Abstract

Accumulation of misfolded or aberrant proteins in neuronal cells is linked with neurodegeneration and other pathologies. How do cellular proteins get misfolded and what could be the probable therapeutic or molecular approaches to counter such alterations inside the cells are not clear. In the present study, it has been demonstrated that treatment of lanosterol diminishes aberrant proteotoxic aggregation and mitigates their cytotoxicity *via* induced expression of co-chaperone CHIP and elevated autophagy. The addition of lanosterol not only reduces aggregation of mutant bona-fide misfolded proteins, but also effectively prevents accumulation of various mutant disease-prone proteotoxic proteins. In routine course of life, nonsteroidal anti-inflammatory drugs are widely prescribed antipyretic, analgesic, and anti-inflammatory drugs. It is a well-proposed notion that treatment of these drugs may induce anti-proliferative effects in numerous cancer cells. Few studies in the past have led to the emergence of the concept that treatment of many of these may induce programmed cell death pathways in cancer cells. However, the underlying precise mechanisms of apoptosis upregulation remain largely unknown. Here, in this study, it was observed that ibuprofen reduces proteasome activity, enhances the aggregation of ubiquitylated abnormal proteins, and elevates the accumulation of crucial proteasome substrates. Ibuprofen treatment leads to mitochondrial abnormalities and release of cytochrome *c* into the cytosol that in turn causes elevated cytotoxicity. Taken together, the present results suggest that modulation of the cellular protein quality control machinery, primarily by using small molecules, can effectively generate anti-tumor effects and may also help in delaying neurodegenerative changes and ageing.

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