

EFFECTS OF ADMINISTRATION OF TARAXACUM OFFICINALE'S EXTRACT ON RENAL PARAMETERS IN CISPLATIN INDUCED NEPHROTOXICITY IN ALBINO MICE

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Date Submitted: March 27, 2019

Date Revised: September 17, 2019

Date Accepted: September 19, 2019

ABSTRACT

OBJECTIVE: To assess biochemical markers after administering *Taraxacum officinale*'s extract in cisplatin induced nephrotoxic albino mice.

METHODS: It was an experimental study, carried out on thirty albino mice categorized into six groups i-e. normal control (saline only), negative control (cisplatin-25mg/kg body weight intraperitoneally) and experimental groups (E1 to E4) (*Taraxacum officinale*'s extract at doses 100 mg, 200 mg, 400 mg and 800 mg per kg body weight respectively intraperitoneally followed by single dose of cisplatin-25 mg/kg body weight intraperitoneally). Effects of *Taraxacum officinale*'s extract on kidney were assessed by biochemical markers i-e. blood urea and creatinine.

RESULTS: Comparison of blood urea levels in experimental groups (E1, E2, E3 & E4) was much lowered (242 ± 36.6 mg/dl, 176.8 ± 23.9 mg/dl, 179.4 ± 69.5 mg/dl, 186.6 ± 69.05 mg/dl respectively) than the negative control (363 ± 111.1 mg/dl) [p value < 0.05]. Comparison of serum creatinine in negative control versus experimental groups respectively was decreased but statistically insignificant (serum creatinine levels of experimental groups were 1.60 ± 0.65 mg/dl, 1.89 ± 0.32 mg/dl, 1.66 ± 0.62 mg/dl, 1.84 ± 0.55 mg/dl while serum creatinine of negative control was 1.97 ± 1.06 mg/dl) [p value > 0.05].

CONCLUSION: *Taraxacum officinale*'s extract (dandelion) significantly reduces the effects of renal toxicity produced by the cisplatin but was unable to completely revert cisplatin-induced nephrotoxicity in mice.

KEY WORDS: *Taraxacum* (MeSH); *Taraxacum Officinale* (MeSH); Biomarkers (MeSH); Cisplatin (MeSH); Nephrotoxicity (Non-MeSH); Herbal drugs (Non-MeSH); Urea (MeSH); Creatinine (MeSH); Antioxidants (MeSH).

THIS ARTICLE MAY BE CITED AS: Javaid A, Zafar S, Khattak M, Khan F, Wadud S. Effects of administration of *Taraxacum officinale*'s extract on renal parameters in cisplatin induced nephrotoxicity in albino mice. *Khyber Med Univ J* 2019;11(3):156-9. DOI: 10.35845/kmuj.2019.19172

INTRODUCTION

Kidney, the vital organ, performing important excretory functions,¹ having peculiar cells as well as increased vascularity (20% of cardiac output) is liable for elimination along with concentration of vast range of drugs as well as toxins.² Adverse effects on kidney by therapeutic agents [non-steroidal anti-inflammatory drugs (NSAID's), aminoglycosides, chemotherapeutic agents] and toxins

include acute renal shut down, chronic interstitial nephritis, nephritic syndrome etc.³

A potent chemotherapeutic agent, cisplatin is used for the treatment of wide variety of tumors including testicular tumor, head and neck carcinomas, ovarian germ cells and epithelial cancers, carcinoma of endometrium / cervix, malignant melanoma, bladder cancer, lung cancer (non-small cell type), cancer of adrenal

cortex and penile carcinoma.⁴ Approximately 35% of the patients receiving cisplatin as a chemotherapy develop nephrotoxicity⁵ which is progressive as well as concentration-dependent.⁶

Before 16th century, herbs were mostly used for treatment of diseases till the development of synthetic drugs.⁷ However, the adverse effects and contraindications of chemical drugs favored the use of plants again. According to archeological studies mankind was aware about the herbal curative properties in ancient times.⁸⁻¹⁰ More than 3.3 billion human beings in developing countries take advantage of medicinal plants oftenly.¹¹ Many herbs available in Pakistan have shown their nephroprotective and hepatoprotective role.^{12,13} Numerous other plants of our landscape still need valuable exploration for the prevention as well as treatment of renal diseases. *Taraxacum officinale*, one of such herbs needs to be evaluated for its nephroprotective effects.

Taraxacum officinale (dandelion) is a flowering herbaceous, perennial plant of the family Asteraceae (Compositae) not only found in Asia but also has been seen mostly in the vicinity of Europe, Southern parts of Africa, America, New Zealand, India, Australia and Canada. Mainly it is a weed belonging to warmer temperate zones¹⁴ sprouting along the edges of roads, in gardens as well as at the coastlands.¹⁵

Taraxacum officinale's extract is known to provide many health benefits (hepato-protective, anti-cancerous, anti-bacterial, anti-parasitic, antioxidant, anti-inflammatory, hypoglycemic, lipid lowering and diuretic effects).¹⁶ However, no remarkable work has been done as far as the nephroprotective role of

TABLE I: EFFECTS OF CISPLATIN AND TARAXACUM OFFICINALE'S EXTRACT ADMINISTRATION ON BLOOD UREA AND SERUM CREATININE IN ALBINO MICE

Treatment Groups	Blood Urea (mg/dl)	Serum Creatinine (mg/dl)
Normal Control (normal saline only)	32.4±6.71	0.46±0.24
Negative Control (Cisplatin only 25mg/kg)	363±111.1	1.97±1.06
<i>Taraxacum officinale</i> 100 mg/kg (E1) + Cisplatin 25mg/kg	242.0±36.6*	1.60±0.657
<i>Taraxacum officinale</i> 200 mg/kg (E2) + Cisplatin 25mg/kg	176.8±23.9*	1.89±0.321
<i>Taraxacum officinale</i> 400 mg/kg (E3) + Cisplatin 25mg/kg	179.4±69.5*	1.66±0.618
<i>Taraxacum officinale</i> 800 mg/kg (E4) + Cisplatin 25mg/kg	186.6±69.05*	1.84±0.550

* p<0.05

Taraxacum officinale is concerned.

Our rationale was to document the protective role of *Taraxacum officinale* on renal functions for which we assessed biochemical markers (blood urea, serum creatinine) after administering *Taraxacum officinale*'s extract in cisplatin induced nephrotoxic albino mice.

METHODS

This study included Swiss albino mice (n=30), weighed 22-35 gms and aged 8-12 weeks of either gender.¹⁷ However, sick and pregnant female albino mice were not included in the study. Mice were given ideal conditions in the animal house facility of Peshawar Medical College, Peshawar, Pakistan i.e., 12 hours of day and night cycles with 25±2°C room temperature. They were provided with standard food and water *ad libitum*. Animals were acclimatized within ten days.¹⁷

Ethical Committee of Peshawar Medical College approved the protocols of animal handling to be applied in the study.

The selected plant was collected from the road sides as well as lawns and gardens of Hasan Garhi near Shami road and Peshawar University Campus, Peshawar in March and April (at peak sprouting time).¹⁸ Methanolic plant extract was prepared and kept in amber colored bottle.¹⁹ Study animals were divided into six groups:

Group I – Normal Control Group

(Normal Saline was given intraperitoneally)

Group II – Negative Control Group (cisplatin only 25 mg / Kg body weight was given intraperitoneally) (animals were slaughtered after 72 hours).

Group III (E 1) – Plant Extract (100 mg / Kg body weight) administration followed by cisplatin (25 mg / Kg body weight) intraperitoneally on 7th day.

Group IV (E 2) – Plant Extract (200 mg / Kg body weight) administration followed by cisplatin (25 mg / Kg body weight) intraperitoneally on 7th day.

Group V (E 3) – Plant Extract (400 mg / Kg body weight) administration followed by cisplatin (25 mg / Kg body weight) intraperitoneally on 7th day.

Group VI (E 4) – Plant Extract (800 mg / Kg body weight) administration followed by cisplatin (25 mg / Kg body weight) intraperitoneally on 7th day.

Five mice were included in each group. The duration of study for group I to group VI was 10 days but for group II it was 72 hours. Animals were slaughtered after seventy-two hours of the cisplatin injection whereas blood samples were drawn by heart puncture technique for calculating blood urea along with serum creatinine levels.

After collection, the blood was centrifuged (4000 rpm for 20 min) to separate serum. Blood urea along with serum creatinine levels were measured. Blood urea was determined by modified Berthelot reaction (enzymatic

calorimetric test) using Human kit (HUMAN Gesellschaft für Biochemica und Diagnostica mbH, Germany).²⁰ Serum creatinine levels were measured through kinetic test (without deproteinization according to Jaffe method) using DiaSys kit (DiaSysDiagnostische Systeme GmbH, Germany).²¹ Both measurements were taken by using Microlab 300 (Merck, Netherland).

For variables such as urea and creatinine, the test of normality was applied and the whole data was found to be normally distributed. Data was presented as mean±SD. Student's T-test was applied using Statistical Package for Social Sciences version 20. P value < 0.05 was considered statistically significant.

RESULTS

Blood urea levels of normal control group was 32.4±6.71 mg/dl while that of negative control group where only cisplatin (25 mg/kg body weight) was given, came out to be 363±111.1 mg/dl which showed significant increase in blood urea (Table I).

The value of serum creatinine of normal control group was 0.46±0.24 mg/dl, whereas the serum creatinine of negative control group, where only cisplatin (25 mg/kg body weight) was given, came out to be 1.97±1.06 mg/dl, which showed significant increase in serum creatinine. These results depicted that cisplatin induced nephrotoxicity was successfully achieved (Table I).

Different doses of plant extract were given and results were obtained. It was determined that by increasing the dose of plant extract (*Taraxacum officinale*) the blood urea levels decreased significantly, meaning an improvement in renal functions (p value < 0.05) (Table I).

However, it is clearly shown in the table that serum creatinine levels remained constantly elevated (except in E-1 and E-3) despite increase in the dose of the plant extract (*Taraxacum Officinale*). We compared the serum creatinine levels of negative control group with all the experimental groups (p value >

0.05)(Table I).

DISCUSSION

The kidney is an essential anatomical structure, which performs various physiological processes. Toxic chemicals or drugs (such as cisplatin) disturb the normal excretory functions of kidney leading to nephrotoxicity.^{22,23}

In present study, animal model is used (single dose of cisplatin 25 mg/kg body weight intraperitoneally) for inducing nephrotoxicity. Yang and his colleagues (2017) had also used the same amount of cisplatin for incurring acute kidney damage.¹⁷ In this experimental study, cisplatin (cis-diamine dichloro platinum-II) induced nephrotoxicity was determined via biochemical markers (blood urea and serum creatinine) Elevated blood urea and creatinine levels were indicating significant cisplatin induced nephrotoxicity, which was also observed in many previous studies.^{17,24,25}

In this study, only blood urea levels were improved by increasing doses of *Taraxacum officinale*'s extract which is in favor of the study by Ali Karakus and colleagues which also showed an improvement in the renal biomarkers with *Taraxacum officinale* administration in CCl₄ induced renal toxicity in rats.²⁶ However, serum creatinine levels after plant extract administration remained elevated and did not revert to normal which is contrary to the work done by Ali Karakus and colleagues. Di Cerbo and colleagues concluded that a diet containing the *Taraxacum officinale*'s improves the serum creatinine, blood urea and urine color in cats diagnosed with stage II and stage III chronic renal failure which also favors the results of our study that the renal toxicity is improved in *Taraxacum officinale*'s treated mice.²⁷ Maham Zafar and her associates also conducted a study on the nephroprotective effects of *Taraxacum officinale* in rats inducing the renal injury with CCl₄. Their results are in agreement to our results showing that the dandelion treatment decreases the nephrotoxic effects of CCl₄ by showing improvement in the serum urea, creatinine and renal histologic findings possibly by increasing antioxidant

defense system.²⁸ Proper comparison with other studies cannot be made as no other remarkable work has been done as far as the nephroprotective role of *Taraxacum officinale* is concerned.

CONCLUSION

Taraxacum officinale's (dandelion) significantly reduce the effects of renal toxicity produced by the cisplatin but was unable to completely revert cisplatin-induced nephrotoxicity in mice.

LIMITATIONS

We carried out the study on whole plant, there is a need for detailed studies on individual parts of *Taraxacum Officinale* as the leaves, roots and stem might have different concentrations of flavonoids, saponins, tannins, alkaloids and phenols.

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AUTHORS' CONTRIBUTIONS

Following authors have made substantial contributions to the manuscript as under:

AJ: Conception and design, acquisition, analysis and interpretation of data, drafting the manuscript, final approval of the version to be published

SZ & FK: Interpretation of data, drafting the manuscript, final approval of the version to be published

MK: Acquisition of data, critical revision, final approval of the version to be published

SW: Study design, critical review, final approval of the version to be published

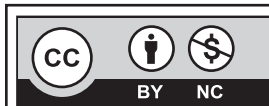
Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

CONFLICT OF INTEREST

Authors declared no conflict of interest

GRANT SUPPORT AND FINANCIAL DISCLOSURE

NIL



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