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Salinomycin induces mouse testicular germ cell apoptosis and changes in Bcl-2 and Bax proteins expression

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Apoptosis, a strictly regulated process involving sequential activation of specific signaling transduction pathways, disturbance of mitochondrial membrane function causing the release of intermembrane proteins into the cytosol and subsequent stepwise degradation of cell. Adverse effect of Salinomycin on male reproductive organs and infertility had been reported, however mechanism involved is still unclear. This study therefore investigates the possibility of apoptosis through the interplay of bcl-2 and bax proteins in mouse testis. Eight groups of mice received 1, 3 and 5 mg/kg Salinomycin and were sacrificed after 28 days of treatment and half of the groups were sacrificed after 28 days withdrawal of the treatment. The role of apoptosis following Salinomycin exposure was evaluated using different techniques. Microarray technology was also used to evaluate effect of Salinomycin on major genes in reproductive pathways. The terminal deoxynucleotidyl transferase-mediated dUTP nick-end-labeling method (TUNEL) shows increased positive staining germ cells in treated testicles across the dose groups (<0.05). Increased number of cells was stained with FITC/PI indicating both early and late apoptosis following Salinomycin exposure. Down regulation of Caspase 3 activity was also observed. Western blot analysis shows down regulation of bcl-2 protein with simultaneous up-regulation of bax apoptosis protein. Data on microarray analysis indicates Salinomycin-induced testicular cell degeneration mediated by apoptosis. A number of the resulting genes involved in reproduction pathways such as Adam 2, participating in sperm-egg membrane binding, the testis-specific factor, Spam, involving in fertility and the transition proteins, Tnp1 and Tnp2, required for chromatin condensation during spermiogenesis, CYP11A1 and STRAD 6 for steroid synthesis are grossly affected. In general, microarray study reveals distinct expression profiles and patterns of each dose of Salinomycin. Conclusively, the study confirmed induction of apoptosis and further established dose dependent- adverse effect of Salinomycin on male reproductive system.

Biography

Olajumoke Omolara Ojo completed her PhD from Jawaharlal Nehru University New Delhi India in 2014 under TWAS-CSIR Postgraduate Fellowship at Central Drug Research Institute Lucknow India. She presented her work in several scientific meetings and also received best poster award at International meeting of Society of Toxicology of India in 2012 held at Indian Institute of Technology Lucknow Research India. Some of her findings were published in PLoS One Journal while some are in communication stage in peer reviewed journals. She is currently a lecturer at Ekiti- State University Ado-Ekiti Ekiti- State Nigeria.

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