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Inhibitory effect of tributyltin on the cell cycle progression in rat testicular leydig cells

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Tributyltin used world-wide in antifouling paints for ships is a widespread environmental pollutant and cause reproductive organs atrophy in rodents. We investigated the effects of tributyltin on rat testicular leydig cells cycle arrest to establishing induction of growth arrest and apoptosis of R2C, rat leydig cells. Our data show that the induction of cell apoptosis and cell cycle arrest at G0/G1 phase by tributyltin might be associated with the induction of p53 and p21, and mediated via the apoptosis-related bcl-2 family proteins. In this report, we further investigated the mechanism involved in the cell cycle arrest induced by tributyltin in R2C cells. The inhibitory effect of tributyltin on the cell cycle progression of R2C cells which arrested cells at the G0/G1 phase was associated with a marked decrease in the protein expression of p53 and an induction in the content of cyclin-dependent kinase (cdk) inhibitor p21 protein. Moreover, this effect was correlated with the elevation in Cyclin D/Cdk 4 complex declined, preventing the phosphorylation of retinoblastoma (Rb) and the subsequent dissociation of Rb/E2F complex. This provides strong evidence that the apoptotic effect of tributyltin, arresting cells at the G0/G1 phase, was exerted by inducing the expression of p21 that, in turn, repressed the activity of cyclin D1/cdk 2 and the phosphorylation of Rb.

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