Thrombus-targeted microbubbles for thrombosis diagnosis

Nanqian Zhou[1,†], Yuzhen Zhao[2,†], Ming Wu[1], Xiao Ding[1], Jianjun Yuan[1] and Haohui Zhu[1,*]

[1]Department of Ultrasonography, Henan Provincial People's Hospital, Zhengzhou 450 003, China

[2]School of Pharmaceutical Sciences, Zhengzhou University, Zhengzhou 450 001, China

Thrombosis remains a significant cause of morbidity and mortality in many cardiovascular and cerebrovascular diseases, and thrombolysis stands out as a promising treatment method. However, the slow diffusion of thrombolytic agents within thrombi leads to delayed recanalisation. Additionally, these agents face limitations in clinical application due to their short circulation time and the risk of hemorrhagic side effects. To address these challenges, we have developed an innovative thrombolytic drug delivery platform for integrated diagnosis and treatment. This platform utilises microbubbles (MB) conjugated with RGDS (Arg-Gly-Asp-Ser) peptide (RGDS-MB). The RGDS-MB system targets thrombi through interaction with αIIbβ3 in activated platelets, ensuring accurate thrombus site diagnosis. These thrombus-targeted MB serve as promising carriers for efficient drug delivery, offering a potential platform for the development of thrombolytic nanomedicines with prospects for clinical translation.

Keywords: Drug delivery, microbubbles, platelets, thrombotic disease, thrombus-targeted

from potentially life-saving interventions[6,7]. Therefore, developing safer and more efficient thrombolytic strategies remains a critical clinical priority.

To address these challenges, targeted and controlled delivery of thrombolytic drugs has emerged as a promising solution, aiming to enhance drug bioavailability, facilitate targeted delivery, and accelerate clot lysis[8,9]. Thrombosis, a physiological process characterised by platelet adhesion, activation, and fibrin formation in response to vascular injury or endothelial cell damage, culminates in blood clot formation[10]. RGDS (Arg-Gly-Asp-Ser) peptides, with their bioactive sequences, selectively bind to platelet receptors like αIIbβ3 integrin[11,12], presenting a compelling strategy for targeted therapy of thrombotic drugs. This targeted approach holds immense potential in the realm of thrombosis management. Additionally, the utilisation of ultrasound microbubbles (MB) for thrombus diagnosis has revolutionised medical imaging[13,14]. These minute bubbles, typically gas-filled, enhance contrast in ultrasound scans, simplifying blood clot detection and monitoring[15,16]. This non-invasive method not only enhances patient safety but also allows real-time visualisation, enabling precise diagnoses and treatment decisions by healthcare professionals.

In the present study, we have functionalised ultrasound