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ABSTRACTS E-BOOK

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REGULATION OF VASCULAR HOMEOSTASIS BY PLANT DERIVED ESTROGENS

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Introduction: Phytoestrogens (PE) such as genistein (Gen) are considered a natural therapy to counteract the risk of cardiovascular diseases in postmenopausal women. Atherosclerosis is a chronic inflammatory process that, in the later step of plaque generation could conduct to vascular calcification (VCa). Revascularization, mainly aided by angiogenesis, represents a survival mechanism for ischemic tissue.
Objectives: We have previously reported that Gen prevents cellular events involved in the early stages of plaque formation. In this work we study the effect of Gen on VCa and angiogenesis.
Methods: Aortic rings (AR); endothelial cells (EC) and vascular smooth muscle cells (VSMC) isolated from aortic explants of female Wistar rats were employed. Cells cultures (VSMC; EC) or AR were *in vitro* exposed to 1-100 nM of Gen.
Results: When the effect of Gen on VCa was assayed, intact aortas were cultured in procalcifying medium (10 mM β-glycerophosphate; 4 mM $CaCl_2$) for 14 days. A significant reduction in calcified areas, revealed by $AgNO_3$ staining, was detected after 10 nM Gen treatment. These results were confirmed by quantification of aortic tissue calcium content (552±43 vs 235±18 ug Ca/mg prot, C vs Gen, $p<0.001$). Since VCa depends on VSMC transdifferentiation into osteoblast, VSMC cells were cultured for 21 days in procalcifying medium. Extracellular calcium content and alkaline phosphatase (ALP) activity were measured as osteoblastic differentiation markers. Gen induced 0,5 and 1-fold reduction in ALP activity ($p<0.05$) and calcium deposition ($p<0.05$) respectively, suggesting an inhibitory action on VSMC transdifferentiation into bone like cells. In view that angiogenesis involves EC proliferation, migration and VEGF synthesis; we studied the role of Gen on these events. Gen (4-96 h) stimulated EC proliferation at all concentrations tested (22-39% above C, $p<0.05$, MTT assay), with higher effect at short time interval treatment. After 72 h of treatment, the PE enhanced EC migration (20%> 66% above C, 10-100 nM, $p<0.01$; wound healing assay). Indeed, Gen increased VEGF synthesis (24.6-68.9 % above C, 1-10 nM Gen; ELISA assay). We confirmed that EC were able to proliferate after VEGF exposure. In order to evaluate new capillaries tube formation, AR were seeded on a collagen matrix and exposed to Gen for 15 d. Gen induced a 10-fold increase in tube formation around AR.
Conclusion: PE exhibits a potential beneficial effect on vascular homeostasis by reducing VCa and promoting angiogenesis.

Disclosure of Interest: None Declared