The natural antioxidant alpha-lipoic acid induces p27(Kip1)-dependent cell cycle arrest and apoptosis in MCF-7 human breast cancer cells.


Abstract

Unlike normal cells, tumor cells survive in a specific redox environment where the elevated reactive oxygen species contribute to enhance cell proliferation and to suppress apoptosis. Alpha-lipoic acid, a naturally occurring reactive oxygen species scavenger, has been shown to possess anticancer activity, due to its ability to suppress proliferation and to induce apoptosis in different cancer cell lines. Since at the moment little information is available regarding the potential effects of alpha-lipoic acid on breast cancer, in the present study we addressed the question whether alpha-lipoic acid induces cell cycle arrest and apoptosis in the human breast cancer cell line MCF-7. Moreover, we investigated some molecular mechanisms which mediate alpha-lipoic acid actions, focusing on the role of the PI3-K/Akt signalling pathway. We observed that alpha-lipoic acid is able to scavenge reactive oxygen species in MCF-7 cells and that the reduction of reactive oxygen species is followed by cell growth arrest in the G1 phase of the cell cycle.
cell cycle, via the specific inhibition of Akt pathway and the up-regulation of the cyclin-dependent kinase inhibitor p27(kip1), and by apoptosis, via changes of the ratio of the apoptotic-related protein Bax/Bcl-2.

Thus, the anti-tumor activity of alpha-lipoic acid observed in MCF-7 cells further stresses the role of redox state in regulating cancer initiation and progression.

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