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Everolimus Loaded Polyvinyl Alcohol Microspheres for Sustained Drug Delivery in the Treatment of Subependymal Giant Cell Astrocytoma

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Abstract : This article aims to develop a sustained release formulation of microspheres containing the mTOR inhibitor Everolimus (EVR) using Polyvinyl alcohol (PVA) to enhance the bioavailability of the drug and to overcome poor solubility characteristics of Everolimus. This paper builds on recent work in the manufacture of microspheres using the sessile droplet technique by freezing the polymer-drug solution by suspending the droplets into pre-cooled ethanol vials immersed in liquid nitrogen. The spheres were subjected to 6 freezing cycles and 3 freezing cycles with thawing to obtain proper geometry, prevent aggregation, and achieve physical cross-linking. The prepared microspheres were characterised for surface morphology by SEM, where a 3-D porous structure was observed. The in vitro release studies showed a 62.17% release over 12.5 days, indicating a sustained release due to good encapsulation. This result is comparatively much more than the 49.06% release achieved within 4 hours from the solvent cast Everolimus film as a control with no freeze-thaw cycles performed. The solvent cast films were made in this work for comparison. A prolonged release of Everolimus using a polymer-based drug delivery system is essential to reach optimal therapeutic concentrations in treating SEGA tumours without systemic exposure. These results suggest that the combination of PVA and Everolimus via a rheological synergism enhanced the bioavailability of the hydrophobic drug Everolimus. Physical-chemical characterisation using DSC and FTIR analysis showed compatibility of the drug with the polymer, and the stability of the drug was maintained owing to the high molecular weight of the PVA. The obtained results indicate that the developed PVA/EVR microsphere is highly suitable as a potential drug delivery system with improved bioavailability in treating Subependymal Giant cell astrocytoma (SEGA).

Keywords : drug delivery system, everolimus, freeze-thaw cycles, polyvinyl alcohol
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