GUEST EDITORIAL OPEN ACCESS

Targeted Thrombolytic Enzymes Delivery

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According to the literature, several years ago, nanobiotechnology has had a significant impact on anticancer drug delivery research, but it has also been felt in efforts to utilize gene delivery nanoscale drugs in several other illnesses[1]. Undoubtedly, cardiovascular disease is an important area that may benefit from the combination of new technologies and innovative treatment procedures[2].

Stroke (IS) and Myocardial Infarction (MI; induced by coronary artery thrombosis), both of which are associated with significant morbidities and ultimately mortality, may be distinguished by the presence of thrombosis as a characteristic feature[2]. The resumption of blood flow as a result of the rapid disintegration of a blood clot is a viable therapy option for a variety of thromboembolic illnesses. Since the late 1970s, fibrin-specific plasminogen activators such as single-chain urokinase-type plasminogen activator (scu-PA), tissue-type plasminogen activator (t-PA), and staphylokinase (Sak) have been widely used in clinics, even though a variety of different types of plasminogen activators (PAs) are already tested[1,2].

A blood clot typically known as a thrombus is mostly composed of fibrin (Factor Ia), in which platelets and erythrocytes are entangled. Indeed, fibrinolysis is a vital stage in hemostasis that is activated by a PA activating plasminogen, an inactive zymogen that catalyzes the process of clotting. Streptokinase is a first-generation thrombolytic enzyme that is produced by bacteria and coheres to circulating plasminogen in the bloodstream. The substrate (which is plasminogen) does not undergo such enzymatic dissociation, and the complex itself shows fibrinolytic activity, which is mediated by plasminogen conformational modification induced by streptokinase binding[3]. On the other hand, tissue-type plasminogen activator (tPA) and its analogs catalyze the conversion of plasminogen into a fibrinolytic enzyme known as plasmin, which is active in the presence of fibrin. Furthermore, tPA is a classic fibrin-mediated envoy, which means that when it attaches to the surface of a fibrin clot, its activity is multiplied by a factor of ten to twenty-five[4].

The intravascular delivery of thrombolytic medicines is required due to the small molecular sizes of the medications, resulting in systemic effects and the induction of the lytic state. Although the dose of tPA is higher than that encountered by a healthy organism, it is only partly provided (0.9 mg/kg for stroke, not more than 90 mg and100 mg for myocardial infarction) due to the rapid degradation of tPA upon delivery. Its blood lodging period is just a few minutes, as opposed to the newer type (Tenecteplase, TNKase®), which has a somewhat longer time to lodge blood. The mechanism of thrombolysis by PA, which involves the rapid enzymatic consumption of essential clotting components (such as Fibrinogen and Factor I), has the potential to produce major bleeding complications in certain patients. Thrombolytic drugs are medicines that might cause serious adverse effects in certain people. Therefore, tailored delivery approaches using nanocarriers are highly recommended[5].

The notion of targeted thrombolysis has been known for more than two decades. According to Dewerchin et al., had developed a single-chain urokinase (scuPA) and antiplatelet antibody bioconjugate was tested in a mouse model to provide proof-of-concept in a mouse model (in terms of bleeding time and clot lysis) [3]. When Liang and colleagues developed tPA and charge-modified anti-fibrin antibodies—a two-part system—in the late 1990s, they discovered that electrostatic couplings between the two parts could be undone by a basic amino acid peptide named protamine, and a therapeutic antagonist named heparin. This was followed by the development of a platelet-focused, electrostatic nanocomplex, which was induced by a therapeutic dose of heparin and has a significant affinity for the active platelet surface (glycoprotein IIIa/ IIb), by employing a peptide sequence of 14-dimers from the gamma-chain of fibrinogen[4].

Endogenous triggers such as thrombin gradients around thrombus were added in a prodrug form of tissue-type plasminogen activator (t-PA), which might be activated by their presence. Over the past ten years, there has also been a continuous growth in interest in studying particle nanocarriers combined with

targeting and release mechanisms for the delivery of thrombolytic medicines. Using a liposomal carrier containing the RGD peptide on the surface, Vaidya and colleagues were able to deliver streptokinase, which was activated by clot shear stresses. It seems that ultrasonic triggered nano-systems such as microbubbles and cationized tPA/ gelatin are a possibility. The last step involves the use of superparamagnetic nanoparticles to deliver thrombolytics to sites in the body[5]. However, the plethora of precedents provided above is only a small selection; readers are encouraged to read recent extensive reviews written by Zenych et al. and Hassanpour et al., to gain a better understanding of thrombolytic medications and nano-based drug delivery techniques for thrombolytics[6,7].

There is no question that interest in this subject is growing and becoming more intense. These systems, like other specialized nano-systems, are, despite their simplicity, difficult to operate. It is hoped that soon, these targeted-based drug delivery systems will overcome the challenges, that pharmaceutical products are facing now, therefore enhancing treatment outcomes for patients suffering from thromboembolic disorders[6].

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