## Bola-shaped Glicocalix[4]arenes for efficient and specific drug delivery systems

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The protein-carbohydrate recognition phenomena can be used for the targeted drug delivery, exploiting the numerous specific carbohydrate receptors present on the cell membrane.<sup>1</sup> Liposomes are well known as drug delivery systems and, in some cases, functionalized with sugar units, they indeed show targeting properties on the basis of these processes.<sup>2</sup> In other examples, the functionalization of the lipid bilayer with bolaamphiphiles gives rise to liposomes with higher rigidity and lower permeability, improving their ability in entrapping molecules.<sup>3</sup>

We recently prepared two new bolaamphiphiles characterized by the presence of active polar heads for targeting, based on calixarenes in the so-called 1,3-alternate geometry and functionalized with four units of glucose and cellobiose (glycocalix[4]arenes).<sup>4</sup> Experiments to determine the incorporation of these glycocalixarenes into lipid bilayers of DOPC liposomes, permeability and entrapment properties of these mixed liposomes, and interaction with a glucose recognition lectin (ConA) were successfully performed.<sup>4</sup> Moreover, targeted delivery experiments were performed towards human breast cancer cells (MDA-MB-231) over-expressing the glucose receptor GLUT1, by using DOPC and DOPC/calixarene mixed liposomes fluorescently labelled with a N-(7-nitrobenz-2-oxa-1,3-diazol-4-yl) (NBD) tagged lipid. The preliminary results collected by laser scanning confocal microscopy indicate that the uptake of liposomes containing the glucosylated calixarenes is significantly higher respect to the uptake of DOPC liposomes suggesting the occurrence of a receptor mediated process. The use of bola-shaped glycocalix[4]arenes could be then a novel successful strategy to functionalize liposomes and obtain drug delivery systems able to target specific lectins, cells and tissues.

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