Nanoparticles, drug carriers in the sub-micron size range, have shown tremendous potential in cell and tissue targeting. However, for water soluble drugs, poor drug encapsulation efficiency and rapid release limit the use of nanoparticles in cellular delivery applications. We have previously reported that surfactant-polymer nanoparticles formulated using dioctyl sodium sulfosuccinate (Aerosol OT™ AOT) and sodium alginate can significantly increase and sustain the cellular delivery of water-soluble molecules, resulting in enhanced therapeutic efficacy. In the present study we demonstrate that incorporation of phospholipids in AOT-alginate nanoparticles further enhances their cellular accumulation and retention. AOT-alginate nanoparticles with or without phospholipids and loaded with a rhodamine as a model drug were formulated using double emulsion process. Kinetics and mechanism of cellular uptake, and retention were evaluated in vitro using a model breast cancer cell line. Addition of phospholipids in AOT-alginate nanoparticles significantly enhanced cellular accumulation and retention of nanoparticle-encapsulated rhodamine. Kinetic studies and metabolic inhibition studies suggest that cellular uptake of phospholipid-containing nanoparticles is mediated through endocytosis. Based on these results, we conclude that AOT-alginate nanoparticles comprising phospholipids are suitable carriers for enhanced and sustained cellular drug delivery.