ABSTRACT

Virus like particles are multimeric, macromolecular protein assemblies. Capsid protein of virus self-assembles to form VLPs, devoid of any genetic material. Structural features of viral capsid makes VLPs amenable for surface modification, cargo encapsulation and protein engineering for biomedical applications. Capsid protein of bacteriophage MS2 forms a 27nm icosahedral VLPs of T=3 symmetry. Change in the subunit interaction causes the change in symmetry, size and nature of particle, often affecting the applications. A point mutation of S37P in MS2 VLPs shifts the size of particle to 17nm with T=1 symmetry. However, does the change in size and symmetry influences the stability and application of mutant MS2 VLPs remain unexplored.
In this present work, we have prepared and characterized the MS2 VLPs together with its engineered variant for its stability, cargo loading efficiency and drug delivery efficacy. Recombinant production of WT and mutant MS2 VLPs have been achieved by expression in Escherichia coli (E.coli) host. The E.coli purified MS2 VLPs were subjected to a series of biochemical and biophysical characterization using plethora of analytical techniques. Interestingly, our results indicated the higher melting temperature of mutant MS2 VLPs as compared to WT, attributed to the different sets of interaction such as hydrogen bonding or hydrophobic interaction at interdimer angle. Furthermore, our findings highlighted that the thermal unfolding of MS2 VLPs follows a sequential process involving particle destabilization, nucleic acid exposure/melting, and disassembly of VLP. This observation underscores the disruption of cooperative intersubunit interactions and protein–nucleic acid interactions, shedding light on the mechanism of heat-induced VLP disassembly.

VLPs offer an advantage for encapsulation of poorly soluble drugs, due to hydrophobic nature of interior core of capsid. MS2 VLPs have been utilized for encapsulation of diverse cargoes via conjugation or passive uptake. In the next part of this work, curcumin, a highly hydrophobic flavonoid molecule has been encapsulated in interior volume of WT and mutant MS2 VLPs. The results depicted the large interior volume of WT, encapsulating more number of curcumin molecules per particle as compared to small size mutant MS2 VLPs. Peptide attachment on the surface of mutant MS2 VLPs suggested for the enhanced surface accessibility of amino acid for conjugation and higher binding affinity to target cells. Together, our work established that mutant MS2 VLPs has potential to be fabricated or modified likewise WT MS2 VLPs. Furthermore, in vitro delivery efficiency of WT and mutant MS2 VLPs were characterized by targeting triple-negative breast cancer (MDA-MB-231) cells. Fabricated and drug formulated WT and mutant MS2 VLPs showed comparable results on cell targeting, biocompatibility, cytotoxicity and apoptosis assessment.

Moreover, mutant-tlyP1 MS2 VLPs depicts higher binding and apoptosis induction, given to higher uptake by cells due to small size of particles. In conclusion, present work characterized and established the engineered variant of MS2 VLP as a potential nanocarrier, in agreement with versatile application of WT MS2 VLPs.