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Positive effects of acellular aortic scaffold on antioxidant activities and cellular homeostasis: an experimental study on cardiomyocytes of infarcted mice

Mahara Hosseinabadi[1], Zohreh Abdolmaleki[2*] and Seyedeh Parastoo Yasini[3]

[1] DVM Graduated, Faculty of Veterinary Medicine, Karaj Branch, Islamic Azad University, Karaj, Iran
[2] Assistant Professor, Department of Pharmacology, Faculty of Veterinary Medicine, Karaj Branch, Islamic Azad University, Karaj, Iran
[3] Assistant Professor, Department of Clinical Sciences, Faculty of Veterinary Medicine, Karaj Branch, Islamic Azad University, Karaj, Iran

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Abstract

Myocardial infarction (MI) has increased in the recent years due to aging as well as lifestyle changes in the population. In the last decades, regenerative medicine has been considered to provide modern and efficient methods for MI patients' therapies. The current study was aimed at investigating the effect of acellular aortic scaffold (AAS) on MI cardiomyocytes to identify the therapeutic potential of this natural biomaterial for MI patients. The study was conducted in five main steps: Preparing MI animal model, preparing MI cells, culture of animal MI cell on AAS, assessment of cell viability (MTT assay) as well as antioxidant and catalytic activities (ROS, TAC, SOD, GPX, and CAT assays) and molecular study on apoptotic and anti-apoptotic factors (qRT-PCR). AAS positively affected the viability rate of MI cells and the GPX and SOD levels were significantly increased in MI cells due to the culture on AAS. The RT-PCR quantification showed a decrease in the levels of of *Cox8* and *Caspase3* expression genes levels in MI cells, cultured on AAS, while an increase in miR-24 expression level was observed in MI cells as a result of culture on AAS. We concluded that acellular aortic scaffold can positively control the catalytic and antioxidant activities, cellular hemostasis, and cell viability of cardiomyocytes after myocardial infarction, demonstrating the potential of such natural biomaterials for cardiac tissue reconstruction. However, to achieve favorable results and ideal therapeutic applications, further studies are required.

Key words: Myocardial infarction, Regenerative medicine, Acellular aortic scaffold, Antioxidant Activity

[*] **Corresponding Author**: Zohreh Abdolmaleki, Assistant Professor, Department of Pharmacology, Karaj Branch, Islamic Azad University, Karaj, Iran
E-mail: zohreh.abdolmaleki@kiau.ac.ir

Refrences

Arnal-Pastor, M., Carlos Chachques, J., Vallés-Lluch, A., & Monleón Pradas, M. (2013). Chapter Biomaterials for Cardiac Tissue Engineering.

Badylak, S. F. (2007). The extracellular matrix as a biologic scaffold material. *Biomaterials, 28*(25), 3587-3593.

Badylak, S. F., Freytes, D. O., & Gilbert, T. W. (2009). Extracellular matrix as a biological scaffold material: structure and function. *Acta biomaterialia, 5*(1), 1-13.

Barnes, C. A., Brison, J., Michel, R., Brown, B. N., Castner, D. G., Badylak, S. F., & Ratner, B. D. (2011). The surface molecular functionality of decellularized extracellular matrices. *Biomaterials, 32*(1), 137-143.

Beattie, A. J., Gilbert, T. W., Guyot, J. P., Yates, A. J., & Badylak, S. F. (2009). Chemoattraction of progenitor cells by remodeling extracellular matrix scaffolds. *Tissue Engineering Part A, 15*(5), 1119-1125.

Brigelius-Flohé, R., & Maiorino, M. (2013). Glutathione peroxidases. *Biochimica et Biophysica Acta (BBA)-General Subjects, 1830*(5), 3289-3303.

Bröker, L. E., Kruyt, F. A., & Giaccone, G. (2005). Cell death independent of caspases: a review. *Clinical Cancer Research, 11*(9), 3155-3162.

Buja, L. M., & Vela, D. (2008). Cardiomyocyte death and renewal in the normal and diseased heart. *Cardiovascular Pathology, 17*(6), 349-374.

Cardona, M., López, J. A., Serafín, A., Rongvaux, A., Inserte, J., García-Dorado, D., . . . Vázquez, J. (2015). Executioner caspase-3 and 7 deficiency reduces myocyte number in the developing mouse heart. *PLoS One, 10*(6), e0131411.

Eitan, Y., Sarig, U., Dahan, N., & Machluf, M. (2010). Acellular cardiac extracellular matrix as a scaffold for tissue engineering: in vitro cell support, remodeling, and biocompatibility. *Tissue Engineering Part C: Methods, 16*(4), 671-683.

Forte, E., Panahi, M., Baxan, N., Ng, F. S., Boyle, J. J., Branca, J., . . . Harding, S. E. (2021). Type 2 MI induced by a single high dose of isoproterenol in C57BL/6J mice triggers a persistent adaptive immune response against the heart. *Journal of Cellular and Molecular Medicine, 25*(1), 229-243.

Fujimoto, K. L., Ma, Z., Nelson, D. M., Hashizume, R., Guan, J., Tobita, K., & Wagner, W. R. (2009). Synthesis, characterization and therapeutic efficacy of a biodegradable, thermoresponsive hydrogel designed for application in chronic infarcted myocardium. *Biomaterials, 30*(26), 4357-4368.

Geng, X., Liu, B., Liu, J., Liu, D., Lu, Y., Sun, X., . . . Kong, B. (2018). Interfacial tissue engineering of heart regenerative medicine based on soft cell-porous scaffolds. *Journal of thoracic disease, 10*(Suppl 20), S2333.

Ighodaro, O., & Akinloye, O. (2018). First line defence antioxidants-superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GPX): Their fundamental role in the entire antioxidant defence grid. *Alexandria journal of medicine, 54*(4), 287-293.

Jawad, H., Ali, N., Lyon, A., Chen, Q., Harding, S., & Boccaccini, A. R. (2007). Myocardial tissue engineering: a review. *Journal of tissue engineering and regenerative medicine, 1*(5), 327-342.

Khan, J. N., & McCann, G. P. (2017). Cardiovascular magnetic resonance imaging assessment of outcomes in acute myocardial infarction. *World journal of cardiology, 9*(2), 109.

Lebovitz, R. M., Zhang, H., Vogel, H., Cartwright, J., Dionne, L., Lu, N., . . . Matzuk, M. M. (1996). Neurodegeneration, myocardial injury, and perinatal death in mitochondrial superoxide dismutase-deficient mice. *Proceedings of the National Academy of Sciences, 93*(18), 9782-9787.

Meezan, E., Hjelle, J. T., Brendel, K., & Carlson, E. C. (1975). A simple, versatile, nondisruptive method for the isolation of morphologically and chemically pure basement membranes from several tissues. *Life sciences, 17*(11), 1721-1732.

Michałek, M., Tabiś, A., Pasławska, U., & Noszczyk-Nowak, A. (2020). Antioxidant defence and oxidative stress markers in cats with asymptomatic and symptomatic hypertrophic cardiomyopathy: a pilot study. *BMC veterinary research, 16*(1), 1-9.

Moghaddam, A. S., Afshari, J. T., Esmaeili, S.-A., Saburi, E., Joneidi, Z., & Momtazi-Borojeni, A. A. (2019). Cardioprotective microRNAs: Lessons from stem cell-derived exosomal microRNAs to treat cardiovascular disease. *Atherosclerosis, 285*, 1-9.

Mukherjee, S., Reddy Venugopal, J., Ravichandran, R., Ramakrishna, S., & Raghunath, M. (2011). Evaluation of the biocompatibility of PLACL/collagen nanostructured matrices with cardiomyocytes as a model for the regeneration of infarcted myocardium. *Advanced Functional Materials, 21*(12), 2291-2300.

Pech, L. G. M., del Carmen Caballero-Chacón, S., Guarner-Lans, V., Díaz-Díaz, E., Gómez, A. M., & Pérez-Torres, I. (2019). Effect of oophorosalpingo-hysterectomy on serum antioxidant enzymes in female dogs. *Scientific reports, 9*(1), 1-13.

Pellegata, A. F., Asnaghi, M., Stefani, I., Maestroni, A., Maestroni, S., Dominioni, T., . . . Mantero, S. (2013). Detergent-enzymatic decellularization of swine blood vessels: insight on mechanical properties for vascular tissue engineering. *BioMed Research International, 2013*.

Plakht, Y., Shiyovich, A., & Gilutz, H. (2015). Predictors of long-term (10-year) mortality postmyocardial infarction: age-related differences. Soroka Acute Myocardial Infarction (SAMI) Project. *Journal of cardiology, 65*(3), 216-223.

Radford, N. B., Wan, B., Richman, A., Szczepaniak, L. S., Li, J.-L., Li, K., . . . Moreadith, R. W. (2002). Cardiac dysfunction in mice lacking cytochrome-c oxidase subunit VIaH. *American Journal of Physiology-Heart and Circulatory Physiology, 282*(2), H726-H733.

Ravi, S., Caves, J. M., Martinez, A. W., Xiao, J., Wen, J., Haller, C. A., . . . Chaikof, E. L. (2012). Effect of bone marrow-derived extracellular matrix on cardiac function after ischemic injury. *Biomaterials, 33*(31), 7736-7745.

Rayman, M. P. (2005). Selenium in cancer prevention: a review of the evidence and mechanism of action. *Proceedings of the Nutrition Society, 64*(4), 527-542.

Reis, L. A., Chiu, L. L., Feric, N., Fu, L., & Radisic, M. (2016). Biomaterials in myocardial tissue engineering. *Journal of tissue engineering and regenerative medicine, 10*(1), 11-28.

Roth, G. A., Huffman, M. D., Moran, A. E., Feigin, V., Mensah, G. A., Naghavi, M., & Murray, C. J. (2015). Global and regional patterns in cardiovascular mortality from 1990 to 2013. *Circulation, 132*(17), 1667-1678.

Vickers, N. J. (2017). Animal communication: when i'm calling you, will you answer too? *Current biology, 27*(14), R713-R715.

Wang, T., Wu, D.-Q., Jiang, X.-J., Zhang, X.-Z., Li, X.-Y., Zhang, J.-F., . . . Huang, C. (2009). Novel thermosensitive hydrogel injection inhibits post-infarct ventricle remodelling. *European journal of heart failure, 11*(1), 14-19.

Wang, Z., Zhang, M., Wang, Z., Li, Q., & Wang, Z. (2020). Mechanistic role of miR-24 and miR-34 in progression in myocardial infarction. *Journal of King Saud University-Science, 32*(1), 1254-1257.