Abstract: Effects of midazolam and lorazepam on the structure of adenosine deaminase (ADA) were studied by molecular dynamics simulation. Adenosine deaminase (ADA) is a cytosolic enzyme, which has been the object of considerable interest, mainly because a congenital defect in the enzyme causes severe combined immunodeficiency disease (SCID) in humans. All calculations were done with gromacs software and Gromose 96 43a1 force field at 300 K. The studied number of midazolam and lorazepam were 6 and 12 molecules. Accessible surface area (ASA), radial distribution function (RDF) and other physical parameters were obtained from analyzing trajectory of molecular dynamics. Results demonstrated that by increasing drug concentration, protein denaturation increase too, therefore enzyme denaturation is more in the presence of higher concentration of drugs. Increase of solvent accessible surface area and protein radius of gyration are good indicators of protein denaturation by these molecules. Variations of helix, beta and coil were analyzed using topology and trajectory files by the VADAR software. Analyzing the secondary structure revealed that both molecules decrease the secondary structure and lorazepam is more effective due to having a smaller size. Therefore increase of beta and coil with decrease of helix structure was observed which confirms simulation results.