



() -

*

pH= /

()

A₁

A₁

)

/

.()

(Clark)

.() (

IV I

.()

.()

.()

.()

.()

-

.()

.

.

()

I

-

.

-

Sprague-Dawely

.()

% /

.

.()

.()

Carcharhinus sorrah

-

)

.

/		/	
(A ₀)		(	
- /		-	
	pH	pH- /	
NaCl			
		()	
		xg	
(BSA)			
()			
(SDS-PAGE)			
SDS -	/ cm)	Q-Sepharose FF	
()		Tris-HCl	(×
R-250		pH- /	
(Lohman)			
		NaCl	
-			
()	%	Sp-Sepharose FF	
		(× / cm)	
/		pH- /	
()			

(Blinded observer method)

() -

B A

(+++)

(+)

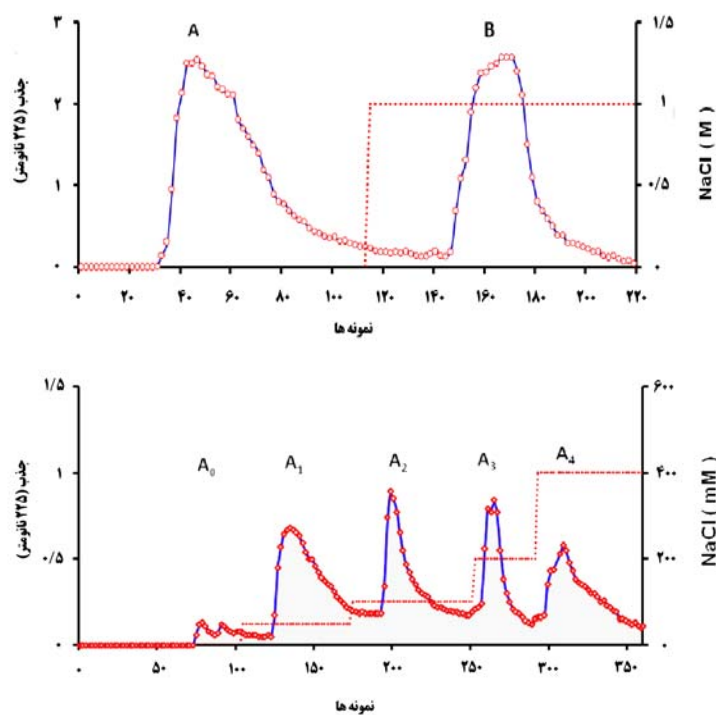
(±)

pH= /

(P < /)

pH= / /

()



(-◇-)

(...) NaCl

pH=

pH= /

Q-Sepharose (A)

A Sp-Sepharose (B)

(-◇-)

(...) NaCl

/

/

 (A_1)

B A

 (A_1)

B A

 $()$

A

 (Rat)

B

)

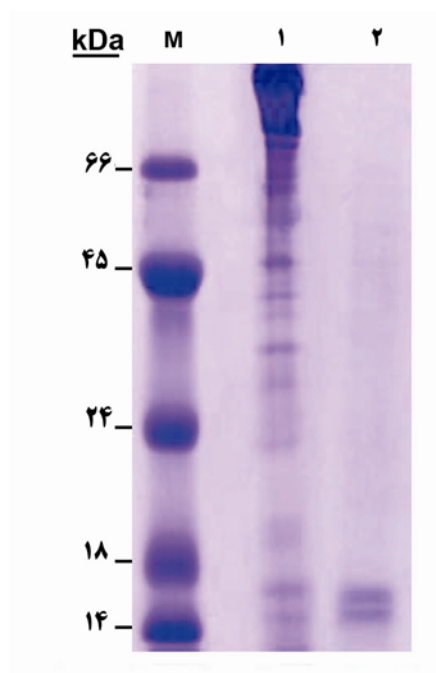
 $(A$

Sp-Sepharose

 (B_1) $()$ A_1

A

 $()$ $()$ A_1



SDS-PAGE

M: R 250

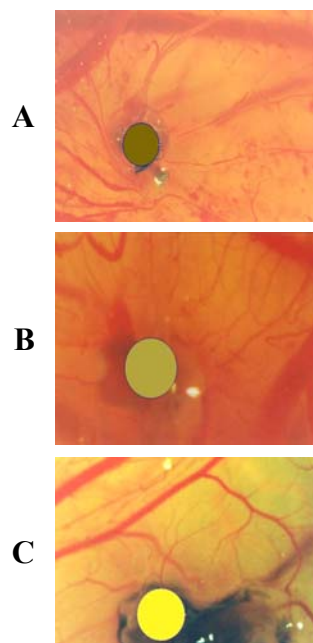
A

.A₀

.()

.()

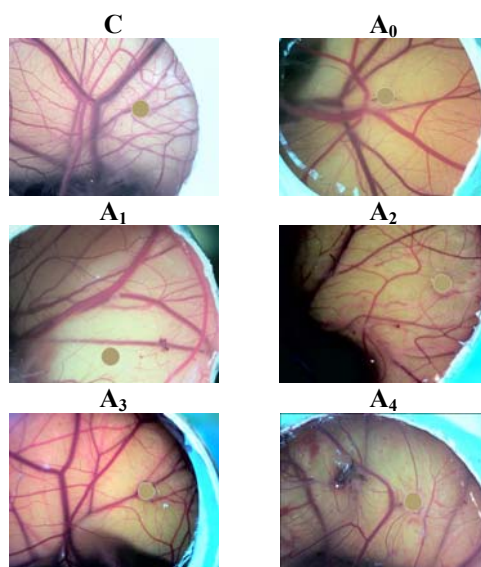
.()



B A :

;B A.

; C.



A₄ A₃ A₂ A₁ A₀ :

.()

Q-Sepharose

.(-)

SDS-

A_1 A

(A B)

A_1

PAGE

.(A_1)

A

.()

-

(Sheu)

(A)

(Wong)

(Liang)

.($P < /$)

A

pH

.()

A

)

.() (

A

Sp-Sepharose

(A_0 - A_4)

.(B)

.($P < /$)

A_1

References:

1. Clark ER, Clark EL. Microscopic observations on the growth of blood capillaries in the living mammal. *Am J Anat* 1939;64: 251-301.
2. Egginton S, Gerritsen M. Lumen formation: in vivo versus in vitro observations. *Microcirculation* 2003;10:45-61.
3. Pepper MS. Manipulating angiogenesis. From basic science to the bedside. *Arterioscler Thromb Vasc Biol* 1997;17:605-19.
4. Mahadevan V, Hart IR. Metastasis and angiogenesis. *Acta Oncol* 1990; 29: 97-103.
5. Lane IW, Comac L. *Sharks Don't Get Cancer*. 1st ed. New York, USA: Avery Pub Group, 1992, 1-192.
6. Brem H, Folkman J. Inhibition of tumor angiogenesis mediated by cartilage. *J Exp Med* 1975;141(2):427-39.
7. Leitner SP, Rothkopf MM, Haverstick DD, et al. Two phase II studies of oral dry shark cartilage powder (SCP) in patients with either metastatic breast or prostate cancer refractory to standard treatment. *Amer Soc Clin Oncol* 1998;17:A240.
8. Hunt TJ, Connelly JF. Shark cartilage for cancer treatment. *Am J Health Syst Pharm* 1995; 52:1756, 60.
9. Spielburg CA, Schuck JM. Novel glycoproteins from bovine cartilage. United State Patent (USP) 1981; No: 4, 243, 582.
10. Cassileth BR. Shark and bovine cartilage therapies. In: *The Alternative Medicine Handbook: The Complete Reference Guide to Alternative and Complementary Therapies*. New York, USA: WW Norton & Company, 1998; 197- 200.
11. Harshbarger JC, Ostrander GK. Cancer in sharks, skates, rays, and other lower fishes. *Proceedings of the American Association for Cancer Research*; 1-5 April 2000; San Francisco, CA, USA, 41: A4848.
12. Saul G. Shark cartilage therapy against cancer. *Nutr Health Forum*. January/February 1997; 14:1-5.
13. Elsdale T, Bard J. Collagen substrata for studies on cell behavior. *J Cell Biol* 1972;54:626-37.
14. Bolis S, Handley CJ, Comper WD. Passive loss of proteoglycan from articular cartilage explants. *Biochim Biophys Acta* 1989;993: 157-67.
15. Markwell MA, Haas SM, Tolbert NE, et al. Protein determination in membrane and lipoprotein samples: manual and automated procedures. *Methods Enzymol* 1981;72:296-303.
16. Laemmli UK. Cleavage of structural proteins during the assembly of the head of bacteriophage T4. *Nature* 1970;227:680-5.
17. Crum R, Szabo S, Folkman J. A new class of steroids inhibits angiogenesis in the presence of heparin or a heparin fragment. *Science* 1985;230:1375-8.
18. Malinda KM, Nomizu M, Chung M, et al. Identification of laminin alpha1 and beta1 chain peptides active for endothelial cell adhesion, tube formation, and aortic sprouting. *Faseb J* 1999;13:53-62.
19. Lane IW, Comac L. *Sharks don't get cancer*. Avery Publishing Group, Inc, 1992.
20. Liu N, Lapcevich RK, Underhill CB, et al. Metastatin: a hyaluronan-binding complex from cartilage that inhibits tumor growth. *Cancer res* 2001;61:1022-8.
21. Evans W, Latreille J, Batist G, et al. AE-941, an inhibitor of angiogenesis: Rationale for development in combination with induction chemotherapy/ radiotherapy in patients with non small cell lung cancer (NSCLC). *Proceedings of the American Society of Clinical Oncology*; 1999; USA, 18: A1938.
22. Juranic ZD, Neskovic-Konstantinovic Z, Stanojkovic TP, et al. The antitumor immune response in HER-2 positive, metastatic breast cancer patients. *J Transl Med* 2005; 3:13.
23. Lane IW. Method of and dosage unit for inhibiting angiogenesis or vascularization in an animal using shark cartilage. United State Patent (USP) ,1991; No: 5,075,112.
24. Balasa, LL. Method of processing animal cartilage. United State Patent (USP). 1987; No: 4, 656, 137.
25. Schinitzky M. Anti-inflammatory composition. United State Patent (USP). 1984; No: 4,473,551.
26. Sheu JR, Fu CC, Tsai ML, et al. Effect of U-995, a potent shark cartilage-derived angiogenesis inhibitor, on anti-angiogenesis and anti-tumor activities. *Anticancer Res* 1998; 18: 4435-41.
27. Liang JH, Wong KP. The characterization of angiogenesis inhibitor from shark cartilage. *Adv Exp Med Biol* 2000;476:209-23.