Pt(IV) complex with O,O'-dibutyl-ethylenediamine-N,N'-di-S,S-(2,2'-dibenzyl)acetic acid ester induces nephrotoxicity in female rats: Protective effect of resveratrol

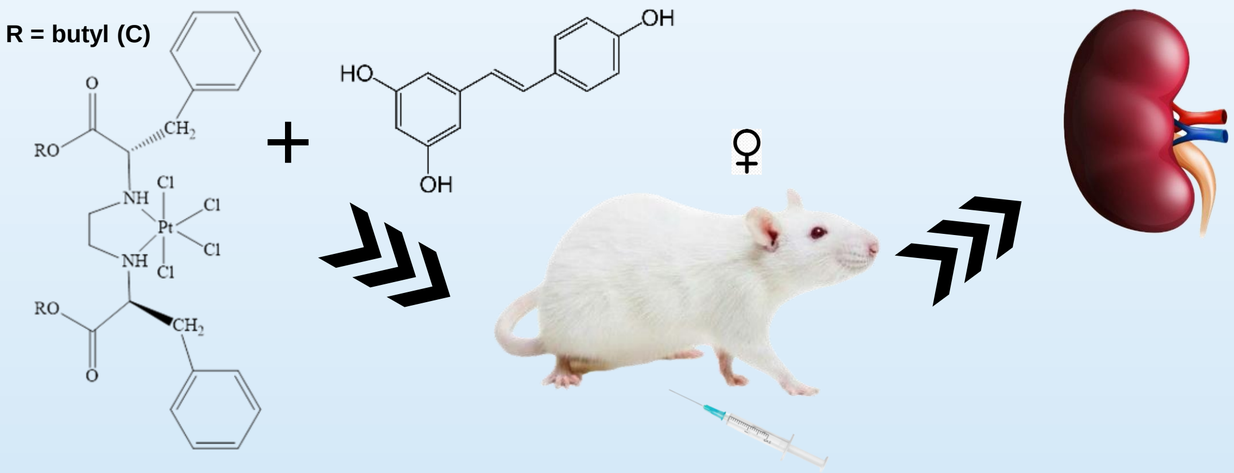
Milica G. Paunović[1*], Miloš M. Matić[1], Ana D. Obradović[1], Vesna D. Stanković[3], Verica V. Jevtić[2], Branka I. Ognjanović[1]

[1]Department of Biology and Ecology, Faculty of Science, University of Kragujevac, Kragujevac; Serbia
[2]Department of Chemistry, Faculty of Science, University of Kragujevac, Kragujevac; Serbia
[3]Institute of Pathology, Faculty of Medical Sciences, University of Kragujevac, Kragujevac; Serbia

[*]e-mail: milica.paunovic@pmf.kg.ac.rs

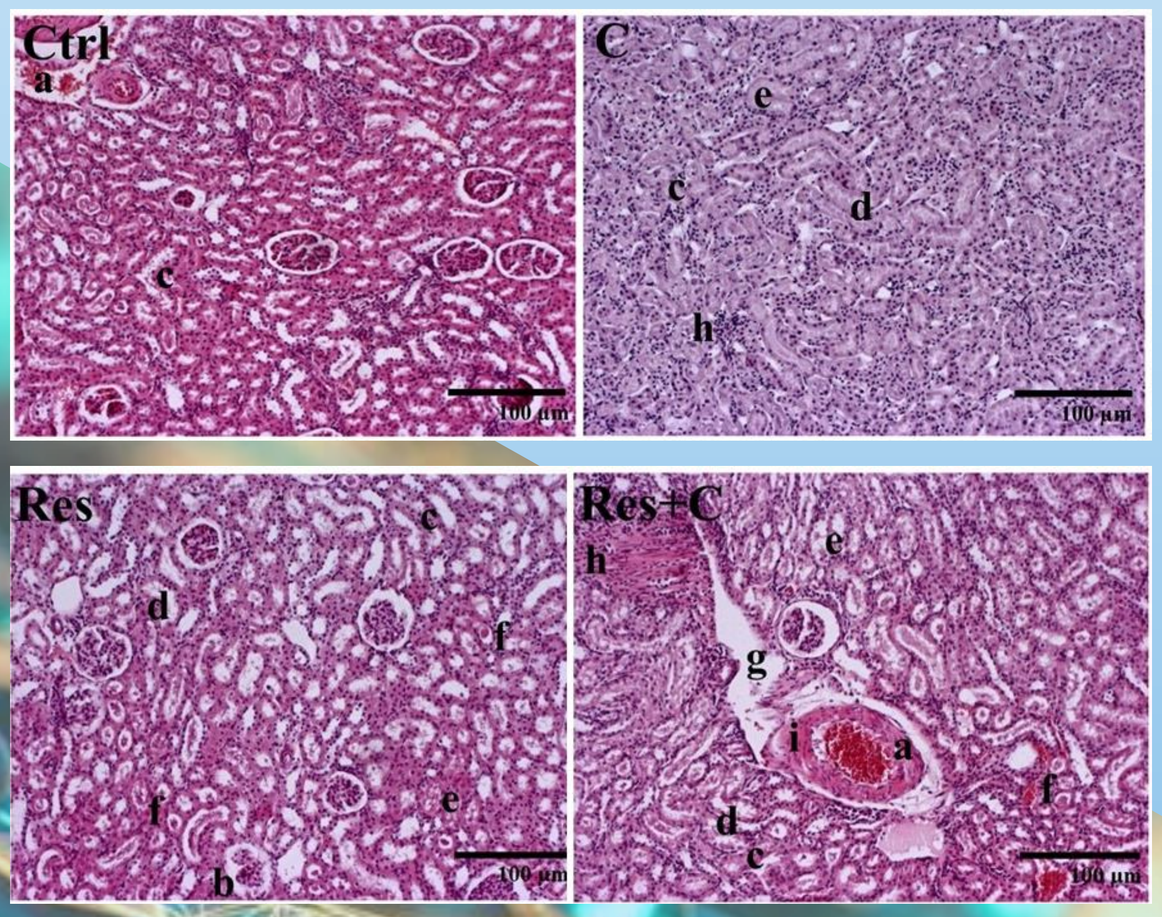
INTRODUCTION

The non-selective effect of chemotherapy drugs frequently results in nephrotoxicity. One of the possible ways of eliminating the accompanying harmful effects of chemotherapy is the creation of new platinum (IV) complexes. In addition, the adjuvant application of chemotherapeutics with derivatives of plant origin, which have pronounced antioxidant and antitumor potential, has proven to be a good strategy in overcoming the aforementioned problems.



Morphological changes	Experimental groups			
	Ctrl	C	Res	Res+C
Congestion	+[a]	+	++	+
Glomerular atrophy	-	+	+	+
Hydropic degeneration of the tubular epithelium	+	++	++	+
Necrosis of tubular epithelial cells	+	++	++	+
Atrophy and desquamation of the tubular epithelium	+	++	++	+
Eosinophilic material in the tubular lumen	-	+	+	+
Interstitial edema	-	+	+	+
Interstitial inflammatory infiltrate	-	+	+	++
Changes in blood vessels	-	+	+	+

[a] (-) without changes; (+) mild; (++) moderate (+++) significant.



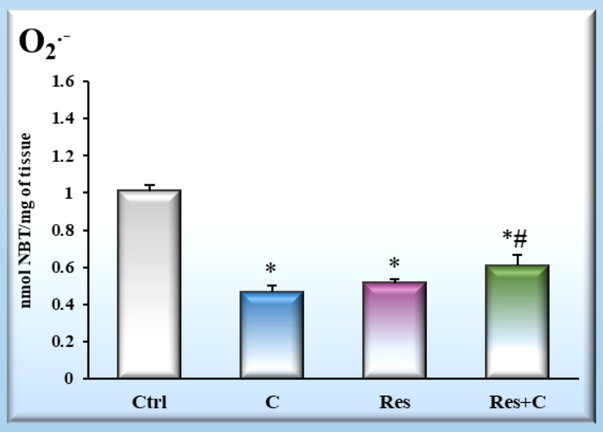
a) Congestion; b) Glomerular atrophy c) Hydropic degeneration of the tubular epithelium; d) Necrosis of tubular epithelial cells; e) Atrophy and desquamation of the tubular epitelium; f) Eosinophilic material in the tubular lumen; g) Interstitial edema; h) Interstitial inflammatory infiltrate; i) Changes in blood vessels

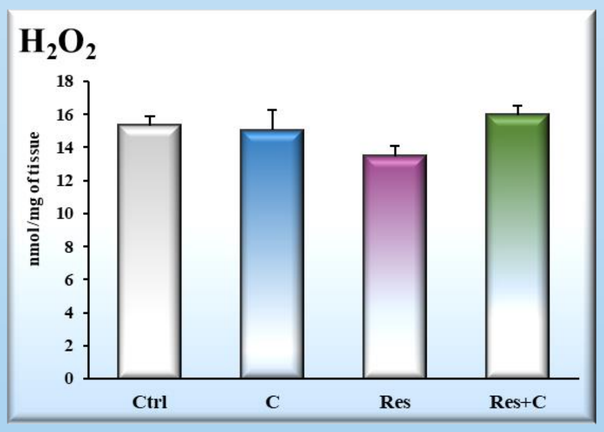
MATERIAL AND METHODES

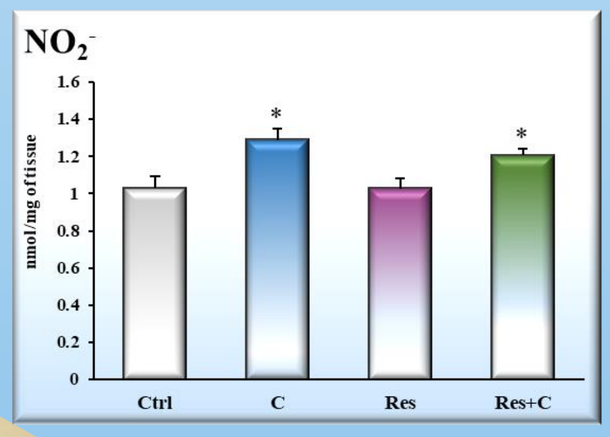
This study aims to investigate the effects of new synthesised Pt(IV) complex containing butyl-esters of the ethylenediamine-N,N'-di-S,S-(2,2'-dibenzyl) acetic acid on the kidneys of Wistar albino rats, as well as potential beneficial effects of resveratrol. The goals were achieved by measuring redox status parameters as well as by histopathological detection of morphological changes in kidney tissue. The tested group of animals were intraperitoneally treated with a single dose of 10 mg/kg b.w. for Pt(IV) complex; 25 mg/kg b.w. for resveratrol; and their combination. The control group was injected only with saline.

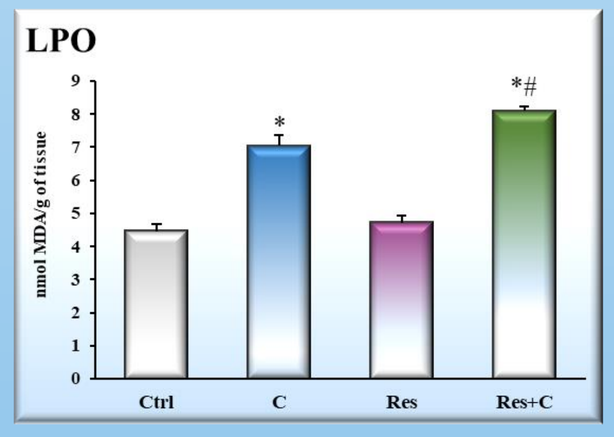
RESULTS

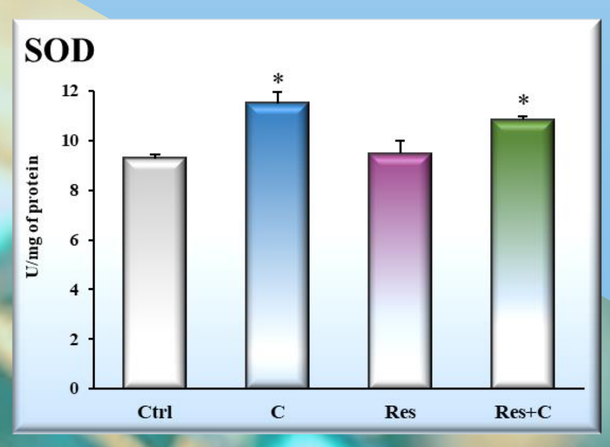
Applied compounds led to a significant decrease in $O_2^{\cdot-}$ compared to control, alone or in combined treatment, while the concentration of H_2O_2 didn't change. As for NO and LPO production and SOD, treatment with complex and combined treatment increased them, while CAT activity was decreased compared to control. In combined acting, resveratrol influenced the normalisation of measured parameters compared to control values, but mostly without statistical significance concerning individual treatments. Additionally, the combined treatment resulted in a significant increase in lipid peroxides compared to control and individual treatments. Regarding histopathological results for both individual treatments, moderate hydrops degeneration, necrosis, atrophy, and desquamation of the tubular epithelium cells were noticed, while other changes were of mild intensity. Apart from a moderately intense interstitial inflammatory infiltrate, the combined treatment primarily produced minor alterations.

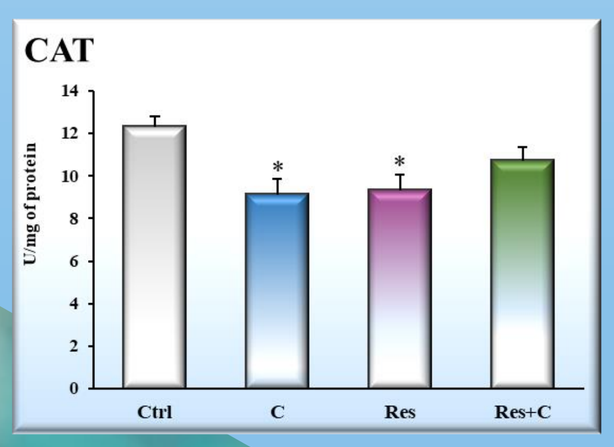












CONCLUSION

Based on the obtained results the newly Pt(IV) complex may cause mild nephrotoxicity, and combined treatment with resveratrol could protect kidney tissue, but not significantly. These findings could be helpful for future research aimed at elucidating the mode of action of the investigated compounds.

Acknowledgements

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