Nanoformulations reduce cardiotoxicity of doxorubicin – *in vivo* animal study

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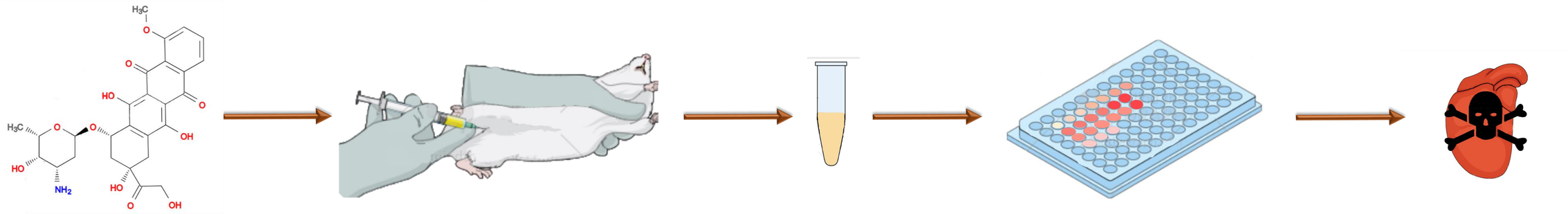
INTRODUCTION

Doxorubicin (DOX) is an effective chemotherapeutic agent prescribed for treatment of various neoplasms. Its major disadvantage and side effect is irreversible cardiomyopathy. This study aimed to investigate if a novel nanoformulation can reduce DOX cardiotoxicity under *in vivo* settings. Biomarkers for cardiotoxicity were serum levels of cardiac troponin T (cTnT) and N-terminal prohormone of brain natriuretic peptide (NT-proBNP), routinely used in the diagnosis of myocardial damage and heart failure. Three different DOX formulations were tested: commercially and clinically approved conventional (DOX) and nanoliposomal DOX formulations (nanoDOX) that were compared with novel nanoformulation based on poly(lactic-co-glycolic acid) (PLGA-DOX).

METHODS

Tested compounds were administered by intraperitoneal application to male and female Wistar rats every 6 days, four times in total. Six days after last administration, rats were sacrificed and the whole blood was sampled in vacutainer tubes without anticoagulant. Afterwards, the whole blood was centrifuged for 25 minutes at 1 200 x *g*. Obtained serum was transferred in clean tubes and used for analysis. cTnT and NT-proBNP were determined in rat serum samples using the enzyme-linked immunosorbent (ELISA) assay. Data were analyzed using Multivariate analysis of variance test (MANOVA) in Statistica Software 13.5.0.17. Only *p* values less than 0.05 were considered statistically significant.



RESULTS

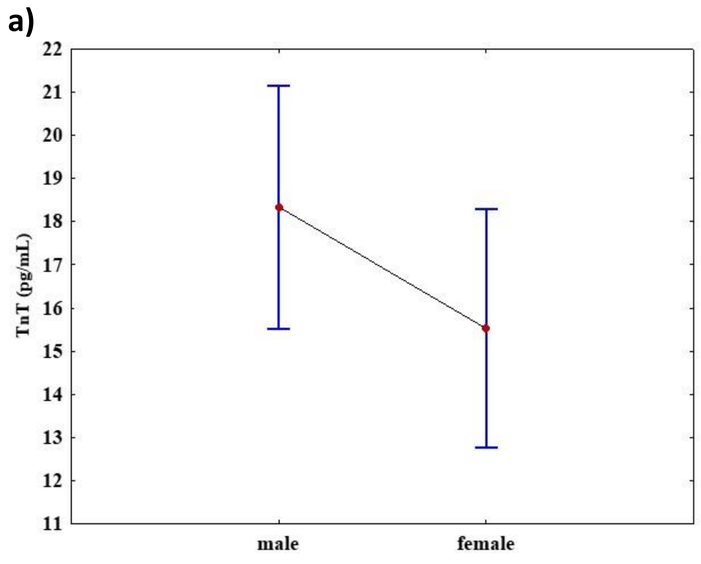


Figure 1. Differences between male and female groups in concentration of Troponin T (TnT) (a) and N-terminal natriuretic peptide (NT-proBNP) (b) and between untreated and treated groups regardless of sex in concentration of TnT (c) and NT-proBNP (d). Significant differences ($P < 0.05$) of the mean values between treated and control samples are denoted with asterisk (*).

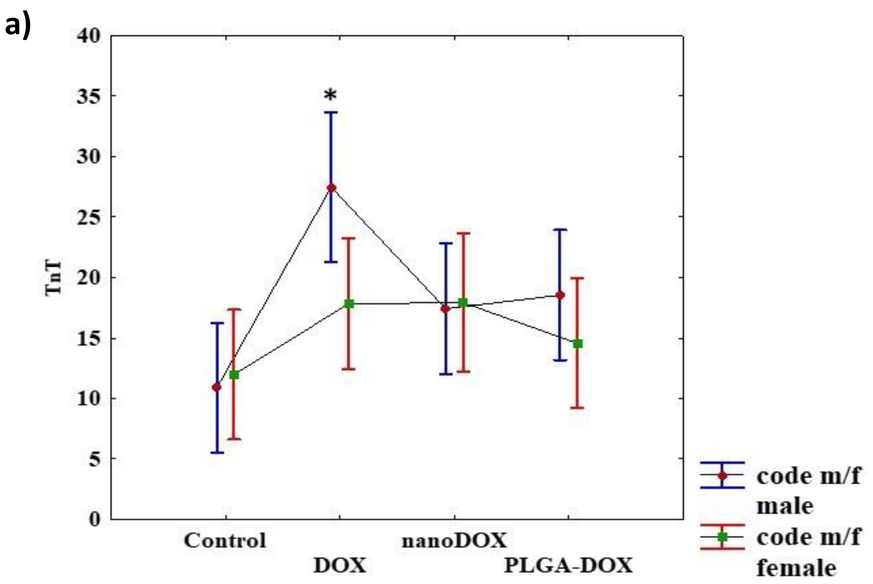


Figure 2. Differences between untreated and treated animals based on sex in concentration of TnT (a) and NT-proBNP (b). Significant differences ($P < 0.05$) of the TI mean values between treated and control samples are denoted with asterisk (*).

CONCLUSION

Significant increase in the TnT concentration was observed in animals treated with DOX, while significant decrease in NT-proBNP concentration was noticed in animals treated with nanoDOX. In males treated with DOX, cTnT was significantly upregulated compared to control animals, while nanoDOX and PLGA-DOX showed no significant effect. Concentration of NT-proBNP decreased in male animals treated with all three types of DOX formulations, while the decrease in concentration was observed in female rats treated with nanoDOX formulation. Obtained results indicate beneficial characteristics of novel nanoformulation towards safer clinical use of antitumor agents and highlight the importance of nanotechnology for cancer medicine.

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