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Investigation of extracts from the medicinal plant *Emblica officinalis* for their preventive properties against cisplatin-induced toxicity

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Abstract

The study assesses the efficacy of medicinal plant extracts in mitigating the toxicity induced by cisplatin. A widely used cancer treatment, cisplatin is associated with severe adverse effects. Investigate the preventative properties of extracts derived from medicinal plants against these adverse effects. Assays will be conducted in vitro and potentially in vivo to determine whether or not these plant extracts can mitigate the toxicity induced by cisplatin in cells and animals. Organ function, cell viability, and oxidative stress indicators may be utilized to assess the protective effects of plant extracts. This research may aid in the development of supplementary medications that reduce the toxicity induced by cisplatin, thereby enhancing the efficacy and acceptability of cancer therapy. Bioactive component extraction from the leaves of medicinal plants, *Emblica officinalis*. The aim of this research is to investigate the protective effect of medicinal plants originating in Chhattisgarh region against cisplatin induced nephrotoxicity. Anti-cancer properties have been empirically demonstrated in these plants

Keywords: *Emblica officinalis*, medicinal plants, cisplatin-induced toxicity, extracts

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Introduction

Solid tumors of the ovary, testis, bladder, and lungs are among the many that cisplatin, a platinum-based chemotherapeutic drug, is used to treat. The high toxicity of cisplatin makes it less useful in the clinic and makes patients less likely to stick to their treatment plans, even if it kills cancer cells. Cisplatin is associated with a number of side effects, the most prevalent of which are constipation, nephrotoxicity, neurotoxicity, and neotoxicity. Along with lowering the patient's quality of life, these side effects can force doctors to lower the dosage or stop treating the cancer patient altogether, which reduces the treatment's effectiveness. Rupal Purena and colleagues (2018) Observed the effectiveness of cisplatin treatment is limited by nephrotoxicity. This study looked at the role of hydroethanolic *Emblica officinalis* leaf extract as a preventative measure against cisplatin-induced nephrotoxicity. Nine groups, each with five male Wistar rats, participated in the fourteen-day study. Group 1 served as a control and received no treatment whatsoever. Injecting 0.9% NaCl intraperitoneally (i.p.) was administered to the second vehicle control group on day eleven. The intraperitoneal administration of cisplatin (12 mg/kg body weight) was scheduled for the same day for all three groups. During treatment, Groups 4, 2, and 400 mg/kg body weight of leaf extract were administered, respectively. The doses of leaf extract administered to groups 7, 8, and 9 were 100, 200, and 400 mg/kg, respectively. Blood samples were collected from both groups on the fourteenth day of the inquiry in order to measure renal function. Incorporating *E. officinalis* leaf extract into cisplatin treatment considerably reduces renal toxicity ($p \leq 0.05$) by lowering serum creatinine and BUN levels, increasing activities of Catalase, SOD, GPx, and GR, and decreasing renal MDA levels. Oral preparations of Amla leaves were associated with less red blood cell histological damage and morphological abnormalities. The results show that *E. officinalis* leaf extract may mitigate cisplatin's toxic effects on the kidneys. The approach of this study includes the use of solvent extraction technologies to extract bioactive components from certain medicinal plants. Traditional medicinal use and early proof of preventive benefits in preclinical investigations informed the selection of these plants. Phytochemical screening is then used to determine whether the extracts include important bioactive components such terpenoids, alkaloids, flavonoids, and phenolic acids. The strong antioxidant capabilities of these substances are thought to mitigate the oxidative damage caused by cisplatin. To evaluate these extracts' protective effects, the experimental design incorporates both in vitro and in vivo models. Organs such as the kidney, liver, and auditory cells that have been cultivated and exposed to cisplatin can be studied in vitro, with or without the use of plant extracts for pre-treatment. Several factors are assessed, including cell viability, inflammatory cytokines, apoptotic signs, and oxidative stress markers such lipid peroxidation levels and reactive oxygen species. After administering cisplatin to animal models, researchers treat them with plant extracts and undertake in vivo experiments. Some examples of endpoints are hearing tests, histological evaluations of tissue samples, and biochemical tests of kidney and liver function. Early findings from these investigations suggest that a number of plant extracts significantly mitigate cisplatin-induced toxicity. So, for example, in both in vitro and in vivo models, extracts that are high in flavonoids and phenolic compounds show strong antioxidant activity, lowering the levels of

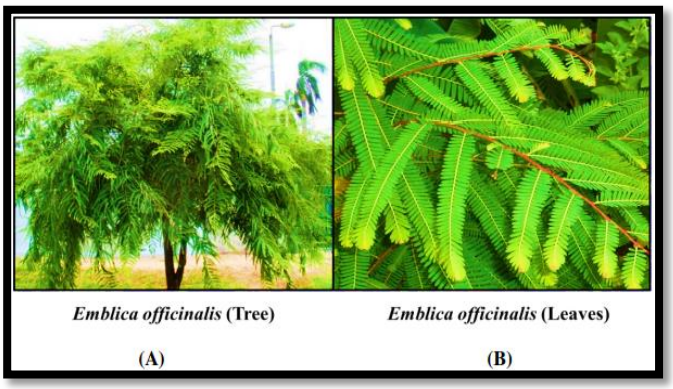
oxidative stress indicators. Apoptosis indicators and inflammatory cytokines are also decreased in these extracts, indicating a complex protective mechanism. Supporting the biochemical results, histopathological examinations show that the treated animals' kidneys and livers had less tissue damage. In addition, tests of auditory function have shown that some extracts can reduce the ototoxicity caused by cisplatin, which means that treated animals can keep their hearing.

Materials and Methods

Collection of plant material and authentication- Leaves of medicinal plants from Chhattisgarh were evaluated for their ethnopharmacological anticancer properties. *Emblica officinalis* (Amla) was selected as the plant.

Processing of plant material - Following a drying period of 4–7 days at room temperature, the leaves were rinsed. The coarsely ground desiccated leaves were deposited in impermeable polythene containers at room temperature prior to use after being ground with a grinder.

Extraction of bioactive components- A Soxhlet extractor (Manufacture: Decibel digital technologies) was employed in conjunction with ethanolic/hydroethanolic solvents to extract 30 grams of pulverized leaves from the aforementioned plants. Incorporating finely ground leaves into the extractor. A cotton cloth was employed to clean the sample into the extraction storage chamber. Following that, the extractor component is affixed to the 250 ml round-bottom vessel containing the solvent for extraction. A heating mantle was utilized to warm the solvent-filled round-bottom flask, while the condenser was connected to the Soxhlet extractor. Following boiling, the solvent was extracted for six to eight hours (eight to ten cycles). The concentrated extract obtained by evaporating the solvent was weighed and preserved at 4˚C until application.



Emblica officinalis: (A) Whole Plant (B) Leaves

In-vivo study of protective role of *Emblica officinalis* hydro-ethanolic leave extract in cisplatin induced nephrotoxicity.

Experimental Animal

The experiment subjects were mature male Wistar rats. Every animal obtained from a reputable source was in good health and immune from any diseases. A separate crate was provided for each of the nine groups to which each animal was randomly assigned with five individuals. To disinfect each confinement, desiccated bedding made of maize fiber was utilized. Husky transformations occurred daily. The animals were provided with water and pellet feed, which was maintained at 22.2>C using a 12-hour light/dark cycle. Prior to the investigation, all animals were acclimated to laboratory conditions for duration of ten days.

Dose Fixation-Three concentrations of hydro-ethanolic extract were selected in accordance with findings from a prior study on the acute toxicity of *E. officinalis* leaf extract (Nain *et al.*, 2012b): 100 mg/kg BW for the minimum dose, 200 mg/kg BW for the intermediate dose, and 400 mg/kg BW for the maximum dose.

Experimental design-There was no animals that were kill or injured. The experiment utilized animals weighing between 150 and 200 g. Each of the nine categories received five participants for the fourteen-day experiment:

Group 1 served as the control and received no therapy. As the vehicle control group, Group 2 was administered 0.9% saline on the eleventh day. On day eleven, a solitary dose of cisplatin in 0.9% saline (12 mg/kg body weight) was administered to Group 3, which served as the control group. Throughout the course of treatment, Group 4 was administered a hydroethanolic *Emblica officinalis* leaf extract at a dosage of 100 mg/kg body weight as the leaf extract control.

As a control throughout the treatment, Group 5 received a hydroethanolic *Emblica officinalis* leaf extract at a concentration of 200 mg/kg body weight.

As a control throughout the treatment, Group 6 received a 400 mg/kg body weight hydroethanolic *Emblica officinalis* leaf extract.

Throughout treatment, Group 7 received 100 mg/kg body weight of *Emblica officinalis* leaf hydroethanolic extract. On day eleven, one milligram of cisplatin per kilogram of body weight in 0.9% saline was administered.

On day eleven, Group 8 was administered a hydroethanolic extract of *Emblica officinalis* leaves at a rate of 200 mg/kg body weight for the duration of the treatment, in addition to a single dose of cisplatin (12 mg/kg body weight) in 0.9% saline. Throughout treatment, Group 9 received 400 mg/kg body weight of *Emblica officinalis* leaf hydroethanolic extract. On day eleven, one milligram of cisplatin per kilogram of body weight in 0.9% saline was administered.

Result and Discussion

According to research conducted by Bahmani *et al.*, (2016) and Lakshmi *et al.*, (2012), medicinal plants contain a wealth of compounds that may have medicinal properties. These compounds could be utilized to create new and improved therapies for various diseases, such as kidney problems, and to lessen or eliminate the negative side effects of many drugs that are already on the market. The effectiveness of cisplatin as an anticancer treatment against various types of cancer is well-known, but its most noticeable side effect is nephrotoxicity. Several synthetic and natural substances have been shown to provide protection against cisplatin-induced nephrotoxicity. However, the described compounds were not able to be used in clinical settings due to inconsistencies between preliminary results and practical evaluations. In cancer biology, the search for a novel medication that protects against nephrotoxicity while maintaining cisplatin's anticancer effects is crucial. The purpose of this study is to examine whether medicinal plants from the Chhattisgarh region can prevent cisplatin-induced kidney damage. These plants have shown anti-cancer capabilities through empirical evidence. Ritesh and Sanmati (2010) cite research showing that 33 medicinal plants from India's Chhattisgarh region exhibit anti-cancer effects against different cancers both in lab tests and in living organisms. *Emblica officinalis* was chosen for this study from among the medicinal plants mentioned before due to the ethnobotanical significance of its leaves. The medicinal plant's leaf extracts were subjected to aqueous and ethanolic/hydro-ethanolic solution analysis in

order to detect phytochemicals and evaluate their antioxidant activity. In order to find out if the most antioxidant-rich leaf extract may prevent cisplatin-induced nephrotoxicity, an in vivo trial was conducted. It appears that several methodologies assess various aspects of antioxidant capacity, as shown by the diversity in antioxidant levels across them. The phosphomolybdate, FRAP, and total reducing power assays all make use of the single electron transfer method (Badrinath *et al.*, 2010). But DPPH and ABTS combine hydrogen transfer with single electron transfer to achieve their goals. *Emblica officinalis* hydro-ethanolic leaf extract (AET) had the greatest antioxidant capacity of all the leaf extracts tested. Quantitative and spectral investigations corroborated the finding that the high concentration of vitamin and phenolic components in the extract was the primary culprit. The next step is to choose which samples will undergo further analysis. Research has shown that the polyphenols found in amla leaves have anti-oxidant, anti-carcinogenic, and anti-diabetic effects. Nain *et al.*, (2012)a, Asmawi *et al.*, (1993), Moilanen (1997), and Nain (2012)b all found that these phytochemicals significantly inhibited oxidative stress. In comparison to the other leaf extracts tested, the hydro-ethanolic *Emblica officinalis* extract showed the greatest antioxidant capacity. A hydro-ethanolic leaf extract of *Emblica officinalis* is used to reduce the nephrotoxicity caused by cisplatin. This study utilized male Wistar rats to examine the potential protective benefits of a hydro-ethanolic leaf extract from *Emblica officinalis* against cisplatin-induced nephrotoxicity. The rats were divided into several groups based on their exposure to cisplatin: control rats, rats treated with cisplatin at dosages of 12, 200, and 300 mg/kg BW, and rats treated with cisplatin at doses of 100, 200, and 300 mg/kg bw. The animals were slaughtered on the fourteenth day following thirteen days of administration of cisplatin and thirteen days of administration of leaf extract, respectively. The dose of the leaf extract was fixed according to the findings of an earlier study on its acute toxicity (Nain *et al.*, 2012b). One of the most common chemotherapeutic agents used to treat solid malignant illnesses is cisplatin, which is based on platinum. It can be used either alone or in conjunction with other medications for therapeutic purposes, and it can also be used as an adjuvant. The most serious side effect of cisplatin is nephrotoxicity, which happens when cisplatin concentrations rise and build up. It is used to treat cancer. Current methods used to reduce nephrotoxicity are thought to be insufficient. Also, since cisplatin is so vital in chemotherapy, we need to find ways to treat it that won't hurt our kidneys but won't reduce its effectiveness either. At present, the most secure course of action for creating novel treatment approaches is pharmaceuticals sourced from plants. Given the well-documented medicinal properties of plants and their constituents, this study set out to determine whether medicinal herbs sourced from Chhattisgarh could mitigate the kidney damage caused by cisplatin. Due to their ethnobotanical importance, the medicinal plant *Emblica officinalis* (Amla) sourced from the Indian state of Chhattisgarh was chosen for this study. Experiments have shown that this plant possesses anti-cancer properties. The presence of phytochemicals and antioxidant potential are the primary criteria for evaluating leaf extracts of the plant described earlier. In order to find out if the chosen leaf extracts can prevent cisplatin-induced nephrotoxicity.

Anticancer effects of hydroethanolic fractions of the leaves of *E. officinalis* in vitro

Fractions 3 and 7, after purification, were tested for antiproliferative activity using the SRB assay. There was no substantial activity (GI50 > 80) according to the results obtained from the analysis conducted on three human cancer cell lines: SK-OV-3, A498, and T-24. Figure 4.8 shows that when tested on the cell lines stated earlier, fractions 3 and 7 show very little antiproliferative efficacy. The GI50, the concentration of a chemical needed to inhibit cell growth by 50%, was typically considered significant when it was less than 10. Conversely, comparable numbers of viable cells showed that fractions 3 and 7 strongly suppressed the proliferation of the triple negative breast cancer cell lines MDA-MB-231 and MDA-MB-468. Crude extracts (AET) and fractions 3 and 7 showed antiproliferative activity that was similar to one another. Along with a large number of fragmented and condensed nuclear DAPI-stained cells, cells treated with cisplatin and fractions (fraction 3 and 7) showed active caspase 3 (red) staining that localizes with nuclei (blue). Immunofluoresence analysis was used to obtain the data that is displayed here.

A study involving histopathology- No pathological changes were noted in kidney segment tissues stained with hematoxylin and eosin in the vehicle and normal control groups, as well as in groups that received leaf extracts at varying concentrations. Element A, element B, element D, element F, and element H make up Figure 4.11. Significant damage was observed in the group that received cisplatin treatment [figure 4.11 C]. Necrosis, cellular hypertrophy, glomeruli degeneration, and Bowman's capsule sloughing were all components of this injury. Additionally, during the process of epithelial cell discharge, the distal and proximal convoluted tubules dilated. Certain tubular cell sections of the kidneys from both the control and leaf extract groups showed disruptions and polymorphic nuclei. Subjects exposed to different amounts of leaf extract in addition to cisplatin showed less necrosis, cellular edema, and Bowman's capsule sloughing in the renal tubules compared to the cisplatin-treated group (figure 4.11. E, G, I). Compared to the group that got 400 mg/kg BW, tubular damage was considerably reduced in the 100 mg/kg and 200 mg/kg BW groups that received leaf extract. This finding implies that there is a possibility of renal tissue toxicity due to excessive administration of leaf extract. If there is too much leaf extract in the body, the kidneys may have to work harder to filter it out.

Blood cell shape as affected by cisplatin and leaf extract - It was hypothesized that rodent blood cells treated with cisplatin would exhibit an abnormal morphology, lysis of red blood cells characterized by the disintegration of cell membranes, and aggregation of nuclear material. In contrast, the blood cells of the control rodents and those that received leaf extract exhibited a uniform morphology and were devoid of any indications of toxicity, as opposed to the cisplatin-treated group.

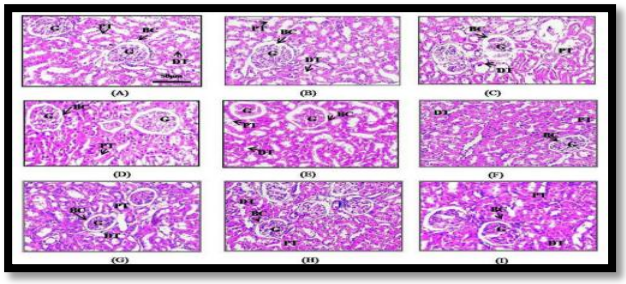


Fig: 4.8 Histopathological Study: (A) Normal control (B) Cisplatin (C) Vehicle control (D) AET 100 mg/kg (E) AET 100 mg/kg + CIS (F) AET 200mg/kg (G) AET 200mg/kg + CIS (H) AET 400mg/kg (I) AET 400mg/kg + CIS. AET= Amla ethanolic extract, CIS= Cisplatin, BC= Bowman's capsule, G= Glomerulus, PT= Proximal Tubule, DT= Distal Tubule.

Cisplatin and leaf extract's effects on total body mass index and the kidney-to-body mass ratio-The results, presented in Table 4.10, indicate that the cohort that received cisplatin treatment experienced a substantial increase ($p \leq 0.05$) in the kidney/body weight ratio and a significant decrease ($p \leq 0.01$) in body weight in comparison to the control group, which received cisplatin as-is. Comparing the normal control to the groups (groups 4-6) that received *E. officinalis* hydro-ethanolic leaf extract alone at varying concentrations, neither body weight reduction nor an increase in the kidney/body weight ratio ($p > 0.05$) were statistically significant. Nevertheless, the aforementioned parameters exhibited substantial changes ($p \leq 0.05$) in the cisplatin-treated groups (group 7) and group 8), which received leaf extract at concentrations of 100 mg/kg BW and 200 mg/kg BW, respectively. On the contrary, group 9, which were administered 400 mg/kg BW of cisplatin, did not undergo any such alteration in comparison to the aforementioned group.

Table 4.10.: The effects of cisplatin and leaf extract on total body mass index and kidney-to-body mass ratio

Groups	%Changeinbodyweight(g)	(Kidney/bodyweightratio)X 1000
NormalControl	+9.22±0.32	9.28±0.30
VehicleControl	+6.08±1.50^{ns}	9.44±0.13^{ns}
Cisplatin	-3.59±0.19**	11.37± 0.02*
AET100mg/kg	+6.89±0.90^{ns}	6.97±0.02^{ns}
AET200mg/kg	+7.16±1.69^{ns}	7.45±0.36^{ns}
AET400mg/kg	+9.71±1.68^{ns}	7.75±0.11^{ns}
AET 100+ Cis	-1.90±0.42$^{\#}$	9.23±0.2$^{\#}$
AET 200+ Cis	-1.80±0.30$^{\#}$	9.03±0.28$^{\#}$
AET 400+ Cis	-2.14±0.40^{NS}	10.01±0.61^{NS}

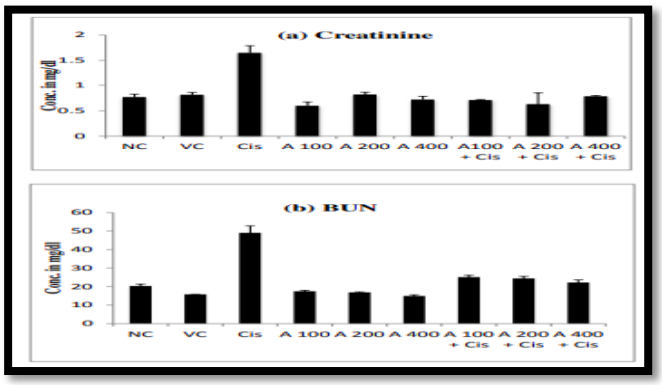
Assuming n=5, values are presented as mean ± SEM. The significance levels are as follows: **P ≤ 0.01 versus normal control, *P ≤ 0.05 versus normal control, #P ≤ 0.05 versus cisplatin, NS = Non-Significant versus cisplatin, and ns = Non-Significant versus normal control. Assay: AET = ethanolic extract of Amla; Cis = Cisplatin.

Table 4.11.: Effect of E. officinalis leaf extract in cisplatin induced Serum Creatinine and Blood Urea Nitrogen (BUN) level in normal, leaf extract and Cisplatin treated rats.

Groups	Creatinine(mg/dl)	BUN(mg/dl)
NormalControl	0.77±0.06	20.29± 0.98
VehicleControl	0.82±0.04^{ns}	15.74± 0.06^{ns}
Cisplatin	1.65±0.14*	49.04± 3.81*
AET100mg/kg	0.6 ±0.07 ^{ns}	17.40± 0.51^{ns}
AET200mg/kg	0.82±0.04^{ns}	16.86± 0.18^{ns}
AET400mg/kg	0.72±0.07^{ns}	14.87± 0.61^{ns}
AET 100+ Cis	0.71±0.01$^{\#}$	25.09±0.98$^{\#}$
AET 200+ Cis	0.63±0.22$^{\#}$	24.37± 1.14$^{\#}$
AET 400+ Cis	0.79±0.01$^{\#}$	22.14± 1.43$^{\#}$

The values are presented as mean ± SEM, assuming n=5. The following are the levels of significance: NS = non-significant in comparison to cisplatin, p ≤ 0.05 versus normal control, and * p ≤ 0.05 versus cisplatin. AET=ethanolic extract of Amla; Cis=cisplatin; for assay.

Blood urea nitrogen and serum creatinine levels as affected by cisplatin and leaf extract The concentrations of serum creatinine and BUN in the vehicle control group, as well as in groups administered different doses of leaf extract, are both determined to be within the anticipated ranges and do not differ significantly from the control group in a statistical sense (refer to figure 4.9 and table 4.11). On the contrary, the aforementioned parameters exhibited a significant increase ($p \leq 0.05$) in the groups that received cisplatin treatment in comparison to the control group that received conventional treatment. In comparison to rats treated with cisplatin (Groups 7-9), rats that were administered leaf extract at concentrations of 100 mg/kg, 200 mg/kg, and 400 mg/kg bodyweight demonstrated a statistically significant decrease ($p \leq 0.05$) in elevated serum creatinine and BUN levels.



Induced renal toxicity by cisplatin: the role of *E. officinalis* leaf extract (a) Creatinine and (b) Blood Urea Nitrogen (BUN) level in normal, leaf extract and Cisplatin treated rats. VC = Vehicle Control, NC = Normal Control, Cis. = Cisplatin, A = *E. officinalis* hydro ethanolic leaf extract.

11. Correlation between Cisplatin and oxidative stress indicators and leaf extract

To assess the renal toxicity of cisplatin, several enzymatic and non-enzymatic antioxidant markers were investigated in rodent models. This was done in consideration of the treatment's predominant mechanism of action, which is oxidative stress. The current study observed a substantial reduction in the activities of several antioxidant enzymes (CAT, SOD, GPx, and GR) following treatment with cisplatin [table 4.12; figure 4.10 (A-D)]. In addition, in comparison to the normal control group, renal MDA concentrations were increased (table 4.13; figure 4.10 (E); $p \approx 0.01$). Following cisplatin treatment, the subsequent effects on rodents of leaf extracts administered at weight-based concentrations of 100 mg/kg, 200 mg/kg, and 400 mg/kg BW are as follows:

4.12 Catalase (CAT) activity and the effects of leaf extract

Rats in groups 7 and 8, which were given leaf extract at doses of 100 mg/kg and 200 mg/kg BW, exhibited a significantly increased CAT activity ($p \leq 0.05$) in comparison to the group that was treated with cisplatin. However, it is worth noting that the CAT activity of rodents in group 9, which received the highest dose, did not increase in a statistically significant manner (see table 4.12 and figure 4.10A).

4.13 Implications for superoxide dismutase (SOD) activity due to leaf extract

The SOD activity of all groups (groups 7-9) that received leaf extract at different concentrations was significantly ($p \leq 0.05$) higher than that of the group of rodents treated with cisplatin, as shown in Table 4.12 and Figure 4.10 (B).

4.14 Assessment of glutathione peroxidase (GPx) activity by use of a leaf extract

GPx activity was significantly reinstated to baseline levels across all concentrations of leaf extract (groups 7-9), in contrast to the group that received cisplatin treatment. Nevertheless, the effect was considerably more pronounced ($p \leq 0.001$) when the dosage was established at 200 mg/kg BW (see figure 4.10 (C) and table 4.12).

4.15 Glutathione reductase (GR) activity and its relationship to leaf extract

The GR activity demonstrated a significant elevation ($p \leq 0.05$) in groups 7-9 when leaf extract was administered at all

eight concentrations, in comparison to the group that received cisplatin [table 4.12; figure 4.10 (D)].

Table 4.12.: The impact of *E. officinalis* leaf extract on antioxidant enzymes in rats that were untreated, given leaf extract, or given cisplatin.

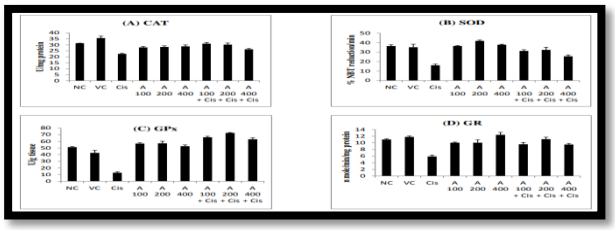
P ≤ 0.05 versus normal control, **P ≤ 0.01 versus cisplatin, ### p ≤ 0.001 versus cisplatin, **P ≤ 0.01 versus cisplatin; NS denotes non-significant differences in comparison to cisplatin and normal control, respectively, assuming n=5. AET=ethanolic extract of Amla; Cis=cisplatin; for assay.

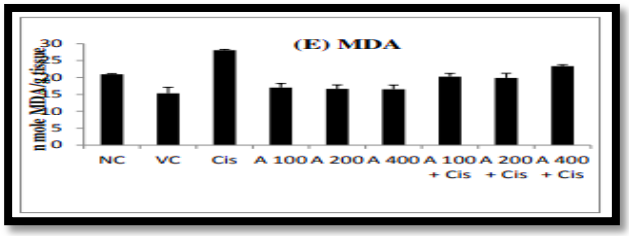
Groups	Catalase (U/mg protein)	SOD (%NBT reduction/min)	GPx(U/g tissue)	GR (nmole/min/mg protein)
NormalControl	31.41±0.06	36.45±1.36	51.28±0.89	11.00±0.21
VehicleControl	35.72±1.65^{ns}	35.18±3.31^{ns}	42.65±3.80^{ns}	11.79±0.27^{ns}
Cisplatin	22.45±0.47**	16.13±1.16**	12.83±1.37**	05.90±0.39**
AET100mg/kg	27.84±0.79^{ns}	36.46±0.64^{ns}	56.69±1.16^{ns}	10.04±0.19^{ns}
AET200mg/kg	28.22±0.99^{ns}	41.88±0.92^{ns}	57.04±3.07^{ns}	10.04±0.86^{ns}
AET400mg/kg	28.75±1.27^{ns}	37.82±0.50^{ns}	52.73±2.07^{ns}	12.41±0.75^{ns}
AET 100+Cis	31.00±0.98$^{\#}$	31.27±1.21$^{\#}$	66.11±1.45$^{\#\#}$	9.97±0.54$^{\#}$
AET 200+Cis	30.21±1.39$^{\#}$	32.35±2.85$^{\#}$	72.63±0.50$^{\#\#\#}$	11.11±0.58$^{\#}$
AET 400+Cis	26.25±0.78^{NS}	25.60±1.47$^{\#}$	63.03±2.25$^{\#\#}$	09.49±0.29$^{\#}$

Rats administered Cisplatin, *E. officinalis* leaf extract, or a control group had their renal MDA levels measured.

Groups	MDA (nmoleMDA/g tissue)
NormalControl	20.95±0.22
VehicleControl	15.34±1.74^{ns}
Cisplatin	28.06±0.21**
AET100mg/kg	17.02± 1.21^{ns}
AET200mg/kg	16.65±1.17^{ns}
AET400mg/kg	16.53±1.23^{ns}
AET 100+Cis	20.23± 0.98$^{\#}$
AET 200+Cis	19.89±1.38$^{\#}$
AET 400+Cis	23.35± 0.41$^{\#}$

The values are presented as mean ± SEM, assuming n=5. NS = Non-Significant versus Cisplatin; ns = Non-Significant versus Normal Control; P ≤ 0.05 versus cisplatin; **P ≤ 0.01 versus normal control; *P ≤ 0.05 versus cisplatin. The ethanolic extract of Amla is denoted as AET, whereas Cisplatin is denoted as Cis.





7. Effect of *E. officinalis* leaf extract on antioxidant enzymes and MDA level in normal, leaf extract and Cisplatin treated rats: (A) Superoxide dismutase (SOD) (B) Catalase (CAT) (C) Glutathione Peroxidase (GPx) (D) Glutathione Reductase (GR) (E) renal Malondialdehyde (MDA). Cis. = Cisplatin, NC= Normal Control, VC = Vehicle Control, A= *E. officinalis* hydro ethanolic leaf extract.

When administered orally at concentrations of 100 mg/kg, 200 mg/kg, and 400 mg/kg of leaf extract, renal tissue MDA levels were significantly decreased (p ≤ 0.05) compared to the group treated with cisplatin [table 4.13; figure 4.10 (E)].

Recommendation

Pharmacology and medical research must assess medicinal plant extracts' cisplatin-toxicity protection. Chronic cisplatin, a chemotherapy medication, often causes neurotoxicity and nephrotoxicity, reducing its clinical value. Researchers may find complementary or alternative medicines that improve cisplatin efficacy and reduce toxicity by investigating medicinal plant extracts. Researchers can find plant extracts that protect against cisplatin-induced toxicity using in vitro and in vivo investigations, biochemical assays, and animal models. This research has promise for developing novel therapeutic strategies to improve cancer patients' quality of life and survival rates.

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