We demonstrated previously that antiproliferative effect of amlodipine, a dihydropyridine Ca\(^{2+}\) channel blocker, on human epidermoid carcinoma A431 cells, involved G1 cell cycle arrest. In this study, we examined the effects of amlodipine on G1 cell cycle regulatory molecules by Western blotting and in vitro kinase assays. Amlodipine treatment of A431 cells resulted in a decrease in phosphorylation of retinoblastoma protein (pRB), a regulator of G1 to S phase transition, reduction of protein levels of cyclin D1, and increased expression of p21\(^{\text{Waf1/Cip1}}\), a cyclin-cyclin dependent kinase (CDK) inhibitor. Concomitantly, CDK2-, CDK4-, and their partners cyclin E- and cyclin D1-associated kinase activities were decreased. The amlodipine-induced reductions in the cyclin D1 protein level and in CDK2 kinase activity were reproduced by a dihydropyridine derivative, nicardipine, having an inhibitory effect on A431 cell growth, but not by nifedipine, lacking the antiproliferative activity. Our results demonstrate that amlodipine caused G1 cell cycle arrest and growth inhibition in A431 cells through upregulation of p21\(^{\text{Waf1/Cip1}}\), inhibition of CDK/cyclin kinase activities, and reduced phosphorylation of pRB.