

A cyanoacrylate/triethyl citrate/nanosilica-based closure glue with wet-adhesion capability for treatment of superficial varicose veins

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Table S1 The adhesive capability of FAL-006 and Butyl-CA

Group	Shear tension strength (kPa)	T-peel strength (N cm ⁻¹)	Tension Strength (MPa)	Wound closure strength (N)
FAL-006	277.2 ± 52 kPa	7.16±2	13.44±0.8	15.6±5
Butyl-CA	301.5 ± 35 kPa	6.84±2.4	10.4±2.88	19±4

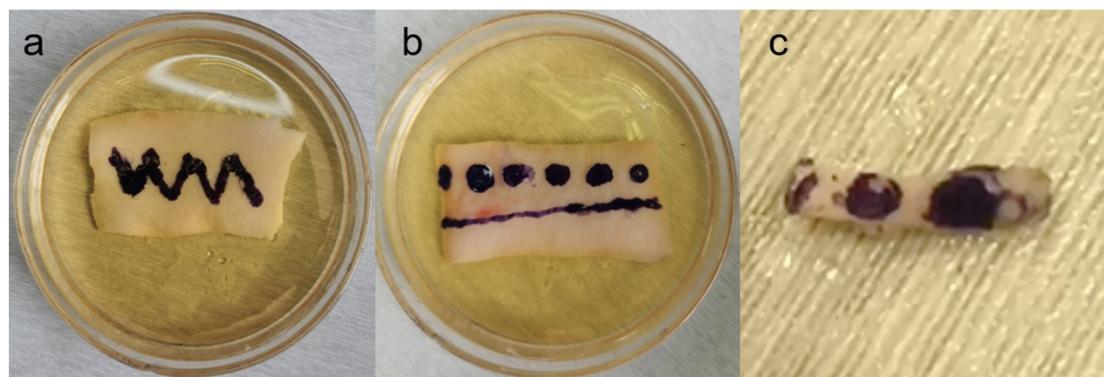


Fig.S1 Strong underwater adhesion to tissue in serum. (a) Underwater writability on pig skin, (b) underwater sustainable extrusion in pig skin, (c) Extrusion moulding and localization of blood vessels by FAL-006 in serum

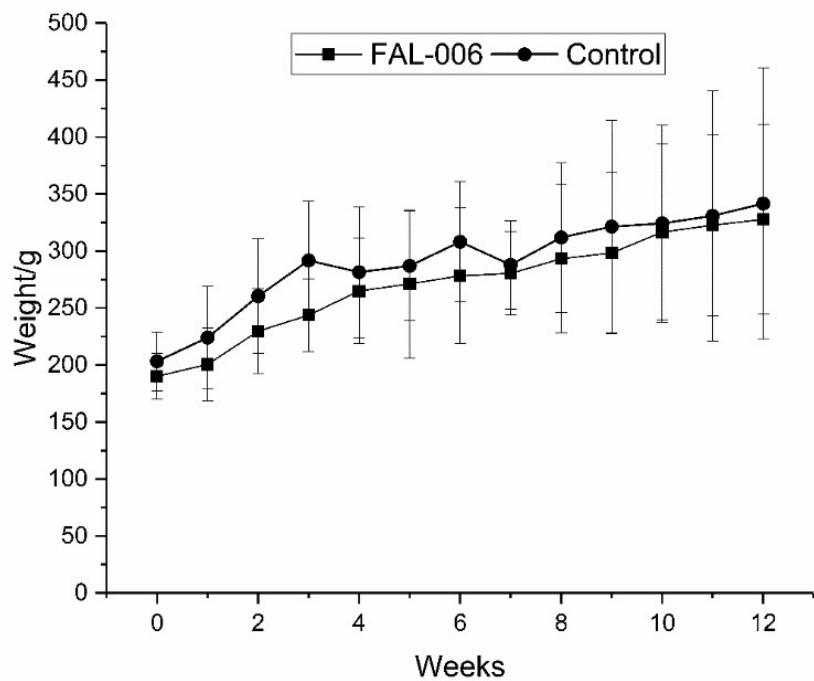


Fig.S1 Body weights of rats in the sub-chronic toxicity test

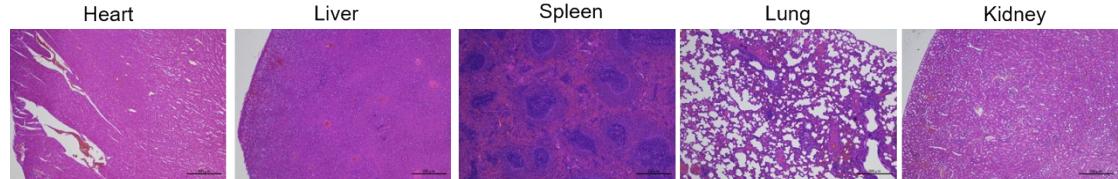


Fig.S2 Pathological analysis of the rats half a month after injection with FAL-006. The heart, liver, spleen, lung, kidney and skin were stained by H&E. Bar scale=500 μm .

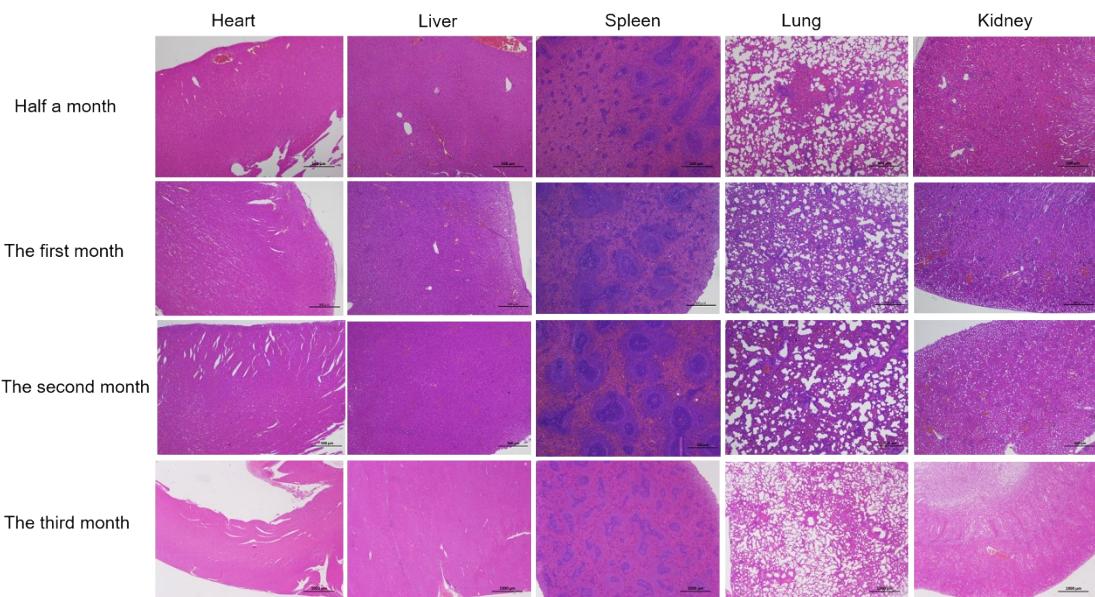


Fig.S3 Pathological analysis of the rats after injection with FAL-006. The pictures were taken at half a month, 1 month, 2 months, and 3 months after injection. Their hearts, livers, spleens, lungs, kidneys and skin were stained by H&E. Bar scale=500/1000 μm .

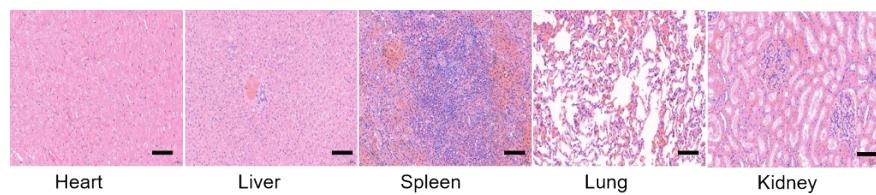


Fig.S5 Closure test of lower extremity vein of sheep with FAL-006. Their hearts, livers, spleens, lungs and kidneys were stained by H&E. Bar scale=500 μm .

Table S2 The serum index of rats in the acute toxicity test

Serum index	Experimental group	Control
AST (U/L)	99.99±13.23	120.61±18.25
γ-GT (U/L)	3.71±0.45	4.38±1.22
ALP (U/L)	269.02±113.21	280.12±90.16
BUN (mg/dL)	16.15±2.35	17.17±5.06
CR (μmol/L)	34.89±7.66	50.78±8.71
TG (mmol/L)	1.58±0.24	1.38±1.05
TC (mmol/L)	3.09±0.49	2.11±4.02
GLU (mmol/L)	7.19±1.25	11.05±1.23
TP (g/L)	69.99±4.12	70.68±10.55
Na (mmol/ L)	158.54±10.03	143.69±0.87
Cl (mmol/l)	110.35±2.75	102.11±2.57
Ca (mmol/ L)	2.62±0.34	2.51±0.26
P (mmol/ L)	3.35±0.41	3.18±0.91
K (mmol/ L)	4.91±0.65	7.13±1.08

Table S3 The serum index of rats in the sub-chronic toxicity test

Serum index	Half a month	First month	Second month	Third month	Control
GT (U/L)	4.16±1.99	3.23±1.20	4.38±0.36	3.73±0.85	4.38±1.22
ALB (g/L)	34.97±3.06	38.47±2.23	39.85±2.07	35.67±0.86	25.16±8.31
ALP (U/L)	239.29±52.17	267.76±133.46	266.22±15.92	270.15±28.92	280.12±90.16
BUN (mg/dL)	21.89±1.35	16.43±1.45	17.38±1.38	23.84±5.62	17.17±5.06
TG (mmol/L)	1.53±0.30	1.54±0.05	2.01±0.34	2.16±0.74	1.38±1.05
TC (mmol/L)	3.19±0.19	3.22±0.38	3.47±0.65	2.82±0.37	3.11±3.02
GLU (mmol/L)	6.29±1.32	7.62±1.17	6.40±0.46	5.37±0.38	11.05±1.23
TP (g/L)	70.88±4.61	77.37±6.87	79.12±4.21	73.64±3.23	70.68±10.55
Na (mmol/L)	123.22±1.01	163.23±0.52	145.30±1.27	135.51±14.76	143.69±0.87
Cl (mmol/L)	127.09±3.41	106.59±1.02	113.07±1.83	109.73±0.43	102.11±2.57
Ca (mmol/L)	2.37±0.08	2.52±0.06	2.10±0.23	2.26±0.35	2.51±0.26
P (mmol/L)	3.47±0.20	2.66±0.26	2.20±0.16	2.75±0.39	3.18±0.91
K (mmol/L)	7.54±1.35	4.36±0.33	5.81±0.29	3.53±0.23	7.13±1.08

Table S4 The results of skin irritation induced by FAL-006 in rabbits

Table S5 The results of skin sensitization test induced by FAL-006 in guinea pigs

Animal number	Normal saline extract				Cottonseed oil extract			
	FAL-006		control		FAL-006		control	
	24h	48h	24h	48h	24h	48h	24h	48h
score	1	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0
	3	0	0	0	0	0	0	0
	4	0	0	0	0	0	0	0
	5	0	0	0	0	0	0	0
	6	0	0	0	0	0	0	0
	7	0	0	0	0	0	0	0
	8	0	0	0	0	0	0	0
Incidence of positive excitation results (%)								
		0		0		0		0

Table S6 The results of Intracutaneous irritation test induced by FAL-006 in rabbits

Time	Animal number	Normal saline extract				Cottonseed oil extract			
		FAL-006		Control		FAL-006		Control	
		erythema	edema	erythema	edema	erythema	edema	erythema	edema
24h	1#	0	0	0	0	0	0	0	0
	2#	0	0	0	0	0	0	0	0
48h	1#	0	0	0	0	0	0	0	0
	2#	0	0	0	0	0	0	0	0
72h	1#	0	0	0	0	0	0	0	0
	2#	0	0	0	0	0	0	0	0
total	1#	0		0		0		0	
score	2#	0		0		0		0	

Table S7 The blood routine examination of sheep before and after surgery

Blood routine index	Before surgery	After surgery	Normal range
WBC ($10^9/L$)	7.96	7.15	5.80~25.00
Neu # ($10^9/L$)	4.38	2.91	2.12~10.10
Lym # ($10^9/L$)	2.88	3.45	3.12~22.10
Mon # ($10^9/L$)	0.09	0.1	0.00~1.42
Eos # ($10^9/L$)	0.61	0.69	0.00~1.32
Bas # ($10^9/L$)	0	0	0.00~0.35
Neu (%)	0.551	0.406	0.130~0.580
Lym (%)	0.361	0.482	0.350~0.830
Mon (%)	0.012	0.014	0.000~0.110
Eos (%)	0.076	H 0.098	0.000~0.080
Bas (%)	0	0	0.000~0.025
RBC ($10^{12}/L$)	14.4	16.91	10.00~21.00
HGB (g/L)	84	99	62~135
HCT (%)	0.238	0.295	0.190~0.360
MCV (fL)	16.5	17.5	13.0~23.0
MCH (pg)	5.8	5.3	4.2~7.8
MCHC (g/L)	353	364	300~380
RDW-CV (%)	0.268	0.251	0.180~0.300
RDW-SD (fL)	19	18.6	12.1~23.1

Table S8 The serum index of sheep before and after surgery

The serum index	Before surgery	After surgery
ALT (U/L)	38.472	31.394
AST (U/L)	144.181	129.389
ALB (g/L)	31.51	36.940
UREA (mmol/L)	11.5	8.215
CREA (μ mol/L)	77.923	57.644
γ -GT (U/L)	48.718	68.847
DBIL (umol/L)	9.84	5.606
TBIL (umol/L)	13.402	9.595
ALP (U/L)	122.856	143.657
UA (umol/L)	86.08	69.928
TBA (umol/L)	4.579	3.586