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**O.M. Kaleinikova, A.P. Lytvynenko, V.O. Sribna,
T.V. Blashkiv, T.Yu. Voznesenskaya**

O.O. Bogomoletz Institute of Physiology, NAS of Ukraine
4, Akademika Bohomoltsia Str., Kyiv, Ukraine, 01024
syana_ds@ukr.net

SIRT1 ACTIVATION AND SIRT2 INHIBITION DIFFERENTIALLY MODULATE APOPTOSIS AND AUTOPHAGY IN SPERMATOZOA UNDER OXIDATIVE STRESS

Aim. To evaluate the effects of resveratrol (a SIRT1 (Silent Information Regulator proteins) activator) and AGK-2 (a SIRT2 inhibitor) on sperm cell viability and cell death pathways under H_2O_2 -induced oxidative stress in vitro. **Methods.** Experiments were performed using spermatozoa obtained from adult albino laboratory mice (25–30 g). Oxidative stress was induced by incubation with H_2O_2 (500 μ M). Resveratrol was applied at concentrations of 2, 20, and 200 μ M, while AGK-2 was used at concentrations of 5, 10, 50, and 100 μ M. The proportions of viable, apoptotic, necrotic, and autophagic sperm cells were assessed following incubation. Statistical significance was accepted at $p < 0.05$. **Results.** Exposure to H_2O_2 -induced oxidative stress significantly decreased sperm cell viability and increased the proportions of apoptotic, necrotic, and autophagic cells compared with the control group ($p < 0.05$). Pre-incubation with resveratrol under oxidative stress conditions increased the proportion of viable spermatozoa and reduced apoptotic cell death in a concentration-dependent manner. The strongest protective effect was observed at 200 μ M, where the percentage of viable cells increased and apoptotic cells decreased significantly compared with the oxidative stress group ($p < 0.05$). Resveratrol also reduced the proportion of autophagic cells, with the greatest effect observed at 200 μ M ($p < 0.05$). In contrast, pre-incubation with AGK-2 did not significantly affect the proportions of viable, apoptotic, or necrotic sperm cells under oxidative stress conditions. However, AGK-2 markedly reduced the proportion of autophagic cells, with the most pronounced effect observed at 100 μ M compared with the oxidative stress group ($p < 0.05$). **Conclusions.** The findings indicate the distinct functional roles of sirtuins in spermatozoa exposed to oxidative stress. Activation of SIRT1 by resveratrol predominantly suppresses apoptotic and necrotic cell death, whereas inhibition of SIRT2 by AGK-2 primarily attenuates autophagic cell death. These results support the hypothesis that SIRT1 is mainly involved in the regulation of apoptosis, while SIRT2 plays a more prominent role in the regulation of autophagy in spermatozoa under oxidative stress conditions.

Keywords: sirtuins; oxidative stress; spermatozoa; apoptosis; autophagy; cell viability.

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