Cell-based screening of antistress activity of some phytochemicals: Identification, validation, and relevance to old-age related pathologies

Zhang H[1], Kaul SC[2] and Wadhwa R[2]*

[1]Graduate School of Science and technology, University of Tsukuba, Ibaraki 305-8575, Japan
[2]AIST-INDIA DAILAB, National Institute of Advanced Industrial Science & Technology (AIST), Tsukuba - 305 8565, Japan

E-mail: renu-wadhwa@aist.go.jp

Background- A variety of environmental stresses have been shown to contribute to poor quality of life, tissue dysfunctions and ailments including metabolic disorders, cognitive impairment, and accelerated aging. Oxidative stress (an imbalance between the production and processing of highly reactive oxygen species) is largely associated with these phenotypes. Whereas drug development and disease therapeutics have advanced remarkably in last three decades, there are still limited options for stress management. Since the later can effectively decrease the disease burden, we aimed to screen phytochemicals with anti-oxidative stress activity using cell-based assays.

Methods- Brain-derived cells were subjected to chemical models of oxidative (paraquat), metal (cadmium nitrate) or hypoxia (cobalt chloride) stresses. Stressed cells were allowed to recover either in the control or phytochemical supplemented culture medium. Cell survival and protein expression/signaling were analyzed to select the useful compounds and/or plant extracts.

Results- Cells subjected to paraquat stress showed decrease in their viability. Three rounds of blind screening of the 24 phytochemicals resulted in identification of 5 compounds that caused better recovery of cells. The selected compounds were examined for their ability for protection against metal and hypoxia stresses induced by cadmium nitrate and cobalt chloride, respectively. Based on these 3D-anti stress protection ability, Withanone (Wi-N) and triethylene glycol (TEG) were selected for molecular validation. We found that whereas stress caused increase in (i) apoptosis (ii) ROS accumulation coupled with mitochondrial depolarization (iii) DNA double-strand break (iiii) protein aggregation, the selected compounds and the Ashwagandha extracts (known to possess these compounds) caused remarkable protection. Furthermore, both Wi-N and TEG caused differentiation of C6 glioblastoma and IMR-32 neuroblastoma as evidenced by the respective differentiated cell morphology and increased expression of biomarkers.

Conclusion- The results suggested that Wi-N, TEG, their mixture, and the natural resource (Ashwagandha) possess potent antistress activity that may be useful for management of old-age-related ailments.