Biphasic Dose-Dependent Effect of Lithium Chloride on Survival of Human Hormone-Dependent Breast Cancer Cells (MCF-7).

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Source
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Abstract
Lithium, the first element of Group I in the periodic system, is used to treat bipolar psychiatric disorders. Lithium chloride (LiCl) is a selective inhibitor of glycogen synthase kinase-3β (GSK-3β), a serine/threonine kinase that regulates many cellular processes, in addition to its role in the regulation of glycogen synthase. GSK-3β is emerged as a promising drug target for various neurological diseases, type-2 diabetes, cancer, and inflammation. Several works have demonstrated that lithium can either inhibit or stimulate growth of normal and cancer cells. Hence, the present study is focused to analyze the underlying mechanisms that dictate the biphasic oncogenic properties of LiCl. In the current study, we have investigated the dose-dependent effects of LiCl on human breast cancer cells (MCF-7) by assessing the consequences on cytotoxicity and protein expressions of signaling molecules crucial for the maintenance of cell survival. The results showed breast cancer cells respond in a diverse manner to LiCl, i.e., at lower concentrations (1, 5, and 10 mM), LiCl induces cell survival by inhibiting apoptosis through regulation of GSK-3β, caspase-2, Bax, and cleaved caspase-7 and by activating anti-apoptotic proteins (Akt, β-catenin, Bcl-2, and cyclin D1). In contrast, at high concentrations (50 and 100 mM), it induces apoptosis by reversing these effects. Moreover, LiCl also alters the sodium and potassium levels thereby altering the membrane potential of MCF-7 cells. Thus it is inferred that LiCl exerts a dose-dependent biphasic effect on breast cancer cells (MCF-7) by altering the apoptotic/anti-apoptotic balance.

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