P3252 | BENCH
The olive constituent oleuropein prevents cardiac doxorubicin-induced changes in eNOS expression, apoptotic mediators and energy metabolism in rats

I. Andreadou1, K. Ioannidis1, S. Kostidis1, F. Sigala2, D. Farmakis3, A.L. Skalskou1, D.T.H. Kremastinos2, M. Anastassiou-Nana3, E. Mikros1, E.K. Iliodromitis1, 1University of Athens, Faculty of Pharmacy, Athens, Greece; 2University of Liege (ULg), GIGA-Cardiovascular Sciences, Liege, Belgium; 3University of Athens, Faculty of Pharmacy, Athens, Greece;

Purpose: Doxorubicin (DXR) causes cardiotoxicity through nitro-oxidative stress, but the exact pathogenesis is not fully elucidated. Oleuropein (OLEU), a polyphenolic constituent of olive oil and its products, prevents acute and chronic DXR-induced cardiotoxicity. We evaluated mechanisms potentially involved in chronic DXR cardiotoxicity, including eNOS, pro-apoptotic mediators and energy metabolism as well as OLEU impact on these mechanisms.

Methods: Ninety rats were divided into 6 groups: Control group, no treatment; OLEU-70 and OLEU-140 groups, 70 and 140 mg/kg of OLEU, respectively, given intraperitoneally (p.i) for 2 weeks; DXR group, 18mg/kg of DXR i.p, divided into 6 equal doses and given over a period of 2 weeks; OLEU-70-DXR and OLEU-140-DXR groups, combined OLEU and DXR as previously described. The rats were finally sacrificed and the hearts were excised for tissue assessment of eNOS, Akt and AMPK by immunohistochemistry and Western-Blot. NMR spectra of tissue extracts was also recorded and analyzed further by multivariate statistics. Results: DXR group had lower eNOS, Akt and AMPK activation compared to controls and all OLEU groups. The NMR-based metabonomic study depicted differences in the metabolic profile of DXR compared to all other groups (Figure)

Conclusions: NMR based metabonomic study depicted differences in the metabolic profile of DXR compared to all other groups. NMR based metabonomic study depicted differences in the metabolic profile of DXR compared to all other groups. NMR based metabonomic study depicted differences in the metabolic profile of DXR compared to all other groups. NMR based metabonomic study depicted differences in the metabolic profile of DXR compared to all other groups.

P3252 | BENCH
Potential etiology of diabetic cardiomyopathy

Y. Bai, J. Zhou, A. Sun, J. Qian, Y. Zou, J. Ge, Shanghai Institute of Cardiovascular Diseases, Zhongshan Hospital-Fudan University, Shanghai, China, People's Republic of

The objective of the current study was to determine whether the negative effects of diabetes on the adult heart are dictated by defects in resident cardiac stem cells (CSCs) and lineage commitment. Type I insulin-dependent diabetes mellitus (IDDM) was induced in mice by streptozotocin administration. The kinetics of CSCs and cardiomyocytes was measured 1, 3, 5, 10, 30, 60, and 90 days after the onset of diabetes, by analyzing 14C birth dating of cardiac cells by Accelerator Mass Spectrometry, which gives the information of the turnover of cardiomyocytes and CSCs in the presence and absence of diabetes. Additionally, the number of cardiomyocytes dying by apoptosis and necrosis were measured

Conclusions: The developed multi-scale model inferring ventricular and atrial contraction from a sarcomere model correctly represents the left atrial behavior and responds to IVCO experiments as physiologically expected.

P3254 | BENCH
Structural modifications of apelin-12 molecule differentially affect cardiac function

S.V. Lakomkin, E.V. Lukoshkova, V.V. Erimshtein, V.L. Lakomkin, A.A. Abravm, Z.D. Despalova, S.N. Tereschenko, V.L. Kapelko. Cardiology Research and Production Center, Institute of Clinical Cardiology, Moscow, Russian Federation

Methods: We used a multi-scale model of the cardiovascular system in which left ventricular and atrial pressures are inferred from a sarcomere model. In this model, we reproduced IVCO experiments by a fourfold increase of the vena cava resistance. As in experimental settings, we observed the variation of measurements before and after modification of the resistance. These measurements were: maximum a and v waves, pressure and maximum early and late ventricular filling.

Results: Among the 8 measurements, in the model, 7 followed a similar decrease as experimentally observed. The only measurement that increased was the slope of the v wave. A possible reason for this discrepancy could be that in experimental protocols, vena cava is obstructed far from the heart. In our model, since the vena cava is only represented by a windkessel model, this geographical difference cannot be accounted for.

Conclusion: Impaired eNOS, Akt and AMPK expression and cardiac energy metabolism disruption is involved in chronic DXR cardiotoxicity; OLEU prevented those changes, thus providing a potential protective agent against DXR-induced cardiomyopathy.

References:


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P3255 | BENCH
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