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Development of Drug Delivery Systems for Endoplasmic Reticulum Amino Peptidases Modulators Using Electrospinning

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Abstract : The administration of endoplasmic reticulum amino peptidases (ERAP1 or ERAP2) inhibitors can be used for therapeutic approaches against cancer and auto-immune diseases. However, one of the main shortcomings of drug delivery systems (DDS) is associated with the drug off-target distribution, which can lead to an increase in its side effects on the patient's body. To overcome such limitations, the encapsulation of four representative compounds of ERAP inhibitors into Polycaprolactone (PCL), Polyvinyl-alcohol (PVA), crosslinked PVA, and PVA with nanoparticles (liposomes) electrospun fibrous meshes is proposed as a safe and controlled drug release system. The use of electrospun fibrous meshes as a DDS allows efficient solvent evaporation giving limited time to the encapsulated drug to recrystallize, continuous delivery of the drug while the fibers degrade, prevention of initial burst release (sustained release), tunable dosages, and the encapsulation of other agents. This is possible due to the fibers' small diameters and resemblance to the extracellular matrix (confirmed by scanning electron microscopy results), high specific surface area, and good mechanical strength/stability. Furthermore, release studies conducted on PCL, PVA, crosslinked PVA, and PVA with nanoparticles (liposomes) electrospun fibrous meshes with each of the ERAP compounds encapsulated demonstrated that they were capable of releasing >60%, 50%, 40%, and 45% of the total ERAP concentration, respectively. Fibrous meshes with ERAP_E compound encapsulated achieved higher released concentrations (75.65%, 62.41%, 56.05%, and 65.39%, respectively). Toxicity studies of fibrous meshes with encapsulated compounds are currently being accessed in vitro, as well as pharmacokinetics and dynamics studies. The last step includes the implantation of the drug-loaded fibrous meshes in vivo.

Keywords : drug delivery, electrospinning, ERAP inhibitors, liposomes
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