POSSIBLE PROTECTIVE ROLE OF RESVERATROL-LOADED LIPOSOMES IN A RAT MODEL OF DOXORUBICIN-INDUCED CARDIOTOXICITY

Nadia Amin Sharaf Eldin, Sahar Aly Omar, Hala M. Abd El-Mouaty, Lamia A. Heikal,* Maha Hammady

Histology and Cell Biology, Faculty of Medicine, Alexandria University, Pharmaceutics, Faculty of Pharmacy,* Alexandria University.

Introduction

Doxorubicin (DOX) is a highly effective and widely used chemotherapeutic agent in treating wide variety of tumors. Unfortunately, cardiotoxicity is its most serious side effect, which is directly linked to the oxidative stress caused by DOX. Resveratrol (RSV) is a powerful antioxidant, but its low bioavailability limits its use. Multilamellar liposomes are lipid nanocarriers. They are recently used as a carrier to enhance the bioavailability of many drugs by increasing their plasma half-life.

Aim of the work

The current study was designed to histologically assess the myocardial alterations following induction of cardiotoxicity in adult male albino rats by doxorubicin and to evaluate the possible protective efficacy of RSV-loaded multilamellar liposomes on DOX-induced cardiotoxicity.

Materials and Methods

The present study was conducted over 5 successive weeks on 30 adult male albino rats which were categorized into 2 equal groups. **Group I** which was subdivided randomly into 3 equal subgroups: subgroup IA (the control subgroup) received physiological saline twice/week by intraperitoneal (i.p) injection, subgroup IB received daily oral suspension of unloaded multilamellar liposomes and subgroup IC received daily oral suspension of RSV-loaded multilamellar liposomes. **Group II** which was also equally subdivided into 3 subgroups (IIA, IIB and IIC), all of which received i.p injection of add the dose DOX twice/week ~~I.~~P. for 5 successive weeks. In addition, subgroups IIB and IIC received daily oral suspension of unloaded multilamellar liposomes, and RSV-loaded multilamellar liposomes respectively. At the end of the experiment, cardiac apices specimens of all rats were obtained, processed and examined by both light and electron microscopes.

Results

1- Light microscope: Examination of H&E-stained ventricular myocardial sections of subgroup IA revealed the classical histological structure of cardiac muscle fibers (Fig.1). Furthermore, histological examination of cardiac sections of subgroups IB and IC revealed similar appearance to that of subgroup IA.

While examination of myocardial sections of subgroups IIA and IIB revealed prominent structural alterations in the form of variable degrees of interrupted muscle fibers and wide interstitial spaces (Fig.2). Sections of subgroup IIC showed evident amelioration of DOX-induced myocardial lesions, although some lesions were infrequently encountered (Fig.3).

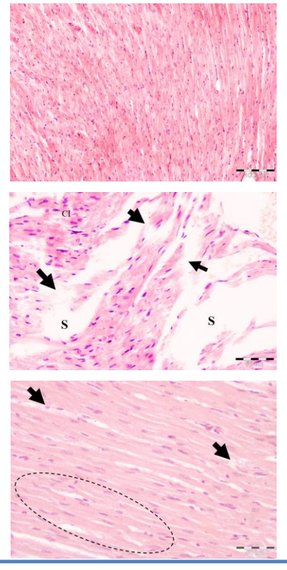

Figure 1: Light photomicrograph of ventricular myocardium of subgroup IA showing the classical myocardial structure. (H&E stain, Mic. Mag. × 200)

Figure 2: Light photomicrograph of a rat myocardium of subgroup IIA showing interrupted muscle fibers (arrow) and wide interstitial spaces (S). (H&E stain, Mic. Mag. × 400).

Figure 3: Light photomicrograph of a rat myocardium of subgroup IIC showing some wavy cardiac muscle fibers (dotted circle) and few interrupted fibers (arrows). (H&E stain, Mic. Mag. × 400).

2- TEM: Examination of myocardia of subgroups (IA, IB & IC) revealed normal cardiomyocytes, with central euchromatic nuclei and regularly arranged myofibrils (Fig.4), while subgroups IIA and IIB revealed evident myocardial lesions. Many cardiomyocytes exhibited irregular sarcolemma, in addition to waviness of myofibrils, interruption, and even focal areas of myofibrillar loss with widening of the intervening spaces and loss of identifiable sarcomeres (Fig.5). Considerable preservation of the myocardial structure was recognized on ultrastructural examination of subgroup IIC. Most of the cardiomyocytes exhibited the classical control picture. Nevertheless, some cardiomyocytes still depicted noticeable structural alterations (Fig.6).

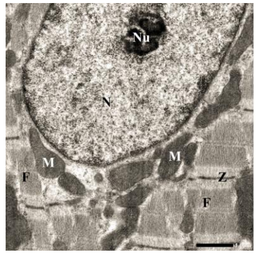

Figure 4: TEM photomicrograph of subgroup IA myocardium, revealing centrally located euchromatic nucleus (N), it shows regular outlines. M; mitochondria, F, myofilaments, Z; Z-line, Nu, nucleolus. (Mic. Mag. × 5000)

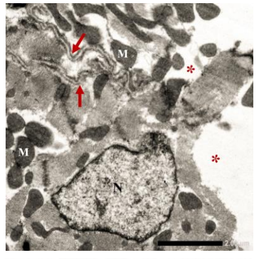

Figure 5: TEM photomicrograph of ventricular myocardium of subgroup IIA showing disrupted myofibrils and wide areas of rarefied sarcoplasm (asterisk). Irregularly arranged bizarre- shaped mitochondria (M) are also seen. Notice the distorted intercalated disc with mildly separated irregular transverse portion (arrow) that is almost devoid of intercellular junctions. N; irregular nucleus of cardiomyocyte. (Mic. Mag. ×3000).

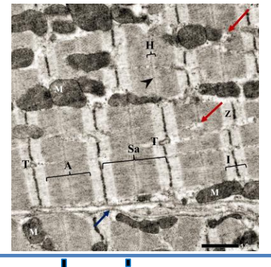

Figure 6: TEM photomicrograph of ventricular myocardium of subgroup IIC showing parts of two adjacent cardiomyocytes with normal cross-banding appearance of myofibrils. One cell depicts small foci of interrupted myofilaments (red arrow), the other exhibits slightly irregular sarcolemma (blue arrow). A; A-band, H; H-zone, I; I-band, M; mitochondria, Sa; sarcomere, T; T-tubule, Z; Z- line, arrowhead; M-line. (Mic. Mag. × 5000).

Conclusion

Resveratrol-loaded multilamellar liposomes have a protective role on doxorubicin-induced cardiotoxicity in adult male albino rats proved by histological studies.

2022©Alexandria Faculty of Medicine
CC-BY-NC