

Supporting Information:

Calculation of the number of free carboxylic acid groups per USPIO:

The numbers of carboxylic groups coated on an USPIO:

According to the TGA analysis, the weight ratio of PAA to USPIOs is 1.611, which means one gram of USPIOs could be coated by 1.611 gram of PAA.

The mass of an USPIO with 4.5 nm size can be calculated according to the following equations:

$$m = \rho V ; \quad V = (4/3) \pi \times r^3$$

Where ρ is the density of Fe_3O_4 (5.2 g/cm^3), V is the volume of an USPIO and r is the radius of USPIO.

$$\begin{aligned} m &= 5.2 \times (4/3) \times 3.14 \times (4.5/2)^3 \times 10^{-21} \\ &= 2.48 \times 10^{-19} \text{ (g)} \end{aligned}$$

The numbers of USPIOs (N_{USPIOs}) with mass of 1g: $N_{\text{USPIOs}} = 1/2.48 \times 10^{-19}$

The numbers of PAA (MW 5000) with mass of 1.611 g:

$$N_{\text{PAA}} = (1.611/5000) \times 6.02 \times 10^{23}$$

Therefore, the number of PAA per USPIO is: $N_{\text{PAA}}/N_{\text{USPIOs}} = 48$

The molecular weight of the repeat unit of PAA (CHCOOH-CH_2) is 72.

Therefore, the number of carboxylic groups in one PAA (MW 5000) molecule is determined to be 69.

The numbers of carboxylic groups per USPIO is determined to be 3312.

Free carboxylic groups per USPIO:

According to the titration curve, the amount of NaOH used for neutralizing protons in carboxylic groups in PAA@USPIOs can be calculated:

$$(x_2 - x_1) \times 0.1 = 0.06368 \text{ (mmol)}$$

The sample volume for titration is 0.4 mL, thus the concentration of free carboxylic groups on PAA@USPIOs is around 0.16 M. The number of free carboxylic groups in one liter of sample is calculated to be $0.16 \times 6.02 \times 10^{23}$

The USPIO concentration for the titration is 8.72 mg/mL, therefore the number of USPIOs in one liter of the sample can also be determined:

$$8.72 / (2.48 \times 10^{-19})$$

Therefore the free carboxylic groups per USPIO are determined to be 2739.



Figure S1 Photograph of PAA@USPIOs produced in one batch

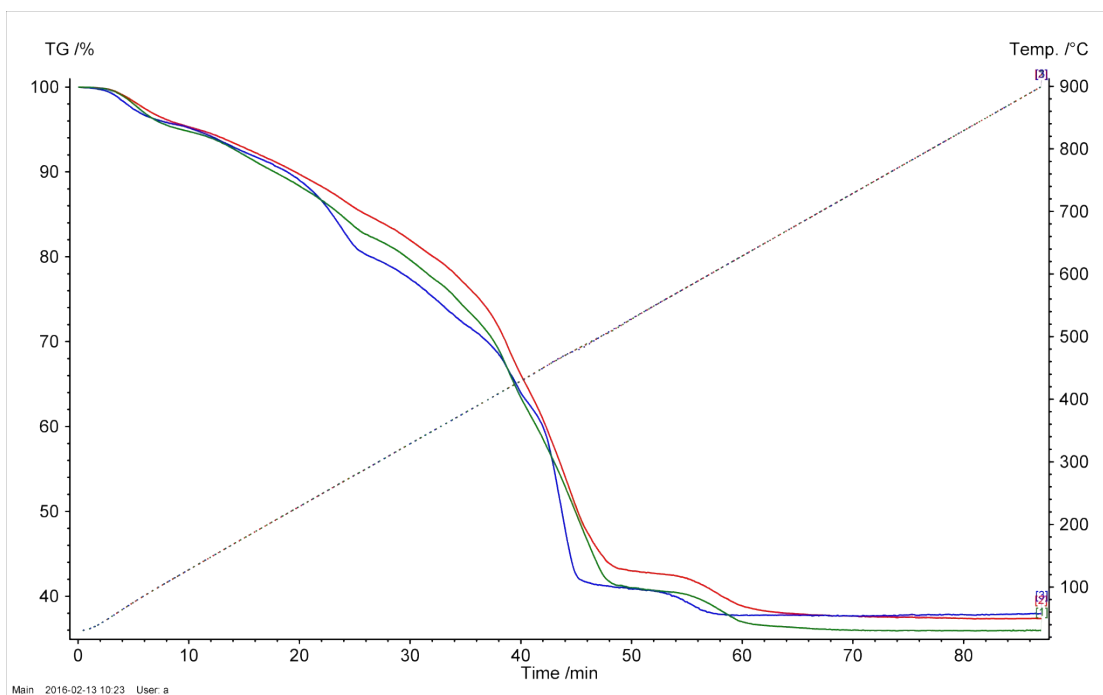


Figure S2 Typical TGA curve of PAA@USPIOs

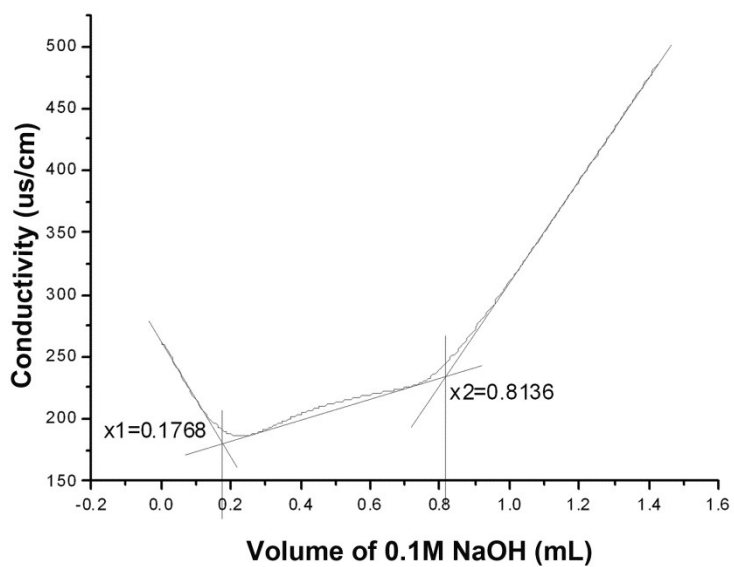


Figure S3 Auto acid-base titration curve PAA@USPIOs

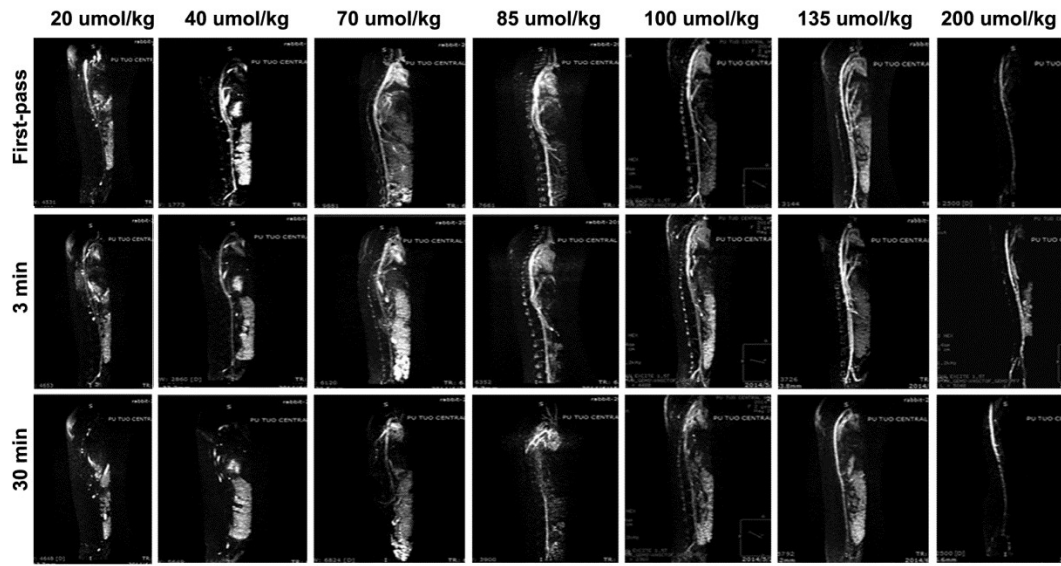


Figure S4 Dose optimization of PAA@USPIOs for MRA of rabbits.

Table 1 Hematology analysis

Test	unit	control	0.73 mmol/kg	1.46 mmol/kg	2.92 mmol/kg
Hematological					
RED	$\times 10^9/L$	8.88 \pm 0.33	9.38 \pm 0.33	9.06 \pm 0.54	10.27 \pm 0.21
WBC	$\times 10^{12}/L$	6.60 \pm 1.70	5.05 \pm 1.06	12.78 \pm 0.31 \uparrow	17.4 \pm 0.31 \uparrow
HGB	g/L	133 \pm 2.82	136 \pm 1.41	130.5 \pm 2.38	136 \pm 3.61
MCV	fL	45	44 \pm 1.41	43.75 \pm 0.96	44.33 \pm 1.53
MCH	pg	14.95 \pm 0.91	14.45 \pm 0.35	14.85 \pm 0.29	15.07 \pm 0.57
MCHC	g/L	334.50 \pm 2.12	328.50 \pm 0.71	338.75 \pm 2.22	338 \pm 0.71
LY	%	80.9 \pm 1.27	87.8 \pm 4.10	78.2 \pm 0.5	83.95 \pm 1.34
NE	%	12.7 \pm 1.27	12.4 \pm 0.27	19.5 \pm 0.54 \uparrow	16.9 \pm 1.76 \uparrow
PLT	$\times 10^9/L$	724 \pm 84	856 \pm 192	768 \pm 73	688 \pm 171

Table 2 Blood biochemical assay

Test	unit	control	0.73 mmol/kg	1.46 mmol/kg	2.92 mmol/kg
ALT	U/L	41.0 \pm 6.4	87.1 \pm 2.1 \uparrow	106 \pm 3.0 \uparrow	261.2 \pm 4.4 \uparrow
ALP	U/L	282.5 \pm 7.78	169.7 \pm 6.9 \downarrow	186.2 \pm 6.3 \downarrow	154.6 \pm 1.9 \downarrow
ALB	g/L	38.5 \pm 1.8	34.2 \pm 1.1 \downarrow	34.9 \pm 0.8 \downarrow	39.1 \pm 0.6 \uparrow
AST	U/L	101.5 \pm 12.0	154.5 \pm 2.0 \uparrow	288.5 \pm 10.0 \uparrow	320.5 \pm 7.6 \uparrow
BUN	mmol/L	7.69 \pm 0.06	6.12 \pm 0.10 \downarrow	6.07 \pm 1.0 \downarrow	7.01 \pm 0.03 \downarrow
CRE	mmol/L	10.50 \pm 0.70	10.7 \pm 0.89	8.11 \pm 0.52 \downarrow	8.26 \pm 1.11 \downarrow