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Supporting Information

DHDMIQK(KAP): A novel nano-delivery system of dihydroxyl-

tetrahydro-isoquinoline-3-carboxylic acid and KPAK towards the

thrombus

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Experimental section

1. ¹HNMR spectrum of DHDMIQK(KAP)





2. ¹³CNMR spectrum of DHDMIQK(KAP)



Fig. S2 ¹³CNMR spectrum of DHDMIQK(KAP).





Fig. S3 COSY 2D NMR spectrum of DHDMIQK(KAP).

4. NOESY 2D ¹HNMR of DHDMIQK(KAP)



Fig. S4 NOESY 2D ¹HNMR of DHDMIQK(KAP).

5. HPLC purity of DHDMIQK(KAP)

A Waters 2695 HPLC system with a Waters 2996 PDA was used. The sample was analyzed on a Waters XTerra C₁₈ reversed-phase column (column 4.6×150 mm, 3.5 µm; Waters Limited, Hertfordshire, UK). Onto the column, 5 µL of a solution of DHDMIQK(KAP) in acetonitrile was injected. The mobile phase was acetonitrile containing trifluoroacetic acid (0.1%). The flow rate was 1 mL/minute. The UV detector was set to a scanning range of 200-400 nm, and a wavelength of 254 nm was used to monitor DHDMIQK(KAP), of which the retention time was 5.366 minutes and the purity was 98.93%.



Fig. S5 HPLC purity of DHDMIQK(KAP).

6. ESI(+)/FT-MS spectrum of DHDMIQK(KAP)

The FT-MS spectrum of DHDMIQK(KAP) in water are shown in Fig. S6A which gives a positive ion peak of $[1/2M + H]^+$ at 1986.17767, the mass of a hexamer plus H, a positive ion peak of $[1/2M + H]^+$ at 1654.47219, the mass of a pentamer plus H, a positive ion peak of $[M + H]^+$ at 1985.18013, the mass of a trimer plus H, a positive ion peak of $[M + H]^+$ at 1323.78001, the mass of a dimer plus H, a positive ion peak of $[M + H]^+$ at 1323.78001, the mass of a dimer plus H, a positive ion peak of $[M + H]^+$ at 662.38787, the mass of a monomer plus H. Fig. 6B is a qCID spectrum, the pentamer is the fragmentation product of the pentamer. Fig. 6C is a qCID spectrum, the monomer is the fragmentation product of the dimer.





Fig. S6 ESI(+)/FT-MS full scan spectrum (A) and qCID ion scan spectrum (B-D).

7. Biodistribution of DHDMIQK(KAP)





Fig. S7 FT-MS spectra of the extracts of the thrombus and blood of DHDMIQK(KAP) treated rats. (A) FT-MS spectrum of the extract of the thrombus and the amplified ion peak of DHDMIQK(KAP)and ion peak of KPAK; (B) FT-MS spectrum of the extract of the thrombus and the amplified anion peak of 6,7-dihydroxy-1,1-dimethyl-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid.