Amlodipine, a dihydropyridine Ca$_{2+}$ channel blocker, induces G1 cell-cycle arrest in human epidermoid carcinoma A431 cells

We have demonstrated that amlodipine, a dihydropyridine Ca$_{2+}$ channel blocker, exhibits the antitumor effect on human epidermoid carcinoma A431 cells both in vitro and in vivo. However, the mechanism is still unknown. Therefore, we investigated the molecular mechanism of action by which amlodipine inhibits the cell proliferation. Cell cycle of A431 cells was examined by flow cytometric analysis. Western blotting was used to evaluate protein levels of regulators in the cell cycle. Amlodipine treatment (20-30 µM for 24 hrs) induced G1 phase accumulation, which was associated with decrease in the phosphorylated form of the retinoblastoma protein (pRB), a regulator of the G1-S phase transition. Under this condition, expression of cyclin D1 and cyclin-dependent kinase 4 (CDK4), G1-specific cell cycle proteins, as well as E2F1 transcription factor were decreased. On the other hand, expression of p21$^{Waf1/Cip1}$, an inhibitor protein of CDK/cyclin complexes, was increased by amlodipine. The present data demonstrates that amlodipine induced expression of p21$^{Waf1/Cip1}$ and concomitantly inhibited CDK4 and CDK4-mediated phosphorylation of pRB, which resulted in G1 cell-cycle arrest.