Targeted Delivery of Throbolytic Agent, Reteplase, Using Shear Activated Nanotherapeutics and RGD Modified Peptides

Shokouh Arjmand¹, Payam Khazaeli², Parinaz Amiri Moghadam¹

¹-Student of Pharmacy, School of Pharmacy, Kerman University of Medical Sciences
²-Professor of pharmaceutics, School of Pharmacy and Pharmaceutical Research Center, Kerman University of Medical Sciences

Abstract: Thrombosis is one of the major causes of mortalities in developed countries and it plays a crucial role in the pathogenesis of atherosclerosis, venous thromboembolism, stroke and myocardial infarction. The significance of antithrombotics' adverse effects specially the risk of hemorrhage and many interactions which can be life threatening have circumscriptively limited the safe use of these agents. A number of lines of evidence have depicted that use of polymeric systems would remarkably circumvent the drawbacks of thrombolytic drugs and provide a promising area of research to ensue an effective dosage form for patients suffering from these diseases. Thereby, we make our minds up to design a study to check reteplase activity using shear activated nanotherapeutics (SANTS) as its carrier not only to enhance its half life but its specificity. RGD modified peptides are also used to augment reteplase activity by inhibiting glycoprotein IIb/IIIa and offer a way to deliver it targetedly. Due to the longer obtained half-life and its selectivity, it can be envisioned as a worth considering candidate for preventing thrombosis and its subsequent aftermaths. At first step we try to prepare SA-NT and test their machano-sensitivity. Pad-Pc-Pad vesicles were prepared by using rotary evaporation. To test the mechanical properties of the corresponding nanocontainers, we prepared LUVET, The liposomes contained 5(6)-carboxyfluorescein at a self-quenching concentration during encapsulation. When the dye is released from the liposome into the medium it dilutes, leading to fluorescence dequenching, and is therefore detectable using fluorescence spectroscopy. Afterward, we will try to load drug and evaluate the physico-chemical properties. In sum, we have addressed the question whether reteplase loaded in shear-activated nanotherapeutics can be used as a novel preventive thrombolytic agent. It should be pointed out that the results of this study would lead to a promising dosage form with fewer side effects and interactions, more patients' compliance and targeted delivery of reteplase which brings about its greater efficiency.

Keyword: Reteplase, Shear activated nanotherapeutics, RGD modified peptide, Thrombosis