Abstract: Introduction: G-quadruplexes are an attractive target for drug design because they are found in biologically important regions. Formation of G-quadruplex in the purine-rich strand in the c-Myc promoter could block transcription of this oncogene. c-Myc is one of the best known oncogenes, and it is overexpressed in various cancer cells. Several DNA binding ligands with antibiotic effects exhibited G-quadruplex binding activities. Here, interaction of c-Myc G-quadruplex with ActinomycinD (ActD) has been investigated by molecular dynamic simulation. ActD is a natural antibiotic and anticancer agent that inhibits the transcription of genes by interacting with a GC-rich duplex, a single-stranded or hairpin form of DNA, and then interfering with the action of RNA polymerase. Method: In this study the complex formation between actinomycin-D and G-quadruplex is simulated by the Amber molecular dynamics package. The molecules were placed in a truncated octahedral TIP3P water box and neutralized by K+ ions. The salt concentration of 100 mM KCl was added to the simulation environment. We have performed Molecular Dynamic simulation to study interactions between ActD and the quadruplex. Results: Analysis of molecular dynamics revealed that a very stable complex forms between the G-quadruplex and ActD, after a few nanoseconds. The major interactions responsible for stability are the hydrophobic interactions between the upper G-quartet surface and the ActD aromatic rings. The overall structure of the quadruplex is distorted in a way to engulf the lower part of the ActD molecule. Conclusions: Anticancer effect of ActD can be related to its binding to c-Myc G-quadruplex structure.