Fabrication of Engineered Heart Tissue as a New Tool for Drug Screening and Diseased Heart Studies

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Introduction: Culturing cardiomyocytes in a collagen matrix creates a coherently contractile 3D tissue named as engineered heart tissue (EHT) which serves as a model of normal or diseased heart. This could provide a reliable in vitro model for drug testing and as a novel treatment for salvaged myocardium after infarction. We herein developed an EHT from chick embryonic cardiomyocytes for the first time in Iran.

Methods: The cardiac cells were isolated from 11-day old embryonic chicken by enzymatic digestion and then engrafted in collagen matrix. These cells then were casted in 8-well polycarbonate mold with a $5x10^6$ cardiomyocyte density in each well (mold, N=4). Tissue formation process was observed using inverted microscope. In order to evaluate tissue characteristics, mono-phasic Action Potential Duration (APD), Sinus Rate (SR) and Contractile force measurement were done for each tissue before and after injection of a β-adrenergic drug (Epinephrine 0.1 µM). Electrophysiological tests were recorded using silver electrodes. Contractile forces of EHTs were measured by an isometric force transducer.

Results: The EHTs started to beat spontaneously after 4-6 days with a rate of 120-140/min. The contractile force measures significantly increased from 0.2±0.001 µN to 0.4±0.0014 µN in response to β-adrenergic stimulation ($p<0.01$). Tissue recordings revealed that SR decreased from 839.8±3.07 ms to 437.7±3.45 ms ($p<0.0001$) before and after epinephrine and action potential duration (APD) decreased from 206.6±6.73 ms to 187.9±2.05 ms ($p<0.02$).

Conclusion: It seems that EHT contains many physiological characteristics of a cardiac tissue and acts as a functional model, suitable for being considered to use in regenerative medicine and a platform for drug tests.

Keywords: Engineered Heart Tissue, Drug screening, Electrophysiological tests.