Arbutin abrogates cisplatin-induced hepatotoxicity via upregulating Nrf2/HO-1, and suppressing NF-κB/TNF-α and caspase-3/Bax signaling in rats

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MRC- 2023, Manipal Academy of Higher Education, Manipal

Abstract ID: MRCHS014

Introduction

Cisplatin (CP) is a potent anticancer agent widely employed in chemotherapy

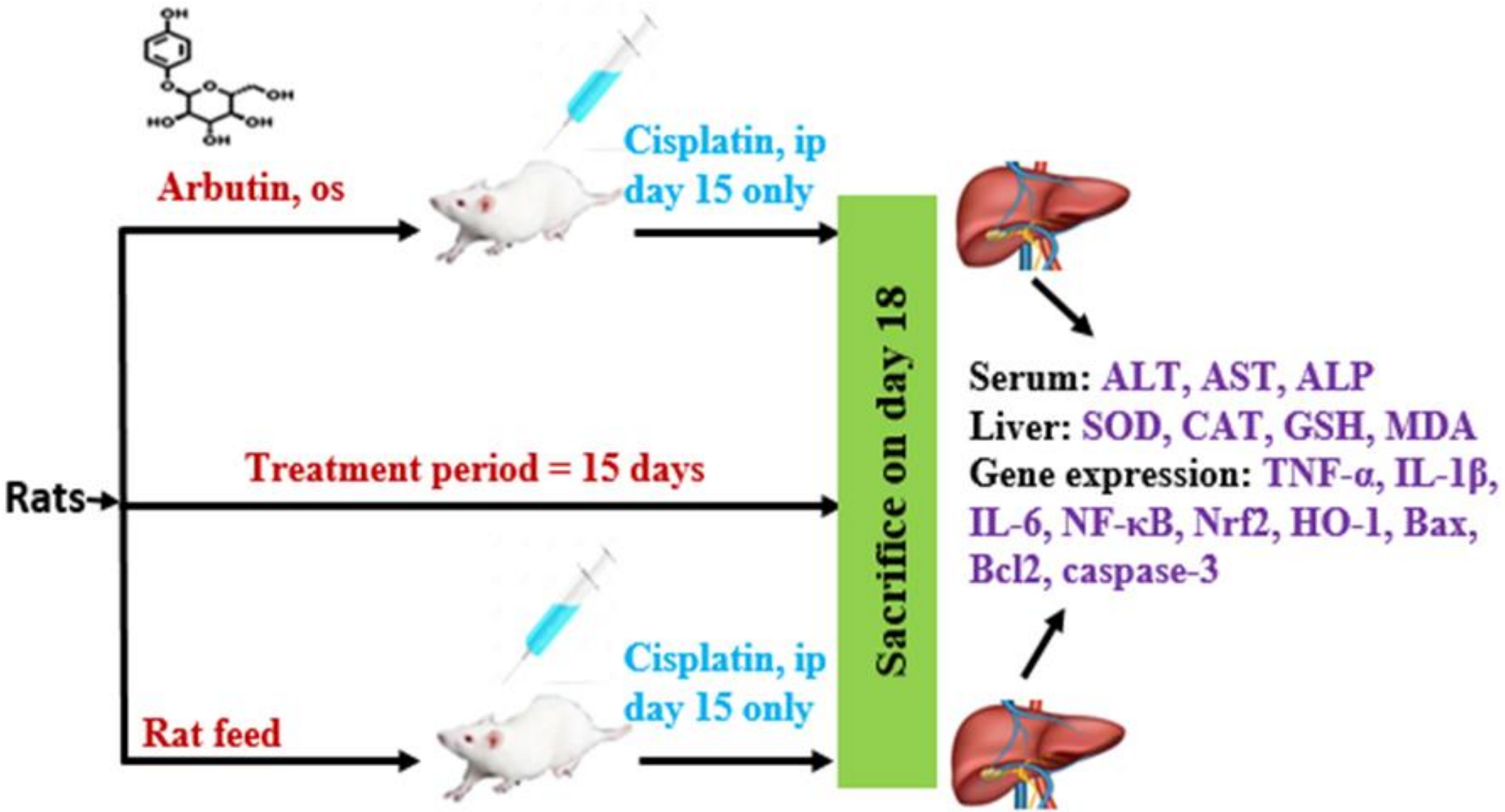
However, CP exerts non-targeted toxicity on healthy organs, including the liver (Jiang et al, 2023; Famurewa et al, 2020)

CP side effect toxicity is related to activation of oxidative inflammation and apoptotic signaling (El Shaffei et al, 2021; Huang et al, 2021)

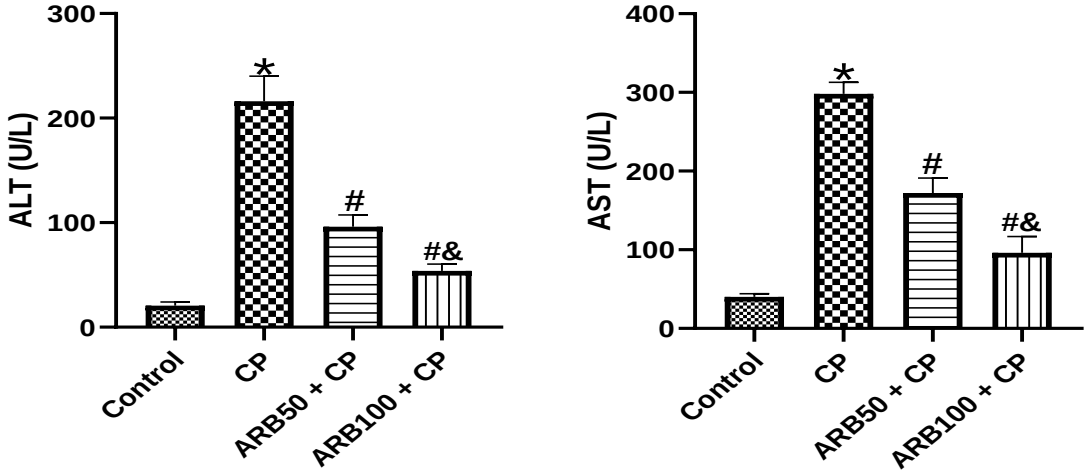
Arbutin is a natural compound with antioxidant and anti-inflammatory actions

Therefore, the study explored whether arbutin could prevent CP-induced liver toxicity

Methodology



Results



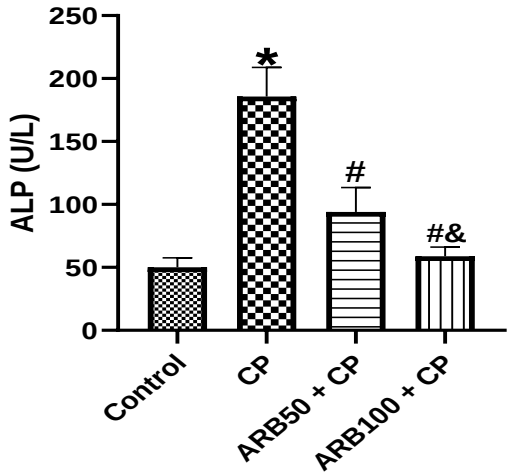
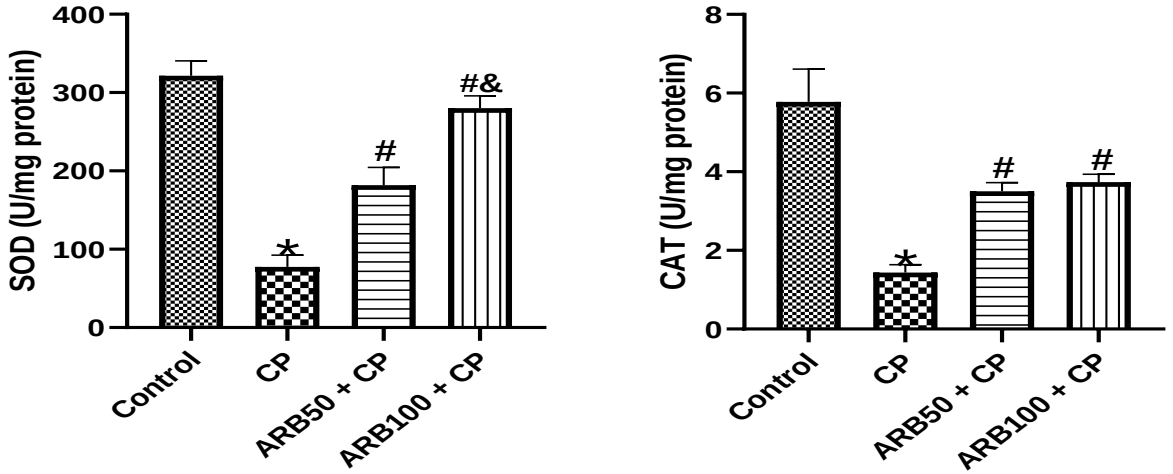


Fig. 1: Effect of arbutin on liver enzymes in CP-injected rats.*Sig against control group; #Sig against CP group; &Sig against ARB50 + CP group; $p < 0.05$



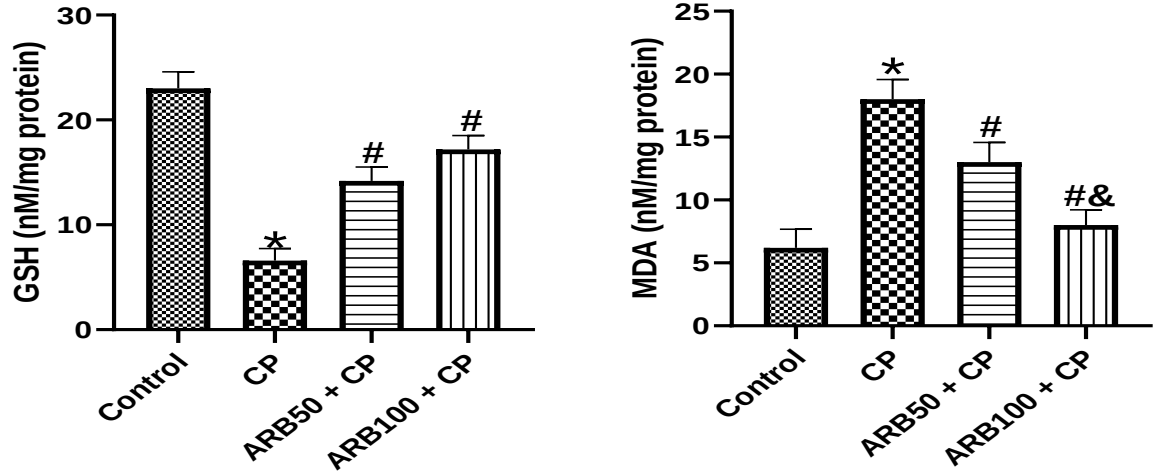


Fig. 2: Effect of arbutin on liver oxidative stress markers in CP-injected rats

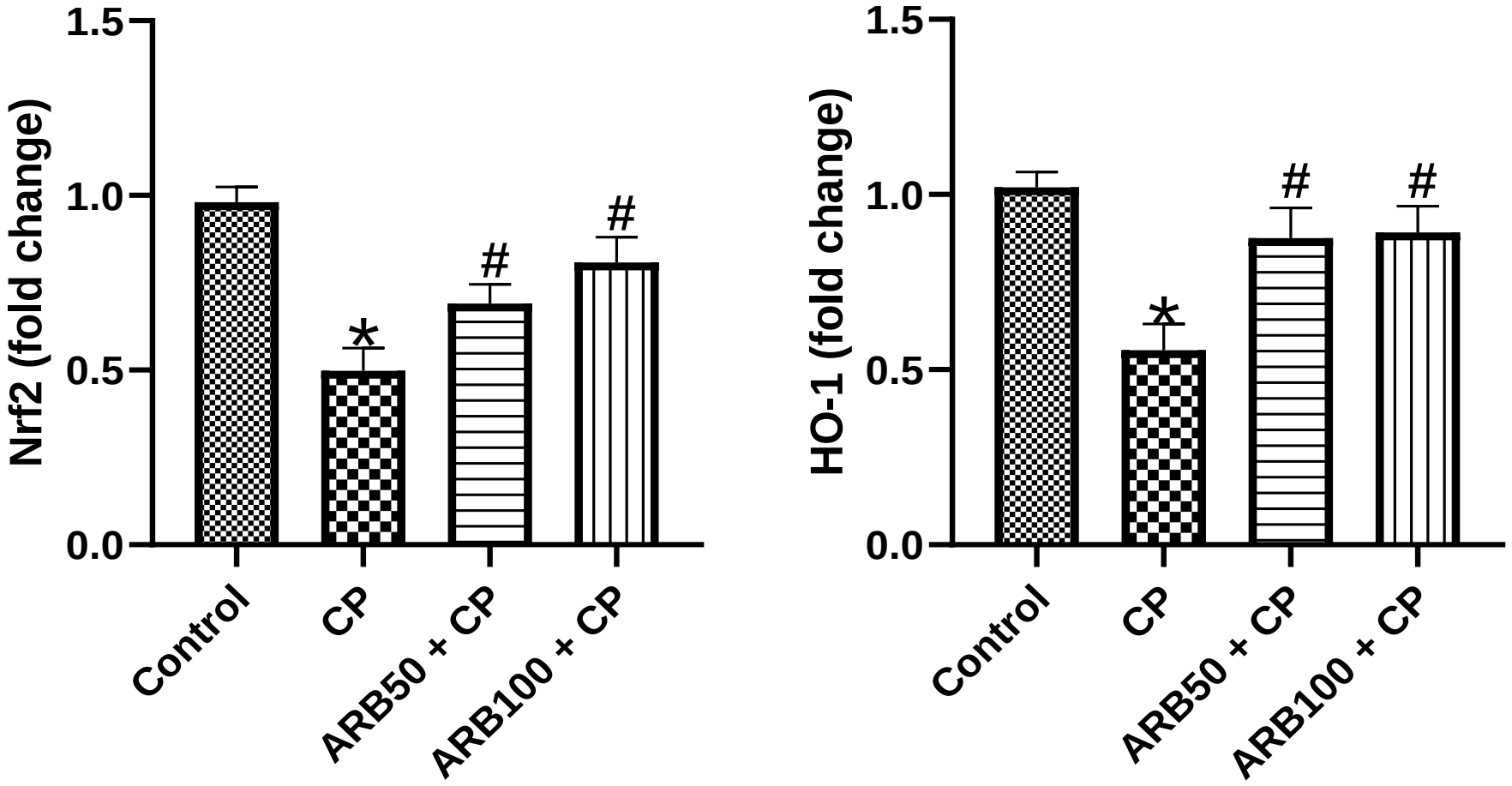


Fig. 3: Effect of arbutin on hepatic Nrf2 and HO-1 gene expressions in CP-injected rats.
***Significant against control group; #Significant against CP group; $p < 0.05$**

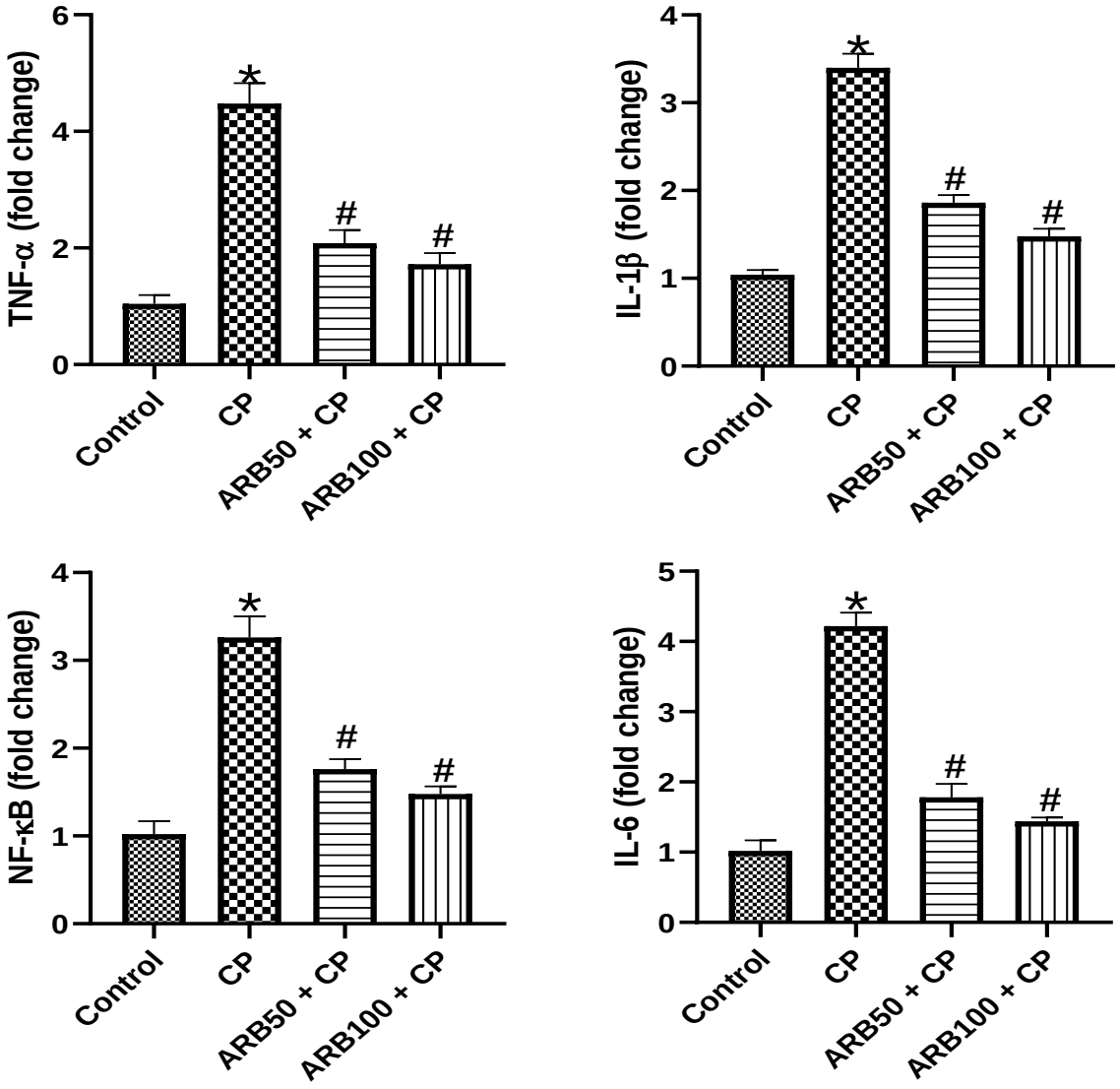


Fig. 4: Effect of arbutin on NF-κB & cytokines in CP-injected rats P<0.05

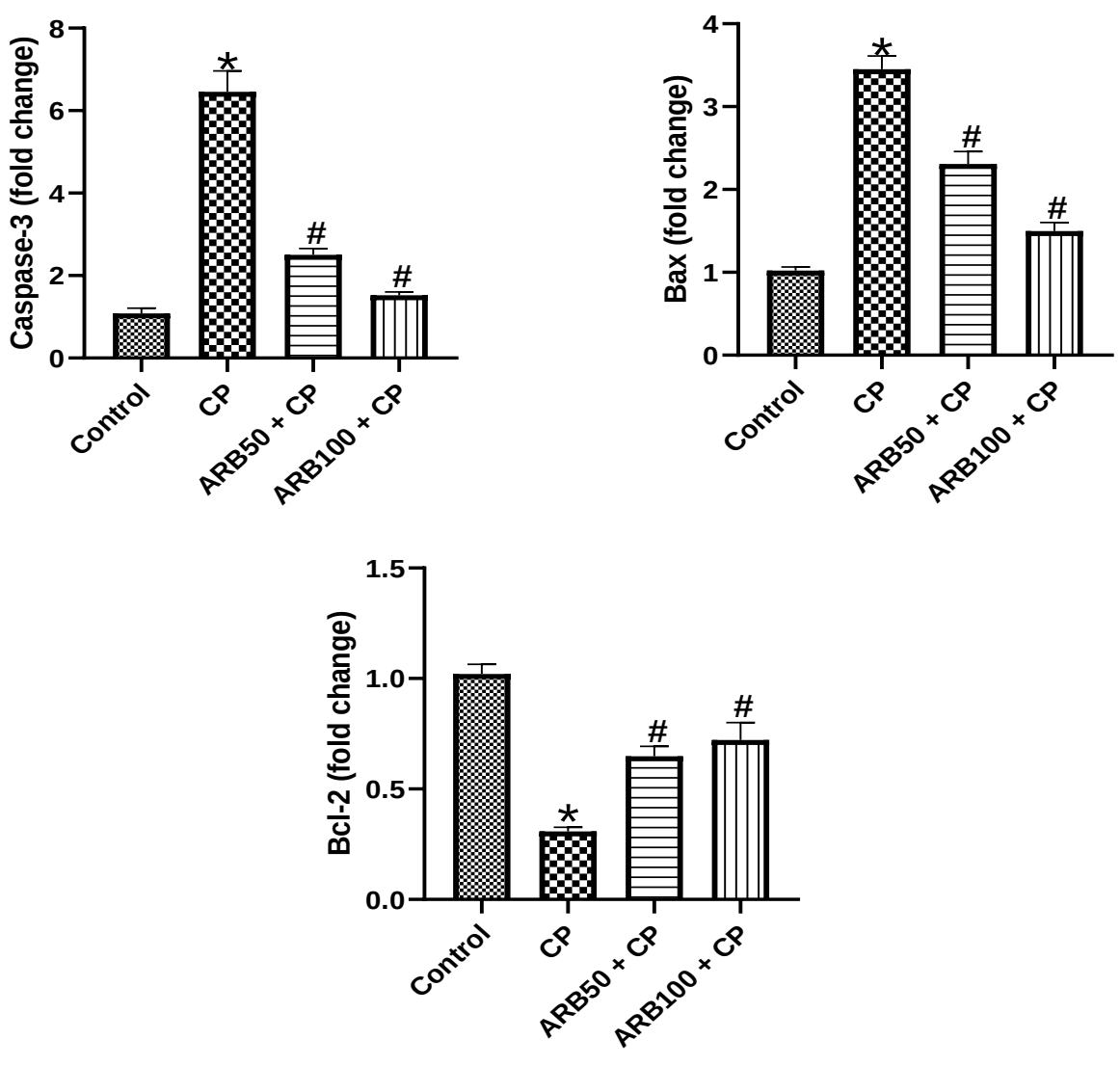
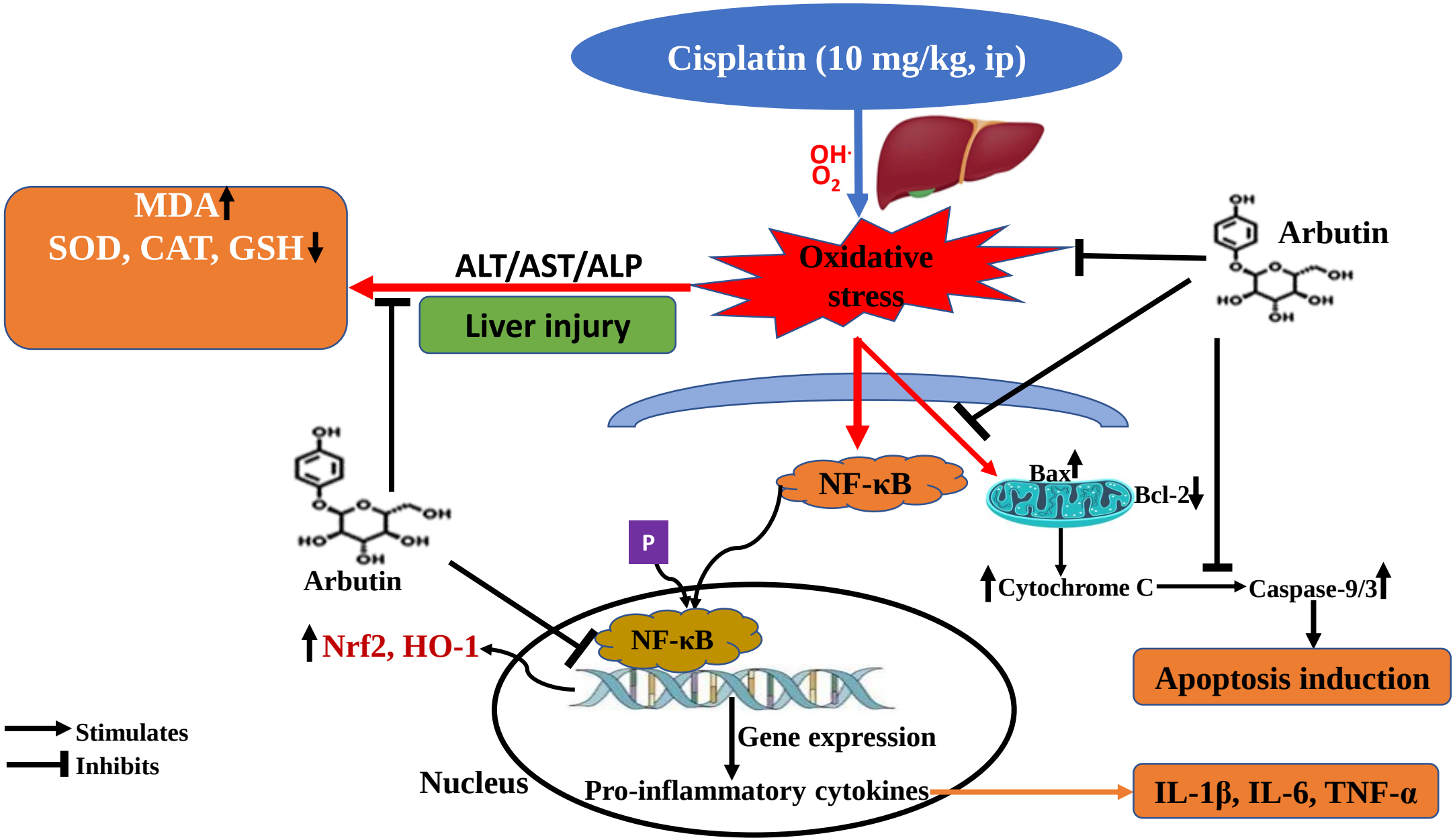


Fig.5: Effect of arbutin on apoptotic markers in CP-injected rats. P<0.05

Schematic representation of the possible actions of cisplatin and arbutin in the rat liver



Conclusions

These findings suggest that CP induces liver toxicity via oxidative stress-mediated inflammation and apoptosis

Arbutin is a potential protective adjuvant against CP-induced hepatotoxicity via inhibition of hepatic oxidative stress, inflammation, and apoptosis

However, there is an unmet need for clinical studies to verify our findings in this study.

References

El Shaffei I, Abdel-Latif GA, Farag DB, Schaalan M, Salama RM. Ameliorative effect of betanin on experimental cisplatin-induced liver injury; the novel impact of miRNA-34a on the SIRT1/PGC-1alpha signaling pathway. J Biochem Mol Toxicol 2021; 35(6): 1-14

Famurewa AC, Ekeleme-Egedigwe CA, Onwe CS, Egedigwe UO, Okoro CO, Egedigwe UJ, Asogwa NT. Ginger juice prevents cisplatin-induced oxidative stress, endocrine imbalance and NO/iNOS/NF-kappaB signalling via modulating testicular redox-inflammatory mechanism in rats. Andrologia 2020; 52(10): e13786.

Huang Y, Liu C, Song X, An M, Liu M, Yao L, Famurewa AC, Olatunji OJ. Antioxidant and Anti-inflammatory Properties Mediate the Neuroprotective Effects of Hydro-ethanolic Extract of Tiliacora triandra Against Cisplatin-induced Neurotoxicity. J Inflamm Res 2021; 14: 6735-6748

Jiang Y, Li Z, Ma Q, Dong W, Yao Q, Yu D. Aucubin protects mouse cochlear hair cells from cisplatin-induced
ototoxicity via activation of the PI3K/AKT/STAT3 pathway. Biochem Pharmacol 2023; 209: 115440

Acknowledgement/Appreciation

1. Department of Biotechnology, Ministry of Science and Technology, Government of India, for the award of 1-year **DBT-TWAS Postdoctoral Fellowship**

2. My amiable and respected Indian Host, **Prof. Dr. K Sreedhara Ranganath Pai**, Department of Pharmacology, MCOPS, Manipal

3. The VC and Managers of MAHE for their acceptance and hospitality

Thanks

for

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audience.