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Editorial

Melatonin as a Promising Radiation Countermeasure

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The term radiation countermeasure targets drugs used for the prevention (radioprotectors), mitigation (radiomitigators) and treatment (therapeutics) of acute radiation injury. Also, radiation countermeasures are needed for the effective medical management of nuclear accidents, and for the deployment of emergency responders for the clean-up operations. In the present global perspectives nuclear/radiation fears arising due to catastrophic accidents due to natural or man-made disasters including threats from the rogue nations and terrorists organizations, several government agencies including Department of Atomic Energy (DAE), Defence Research and Development Organization (DRDO), Indian Council of Medical Research (ICMR), and many others have started radiation countermeasures program and prioritize it for the development of novel and non-toxic agents that can attenuate the deleterious side effects of ionizing radiation.

Melatonin (N-acetyl-5-methoxytryptamine) is nature's most versatile molecule and the chief secretory product of pineal gland in the brain. Several studies reported in the public domain suggested that melatonin is among one of the molecule functioning directly as free radical scavenger and indirectly as an antioxidant. The free radical scavenging ability of melatonin was used as a rationale to prove its cytoprotective efficiency through *in vitro* and *in vivo* systems. A series of investigations by Vijayalaxmi., *et al.* and others on both *in vitro* and *in vivo* systems have confirmed that melatonin, as a cytoprotective molecules, protects most of the major biological macromolecules from the negative/harmful side effects of ionizing radiations [1,2].

In line with this notion, we have reported that melatonin protected hematopoietic, immunological, gastrointestinal, reproductive and antioxidant systems of whole-body ^{60}Co γ-irradiated mice, which were studied through survival, histopathology, immunophenotyping, DNA strand breaks, colony forming unit activity of hematopoietic progenitor stem cells (HPSCs), sperm abnormalities, sperm viability and motility index, antiradical and antioxidant assays and pro-versus-anti-apoptotic protein markers [3-6]. Our results demonstrated that, a single prophylactic dose of melatonin pre-treatment significantly reduced the mortality of whole-body irradiated (WBI) mice [3,4]. Melatonin pre-treatment protected gastrointestinal system from radiation-induced oxidative injury by decreasing lipid peroxidation, DNA strand breaks, altered expression pattern of apoptotic signaling proteins and increasing epithelial crypt cells regeneration [3,4]. It also inhibited gut bacterial translocation to spleen, liver and kidney [3,4]. Further studies showed that melatonin pre-treatment protected hematopoietic system injury by increasing the HPSCs in bone marrow of WBI mice [3], and also protect immunological system by increasing T cell sub-populations and decreasing DNA strand breaks and apoptosis in spleen of WBI mice [3-5]. In contrast, melatonin pre-treatment inhibited γ-ray-induced lipid peroxidation and DNA strand breaks in testes of WBI mice [6]. We also showed that radiation-induced spermatogenic cells (spermatogonia, spermatocyte and spermatid) depletion in seminiferous tubules as well as sperm abnormalities, motility and viability index in cauda-epididymis were markedly prevented by melatonin pre-treatment [6], thereby, protected reproductive system. The molecular mechanism of melatonin pre-treatment is largely unknown, most likely by inhibiting ATM-dependent p53 apoptotic signaling proteins- ATM, p53, p21, Bax, cytochrome C, caspases-3 and caspases-9. The reductions of apoptotic proteins were associated with the increase in anti-apoptotic-Bcl-x protein. Keeping the above in view, melatonin pretreatment appears to be very effective radioprotective agents in rescuing radiation-induced reproductive, hematopoietic, immunological, and gastrointestinal systems injuries in murine. Further, cytoprotective studies and their validation using other animal models for their pharmacological application may be warranted.

In futuristic, it will be interesting to see the mechanism by which melatonin elicits antioxidant effects through the regulation of redox-sensitive Nrf2 transcription factors and inhibition of NF-κB mediated pro-inflammatory genes against radiation. Nrf2-NFκB cross-talk is also very unclear. Therefore, analyzing cross-talk between Nrf2 and NF-κB against radiation may show a role for melatonin as a mechanistic model.

Bibliography

1. Vijayalaxmi., *et al*. "Melatonin as a radioprotective agent: a review". *International Journal of Radiation Oncology, Biology, Physics* 59.3 (2004): 639-653.

2. Zhang HM., *et al*. "Melatonin: a well-documented antioxidant with conditional pro-oxidant actions". *Journal of Pineal Research* 57.2 (2014): 131-146.

3. Khan S., *et al*. "Melatonin attenuates 60Co γ-ray-induced hematopoietic, immunological and gastrointestinal injuries in C57BL/6 male mice". *Environmental Toxicology* 32.2 (2017): 501-518.

4. Khan S., *et al*. "Melatonin attenuates γ-ray-induced hematopoietic and gastrointestinal injury in mice". India: Institute of Nuclear Medicine and Allied Sciences (2014).

5. Khan S., *et al*. "Melatonin and sesamol protects spleenocytes against ^{60}Co γ-irradiation induced damages in male C57BL/6 mice". India: KS Hegde Medical Academy (2013).

6. Khan S., *et al*. "Radioprotective potential of melatonin against ^{60}Co γ-ray-induced testicular injury in male C57BL/6 mice". *Journal of Biomedical Science* 22 (2015): 61.

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