

表6.  $\text{VCR}10^{-7}\text{M} + \text{Cyclosporin A} + \text{Cepharanthine}$

K 562 / VCR

		Cepharanthine				
		10	5	1	0.5	0.1
( $\mu\text{g/ml}$ )						
5		69.3 $\pm$ 2.7	64.2 $\pm$ 3.1	63.5 $\pm$ 0.3	46.2 $\pm$ 2.1	46.8 $\pm$ 1.2
1		62.2 $\pm$ 3.1	55.0 $\pm$ 1.7	46.6 $\pm$ 2.8	37.4 $\pm$ 2.1	25.5 $\pm$ 3.1
0.5		66.0 $\pm$ 4.1	45.7 $\pm$ 1.9	33.6 $\pm$ 5.8	23.1 $\pm$ 2.2	29.7 $\pm$ 5.8
0.2		48.7 $\pm$ 2.2	43.2 $\pm$ 0.5	35.5 $\pm$ 2.9	22.2 $\pm$ 8.4	25.5 $\pm$ 3.1
Cyclosporin A						
Control absorbance		0.979 $\pm$ 0.035				

Each value represents the mean  $\pm$  standard deviation at least eight determinations



表7. The effect of cyclosporin A or Cepharanthine for K562 cells

K562 / wild

	Adjuvant drug 濃度								Control absorbance
	100	50	25	10	5	2.5	1	0.1	
( $\mu\text{g/ml}$ )									
Cepharanthine	69.2 $\pm 1.2$	45.1 $\pm 3.4$	42.0 $\pm 1.8$	28.5 $\pm 3.2$	20.2 $\pm 2.2$	15.4 $\pm 4.1$	12.8 $\pm 2.1$	9.5 $\pm 1.9$	0.871 $\pm 0.032$
Cepharanthine + ADM $\cdot 10^{-8}\text{M}$	68.5 $\pm 3.5$	40.2 $\pm 2.1$	41.5 $\pm 1.2$	25.3 $\pm 1.8$	19.5 $\pm 3.2$	15.9 $\pm 2.5$	13.0 $\pm 6.9$	10.0 $\pm 5.2$	0.857 $\pm 0.037$
Cyclosporin A	72.3 $\pm 4.1$	65.2 $\pm 2.7$	42.3 $\pm 2.1$	30.3 $\pm 3.7$	25.8 $\pm 1.9$	20.7 $\pm 3.5$	17.4 $\pm 2.9$	10.8 $\pm 3.9$	0.967 $\pm 0.028$
Cyclosporin A + ADM $\cdot 10^{-8}\text{M}$	71.9 $\pm 5.1$	63.7 $\pm 3.2$	41.5 $\pm 3.7$	33.4 $\pm 5.1$	24.3 $\pm 2.2$	22.3 $\pm 4.1$	18.2 $\pm 2.1$	13.0 $\pm 4.2$	0.897 $\pm 0.031$

Each value represents the mean  $\pm$  standard deviation at least four determinations



表8. Effect of Cyclosporin A and/or Cepharanthine on <sup>14</sup>C-ADM uptake

<sup>14</sup> C-ADM CyA CR	<sup>14</sup> C-ADM (Control)	<sup>14</sup> C-ADM CyA 1 $\mu$ g/ml	<sup>14</sup> C-ADM CR 1 $\mu$ g/ml	<sup>14</sup> C-ADM CyA 1 $\mu$ g/ml CR 1 $\mu$ g/ml
time (mins)	5082.9 $\pm$ 1620.8	8793.2 $\pm$ 1345.0	9148.7 $\pm$ 191.2	8901.4 $\pm$ 216.7
5	6395.0 $\pm$ 1856.9	10072.2 $\pm$ 434.1	9522.0 $\pm$ 111.7	10054.1 $\pm$ 302.3
15	8600.9 $\pm$ 145.4	9535.9 $\pm$ 369.2	8860.4 $\pm$ 323.9	9094.7 $\pm$ 376.9
30	7813.8 $\pm$ 216.1	8229.7 $\pm$ 263.1	7598.5 $\pm$ 153.7	8010.8 $\pm$ 65.6
60	5608.0 $\pm$ 1272.8	6582.7 $\pm$ 141.6	6442.7 $\pm$ 110.9	6344.7 $\pm$ 234.7
90	4814.1 $\pm$ 117.3	5143.2 $\pm$ 274.1	5079.0 $\pm$ 242.8	5542.4 $\pm$ 71.6
120				

Each value represents the mean  $\pm$  standard deviation at least three determinations

\*P < 0.001 vs Control, \*\*P < 0.01 vs Control, \*\*\*P < 0.05 vs Control



表 9. Effect of Cyclosporin A and/or Cepharanthine on  $^3\text{H}$ -VCR uptake

$^3\text{H}$ -VCR CyA CR	$^3\text{H}$ -VCR (Control)	$^3\text{H}$ -VCR CyA 1 $\mu\text{g}/\text{ml}$	$^3\text{H}$ -VCR CR 1 $\mu\text{g}/\text{ml}$	$^3\text{H}$ -VCR CyA 1 $\mu\text{g}/\text{ml}$ CR 1 $\mu\text{g}/\text{ml}$
time (mins)				
5	239.2 $\pm$ 12.9	478.7 $\pm$ 116.2 *	338.1 $\pm$ 114.8 ***	509.9 $\pm$ 10.5 *
10	339.2 $\pm$ 22.8	536.2 $\pm$ 11.7 *	388.8 $\pm$ 177.1	465.8 $\pm$ 6.5 *
15	339.7 $\pm$ 80.6	532.4 $\pm$ 70.1 **	347.5 $\pm$ 70.1	448.4 $\pm$ 2.9 ***
30	358.7 $\pm$ 40.3	619.8 $\pm$ 56.9 *	292.3 $\pm$ 24.6 **	447.4 $\pm$ 38.0 **
60	355.1 $\pm$ 40.0	491.9 $\pm$ 21.6 *	314.3 $\pm$ 42.0 **	561.7 $\pm$ 18.2 *
90	430.2 $\pm$ 14.6	628.5 $\pm$ 45.9 *	407.8 $\pm$ 33.0	660.2 $\pm$ 31.9 *
120	441.2 $\pm$ 13.0	751.1 $\pm$ 43.3 *	414.1 $\pm$ 32.5 **	674.5 $\pm$ 96.2 *

Each value represents the mean  $\pm$  standard deviation at least three determinations

\*P < 0.001 vs Control, \*\*P < 0.01 vs Control, \*\*\*P < 0.05 vs Control



表10. リスク別, 初発・再発別でみた  
P-glycoprotein の発現

	Onset	Relapse	Total
Standard risk	1/5	0/1	1/6
High risk	2/6	—	2/6
Total	3/11	0/1	3/12







越前屋 竹寅 附図14枚



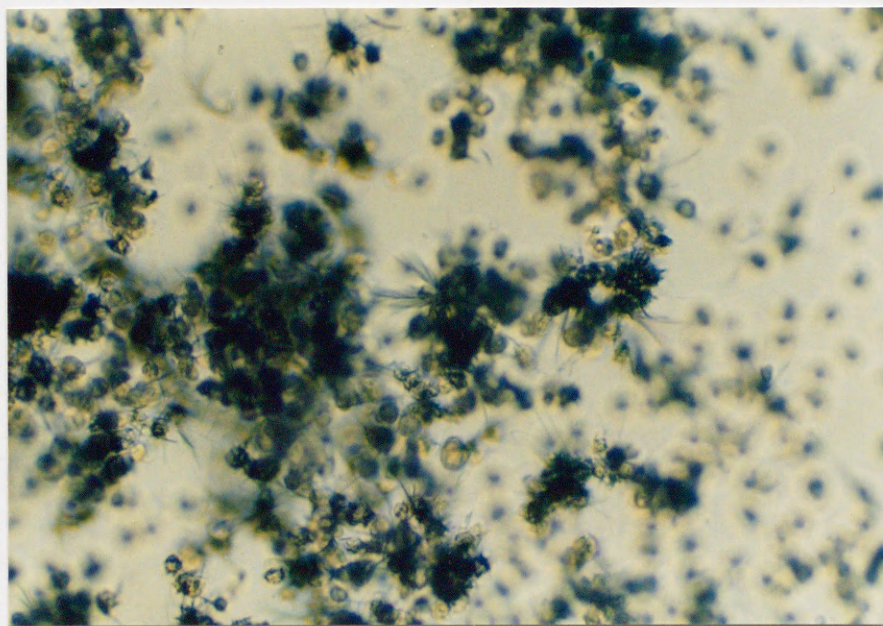


図 1 K562/Wildでのformazan形成状態

粗大顆粒形成、時間とともに針状に細胞外へのびてゆく

(位相差顕微鏡400X)



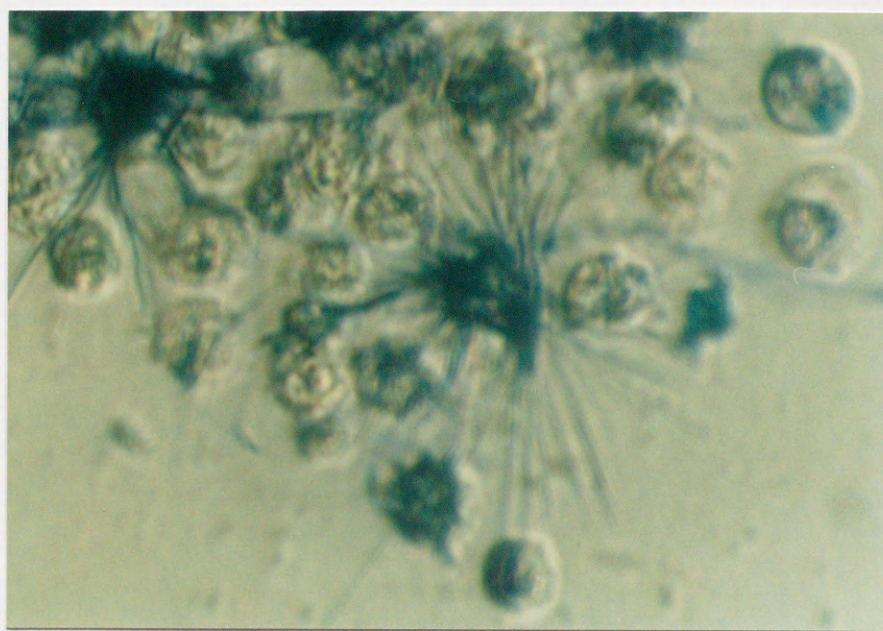


図 2 K562/Wildでのformazan形成状態

(位相差顕微鏡1000x)



K562 / ADM

(μg/ml)	Adjuvant drug 濃度							
	100	50	25	10	5	2.5	1	0.1
Verapamil								
Diltiazem								
Cephazanthine								
Cyclosporin A								
Dipyridamole								
Amphotericin B								
Clorpromazine								
Lidocaine								
Procaine								
Ascorbic acid								
Urokinase (U/ml)	1000	500	100	50	10	5	1	0.1
Trypsin inhibitor								

☒ 著効 : CI 60 % 以上, 
 ☒ 有効 : CI 40 ~ 59 %, 
 ☐ 無効 : CI 40 % 未満

図 3. ADM10<sup>-5</sup> M + Adjuvant drug



K562/VCR

(μg/ml)	Adjuvant drug 濃度							
	100	50	25	10	5	2.5	1	0.1
Verapamil								
Diltiazem								
Cepharanthine								
Cyclosporin A								
Dipyridamole								
Amphotericin B								
Clorpromazine								
Lidocaine								
Procaine								
Ascorbic acid								
Urokinase (U/ml)	1000	500	100	50	10	5	1	0.1
Trypsin inhibitor								







 著効：CI 60%以上，
  有効：CI 40～59%，
  無効：CI 40%未満


図4. VCR $10^{-7}$  M + Adjuvant drug



K 562 / ADM

		Cepharanthine				
(μg/ml)		10	5	1	0.5	0.1
Cyclosporin A	5					
	1					
	0.5					
	0.2					



 著効 : CI 60 % 以上, 
  有効 : CI 40 ~ 59 %, 
  無効 : CI 40 % 未満


 5. ADM10<sup>-5</sup> M + Cyclosporin A + Cepharanthine



K562/VCR





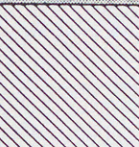





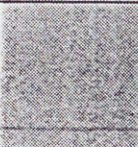

(μg/ml)	Cepharanthine				
	10	5	1	0.5	0.1
Cyclosporin A					
5					
1					
0.5					
0.2					

 著効：CI 60%以上, 
  有効：CI 40～59%, 
  無効：CI 40%未満

 6. VCR10<sup>-7</sup>M + Cyclosporin A + Cepharanthine



K 562 / wild

(μg/ml)	Adjuvant drug 濃度							
	100	50	25	10	5	2.5	1	0.1
Cepharanthine								
Cepharanthine + ADM · 10 <sup>-8</sup> M								
Cyclosporin A								
Cyclosporin A + ADM · 10 <sup>-8</sup> M								




 著効 : C160%以上,  有効 : C140 ~ 59%,  無効 : C140%未満

図 7. The effect of cyclosporin A or Cepharanthine for K 562 cells



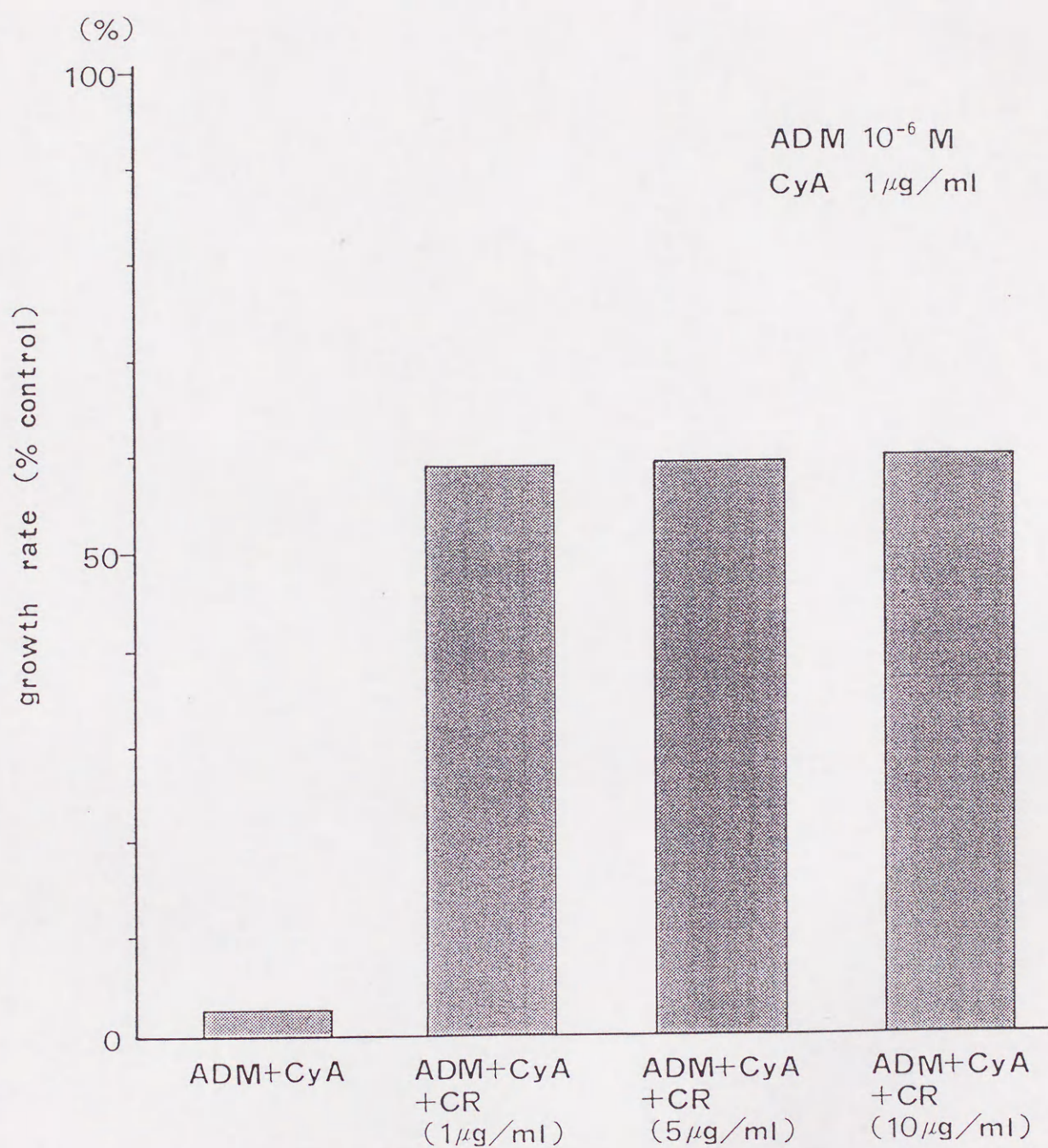


図8.

Growth inhibition assay by suspension culture



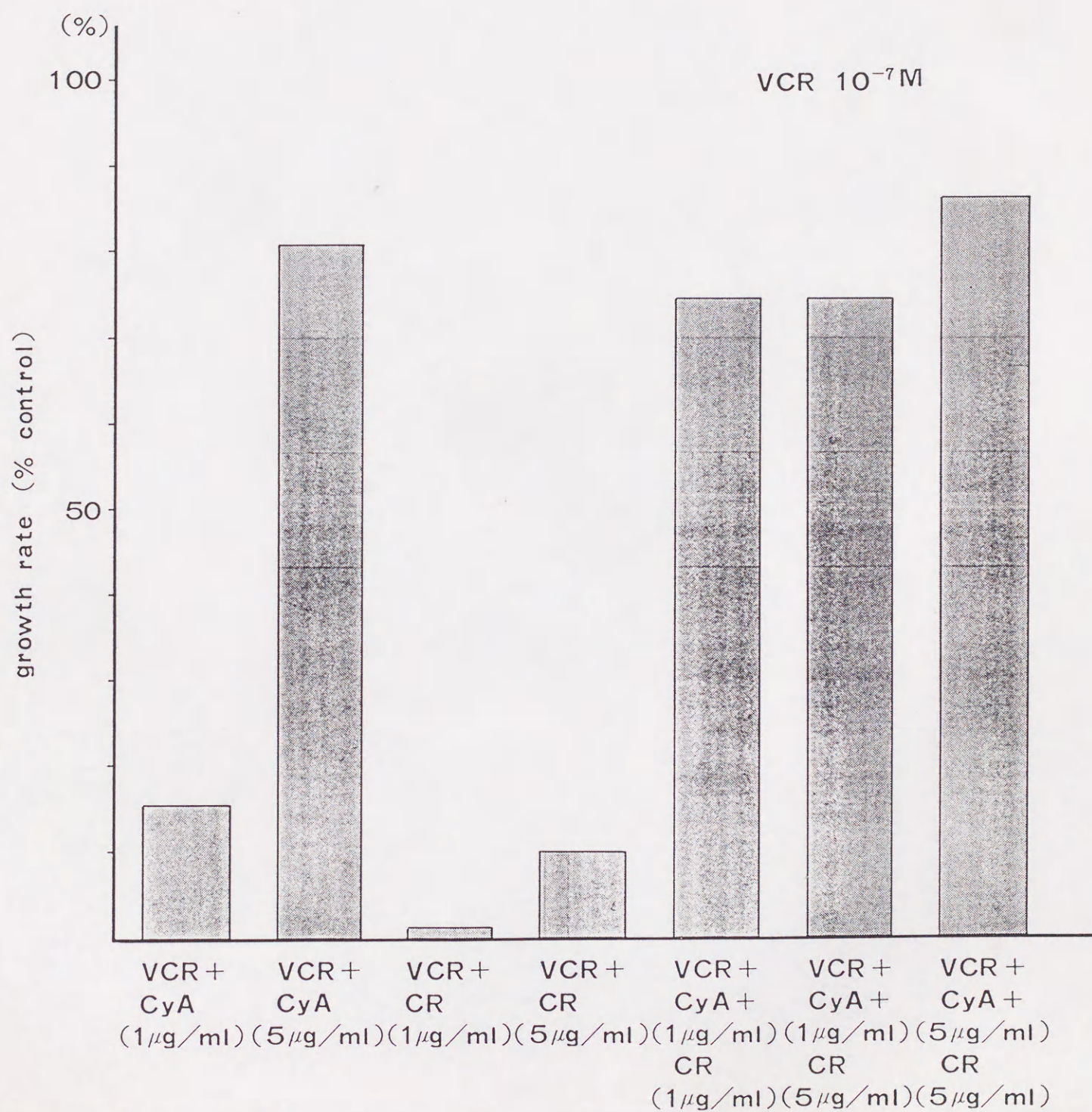


図 9.

Growth inhibition assay by suspension culture



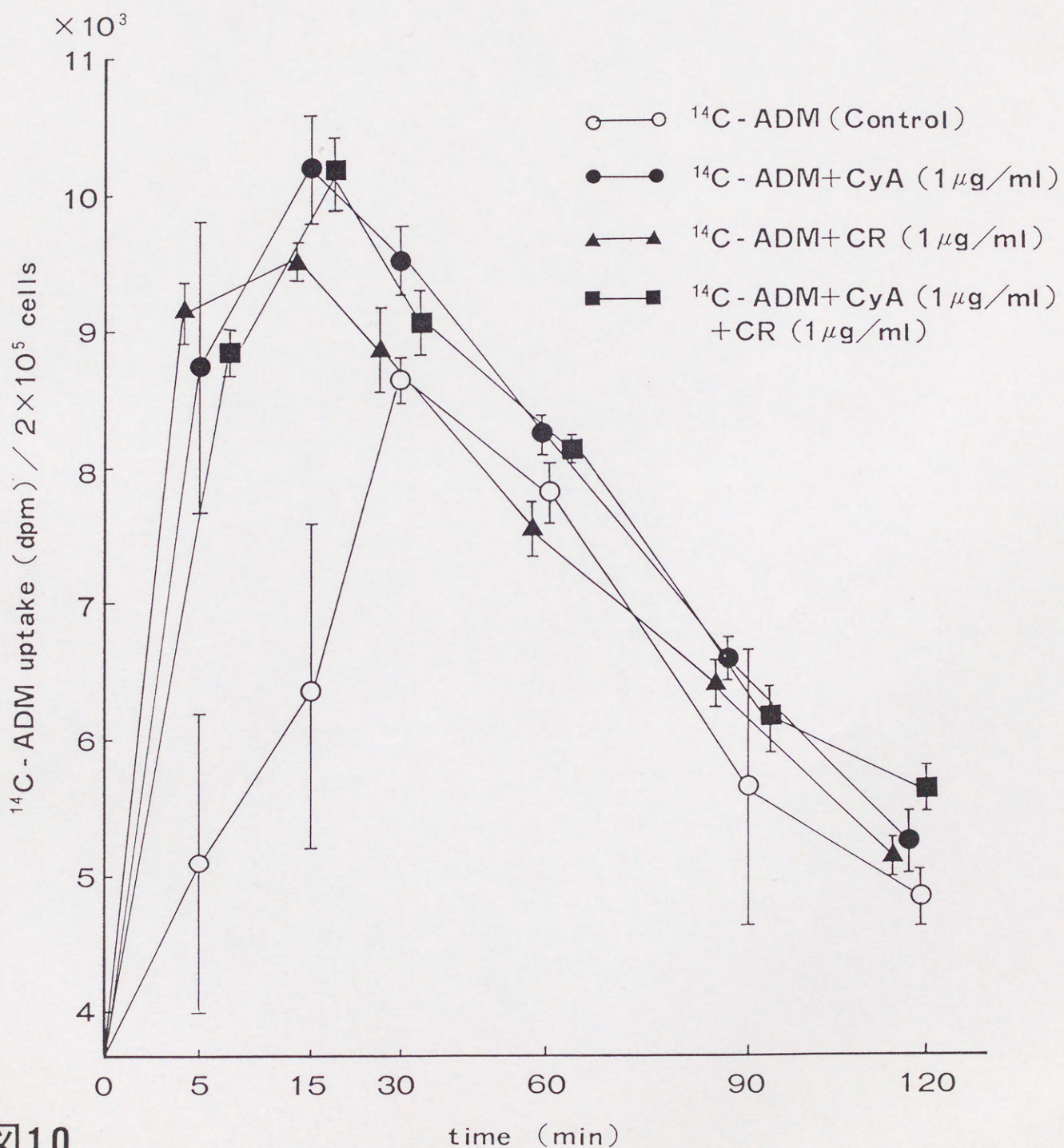


图10.

Effect of CyclosporinA and/or Cephalexin on  $^{14}\text{C}$ -ADM uptake



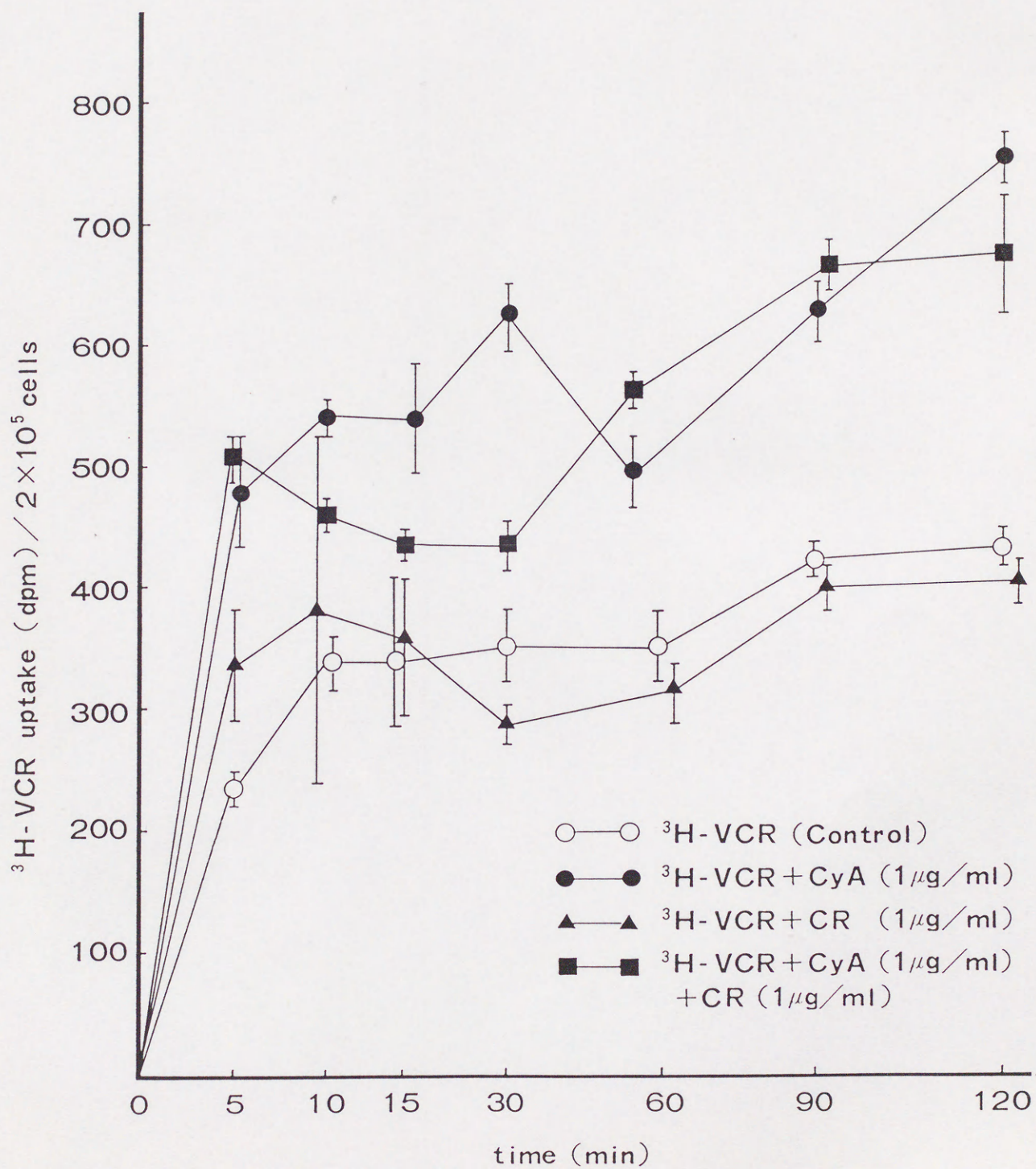


図11. Effect of Cyclosporin A and/or Cepharanthine on  $^3\text{H-VCR}$  uptake



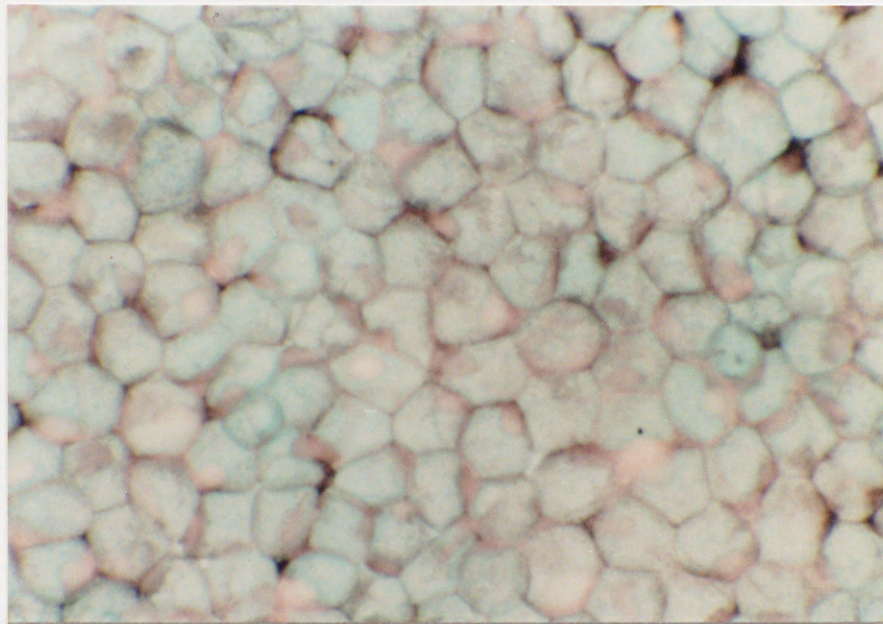


図 1 2 Case 3 の p - g p 染色

(1000X)

黒褐色に染色されている



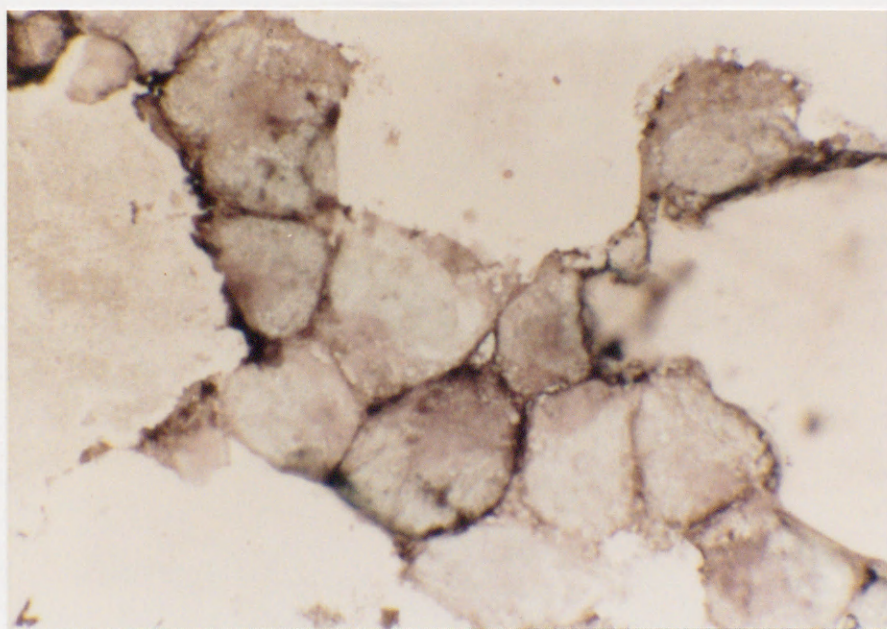


図 1 3 K562/ADMのp-gp染色

(1000x)



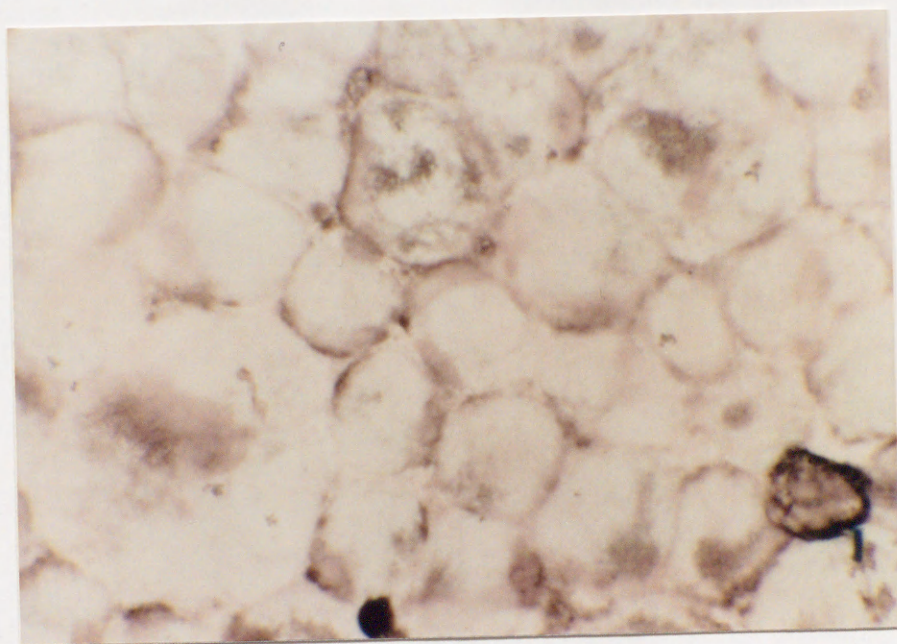


図 1 K562/VCRのp-gp染色

(1000x)



