The field of extracellular vesicle (EV)-based drug delivery systems has evolved significantly through the recent years, and numerous studies suggest that these endogenous nanoparticles can function as efficient drug delivery vehicles in a variety of diseases. Many characteristics of these EV-based drug delivery vehicles suggest them to be superior at residing in the systemic circulation and possibly at mediating therapeutic effects compared to synthetic drug delivery vehicles, e.g. liposomes. In this Commentary, we discuss how some currently published head-to-head comparisons of EVs versus liposomes are weakened by the inadequate choice of liposomal formulation, and encourage researchers to implement better controls to show any potential superiority of EVs over other synthetic nanoparticles.