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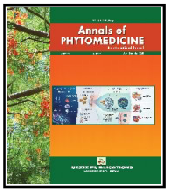

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Cytoprotective potential of quercetin against cisplatin induced cytotoxic insults in diverse renal cell lines NRK-52E, MDCK and HEK293

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Abstract

Cisplatin (cDDP), a platinum based chemotherapeutic agent, remains one of the most widely utilized and efficacious treatment for a broad spectrum of solid malignancies in both human and veterinary oncology. However, its clinical utility is markedly constrained by a pronounced, dose dependent nephrotoxicity. Renal epithelial cell lines such as NRK-52E, MDCK and HEK293 serve as well established *in vitro* models for investigating cDDP induced nephrotoxic mechanisms. The current investigation was designed to evaluate cDDP mediated cytotoxicity and the nephroprotective potential of quercetin (QRT). A concentration of 200 µM cDDP was employed to induce a reproducible cytotoxic response, yielding approximately 10-20% cellular viability, thereby enabling the assessment of QRT protective effects at a graded concentration range (3.125-50 µg/20 µl). Cell proliferation assays revealed that among the tested cell lines, HEK293 exhibited the highest susceptibility to QRT induced proliferative rescue, followed by MDCK and NRK-52E demonstrating the least sensitivity. All three cell lines showed marked vulnerability to cDDP induced cytotoxic stress. Notably, the restoration of 50% cell viability in the presence of cDDP necessitated a higher concentration of QRT in HEK293, compared to MDCK and NRK-52E, respectively. These findings underscore the differential cellular responsiveness to both toxic and protective agents. Furthermore, the elucidation of the molecular underpinnings of QRT mediated cytoprotection offers compelling rationale for its potential inclusion in combinatorial therapeutic regimens to mitigate cisplatin induced nephrotoxicity.

1. Introduction

Cisplatin (cDDP) is a platinum coordinated inorganic complex extensively employed as a cytotoxic chemotherapeutic agent in the treatment of diverse solid malignancies (Li *et al*., 2025). Despite its clinical efficacy, the therapeutic application of cDDP is often hindered by its adverse off target effects, prominently including nephrotoxicity, myelosuppression, ototoxicity and hepatotoxicity (Orasan *et al*., 2025; Verma *et al*., 2025a). Following systemic administration, cDDP is predominantly excreted *via* the renal pathway, where it preferentially accumulates in the S3 segment of the proximal tubular epithelium, leading to nephrotoxic outcomes that are closely linked to the degree of renal injury manifesting as either necrotic or apoptotic cell death (Chen *et al*., 2025).

The pathophysiology of cDDP induced nephrotoxicity is multifactorial, involving intricate biochemical cascades and discrete genomic modifications. Elevated intracellular concentrations of cDDP augment the generation of reactive oxygen species (ROS), primarily through interaction with nuclear DNA, resulting in oxidative stress and subsequent cellular injury (Verma *et al*., 2019; Li *et al*., 2023). The ensuing damage encompasses structural disintegration of the cytoskeleton, compromised intracellular organelles and impairment of membrane bound transport systems, culminating in apoptotic or necrotic cell demise. Notably, investigations utilizing enucleated cellular models suggest that cDDP may also trigger apoptosis via nucleus independent mechanisms, particularly through disruption of endoplasmic reticulum (ER) homeostasis, including perturbation of protein folding and calcium regulation (Tang *et al*., 2023). Further exacerbation of cDDP induced oxidative stress has been attributed to cytochrome $P_{450}2E_1$, which catalyses the formation of highly reactive oxygen intermediates such as hydroxyl radicals, superoxide anions and hydrogen peroxide, thereby amplifying oxidative damage (Verma *et al*., 2025a). Cellular uptake of cDDP is mediated predominantly by copper transporter 1 (CTR1) and organic cation transporter 2 (OCT2); however, once internalized, cDDP can interfere with intracellular antioxidant systems by inactivating protective enzymes such as glutathione and metallothionein (Kannampuzha *et al*., 2025).

In recent years, bioactive polyphenolic compounds derived from natural sources have garnered substantial interest for their potential role in ameliorating drug induced kidney injury, owing to their potent antioxidant, antiinflammatory and metal chelating properties. Among these, quercetin (QRT), a ubiquitous flavonol present in various fruits, vegetables, and medicinal plant species, has emerged as a promising nephroprotective agent (Carrillo-Martinez *et al.,* 2024;

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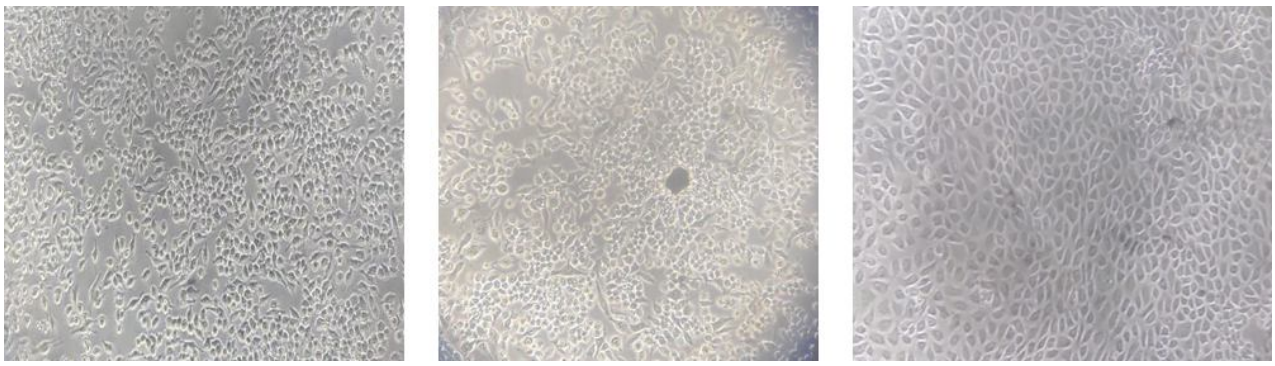
Jian *et al*., 2024). The QRT exhibits broad-spectrum pharmacological activities, including antimicrobial, anticancer and antioxidant effects. Mechanistically, QRT acts by neutralizing free radicals and potentiating the endogenous antioxidant defense system, notably via activation of the nuclear factor erythroid 2-related factor 2 (Nrf2) signaling axis, which is pivotal in cellular redox homeostasis (Baba *et al*., 2024). Additionally, QRT has been reported to inhibit the protein kinase R-like endoplasmic reticulum kinase (PERK) signaling pathway, thereby mitigating ER stress mediated oxidative injury in cDDP exposed NRK-52E cells and conferring protection against acute renal damage (Ju *et al*., 2021). It has also been implicated in the activation of Sirtuin-1 (SIRT1), a NADP-dependent deacetylase involved in modulating cellular aging and stress resistance pathways, thereby offering therapeutic potential in various kidney disorders (Bian *et al*., 2022). Prior experimental studies have demonstrated that QRT can counteract the antiproliferative effects of cDDP in renal epithelial cell lines such as HEK293 and NRK-52E, highlighting its protective efficacy *in vitro* (Casanova *et al*., 2021).

Given this backdrop, the present study was undertaken to systematically evaluate the protective effects of QRT against cDDP induced cytotoxicity across three distinct renal cell lines [NRK-52E (rat origin), MDCK (canine origin) and HEK293 (human origin)] in an effort to delineate cell specific responses and mechanistic insights relevant to nephroprotection.

2. Materials and Methods

2.1 Cell lines culture

Three distinct renal epithelial cell lines NRK-52E (normal rat kidney, of *Rattus norvegicus*), MDCK (madin darby canine kidney, derived from *Canis lupus familiaris*) and HEK293 (human embryonic kidney, of *Homo sapiens*) were obtained from the National Centre for Cell Science (NCCS), Pune, Maharashtra, India. Morphological assessment and routine monitoring of cellular health were performed using an inverted phase contrast microscope (Nikon, ECLIPSE-TS100, Japan). Cells were maintained in dulbecco's modified eagle medium (DMEM), supplemented with 10% fetal bovine serum (FBS) and 1% penicillin streptomycin solution. Cultures were incubated under standard conditions at 37°C in a humidified atmosphere containing 5% CO_2 using a CO_2 incubator (HERA cell 150, Thermo fisher scientific, USA). Representative images of the three cell lines are displayed below:



NRK-52E MDCK HEK293

2.2 Reagents and chemicals

All chemicals and reagents utilized in this investigation were of analytical or cell culture grade. The following were procured from Sigma Aldrich (USA), *viz.,* dulbecco's modified eagle medium (DMEM; Cat. No. D5671), dimethyl sulfoxide (DMSO; Cat. No. D2650), fetal bovine serum (FBS; Cat. No. F7524), dulbecco's phosphate buffered saline (DPBS; Cat. No. D5537), trypan blue solution (Cat. No. T8154), resazurin (Cat. No. RM125), penicillin streptomycin (Cat. No. P4333), trypsin EDTA (Cat. No. TCL006), L-glutamine (Cat. No. TCL012). The following specific agents were used for cytotoxicity assessment and treatment like 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide (MTT); cisplatin (cDDP; Cat. No. PHR1624); quercetin (QRT; Cat. No. S1BB8166V) acquired from Sigma Aldrich Pvt Ltd., USA.

2.3 Assessment of cytotoxicity

To evaluate the cytotoxic potential of cDDP and the protective efficacy of quercetin, three standard cell viability assays MTT, resazurin reduction, and trypan blue exclusion were employed, following established protocols (Mani and Swargiary, 2023). For MTT and resazurin assays, cells were seeded into 96 well microplates at densities ranging from 5,000 to 8,000 cells per well. After 24 h of adherence and acclimatization, cells were exposed to varying concentrations of cDDP (ranging from 50 µM to 800 µM) to determine the optimal dose for cytotoxic induction. Based on preliminary viability screening, 200 µM of cDDP was selected for subsequent experiments, as it consistently produced approximately 75-85% cytotoxicity across cell lines. To evaluate the cytoprotective potential of quercetin, concentrations of 50, 25, 12.5, 6.25, and 3.125 µg/ 20 µl were tested both individually and in cotreatment with 200 µM cDDP. The effects of these treatments were assessed in all three renal epithelial cell lines.

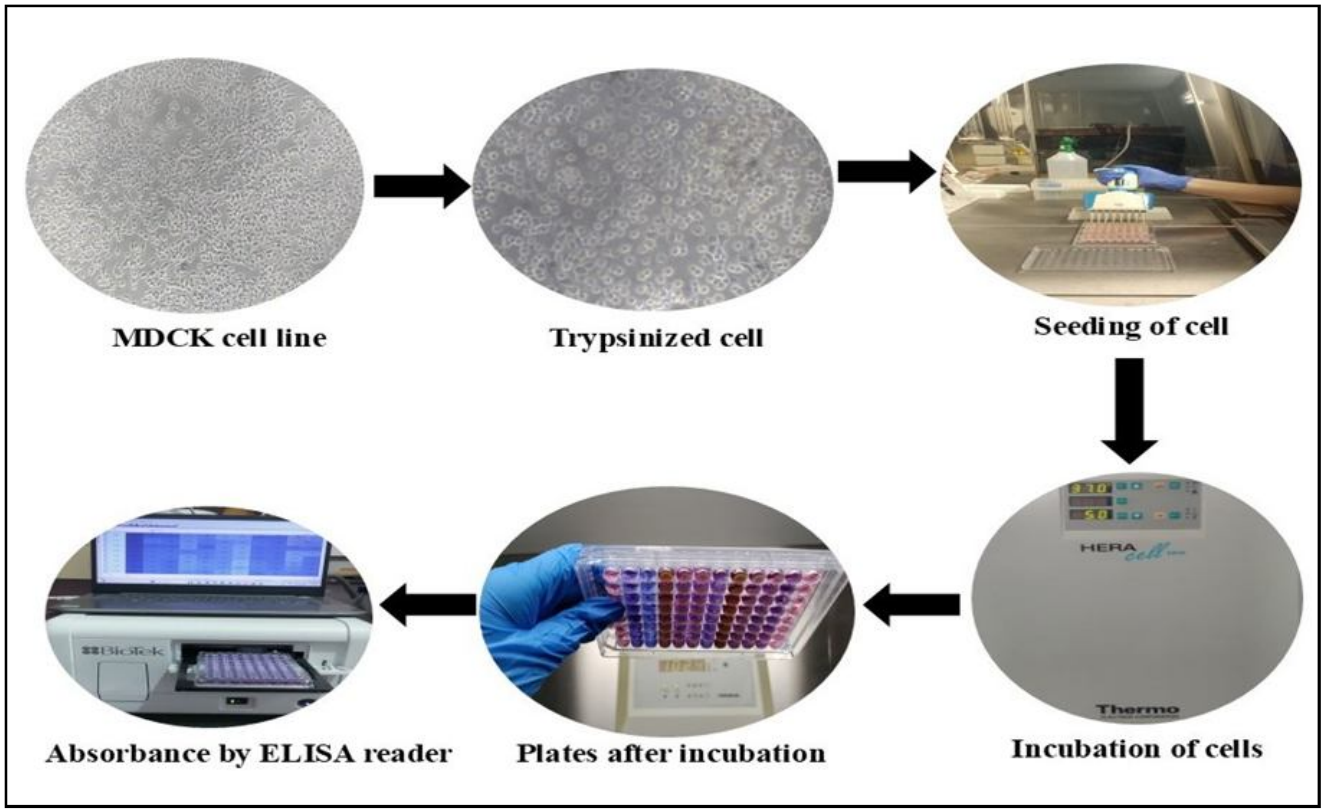
2.3.1 MTT assay

The MTT assay was performed to quantify mitochondrial metabolic activity as an indirect measure of cell viability and proliferation (Ghasemi *et al*., 2023). Briefly, cells were seeded in 96 well plates and incubated for 24 h. After incubation, cells were treated with cDDP and/or QRT as described above. After 24 h of exposure, the medium was removed and 20 µl of MTT solution (5 mg/ml in DPPS) was added to each well. Plates were then incubated for 4 h at 37°C to allow formazan crystal formation. Subsequently, the medium was

replaced with 100 µl of DMSO to solubilize the crystals, and the absorbance was measured at 570 nm using a microplate reader (EPOCH2, BioTek, USA). Results were expressed as the percentage of viable cells relative to untreated control.

2.3.2 Resazurin dye reduction assay

The resazurin assay was employed as a complementary fluorometric method to evaluate cell viability based on metabolic activity and mitochondrial respiration (Petiti *et al*., 2024). Cells and treatments were prepared in 96 well plates as outlined previously. After 24 h of exposure, 20 µl of resazurin working solution was added to each well and the plate was incubated for an additional 4 to 6 h at 37°C. Fluorescence intensity was measured using an excitation/emission wavelength of 560/590 nm, respectively. Data were analysed and interpreted similarly to the MTT assay. A schematic overview of the experimental workflow is presented in the corresponding flowchart.



2.3.3 Trypan blue exclusion assay

Cell viability was further validated using the trypan blue exclusion method (El-Dabae, 2024). Cells were seeded in 6 well plates, treated with cDDP (200 µM) alone or in combination with varying concentrations of QRT for 24 h post-treatment, cells were detached using trypsin EDTA, harvested into microcentrifuge tubes and stained with 0.4% trypan blue solution. Viable (unstained) and non-viable (blue stained) cells were manually counted using a haemocytometer (Neubauer chamber) under a light microscope equipped with a digital camera (MLX with OLYMPUS PEN Lite, Japan). Cell viability percentage was calculated using the formula:

$$\text{Cell viability (\%)} = \frac{\text{Total number of viable cells}}{\text{Total number of cells}} \times 100$$

2.4 Statistical analysis

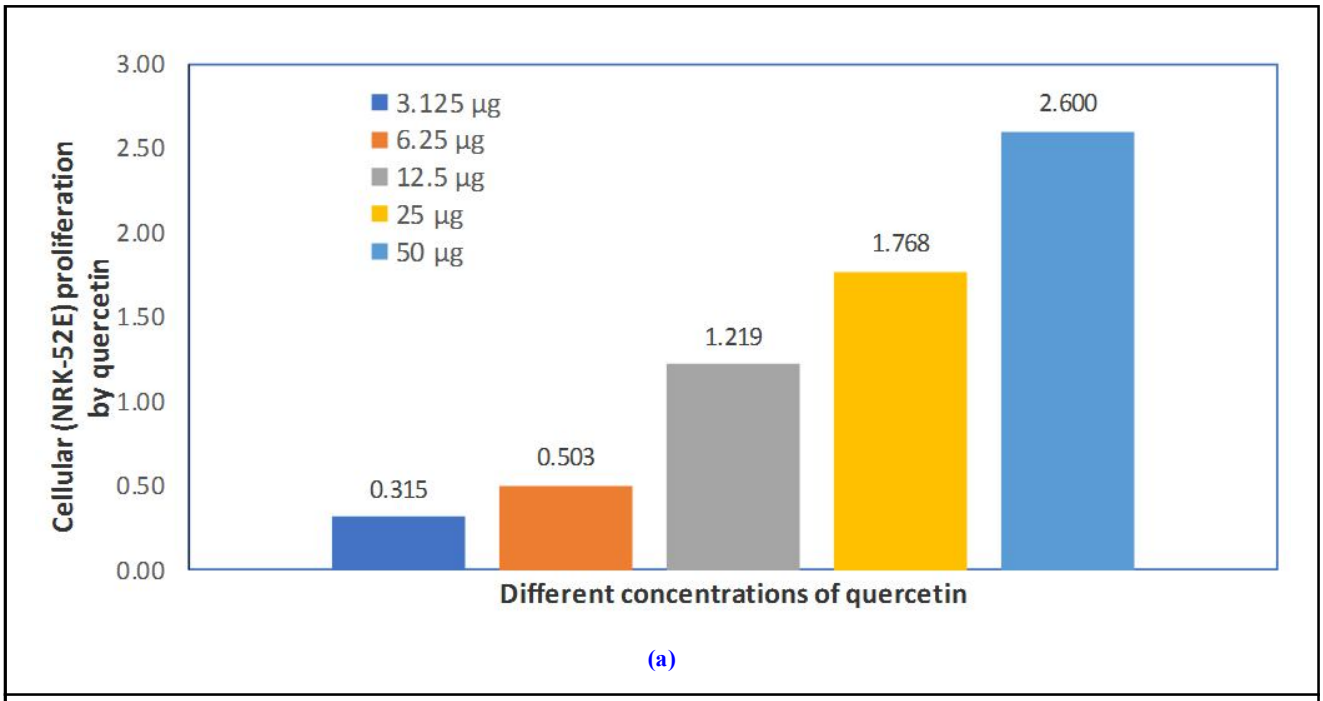
All experimental data were compiled and analysed using GraphPad Prism software. Results were expressed as mean ± standard deviation (SD) for all replicates. Statistical significance was determined using appropriate tests, details of which are provided in the results section.

3. Results

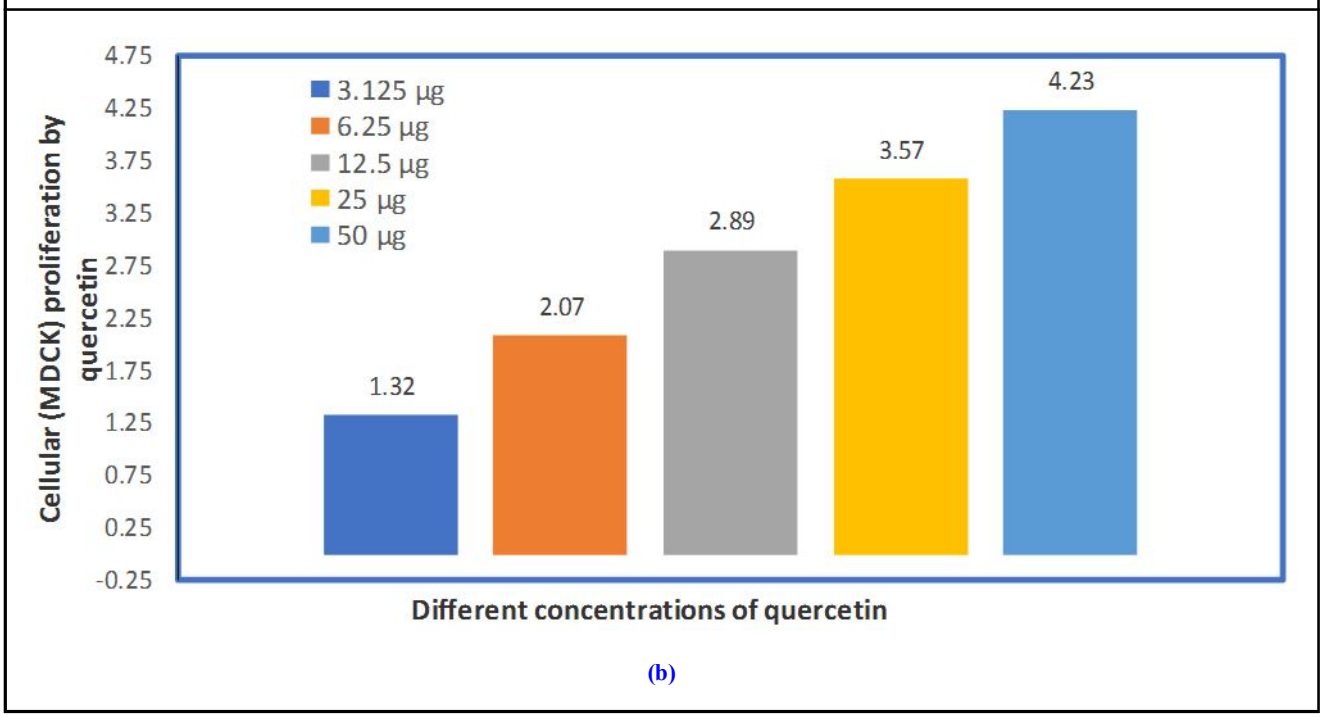
3.1 QRT mediated cytoprotective and proliferative response *via* MTT assay

The MTT assay was employed to quantitatively assess the differential protective effects and proliferative potential of QRT against cDDP induced cytotoxicity in renal epithelial cell lines NRK-52E, MDCK and HEK293 following a 24 h exposure period. All three cell lines were exposed to a fixed cytotoxic dose of 200 µM cDDP, in combination with varying concentrations of QRT (3.125-50 µg/ 20 µl). The extent of cellular recovery and proliferation was determined by measuring mitochondrial dehydrogenase activity. The findings confirmed that QRT conferred a concentration dependent ameliorative effect in all cell lines. In NRK-52E cells, co-treatment with 50 µg/ 20 µl QRT restored proliferation by 1.14-fold, followed by 0.61, 0.38, 0.12 and 0.08 folds increases at 25, 12.5, 6.25, and 3.125 µg/ 20 µl doses, respectively, relative to the cDDP only group. When administered in the absence of cDDP, QRT alone elicited a notable dose-dependent proliferative effect, resulting in 2.6-fold increase at 50 µg/ 20 µl, followed by 1.77, 1.22, 0.50, and 0.32 folds increases at decreasing concentrations. In MDCK cells, QRT demonstrated a similar protective trend though a lesser extent. Coexposure to 50 µg/

20 µl QRT led to a 0.97 folds increase in cell proliferation compared to cDDP treated controls, followed by 0.69, 0.37, 0.28 and 0.04 folds increases at lower QRT doses exposed. In the absence of cDDP, QRT alone induced a robust, dose-responsive proliferation in MDCK cells 4.23 folds at 50 µg/20 µl, with subsequent increases of 3.57, 2.89, 2.07, and 1.32 folds at decreasing concentrations. HEK293 cells displayed the highest intrinsic proliferative response to QRT under normal condition. Exposure to QRT alone resulted in a remarkable 11.07 folds increase in proliferation at 50 µg/20 µl, followed by 8.08, 5.26, 2.87 and 1.53 folds increases at descending doses. Under cDDP induced stress, however, HEK293 cells demonstrated limited amelioration. Co-treatment with QRT yielded 1.06, 0.65, 0.35, 0.09 and 0.03-fold proliferation at 50, 25, 12.5, 6.25, and 3.125 µg/20 µl QRT, respectively. Collectively, these findings confirm the dose dependent protective and proliferative capacity of QRT with HEK293 showing the highest baseline proliferative response, while NRK-52E demonstrated superior resilience and recovery under cDDP induced toxicity. Figures 1 and 2 represent the cellular proliferation and cytoprotection by QRT alone and in presence of cDDP in all three cell lines.



(a)



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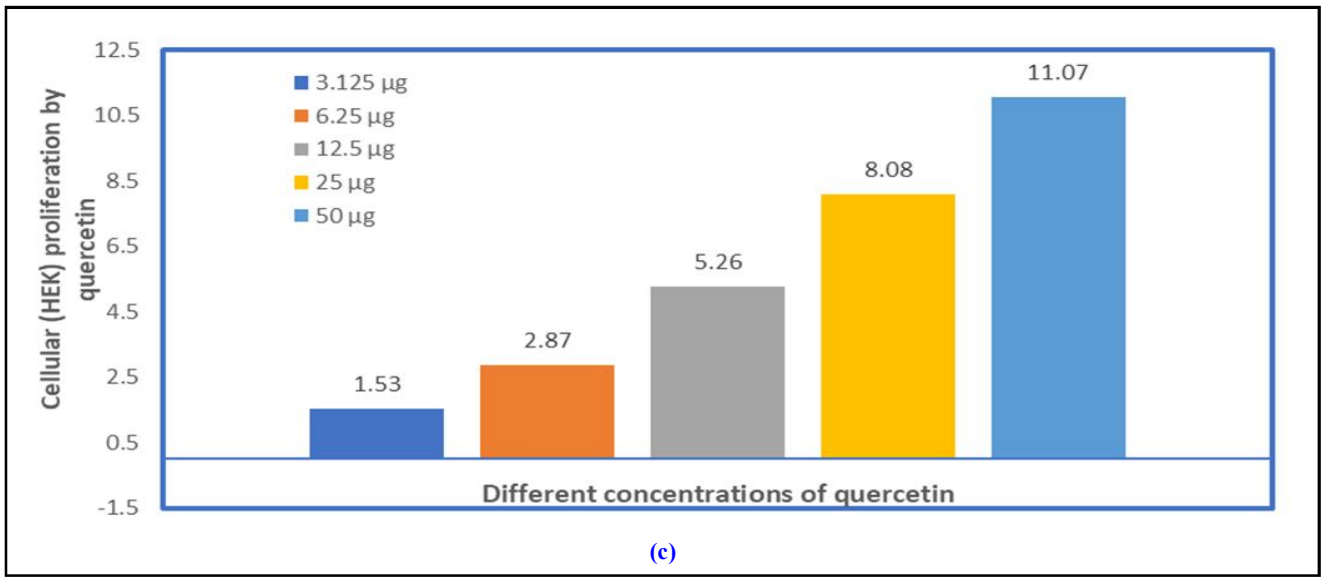
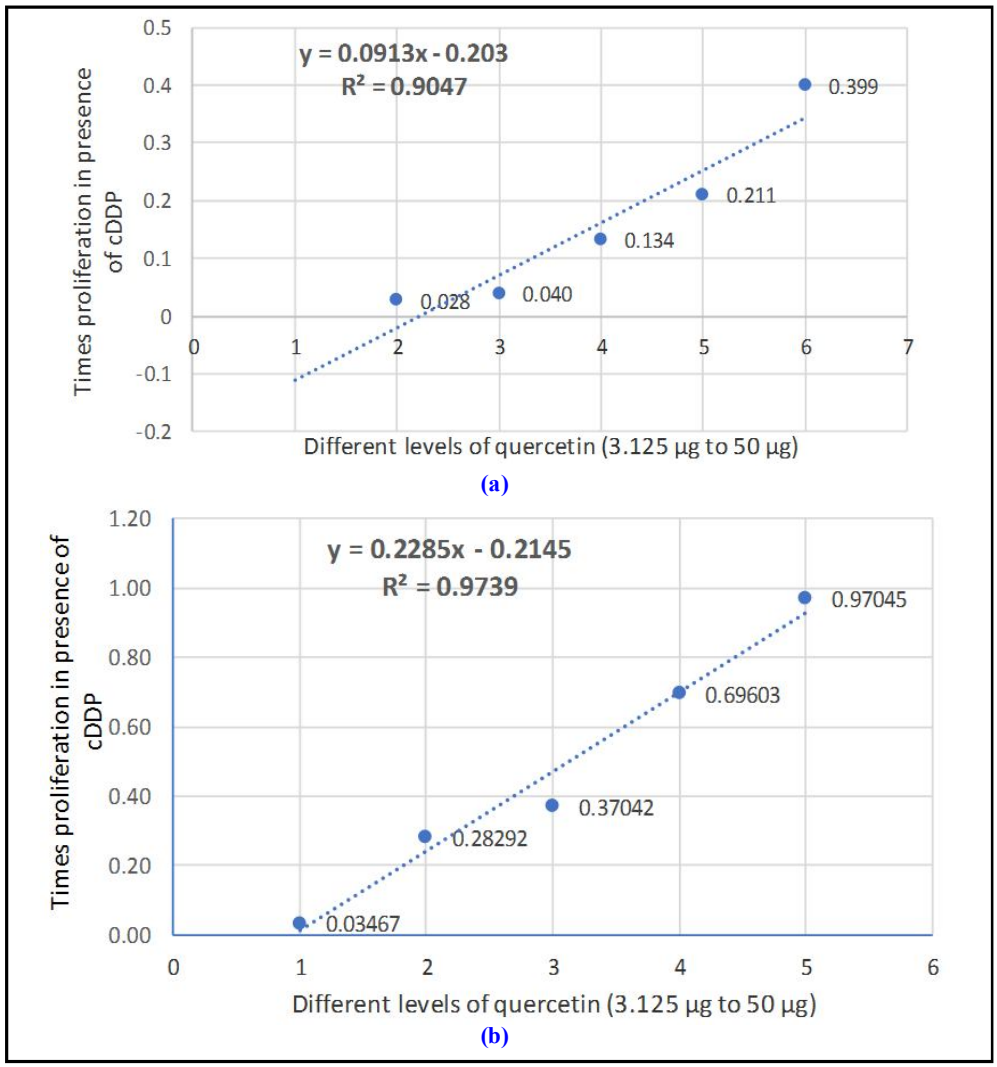


(c)

Figure 1: Dose dependent cellular proliferation of different cell lines, *viz.*, NRK-52E (a) MDCK (b) and HEK (c) on exposure of different concentrations of quercetin using MTT assay.



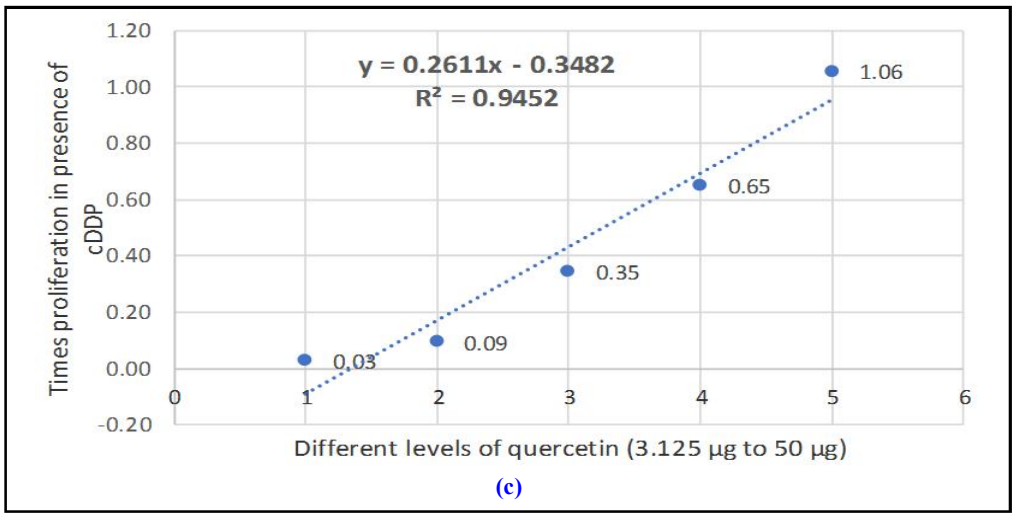
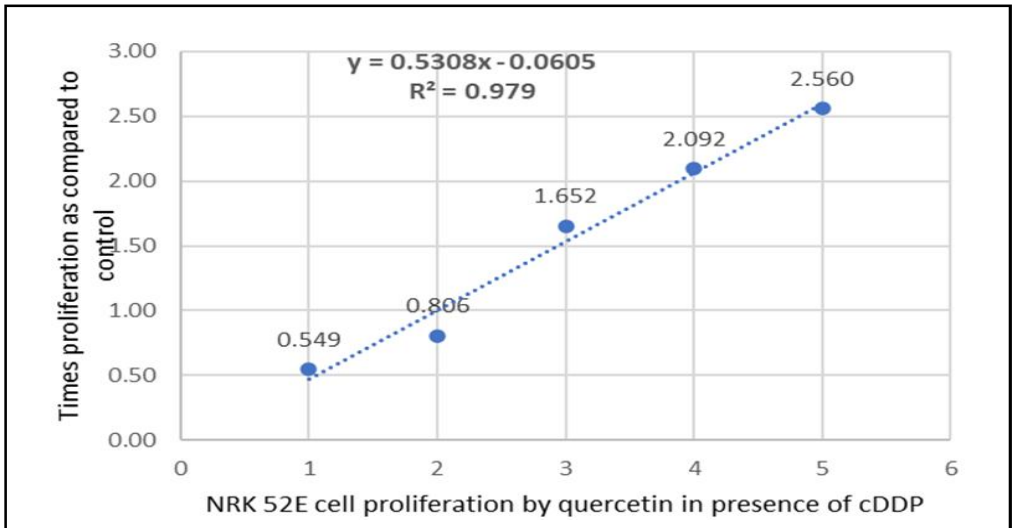
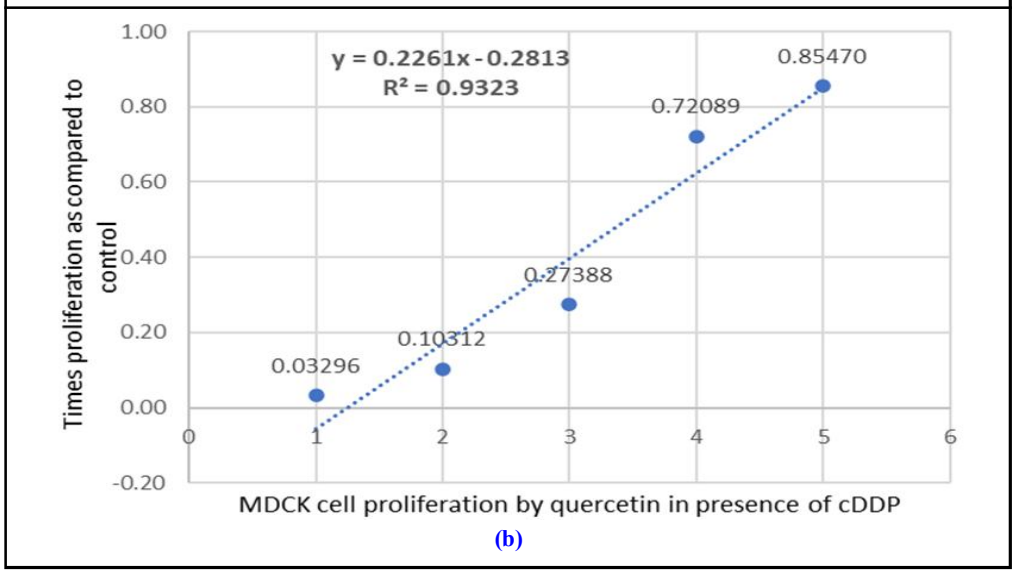
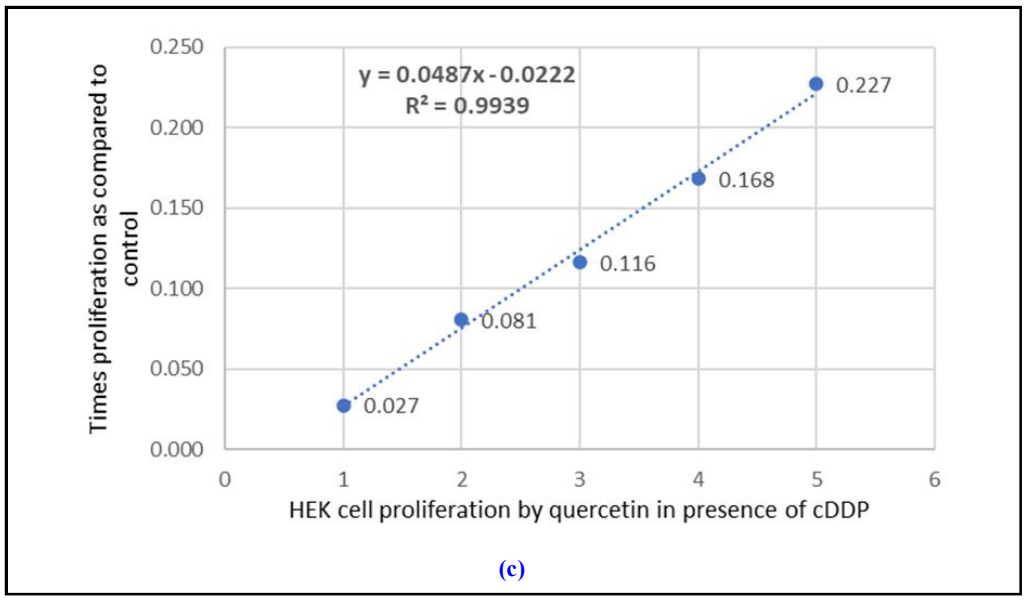


Figure 2: Inhibition of cellular proliferation by cDDP along with concurrent exposure of QRT in different cell lines, *viz.*, NRK-52E (a) MDCK (b) and HEK293 (c) cell lines using MTT assay.







(c)

Figure 3: Inhibition of cellular proliferation by cisplatin (cDDP) and concurrent exposure of quercetin in different cell lines, *viz.*, NRK-52E (a) MDCK (b) and HEK293 (c) cell lines using resazurin assay.

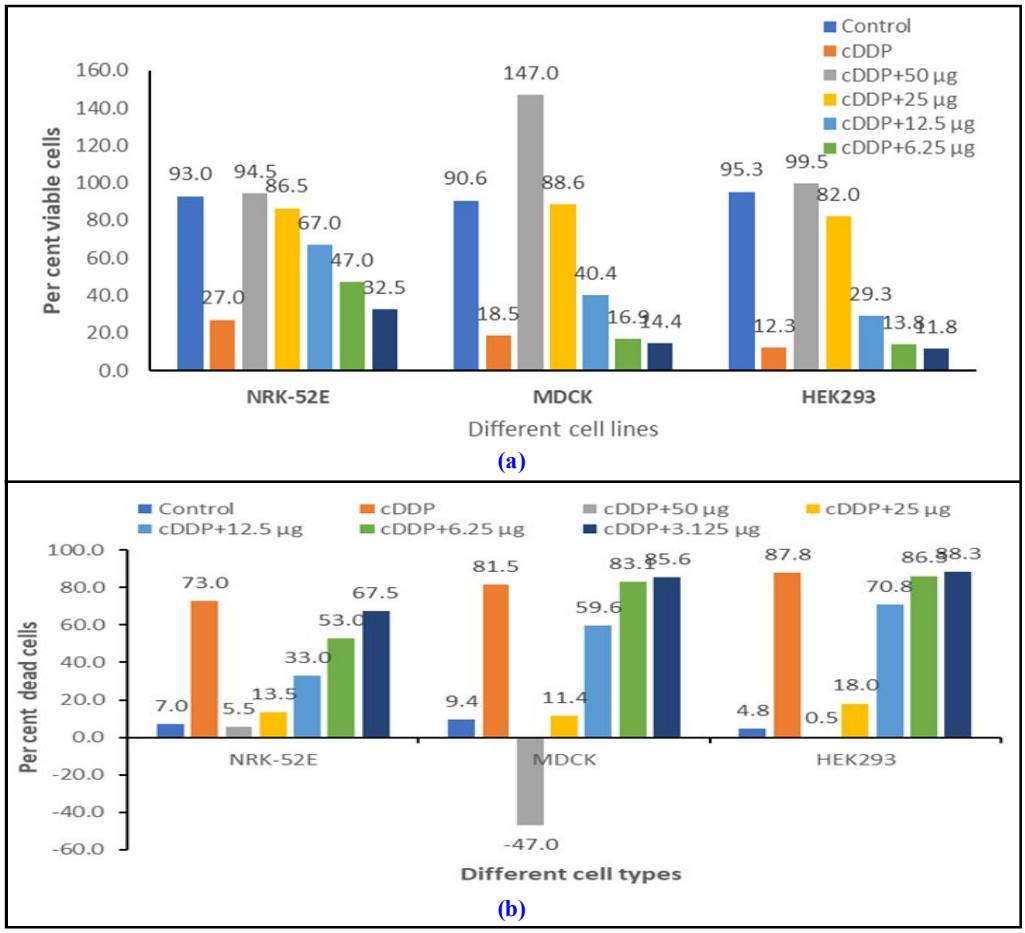


Figure 4: Per cent live (a) and dead cells (b) following exposure of cDDP along with different concentrations of quercetin in different cell lines, *viz.*, NRK-52E, MDCK and HEK293 cell lines using trypan blue assay.

3.2 Cytoprotective assessment using resazurin dye reduction assay

The resazurin dye reduction assay was employed to further corroborate the MTT findings by quantifying mitochondrial metabolic activity as a proxy for cellular viability and proliferation following treatment. Among the three cell lines, NRK-52E again exhibited the highest degree of cytoprotection in response to QRT under cDDP challenge. In the presence of cDDP (200 µM), QRT treatment at 50, 25, 12.5, 6.25 and 3.125 µg/ 20 µl elicited 2.56, 2.09, 1.65, 0.81 and 0.55-fold increases in cell proliferation, respectively. MDCK cells demonstrated moderate protection, with 0.85, 0.72, 0.27, 0.10 and 0.03-fold increases at corresponding QRT concentrations. Conversely, HEK293 cells exhibited a comparatively attenuated response, with fold increases of 0.22, 0.16, 0.11, 0.08 and 0.03 indicating lesser protective effects under cDDP induced oxidative stress. These results reinforce the differential sensitivity of the renal cell lines to both QRT and cDDP. While QRT showed a dose dependent cytoprotective trend in all cell types, NRK-52E was most responsive, followed by MDCK and HEK293 cells showing the least amelioration in this assay. Inhibition of cellular proliferation by cDDP and concurrent exposure of QRT in different cell lines, *viz.,* NRK-52E (a) MDCK (b) and HEK293 (c) using resazurin assay were presented in Figure 3.

3.3 Determination of cell viability by trypan blue exclusion assay

To validate the results obtained from the metabolic assays, cell viability was directly assessed through membrane integrity analysis using the trypan blue exclusion method, distinguishing live (unstained) from dead (stained) cells after 24 h exposure to cDDP (200 µM) alone and in combination with graded concentrations of QRT. In NRK-52E cells, exposure to cDDP alone resulted in a viability of 27%. Cotreatment with QRT significantly improved viability in a dose dependent manner form 94.5% (50 µg/ 20 µl) to 32.5% at 3.125 µg/ 20 µl. In MDCK cells, cDDP exposure alone reduced viability to 18%, whereas QRT cotreatment yielded the following recoveries: 50 µg/ 20 µl: 147% (the viability likely reflects a proliferative overshoot compared to the original seeding density) followed by 88.6% (25 µg/ 20 µl) and 14.4% at 3.125 µg/ 20 µl. For HEK293 cells, baseline viability following cDDP treatment alone dropped to 12.3%.

The QRT cotreatment restored viability at 50 µg/ 20 µl to 99.5%, 25 µg/ 20 µl to 82.0%, 12.5 µg/ 20 µl to 29.3%, 6.25 µg/ 20 µl to 13.8% and 3.125 µg/ 20 µl to 11.8%. The trypan blue assay thus confirmed the cytoprotective efficacy of QRT, particularly at higher concentrations. While all three cell lines exhibited dose responsive improvements in viability, NRK-52E and HEK293 cells showed a pronounced restoration of membrane integrity, with MDCK cells displaying an unusually high apparent viability at the maximal QRT dose. Graphical representation of per cent live (a) and dead cells (b) following exposure of cDDP along with different concentrations of quercetin in different cell lines using trypan blue assay were presented in Figure 4.

4. Discussion

Cisplatin remains one of the most potent and widely employed chemotherapeutic agent in oncology. However, its clinical utility is significantly restricted due to dose limiting nephrotoxicity, which arises from its preferential accumulation in renal proximal tubular epithelial cells, where concentrations can reach up to five folds higher than in plasma due to transporter mediated uptake mechanisms (Mashayekhi-Sardoo *et al*., 2025; Firdous *et al*., 2025). The resultant nephrotoxicity manifests as a complex interplay of DNA damage, inflammatory responses, oxidative stress and programmed cell death, including both apoptosis and necrosis (Hussain *et al*., 2025; Verma *et al*., 2025b). Numerous *in vitro* and *in vivo* studies have corroborated the deleterious renal effects of cDDP and accordingly there is a growing body of research advocating for the use of naturally derived polyphenolic compounds, particularly flavonoids, to ameliorate these toxicities (Fang *et al*., 2021; Luo *et al*., 2025). These agents are known to scavenge free radicals, regulate inflammatory cascades, preserve renal histoarchitecture and promote cellular survival. Quercetin, a widely distributed flavonol has garnered substantial attention owing to its antioxidant, antiapoptotic and cytoprotective capabilities (Raheem *et al*., 2025). The QRT mediates its renoprotective effects by modulating multiple molecular pathways. It scavenges ROS, activates the Nrf2 antioxidant response, suppresses ER stress and inhibits pro-apoptotic pathways (Feng *et al*., 2023). The present investigation evaluated the cytoprotective potential of QRT in three distinct renal tubular epithelial cell lines NRK-52E, MDCK and HEK293 under cDDP induced insults, with the goal of identifying potential interspecies variability in response profiles. Our findings are consistent with prior evidence indicating a dose and time dependent decline in renal epithelial cells viability upon cDDP exposure, as demonstrated in human kidney cell lines such as AD293, where decreased proliferation was mitigated by anti-inflammatory agents like thrombomodulin, known to downregulate ROS generation, ER stress, and apoptotic cell death (Yamamoto *et al*., 2024). Similarly, studies involving LLC-PK1 and HK-2 cells have shown that cDDP induced cytotoxicity can be attenuated by QRT cotreatment, which leads to significant reductions in ROS, lipid peroxidation and glutathione depletion, while simultaneously restoring the expression of key redox modulators such as GPX4 and SLC7A11 (Kuhlmann *et al*., 1998; Shi *et al*., 2024). In alignment with these findings, our results demonstrated that QRT particularly at concentrations $\geq$12.5 µg/ 20 µl significantly enhanced cell viability and proliferation in all three cell lines following cDDP challenge. In NRK-52E cells, even the lower concentrations of QRT (3.125 and 6.25 µg/ 20 µl) exhibited modest protective effects, while higher concentrations (25 and 50 µg/ 20 µl) evidently improved proliferation rates. When administered alone, QRT produced a clear dose dependent stimulatory effect on cell proliferation, with maximal efficacy observed at 50 µg/ 20 µl. These observations validate previous findings where QRT conferred dose responsive cytoprotection in NRK-52E and HK-2 cells through mechanisms involving oxidative stress mitigation and enhancement of cell survival (Munoz-Reyes *et al*., 2022). In MDCK cells, QRT induced cytoprotection was similarly dose dependent. However, the proliferative response at lower concentrations (3.125-6.25 µg/ 20 µl) was relatively subdued. Notably, the maximal dose (50 µg/ 20 µl) resulted in significant cellular recovery, although the degree of protection remained lower than that observed in NRK-52E cells. Interestingly, under non-toxic conditions, QRT elicited a two-fold higher proliferative response in MDCK cells compared to NRK-52E, suggesting intrinsic differences in cell cycle regulation or metabolic response to QRT. These findings are consistent with earlier works in which genistein and resveratrol were shown to protect MDCK cells from oxidative stress, primarily by enhancing intracellular antioxidant capacity and downregulating ROS (Chu *et al*., 2016; Verma *et al.,*

2025a). In HEK293 cells, QRT demonstrated the highest baseline proliferative activity among all three cell lines. While cotreatment with QRT and cDDP restored proliferation in a dose dependent fashion, the cellular response to QRT alone was markedly elevated, suggesting heightened sensitivity of human derived renal epithelial cells to QRT mediated signaling. This could reflect species specific metabolic pathways, enhanced intracellular uptake mechanisms or greater inducibility of antioxidant defense systems in HEK293 cells compared to their rat and canine counterparts.

The robust response of HEK293 cells may also be attributed to differences in transporter expression. Studies have demonstrated that human kidney cells, including HEK293, express higher levels of flavonoid transporters, such as organic anion transporting polypeptides (OATPs) and solute carrier family members, which facilitate increased intracellular accumulation of flavonoids like QRT (Svoboda *et al*., 2011; Kumar and Pandey, 2013). Furthermore, the enzymatic activity of β-glucuronidase is generally higher in human renal cells promoting conversion of quercetin glucuronides into their bioactive aglycone form, thereby enhancing cytoprotective efficacy (Brady *et al.,* 2014; Middleton *et al*., 2000). In contrast, lower expression of such transporters and variation in phase I/II metabolic enzyme profiles in MDCK and NRK-52E cells may limit QRT bioavailability or lead to its rapid detoxification, thereby reducing its therapeutic potential (Hu *et al*., 2002; Martignoni *et al*., 2006). In addition, HEK cells may possess more responsive antioxidant systems, which include a higher basal or inducible expression of Nrf2 regulated genes, contributing to a superior defensive phenotype under oxidative stress (Guillot *et al*., 2008; Yao *et al*., 2007; Brady *et al*., 2014). Moreover, it has been well documented that QRT activates transcriptional pathways such as Nrf2/ARE and upregulates genes involved in ferroptosis resistance, including GPX4 and SLC7A11, which may further explain the heightened resilience of HEK293 cells under oxidative assault (Yang *et al*., 2014). In summary, QRT displayed significant cytoprotective and proliferative effects in all three renal epithelial cell lines examined, both in the presence and absence of cDDP induced cytotoxicity. The efficacy was found to be dose dependent and species specific, with HEK293 cells exhibiting the highest responsiveness, followed by MDCK and NRK-52E. These intercellular differences underscore the importance of cellular context, transporter expression and metabolic competency in modulating the therapeutic response to polyphenolic interventions.

5. Conclusion

The present study investigated the nephroprotective efficacy of QRT in renal tubular epithelial cells derived from human (HEK293), canine (MDCK), and rat (NRK-52E) origins subjected to cDDP induced cytotoxicity. Cisplatin treatment led to significant reduction in cell viability, accompanied by impaired proliferation and increased cell death across all cell types. However, cotreatment with QRT conferred a notable, dose dependent restoration of cellular viability and proliferation, as evidenced by MTT, resazurin and trypan blue assays. These protective effects are attributed to the antioxidant and antiapoptotic properties of QRT, which mitigate ROS mediated damage and enhance cellular defense mechanisms. Among the cell lines tested, HEK293 cells exhibited the greatest proliferative response to QRT, suggesting species-specific variations in cellular uptake, metabolism and antioxidant capacity. The findings support the potential application of QRT as an adjuvant therapeutic agent to alleviate cDDP induced nephrotoxicity in clinical settings. Collectively, these results highlight QRT ability to preserve renal tubular epithelial integrity and support its utility in protective strategies against drug induced renal injury.

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Conflict of interests

The authors have no conflict of interest related to this article.

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