Carbon dioxide-responsive miktoarm polymer-based soft nanoparticles for drug delivery

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Stimuli responsive polymers respond to changes in environment induced by physical, chemical, or biological signals, such as oxidative stress, pH, temperature, glucose levels etc. The specificity and responsiveness of such polymeric nanocarriers as well as their tunable behavior are an attractive feature for drug delivery, as they are subjected to changes only when exposed to a particular trigger, avoiding accumulation and side-effects of drug molecules at undesired sites. Miktoarm polymers continue to provide an ideal platform for developing stimuli-responsive drug delivery nanocarriers, as functional groups that can respond to a specific stimulus can be easily incorporated into the branched architecture. The nanometer size self-assemblies from these amphiphilic miktoarm stars are also known for their superior drug loading ability, while having a low critical micelle concentration. CO_2-responsive polymers have been widely investigated, as the gas is benign, abundant, inexpensive, and easily reversible. These advantages have brought much attention to CO_2-responsive polymers in applications such as CO_2-switchable surfaces, CO_2-switchable nanoreactors and CO_2-responsive self-assemblies. It is, however, less studied as a stimulus in drug delivery. Numerous studies have shown that cancerous sites have elevated levels of CO_2, resulting in impaired respiration in lung cancer patients and threatening the growth of healthy cells. Therefore, CO_2-targeting nanocarriers are needed for delivering drugs to such targeted sites and increasing the drug release rate. We will discuss the design of biocompatible CO_2-responsive AB_2-type amphiphilic miktoarm stars, with a combination of hydrophilic and amine-incorporated hydrophobic segments. A 2:1 ratio of hydrophilic to hydrophobic segment greatly enhances the aqueous solubility. A detailed evaluation of the design, self-assembly, drug loading and release characteristics of these miktoarm star-based assemblies will be discussed.