An existing model of the rat ventricular myocyte was modified to reproduce the experimentally observed differential effects of the fast and slow exogenous Ca2+ buffers BAPTA and EGTA on inactivation of ICa and to investigate the possible cause. The results of the simulations suggest that the different potencies of EGTA and BAPTA on inactivation of ICa are due to their different rates of Ca2+ binding, and thus different intracellular gradients of bound and unbound buffer, causing different rates of diffusion of bound and unbound buffer out of and into the dyadic space. The consequent difference in suppression of the Ca2+ transient in the dyadic space caused different rates of Ca2+ - induced inactivation of ICa in the presence of the two buffers.