The K_{ATP} channel opener diazoxide attenuates mitochondrial Ca^{2+} overload in rat ventricular myocytes

Sunghyun Kang, Nari Kim, Hyun Joo, Jae boum Youm, Won sun Park, Dang Van Cuong, Hyoung kyu Kim, Teaho Kim, Tran Min Khoa, Vu Thi Thu, Hyunju Kim, Hyejin Moon, Hyunsuk Lee, Euiyong Kim and Jin Han*

Mitochondrial Signaling Laboratory, Department of Physiology and Biophysics, College of Medicine, Cardiovascularand Metabolic Disease Center, Biohealth Products Research Center, Inje University, Busan 614-735 Korea

Background: Mitochondrial KATP channel protects the heart from ischemia-reperfusion injury and mediatesischemic preconditioning (IPC). In this study, we intended to characterize the cardiac protection effect of mitochondrial KATP channel opening.

Methods and results: Single rat ventricular myocytes were isolated using enzymatic method. Mitochondrial Ca2+ and inner membrane potential (m) were measured with rhod-2 AM and JC-1, respectively, under laser scanning confocal microscope (LSCM). When rhod-2 AM loaded cells were administrated with ouabain (1 mM), a Na+/K+ ATPase inhibitor, the fluorescence intensity of rhod-2 AM increased by about 120 % of the baseline. The increased rhod-2 AM fluorescence intensity was attenuated when a mitochondrial KATP channel opener, diazoxide (100?M) was added again. However, the mitochondrial Ca2+ decrease by diazoxide was blocked by 5-Hydroxydecanoate (5-HD, 500?M), mitochondria KAPT channel antagonist. Furthermore, in the presence of ouabain, diazoxide depolarized m and reduced the JC-1 fluorescence intensity by about 50 % of the baseline.

Conclusion: These data suggest that the opening of mitochondrial KATP channel leads to depolarization of m, which attenuates mitochondrial Ca2+ overload. Diazoxide might be a useful candidate for the protection from cardiac ischemia /reperfusion injury (I/R).

Key words: Mitochondrial KATP channel, ouabain, diazoxide, JC-1, Rhod-2 AM, 5-HD.