World Academy of Science, Engineering and Technology
International Journal of Bioengineering and Life Sciences
Vol:11, No:04, 2017

Charged Amphiphilic Polypeptide Based Micelle Hydrogel Composite for Dual Drug Release

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Abstract : Synthetic hydrogels, with their unique properties such as porosity, strength, and swelling in aqueous environment, are being used in many fields from food additives to regenerative medicines, from diagnostic and pharmaceuticals to drug delivery systems (DDS). But, hydrogels also have some limitations in terms of homogeneity of drug distribution and quantity of loaded drugs. As an alternate, polymeric micelles are extensively used as DDS. With the ease of self-assembly, and distinct stability they remarkably improve the solubility of hydrophobic drugs. However, presently, combinational therapy is the need of time and so are systems which are capable of releasing more than one drug. And it is one of the major challenges towards DDS to control the release of each drug independently, which simple DDS cannot meet. In this work, we present an amphiphilic polypeptide based micelle hydrogel composite to study the dual drug release for wound healing purposes using Amphotericin B (AmpB) and Curcumin as model drugs. Firstly, two differently charged amphiphilic polypeptide chains were prepared namely, poly L-Lysine-b-poly phenyl alanine (PLL-PPA) and poly Glutamic acid-b-poly phenyl alanine (PGA-PPA) through ring opening polymerization of amino acid N-carboxyanhydride. These polymers readily self-assemble to form micelles with hydrophobic PPA block as core and hydrophilic PLL/PGA as shell with an average diameter of about 280nm. The thus formed micelles were loaded with the model drugs. The PLL-PPA micelle was loaded with curcumin and PGA-PPA was loaded with AmpB by dialysis method. Drug loaded micelles showed a slight increase in the mean diameter and were fairly stable in solution and lyophilized forms. For forming the micelles hydrogel composite, the drug loaded micelles were dissolved and were cross linked using genipin. Genipin uses the free –NH2 groups in the PLL-PPA micelles to form a hydrogel network with free PGA-PPA micelles trapped in between the 3D scaffold formed. Different composites were tested by changing the weight ratios of the both micelles and were seen to alter its resulting surface charge from positive to negative with increase in PGA-PPA ratio. The composites with high surface charge showed a burst release of drug in initial phase, were as the composites with relatively low net charge showed a sustained release. Thus the resultant surface charge of the composite can be tuned to tune its drug release profile. Also, while studying the degree of cross linking among the PLL-PPA particles for effect on dual drug release, it was seen that as the degree of crosslinking increases, an increase in the tendency to burst release the drug (AmpB) is seen in PGA-PPA particle, were as on the contrary the PLL-PPA particles showed a slower release of Curcumin with increasing the cross linking density. Thus, two different pharmacokinetic profile of drugs were seen by changing the cross linking degree. In conclusion, a unique charged amphiphilic polypeptide based micelle hydrogel composite for dual drug delivery. This composite can be finely tuned on the basis of need of drug release profiles by changing simple parameters such as composition, cross linking and pH.

Keywords : amphiphilic polypeptide, dual drug release, micelle hydrogel composite, tunable DDS
Conference Title : ICBE 2017 : International Conference on Biomaterials Engineering
Conference Location : Kyoto, Japan
Conference Dates : April 27-28, 2017