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Synthesis of a Hybrid of PEG-b-PCL and G1-PEA Dendrimer Based Six-Armed Star Polymer for Nano Delivery of Vancomycin

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Abstract : Treatment of infections is compromised by limitations of conventional dosage forms and drug resistance. Nanocarrier system is a strategy to overcome these challenges and improve therapy. Thus, the development of novel materials for drug delivery via nanocarriers is essential. The aim of the study was to synthesize a multi-arm polymer (6-mPEPEA) for enhanced activity of vancomycin (VM) against susceptible and resistant Staphylococcus aureus (MRSA). The synthesis steps of the star polymer followed reported procedures. The synthesized 6-mPEPEA was characterized by FTIR, ^{1}H and $^{13}CNMR$ and MTT assays. VM loaded micelles were prepared from 6-mPEPEA and characterized for size, polydispersity index (PI) and surface charge (ZP) (Dynamic Light Scattering), morphology by TEM, drug loading (UV Spectrophotometry), drug release (dialysis bag), in vitro and in vivo efficacy against sensitive and resistant S. aureus. 6-mPEPEA was synthesized, and its structure was confirmed. MTT assays confirmed its nontoxic nature with a high cell viability (77%-85%). Unimolecular spherical micelles were prepared. Size, PI, and ZP was 52.48 ± 2.6 nm, 0.103 ± 0.047, -7.3 ± 1.3 mV, respectively and drug loading was 62.24 ± 3.8%. There was a 91% drug release from VCM-6-mPEPEA after 72 hours. In vitro antibacterial test revealed that VM-6-mPEPEA had 8 and 16-fold greater activity against S. aureus and MRSA when compared to bare VM. Further investigations using flow cytometry showed that VM-6-mPEPEA had 99.5% killing rate of MRSA at the MIC concentration. In vivo antibacterial activity revealed that treatment with VM-6-mPEPEA had a 190 and a 15-fold reduction in the MRSA load in untreated and VM treated respectively. These findings confirmed the potential of 6-mPEPEA as a promising bio-degradable nanocarrier for antibiotic delivery to improve treatment of bacterial infections.

Keywords : biosafe, MRSA, nanocarrier, resistance, unimolecular-micelles
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