

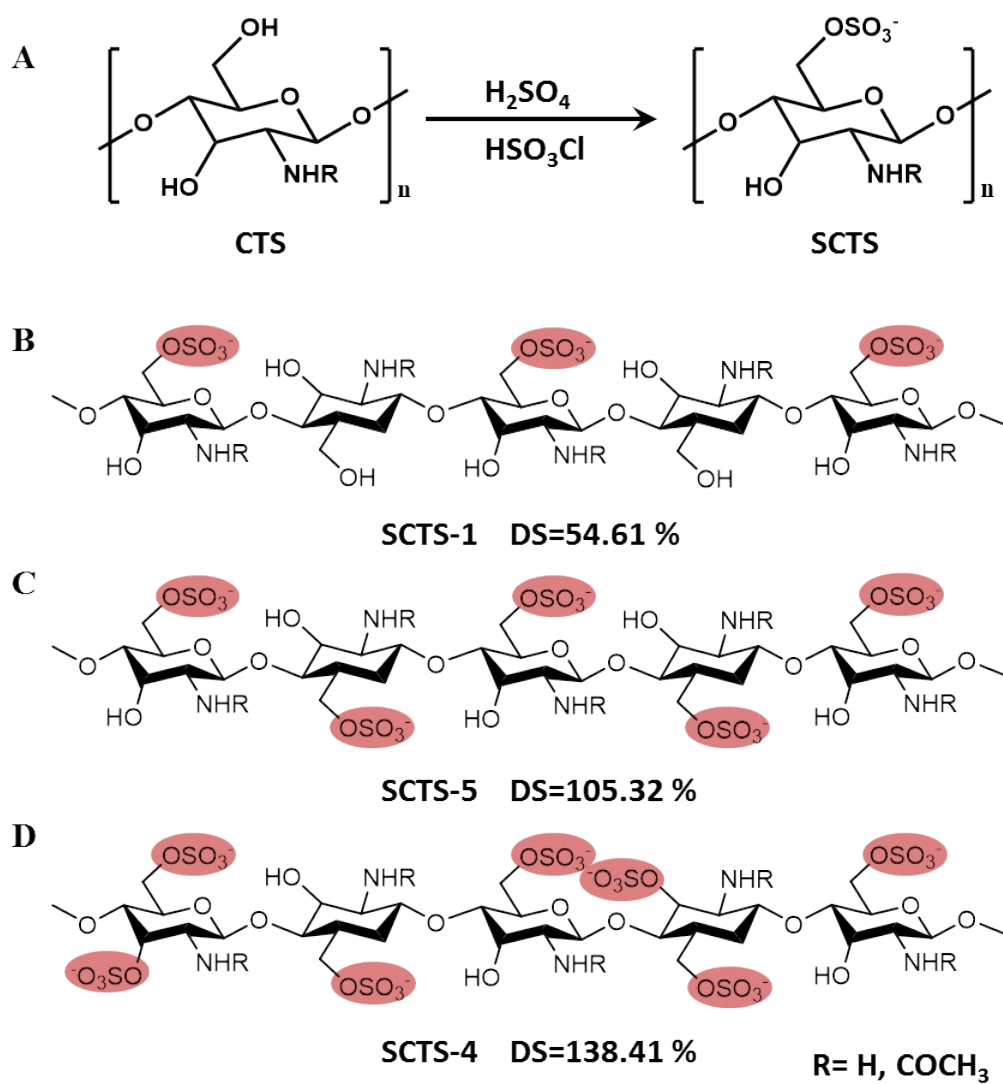
Chitosan Sulfate Inhibits Angiogenesis via Blocking VEGF/VEGFR2 Pathway and Suppress Tumor Growth *in Vivo*

Yingying Li ¹, Wei Wang ^{*1}, Yapei Zhang ¹, Xinyu Wang ¹, Xuefeng Gao ¹, Zhi Yuan

^{*1,2}, and Yu Li ¹

¹ Key Laboratory of Functional Polymer Materials of Ministry of Education, Institute
of Polymer Chemistry, College of Chemistry, Nankai University, Tianjin 300071,
China

² Collaborative Innovation Center of Chemical Science and Engineering (Tianjin),
Tianjin 300071, China



Scheme S1. (A) The synthetic route of SCTS. Structures of (B) SCTS-1 (DS= 54.61%), (C) SCTS-5 (DS= 105.32%), and (D) SCTS-4 (DS= 138.41%).

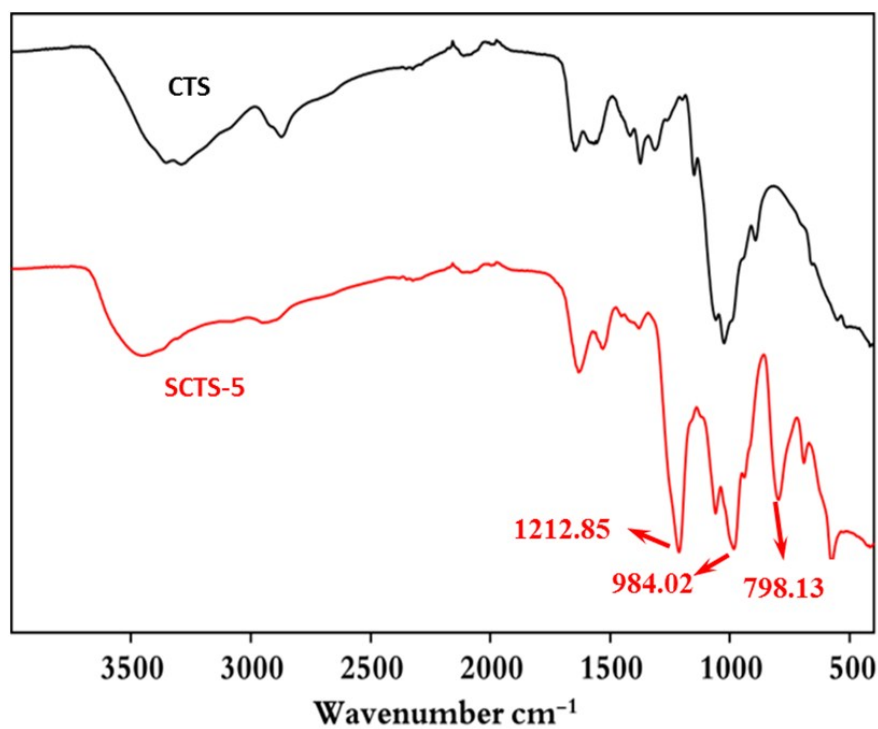


Figure S1. FTIR spectra of CTS and SCTS-5.

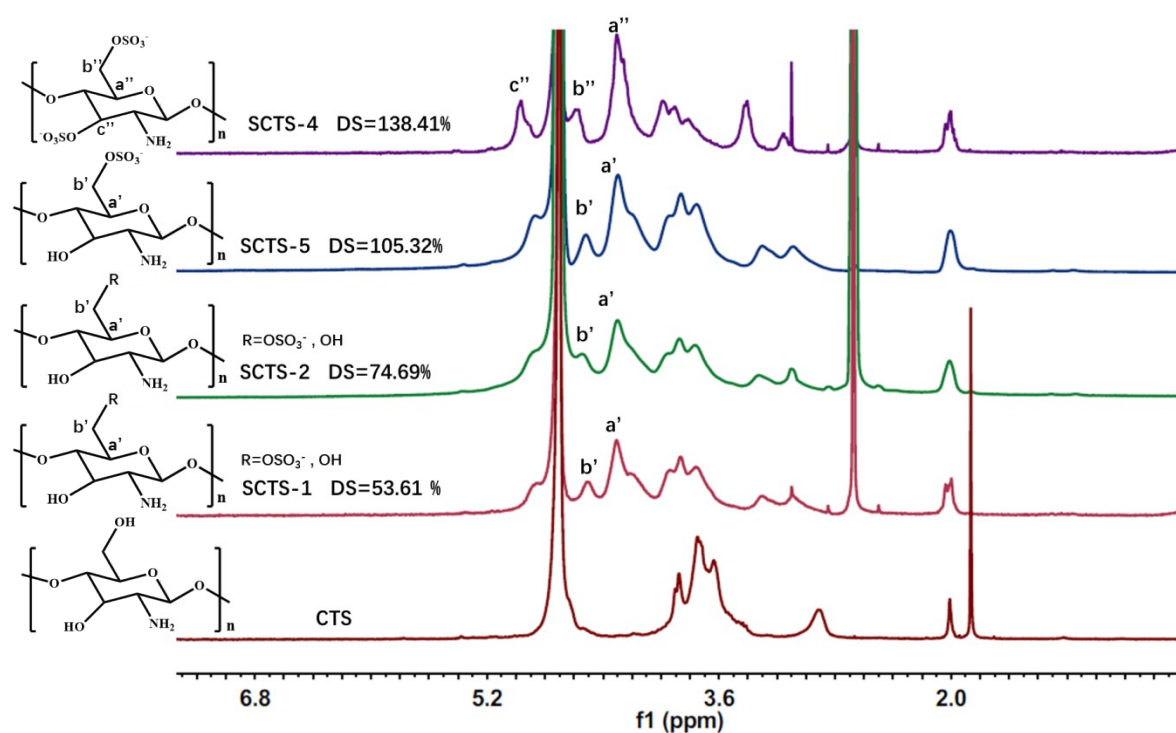


Figure S2. ^1H NMR spectra of the CTS, SCTS-1, SCTS-2, SCTS-4 and SCTS-5.

Table S1. The molecular weight and the DS of SCTS prepared in different reaction conditions

Sample	Sulfonated time (min)	DS (%)	Degradation time (min)	H ₂ O ₂ concentration (wt%)	M _w (×10 ⁴)	PDI
SCTS-1	60	53.61	180	1.5	1.04	1.173
SCTS-2	180	74.68	150	1.5	1.01	1.233
SCTS-3	300	98.71	90	1.5	0.95	1.326
SCTS-4	420	138.41	60	1.5	0.93	1.123
SCTS-5	300	105.32	150	2.5	0.24	1.271
SCTS-6	300	103.67	120	2	0.67	1.097
SCTS-7	300	95.8	60	1	1.38	1.215

DS defined as the number of –SO₃ - groups per 100 glucosamine units of chitosan.

The degradation of chitosan was performed at a temperature of 50°C.

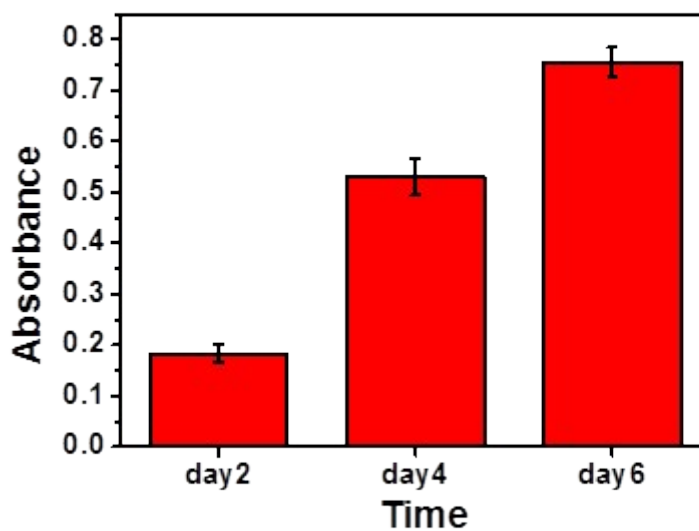


Figure S3. The absorbance of control group in the HUVEC proliferation test at 2, 4 and 6 days

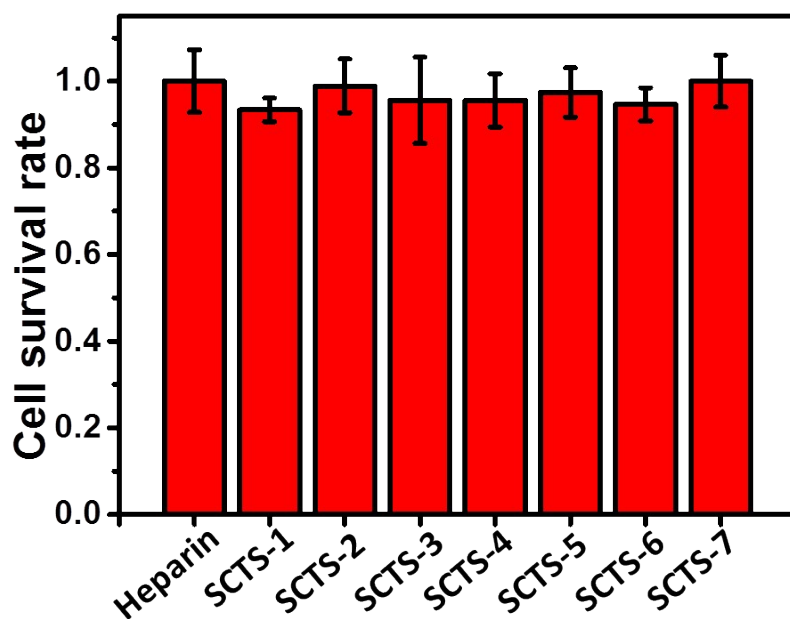


Figure S4. Cell survival rate of HUVEC after co-cultured with SCTS for 24 h

Table S2. Influence of SCTS-5 on the clotting time and bleeding time of mice in vivo

sample	clotting time (min)	bleeding time (min)
control	1.55±0.25	37.50±4.62
SCTS-7	1.80±0.42	46.00±8.21
Heparin	>10	>60