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Nootkatone debilitate bleomycin-induced pulmonary toxicity in lung cancer A549 cells: *In silico* and genomic evolution

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The biggest issue with bleomycin (BLM) chemotherapy is pulmonary damage. BLM manifests oxidative stress via an uncontrolled progression of reactive oxygen species in pneumocystis, a relative deficit of the deactivation enzyme BLM hydrolase and the formation of inflammatory cytokines leading to apoptosis. There have been several attempts to treat patients for this adverse effect by giving them antioxidant rich supplements to minimise free radicals. Compounds that are extracted from plants or that are based on plants emphasise more on curing such patient issues in order to support treatment, rejuvenate, or manage normal metabolism. Hence, in this study we concentrated on pretreatment of lung cancer derived A549 cells with phytocompound nootkatone (NKT) to prevent BLM-mediated oxidative stress. We find in our study, the BLM-exposed cells have displayed morphological anomalies such as shrinkage, blabbing, and chromatin condensation, among others. Yet, even after exposure to BLM, no such abnormalities were seen in NKT pretreated cells. In NKT pretreatment cells, there was a significant surge in endogenous antioxidants and a decrease in lipid peroxidation, in contrast, cells exposed to BLM had lower levels of antioxidants and greater levels of lipid peroxidation. In gene expression analysis, the pro-apoptotic gene *Bcl-2/Bax* and the apoptotic executor caspase 3 were significantly suppressed in the NKT pretreated cells, which attenuated BLM-mediated apoptosis. The current investigation, showed that the NKT pretreatment has displayed merit for pulmonary protective activity against BLM-induced oxidative stress by boosting the intracellular antioxidant defence.

Keyword: Gene expression, Molecular docking, Oxidative stress, Phytocompound