxidative stress either leading to lipid peroxidation, damaging of DNA and protein or on the other hand stimulation of inflammatory cascade, activation of leucocytes adhesion molecules which causes monocytes and macrophage migration at the site of injury followed by renal failure these condition leads to decrease in GFR tubulointerstitial nephritis, renal tubular necrosis or glomerular damage [7].

Dithiocarb (SDDCT) is the major metabolite of disulfiram, acts as a chelating agent, and used as an antioxidant [8]. It has the inhibitory effect of Dopa β-Hydroxylase (DBH), a Cu-containing mono-oxygenase enzyme that has the aptitude for forming noradrenaline (NA) from dopamine (DA) therefore regulating nor-adrenaline (NA) invention [9]. Disulfiram is extremely proficient in the managing of drug obsession that takes action by interfering with the neurotransmitter dopamine [10]. SDDCT is an antagonist of NF-ƘB [11]. Protein produce by NF-KB is used for several cellular activities like DNA transcription, inflammatory cell generation, and increase in life-span of cells and their pathway [12]. SDDCT-Cu plays a critical role as a proteasome inhibitor in cancer cells [13]. The effects of DDTC copper complex in human prostate and breast cancer cells was also reported [14].

MATERIALS AND METHODS:

Chemical and Reagents: The Sodium diethyl-dithiocarbamate-tri hydrate was obtained from AviChem Industry Pvt. Ltd. State. The inducing agent such as Gentamicin and standard drug (Cystone) had received from the drugstore house of HIPER, Lucknow.

Experimental Animals: Albino Wister rats (150-200 g) were procured from an approved vendor and followed the animal ethic clearance from the animal house of HIPER (Hygia Institute of Pharmaceutical Education & Research, Lucknow); the IAEC approved protocol no. HIPER/IAEC/ 23/18/10. All animals were kept in polypropylene cages (six rats per cage) at 25 ± 2 °C temperature with the relative moisture level of 45-55% for twelve hours in darkness and light cycle. All the animals were acclimatized for providing them with laboratory conditions as per as CPCSEA guideline for a week before starting up the experiment. During experimental work and after that, an experimental rat was supplied with conventional pellet diet and water

Experimental Design: After acclimatization, Wistar rats (150-200 g) were divided into five groups having six animals in each group. The study was conducted for 35 days and all the animals (except NC) firstly administered with Gentamicin (100 mg/kg i.p.) for 7 days after that they were divided for treatment groups such as; Group I treated as normal control administered only normal saline; Group II serve as diseased control that was administered with Gentamicin 100 mg/kg i.p. for 7 days. The diseased rats were divided for treatment as Group III rats treated with SDDCT-50 (Sodium Diethyldithiocarbamate Trihydrate 50 mg/kg b.w./ day p.o.); Group IV treated with SDDCT-100 (Sodium Diethyldithiocarbamate Trihydrate 100 mg/kg b.w./day p.o.), and Group V rats were treated with Standard drug (Cystone 500 mg/kg b.w./day p.o.) continued for the next 28 days.

Investigational Parameters: In the last part of the study, the group of each rat weighed on analytical balance and animal were then sacrificed, kidneys removed, and washed thoroughly in cold running water. Further, the organs were quietly placed among the piece of paper and analyzed on an analytical balance.

Urine Sample Collection: The rats were housed in cages for one day for urine collection. The urine was free from other contagion contents. The albino rats were fed water, and no food was given. The content in the urine separated by use of separator and further included for leucocytes, ketone, protein, urobilinogen, blood and bilirubin analysis [15].

KFT Profile in Blood Serum and Electrolytes Concentration: Estimation of serum urea (method:

Urease / GLDH), serum creatinine (method: Jaffe Kinetic), [16] serum uric acid (method: Urease / GLDH), serum albumin (Albumin (BCG) Assay Kit), BUN (method: Berthelot method) was determined in blood serum. And the estimation of electrolytes like sodium, potassium, chloride (method: ISE) was determined.

Antioxidant Activity: Estimation of catalase *(method:* Beer and Sizer), Malondialdehyde (method: Ohkawa *et al*.), Reduced Glutathione (method: Moron *et al*.) and superoxide dismutase (method: Mc Cord and Fridovich) [17-22] was determined by use of tissue supernatant [23] using biodiagnostic kits manufactured by AviChem Industries.

Histopathological Analysis: Kidney tissues were obtained on the last day of the experiment after scarification of albino rats immediately store in ten percent (10%) neutral formalin solution and clean up with seventy percent (70%) of ethanol for histo-pathological analysis. The kidney tissues were then positioned in alcohol series from 70% to 100% alcohol and fixed in paraffin wax by using an embedding machine. The block was then sectioned of five micrometers in thickness using a rotatory ultra-microtome. The mounted slides were analyzed through the light microscope at 10x and 40x after being marked with H & E stain [24].

Statistical Analysis: All statistics information articulated as mean ± SD. Data were evaluated statistically using the ANOVA using graph pad prism software 6. To detect the significance between various groups concerning the control and diseased group, the Bonferroni test was implemented. $^{\#}$P value more than 0.05, 0.01, 0.05, and 0.001 considered as extremely significant, moderate significant and less significant from diseased group, respectively [25].

RESULTS AND DISCUSSION:

Estimation of Physical Parameter: Body Weight, Kidney Weight & Urine Volume: The average weight of the body of animal within Gentamicin treated rat showed a slight decrease ($^{\#}P<0.05$) in body weight (138.67 ± 16.53 gm) as compare to the group of control (200.67 ± 14.52 gm), while there was small raise in *P*-value in weight of body of curing group (170.55 ± 16.53 gm) as well as standard group (188.17 ± 16.20 gm) when equated with set of diseased weight.

The number of animals in Gentamicin (DC) show reduced kidney weight (0.48 ± 0.07) gm, which was statistically significant ($^{\#}P<0.05$) against normal control (0.60 ± 0.09) gm. The higher dose (0.54 ± 0.08) gm shows statistically substantial ($^{*}P<0.01$) against disease control. The other treatment group, such as treatment with lower dose (0.58 ± 0.05) gm and standard group (0.56 ± 0.07) gm does not show any significant improvement when compared with diseased control.

It was observed that the diseased group show a significant decline in the urine volume as compared to normal control. The animal treated by means of SDDCT (higher dose) showed statistically noteworthy rise in value *P* in urine volume when comparison made with diseased control, whereas standard drug-treated rats also showed significant ($^{***}P<0.001$) improvement and comparable with normal control and SDDCT (lower dose) of the treatment group ($^{**}P<0.05$).

TABLE 1: ESTIMATION OF BODY WEIGHT, KIDNEY WEIGHT AND URINE VOLUME OF EXPERIMENTAL ANIMALS

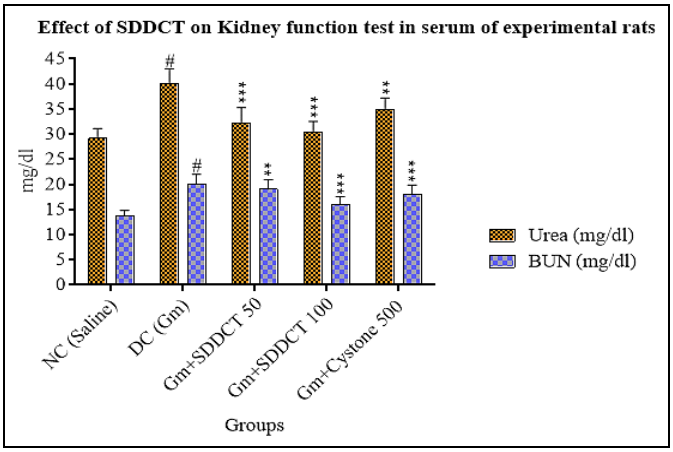
Group	Body Weight (gm)	Urine Volume (ml)	Kidney Weight (gm)
NC (Saline)	200.67 ± 14.52	8.13 ± 1.54	0.60 ± 0.09
Gm (Gentamicin)	138.67 ± 16.53$^{\#}$	3.02 ± 0.52$^{\#}$	0.48 ± 0.07$^{\#}$
Gm + SDDCT 50	140.56 ± 19.06^{NS}	5.20 ± 0.69**	0.58 ± 0.05
Gm + SDDCT 100	170.55 ± 16.53*	7.92 ± 1.06***	0.54 ± 0.08
Gm + Cystone 500	188.17 ± 16.20**	6.87 ± 1.00***	0.56 ± 0.07

Values are given as Mean ± SEM of the animal group (n=6) and expressed in gm and ml. $^{\#}P$ <0.05 statistically significant against normal control, $^{*}P<0.01$, $^{**}P<0.05$ and $^{***}P<0.001$ shows statistical significance against disease control. NS = Non significance.

Estimation of Blood Profile:

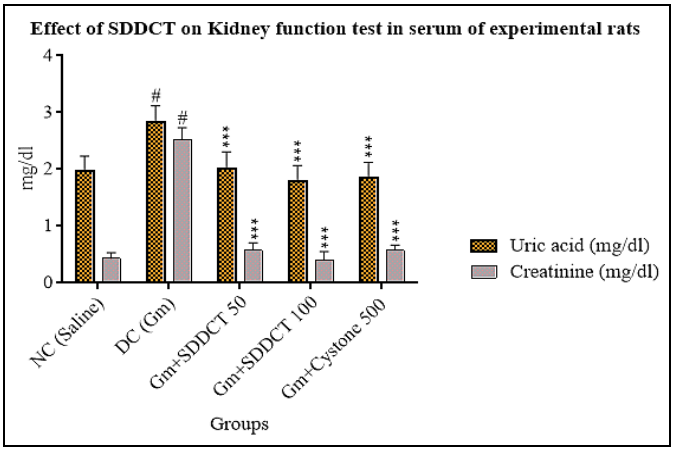
Urea and BUN: It was estimated that the diseased group show significant ($^{\#}P<0.05$) increase in the urea (40.00 ± 3.01 mg/dl), BUN (20.06 ± 1.92 mg/dl), in serum sample when compared to normal control. The animal treated with SDDCT (higher dose) group and standard population showed relevant decline of *P* assessment in urea (30.33 ± 2.21 mg/dl) and BUN (16.06 ± 1.50 mg/dl) while compare through the diseased control whereas the

treated group of SDDCT (lower dose) shows less significant ($^{**}P<0.05$) in BUN (18.05 ± 1.90 mg/dl) in comparative to higher dose of treatment group.



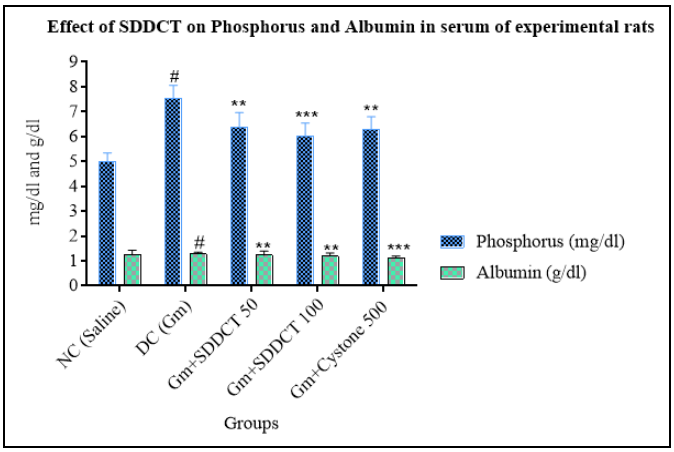
GRAPH 1: ESTIMATION OF KIDNEY FUNCTION TEST IN SERUM UREA AND BUN OF EXPERIMENTAL RATS. Values are given as Mean ± SEM of the animal group (n=6) and expressed in mg/dl. $^{\#}P<0.05$ statistically significant against normal control, $^{**}P<0.05$ and $^{***}P<0.001$ show statistical significance against disease control.

Uric Acid and Creatinine: It was observed that the diseased group show a significantly ($^{\#}P<0.05$) increase in the uric acid (2.83 ± 0.29 mg/dl) and creatinine (2.53 ± 0.20 mg/dl), in the serum sample, when compared with normal control. The animal treated by SDDCT plus a standard group shows a more significant ($^{***}P<0.001$) decline in uric acid and creatinine in comparison to the diseased group. The higher dose of the treatment group shows improvement incomparable to other groups on uric acid (1.80 ± 0.27 mg/dl) and creatinine (0.40 ± 0.15 mg/dl).



GRAPH 2: ESTIMATION OF KFT IN SERUM URIC ACID AND CREATININE OF EXPERIMENTAL RATS. Values are given as Mean ± SEM of the animal group (n=6) and expressed in mg/dl. $^{\#}P<0.05$ statistically significant against normal control, $^{***}P<0.001$ shows statistical significance against disease control.

Phosphorus and Albumin: In the case of phosphorus and albumin, a remarkable enhancement ($^{\#}P<0.05$) in phosphorus was observed during comparison with the normal group. The test group of higher (6.00 ± 0.54 mg/dl) and lower dose (6.38 ± 0.58 mg/dl) considerably ($^{**}P<0.05$ and $^{***}P<0.001$) maintained the level of phosphorus. The treatment groups also show a significant ($^{**}P<0.05$) effect over the albumin while compared with the diseased group. The standard group shows major improvement in *P*-value in albumin (1.12 ± 0.07 g/dl) at the end of the study.



GRAPH 3: ESTIMATION OF KIDNEY FUNCTION TEST IN SERUM PHOSPHORUS AND ALBUMIN OF EXPERIMENTAL RATS. Values are given as Mean ± SEM of the animal group (n=6) and expressed in mg/dl and g/dl. $^{\#}P<0.05$ statistically significant against normal control, $^{**}P<0.05$ and $^{***}P<0.001$ show statistical significance against disease control.

Estimation of Electrolyte Concentration:

Sodium and Chloride: The estimation of electrolytes in serum show that the serum sodium (144.00 ± 2.46 nmol/L) and chloride (106.67 ± 1.38 nmol/L) were increased significantly ($^{\#}P<0.05$) in diseased control when compared by normal control. The test groups and standard group reduces significantly the elevated range of serum electrolytes when compared with the diseased group.

Calcium and Potassium: The estimation of KFT in serum shows that the serum Calcium (12.68 ± 0.57 mg/dl) and potassium (6.28 ± 0.64 nmol/L) were significantly ($^{\#}P<0.05$) greater in diseased control when compared by normal control. The test groups and standard group show significant ($^{**}P<0.05$) reduction within these elevated levels while compared with the diseased group. While the higher dose of treatment group show non-

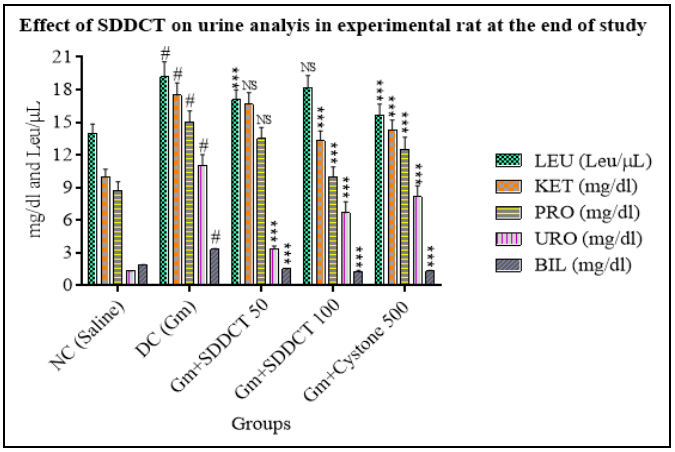
significant improvement of potassium (5.98 ± 0.54 nmol/L) and the lower dose also show non-significant improvement of calcium (9.57 ± 0.30 mg/dl) as compared to the diseased group.

TABLE 2: ESTIMATION OF KIDNEY FUNCTION TEST IN SERUM SODIUM, CHLORIDE, CALCIUM AND POTASSIUM OF EXPERIMENTAL ANIMAL

Group	Sodium (nmol/L)	Chloride (nmol/L)	Calcium (mg/dl)	Potassium (nmol/L)
NC (Saline)	137.50 ± 1.78	103.71 ± 1.37	8.00 ± 0.99	4.80 ± 0.38
Gm (Gentamicin)	144.00 ± 2.46$^{\#}$	106.67 ± 1.38$^{\#}$	12.68 ± 0.57$^{\#}$	6.28 ± 0.64$^{\#}$
Gm + SDDCT 50	140.33 ± 2.06**	104.50 ± 1.36*	9.57 ± 0.30^{NS}	5.25 ± 0.22**
Gm + SDDCT 100	139.17 ± 1.89**	106.00 ± 1.39^{NS}	8.30 ± 1.04**	5.98 ± 0.54^{NS}
Gm + Cystone 500	136.50 ± 1.81**	104.33 ± 1.36*	8.69 ± 0.79**	5.31 ± 0.52**

Values are given as Mean ± SEM of the animal group (n=6) and expressed in nmol/L, mg/dl. $^{\#}$P <0.05 statistically significant against normal control, $^{*}P$<0.01 and $^{**}P$<0.05 show statistical significance against disease control. NS= Non-significance.

Estimation of Urine Analysis: Gentamicin caused a statistical boost ($^{\#}$P<0.05) in leucocyte (19.17 ± 1.40) Leu/µL, ketone (17.50 ± 1.12) mg/dl, protein (15.00 ± 1.04) mg/dl, urobilinogen (11.03 ± 1.00) mg/dl and bilirubin (3.33 ± 0.08) mg/dl. The treatment group of higher doses were found to be effective and significantly (***P<0.001) maintain the elevated level of ketone (13.33 ± 0.89) mg/dl, protein (10.00 ± 0.90) mg/dl, urobilinogen (6.67 ± 1.04) mg/dl and bilirubin (1.30 ± 0.09) mg/dl and leucocyte (17.07 ± 0.91) Leu/µL show non-significant (NS), as compared to diseased group. Ketone (16.67 ± 1.07) mg/dl and protein (13.50 ± 1.03) mg/dl shows non-significant (NS) in a lower dose of the treatment group. The standard group also significantly (***P<0.001) improve these elevated level of leucocyte (15.67 ± 1.00) Leu/µ, ketone (14.33 ± 0.88) mg/dl, protein (12.50 ± 1.12) mg/dl, urobilinogen (8.17 ± 1.00) mg/dl, and bilirubin (1.33 ± 0.08) mg/dl when compared with diseased group.



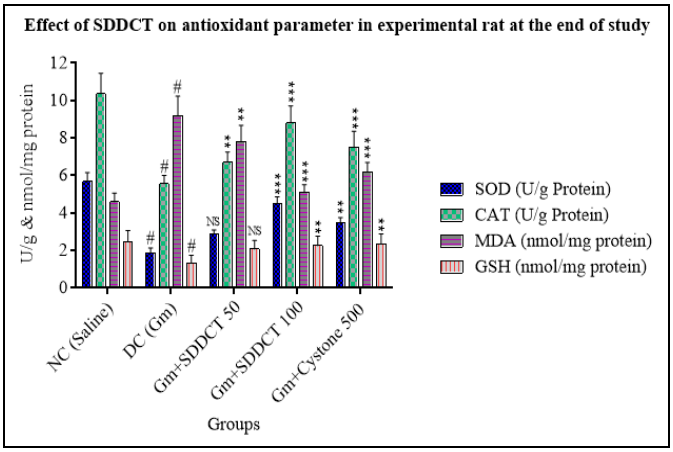
GRAPH 4: ESTIMATION OF URINE ANALYSIS OF LEUCOCYTES, KETONE, PROTEIN, UROBILINOGEN, AND BILIRUBIN AT THE END OF THE STUDY. Values are given as Mean ± SEM of the animal group (n=6) and expressed in Leu/µL and mg/dl. $^{\#}P$<0.05 statistically significant against normal control, $^{***}P$<0.001 shows statistical significance against disease control. NS= Non-significance.

TABLE 3: ESTIMATION OF URINE ANALYSIS OF GLUCOSE, NITRITE, AND BLOOD OF EXPERIMENTAL ANIMAL

Group	GLU (g/dl)	NIT (mg/dl)	BLO (Ery/µL)
NC (Saline)	-	-	-
Gm (Gentamicin)	-	+	++
Gm + SDDCT 50	-	+	+
Gm + SDDCT 100	-	-	-
Gm + Cystone 500	-	-	-

++: moderately present; +: slightly present; -: absent

The estimation of urine analysis shows that the level of nitrite and blood significantly increased in diseased control while no effect observed in the case of glucose. The treatment, as well as the standard group, maintained the elevated levels of nitrite and blood as compared to the diseased group.



GRAPH 5: ESTIMATION OF ANTIOXIDANT ENZYME IN KIDNEY HOMOGENATE SOD, CAT, MDA AND GSH AT THE END OF THE STUDY. Values are given as Mean ± SEM of the animal group (n=6) and expressed in U/g Protein and nmol/mg protein. $^{\#}P$<0.05 statistically significant against normal control, $^{**}P$<0.05 and $^{***}P$<0.001 show statistical significance against disease control. NS= Non-significance

Estimation of Antioxidant Parameter: The evaluation of the antioxidant parameter observed that, diseased group decrease ($^{\#}P$<0.05) the SOD

(1.87 ± 0.26), CAT (5.56 ± 0.45) and reduced glutathione (1.32 ± 0.42) nmol/mg protein action in renal tissue as compared with a healthy controlled. On the other side, the diseased group produces a major increase ($^{**}P<0.05$) in MDA (9.18±1.05) nmol/mg protein activity. The treatment group of higher dose found to be effective by preserving the oxidative damage caused by Gentamicin (100 mg/kg) of SOD (4.48 ± 0.38) U/mg protein, CAT (8.80 ± 0.91) U/mg protein, GSH (2.26 ± 0.51) nmol/mg protein and MDA (5.10 ± 0.41) nmol/mg protein when compared with the diseased group. The standard group also significantly improves this elevated point of SOD (3.47 ± 0.28) U/mg protein, CAT (7.51 ± 0.85) U/mg protein, GSH (2.36 ± 0.53) nmol/mg protein and MDA (6.20 ± 0.50) nmol/mg protein as compared to disease group.

Histopathological Analysis: Histopathological changes observed in cortex and medulla part such as changes in glomeruli, proximal convoluted tubules, and distal convoluted tubules parts. The differences observed were compared in normal control with the diseased group, and the further unhealthy group compared with the treatment group and standard group.

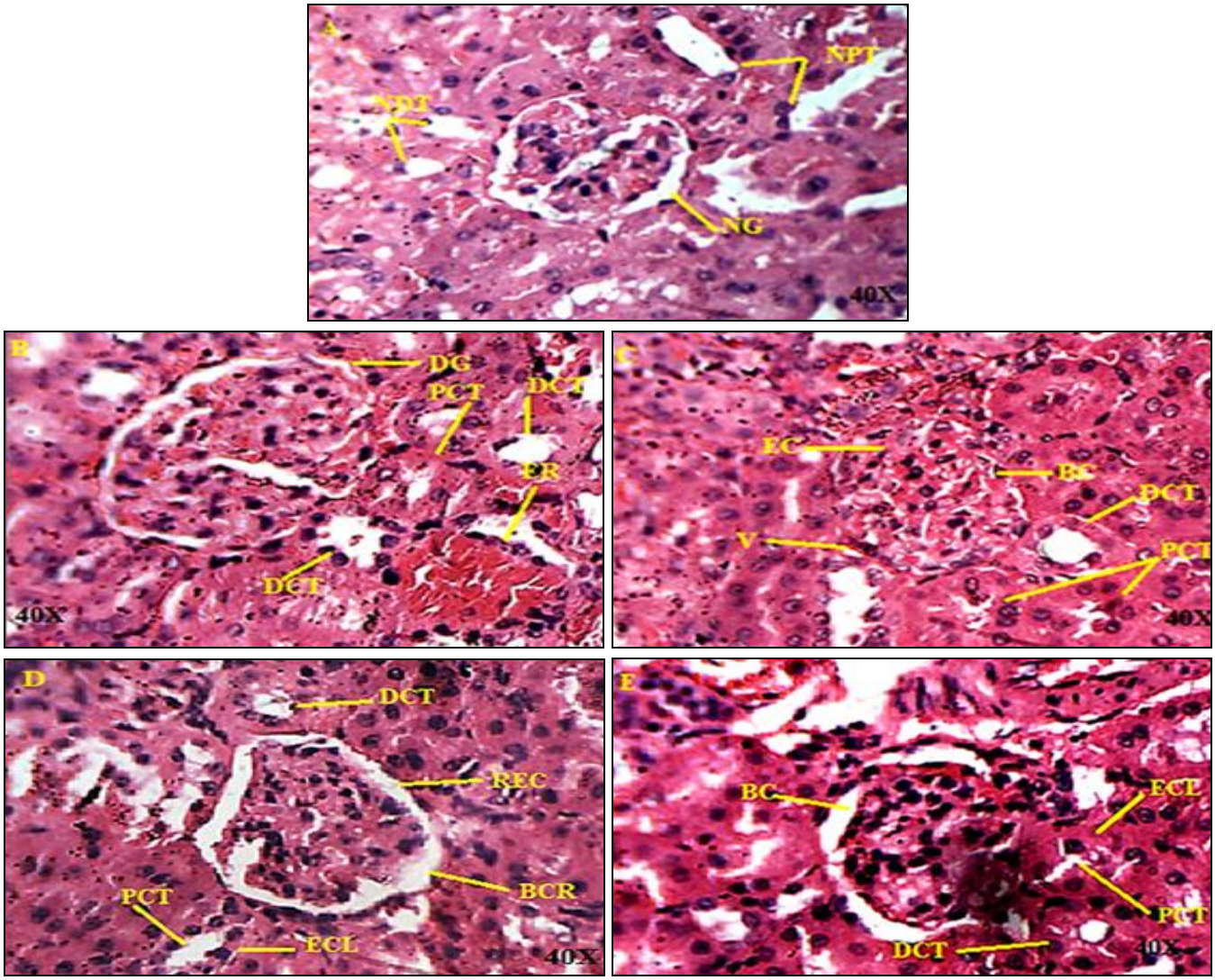


FIG. 1: HISTOPATHOLOGICAL STUDY OF EXPERIMENTAL RAT KIDNEY STAINED THROUGH HEMATOXYLIN AND EOSIN AND OBSERVED UNDER THE LIGHT MICROSCOPE OF 40X. (A) KIDNEY SECTION OF CONTROL RAT SHOWS NORMAL STRUCTURE IN THE CORTEX AND MEDULLA PART. (B) DISEASED CONTROL SHOWS CHANGES IN GLOMERULAR AS WELL AS TUBULAR SIZE AND SHAPE, MARKED NECROSIS THROUGHOUT THE CORTEX AND TUBULAR PART. (C) TEST DRUG (LOW DOSE), THE SECTION SHOWS THE SLIGHT CHANGES IN THE CORTEX AS WELL AS THE MEDULLA PART. THE PROXIMAL CONVOLUTED TUBULE (PCT) DAMAGE APPEARS THROUGH DISRUPTION OF EPITHELIAL CELLS. (D) TEST DRUG (HIGHER DOSE), THE SECTION SHOWS LESS DAMAGE OF EPITHELIAL CELL LINING (ECL) IN PCT. REGENERATION OF BOWMAN'S CAPSULE (BCR) AT THE CORTEX PART. (E) STANDARD DRUG (CYSTONE), THE SECTION SHOWS THE REGENERATION OF SHAPE AND SIZE OF GLOMERULI (GR), BOWMAN'S CAPSULE (BC), AND REGENERATION OF NUCLEI SURROUNDING DCT.

The histological study of experimental rat kidney in normal control shows Normal Glomeruli (NG) in the cortex part and Normal Proximal tubules (NPT) with Normal Distal tubules (NDT) in the medulla. In diseased control group show changes in glomerular as well as tubular size and shape, damaged glomeruli (DG), the destruction of parietal layer, damage of brush border, marked necrosis throughout the cortex and tubular part showing the presence of a large number of erythrocytes (ER). Medulla part shows a various number of ruptured proximal tubules (RPT) filled with blood and absence of a large number of nuclei surrounding the distal convoluted tubules (DCT) in the medulla part. The presence of brush border and less damage to ECL in PCT while the presence of several fresh-looking nuclei in the similar tubule indicate the liveliness of the epithelium. In other tubules, the brush border is totally undamaged and regaining of shape and size of distal convoluted tubules (DCT). Regeneration of Bowman's capsule (BCR) as well as regeneration of epithelial cells of glomeruli (REC) also is seen in the cortex part. Evidence from the histopathological and biochemical investigation supports the nephroprotective potential of SDDCT on experimental rats.

CONCLUSION: Nephron toxicity is among the most common illness of kidneys that occur while the body is subjected to medicines or chemicals which cause kidney damage. Thirty years old Patients are more likely to have diabetes and heart disease, because of which they take numerous medications, and exposed to more investigative and beneficial procedures that potentially harm the kidney function [26]. Nephrotoxicity induced by gentamicin causes excessive production of nitric oxide (NO) due to overproduction of iNOS (inducible nitric oxide synthase) causes a cytotoxic effect on mitochondria to lead to inhibition of electron transport chain (ETC) [27]. Inhibition of ETC leads to the generation of reactive oxygen species causing oxidative stress by a rise in a number of free radicals. Further, stimulate inflammatory cascade and migration of activated monophage and macrophage at the site of injury. Followed by renal injury resulted in Tubulointerstitial nephritis, renal tubular necrosis, and Glomerular damage. On the other hand, the overproduction of calcium has an indirect effect over the ROS and direct effect by an increase in the activator protein and phospholipase A2 (PLA2) cause cell contraction and cell proliferation leading to decrease in GFR by a decrease in ultrafiltration rate resulting in Tubulointerstitial nephritis, renal tubular necrosis, and Glomerular damage. SDDCT, the test drug being a chelating agent, having antioxidant activity found to be useful by showing its effect over gentamicin-induced nephrotoxicity. SDDCT acts either by decreasing the overproduction of ROS or the inhibition of inflammatory cascade. On the other hand, the action of Gentamicin on proximal convoluted tubules on transporter and gentamicin accumulation in membrane central to mitochondrial dysfunction, leading to apoptosis, on the other hand, increase in oxidative stress leads to inflammation further causing nephrotoxicity. The effect of SDDCT was found to improve mitochondrial depletion, action over apoptosis, on oxidative stress and further on inflammation.

So, in this regard, we can say that SDDCT could relieve cell damage caused by Gentamicin and can be used as nephroprotective potential and observed by undergoing various biochemical, physical, and antioxidant parameters. Gentamicin causes loss of appetite, increase in catabolism resulting in acidosis, which is accomplished by anorexia. Hence, food intake also decreases and leads to loss of body weight; this effect is overcome by a high dose (100 mg/Kg) of SDDCT, which may cause suppression of increase calcium level. The increase in kidney weight may occur due to edema of parenchyma cell caused by Gentamicin that initiates renal inflammation. The higher dose (100 mg/kg) of SDDCT was found effective in decreasing the level of kidney weight; it may act by inactivating inflammatory cell-protecting from renal inflammation.

In case of elevated level of biochemical parameter like BUN, creatinine, urea, uric acid and electrolytes was observed in Gentamicin-induced nephrotoxicity resulting in a marked increase in these parameters, the increase in these parameters may be due to action of Gentamicin on ROS that leads to increase in ROS causing destruction in renal vasculature leading to mesangial cell contraction, alteration in surface area of filtration, thus resulting in decrease in GFR.

Since, plasma creatinine concentration is related to GFR, it seems that increased plasma creatinine concentration was due to a decrease in GFR. The effect of SDDCT may be ROS leading to a decrease in oxidative stress, thus protecting antioxidant defense mechanism [28].

Our findings have provided strong evidence that SDDCT may provide protective effects against gentamicin-induced nephrotoxicity in rats. This defensive effect might be due to its antioxidant and anti-inflammatory properties or other pathways which require further studies.

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CONFLICTS OF INTEREST: The author(s) confirm that this article content has no conflict of interest.

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