Expression of Kv4.xion channels reorganized on cardiomyocytes with altered mechanical and physiological parameters influenced by ophiobolins

Viktoria Szuts [1,3], Bencsik Otto [2], Zsolt Szegletes [1], Ferenc Otvos [1], George Váro [1], Antal Véha [3], Andras Szekeres [2], Csaba Vágvölgyi [2], Katalin Halasy [4]

[1] Biological Research Centre, Hungarian Academy of Science, Szeged, Hungary
[2] Department of Microbiology, Faculty of Science and Informatics, University of Szeged, Hungary
[3] Department of Food and Engineer, Faculty of Engineering, University of Szeged, Szeged, Hungary
[4] Department of Anatomy and Histology, University of Veterinary Sciences, Budapest, Hungary

E-mail address of presenting author: szutsvik@hotmail.com
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Nowadays the effects of the secondary metabolites come into sight since they can influence the electrolit balace in humans or animals but the biological consequence is poorly understood. Ophiobolins are major members of the ophiobolin complex of phytotoxic metabolites, and they possess antitumor, antibacterial, antifungal activities. However, knowledge of effects of ophiobolins on ion channels is very limited. The voltage dependent transient outward currents (Ito) are determined by Kv4.2 and Kv4.3 ion channels where the activity of fast and slow components of Ito (Ito,f and Ito,s) currents is not obligately dependent upon the expressed level of Kv4.x transcript. Increasing evidence points to a role of HMGB1 as underlying factors and SAP97 related to inflammation. The SAP97 associates with Kv4 type channels in complex modulating their kinetic properties. Our hypothesis was that the SAP97 mainly localises in the intercalated discs of the cardiac muscle therefore the altered expression of ion channels are presumably involved in the inhibition of normal mechanical parameters and physiological function of transient outward current (Ito). The aim was to use purified ophiobolins as an effective molecular tool in the study of cardiomyocyte inflammation. In this swot we have investigated the mechanical factors by atomic force microscope technique (AFM) and the surface expression of Kv4 ion channels on the cardiomyocytes using electron microscope, immunofluorescence and patch-clamp methods. Atomic force microscopy study showed that the elasticity of the cell surface, the Young modulus is moderately changed as well as the cell volume and the highest of the cells in the presence of low ophiobolin concentration. However, after treatment of ophiobolin the SAP97 binding to Kv4.3 channels and distribution of their complexes are altered in the membrane and physiological behaviour of cardiomyocytes as compared to control. A growing body of research use using these new reductionist models of inflammation on cardiomyocytes are demonstrating a role of SAP97 in specific ion channel stability important for cardiac functions. These results suggest that SAP97 deactivation or reduction can lead (directly or indirectly) to changes in the functional cell surface expression of Kv4.x channels with mechanical parameters, with biophysical and biochemical properties of cardiac Ito current. These results could help to develop a new test for the effects of the secondary metabolites.
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