### CHAPTER IV

#### RESULTS

The Effect of Intravenous ALK. 3a-dihydrocadambine, on Systemic Blood Pressure and Heart Rate.

An IV injection of the ALK ( $3\alpha$ -dihydrocadambine) in various doses, 0.8, 1.6, 3.2, 6.4, 16.0, and 24.0 mg/kg B.W., caused dose-dependent reduction in both systolic and diastolic blood pressure (Figure 5, 6, 7). In terms of timeaction, AP, as well as systolic and diastolic blood pressure began to fall immediately after injection and the peaks were always reached by 40 seconds after injection (Figure 5, 8, Table 4). These effects were still evident about 30 minutes and then returned to base line. The corresponding values of the decreasing effect at each dose in percentage averaged were  $4.19 \pm 1.01$ ,  $5.80 \pm 0.86$ ,  $17.06 \pm 1.52$ ,  $26.46 \pm 2.82$ ,  $25.65 \pm 2.97$  and  $24.56 \pm$ 4.83 for systolic blood pressure; in case of the diastolic blood pressure, values attained were  $13.03 \pm 1.11$ ,  $18.61 \pm 1.66$ ,  $25.76 \pm 1.05$ ,  $43.19 \pm 3.32$ ,  $39.49 \pm 4.89$  and  $37.03 \pm 4.53$  in doses ranging from 0.8 to 24.0 mg/kg B.W. (Table 1,2 and Figure 6,7). However, using student's paired t- test to analyze these data, significant reduction in systolic, diastolic and also MAP were observed in every doses when compared to those base-line measurements (Table 1,2,3 Figure 6,7).

The placebo injection of 10%PEG in NSS intravenously evoked no significant systemic change (Table 4 and Figure 8).

In Table 5., heart rate was also decreased initially by IV ALK and then followed by increasing when the maximum hypotensive effect was

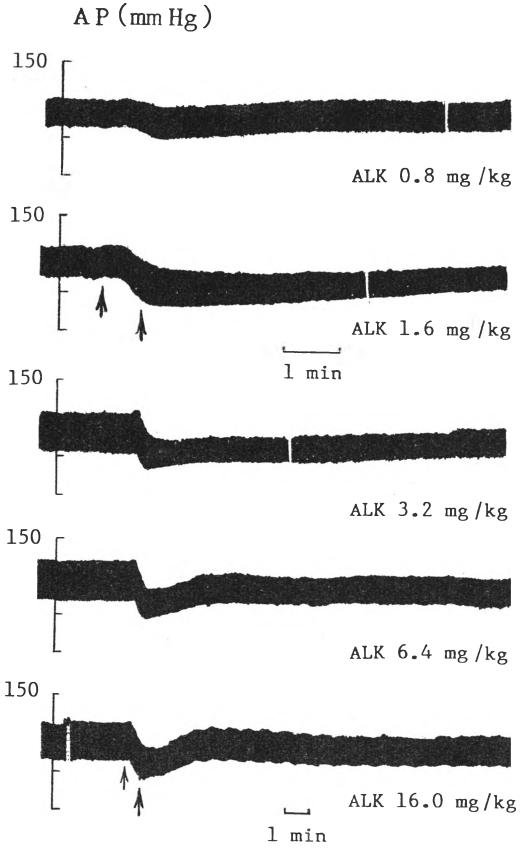


Figure 5. Changes in arterial pressure at base line after intravenous administration of ALK in various doses 0.8, 1.6, 3.2, 6.4 and 16.0 mg/kg.

DOSE	NUMBER	SYSTOLIC BLOOD PRESSURE						
OF ALK	OF		(mn	nHg)				
(mg/kg)	ANIMAL	BEFORE ALK	AFTER ALK	DECREASE	%DECREASE			
0.8	8	126.63 ± 12.53	121.25 ± 11.87	5.38 ± 1.39	4.19 ± 1.01****			
1.6	10	112.70 ± 11.15	106.20 ± 10.59	6.50 ± 1.25	5.80 ± 0.86****			
3.2	10	111.50 ± 6.50	92.60 ± 5.75	18.90 ± 1.85	17.06 ± 1.52*****			
6.4	8	103.63 ± 7.08	76.00 ± 5.49	27.63 ± 3.41	26.46 ± 2.82****			
16.0	8	125.25 ± 14.53	94.25 ± 12.29	31.00 ± 4.37	25.65 ± 2.97*****			
24.0	8	136.63 ± 11.27	100.38 ± 6.41	36.25 ± 9.97	24.56 ± 4.83****			

<u>Table 1.</u> Decreasing effect of intravenous ALK on systolic blood pressure in anaesthetized tree shrews. Values represent the mean  $\pm$  S.E.M. Significant symbols: \*\*\*\* p < 0.005; \*\*\*\*\* p < 0.005, Student's paired t- test.

DOSE	NUMBER		DIASTOLIC BLOOD PRESSURE						
OFALK	OF		(mn	nHg)					
(mg/kg)	ANIMAL	BEFORE ALK	AFTER ALK	DECREASE	%DECREASE				
0.8	8	59.88 ± 4.82	52.00 ± 4.17	7.88 ± 0.93	13.03 ± 1.11*****				
1.6	10	65.40 ± 8.49	53.60 ± 7.72	11.80 ± 1.36	18.61 ± 1.66****				
3.2	10	74.70 ± 7.84	58.20 ± 7.42	16.50 ± 0.65	25.76 ± 1.05****				
6.4	8	51.38 ± 5.97	2925 ± 3.71	22.13 ± 3.49	43.19 ± 3.32*****				
16.0	8	73.25 ± 12.37	46.13 ± 10.66	27.13 ± 3.73	39.49 ± 4.89****				
24.0	8	78.25 ± 8.02	49.00 ± 6.23	29.25 ± 5.53	37.03 ± 4.53*****				

 $\label{eq:total_condition} \begin{array}{l} \underline{\text{Table 2.}} \ \ \text{Decreasing effect of intravenous ALK on diastolic blood pressure in} \\ \text{anaesthetized tree shrews. Values represent the mean $\pm$ S.E.M.} \\ \text{Significant symbols: *****} \ \ \rho < 0.0005, \ \text{Student's paired $t$ - test.} \end{array}$ 

DOSE	NUMBER	MEAN ARTERIAL PRESSURE						
OF ALK	OF		(mn	nHg)				
(mg/kg)	ANIMAL	BEFORE ALK	BEFORE ALK AFTER ALK DECREASE %DECRE					
0.8	8	78.50 ± 5.06	71.89 ± 4.55	6.61 ± 0.69	8.38 ± 0.55*****			
1.6	10	84.27 ± 9.30	75.64 ± 8.73	8.63 ± 0.89	10.66 ± 1.02*****			
3.2	10	81.69 ± 5.91	66.66 ± 5.44	15.03 ± 0.77	18.97 ± 1.15*****			
6.4	8	68.79 ± 5.98	44.83 ± 3.99	23.96 ± 3.28	34.46 ± 2.86*****			
16.0	8	90.59 ± 12.79	62.15 ± 10.76	28.44 ± 3.45	32.95 ± 3.63*****			
24.0	8	97.73 ± 8.78	66.13 ±6.09	31.60 ± 6.88	31.15 ± 4.39*****			

<u>Table 3.</u> Decreasing effect of intravenous ALK on mean arterial pressure in anaesthetized tree shrews. Values represent the mean  $\pm$  S.E.M. Significant symbols: \*\*\*\*\* p < 0.0005, Student's paired t- test.

# ALK concentration (mg/kg)

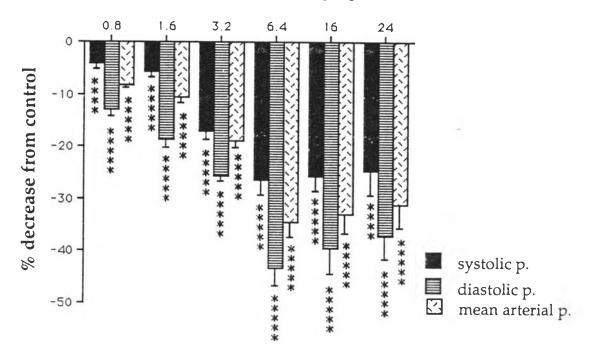


Figure 6. Dose-dependent decreases in systolic, diastolic and mean arterial pressure produced by intravenous administration of ALK. The ordinate scale is percent decrease in arterial pressure; the abscissa scale is dose of ALK in mg/kg B.W. Standard errors of the mean are indicated on each histogram.

Significant symbols: \*\*\*\* p< 0.005 \*\*\*\*\* p< 0.0005, Student's paired t-test

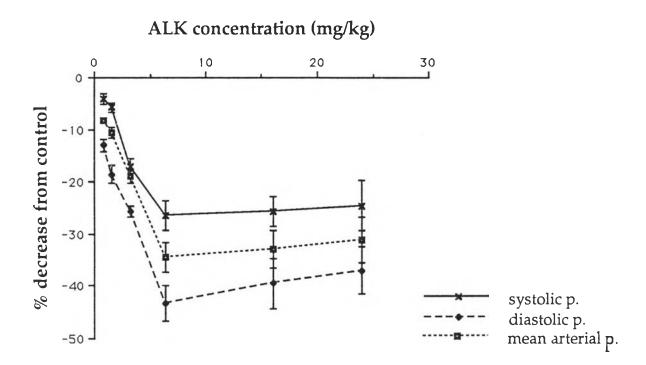


Figure 7. The concentration response curves for hypotensive effect after intravenous administration of ALK 0.8, 1.6, 3.2, 6.4, 16.0 and 24.0 mg/kg B.W. The ordinate scale is percent decrease in arterial pressure; the abscissa scale is dose of ALK in mg/kg B.W. Values represent the mean  $\pm$  S.E.M.

DOSEOFALK	%СНА	ANGE IN A	RTERIAL PR	RESSURE AF	TER ALK A	DMINISTRA	ATION
(mg/kg)	0.6 min	1 min	2 min	3 min	5 min	10 min	20 min
0.0 (10% PEG)							
SYSTOLIC P.	-1.10±0.75	1.00±1.63	-0.49±0.99	-1.79±1.38	-1.40±1.58	1.01±3.08	5.60±5.59
DIASTOLIC P.	-2.05 <b>±</b> 2.07	-3.70±1.83	-3.55±4.04	-4.28±3.04	-3.38±3.45	1.53±4.49	0.73±3.79
MAP	-1.78±1.03	-2.38±1.71	-2.17±1.94	-3.03±1.98	-2.45±2.10	1.82±3.52	2.67±4.39
3.2							
SYSTOLIC P.	-10.17±1.35	-10.52±1.52	-13.23±1.92	-12.16±2.15	-10.33±2.02	-10.28±1.99	-9.9 <b>4</b> ±3.14
DIASTOLIC P.	-28.52±3.20	-27.48±3.26	-22.73±3.41	-16.58±3.39	-12.37±2.56	-8.73±2.77	-7.68±2.36
MAP	-18.87±2.07	-18.63±2.25	-17.75±2.59	-14.31±2.64	-11.26±2.19	-9.48±2.17	-8.76±2.53
6.4					1		
SYSTOLICP.	-10.94±6.56	-14.68±5.73	-18.69±3.28	-16.88±4.91	-14.08±5.36	-13.85±1.44	-13.32±2.13
DIASTOLICP.	-31.07±9.67	-33.58±8.77	-23.91±8.41	-16.09±9.19	-13.44±7.57	-11.28±6.29	-7.82±5.22
MAP	-20.89±8.00	-23.89±6.77	-20.12±4.62	-16.13±6.66	-13.58±6.29	-13.69±4.69	-10.81±3.57

Table 4. Comparison of the percent changes in arterial pressure produced by intravenous ALK 0.0 (10% PEG), 3.2 and 6.4 mg/kg as function of the time. Values represent the mean± S.E.M.

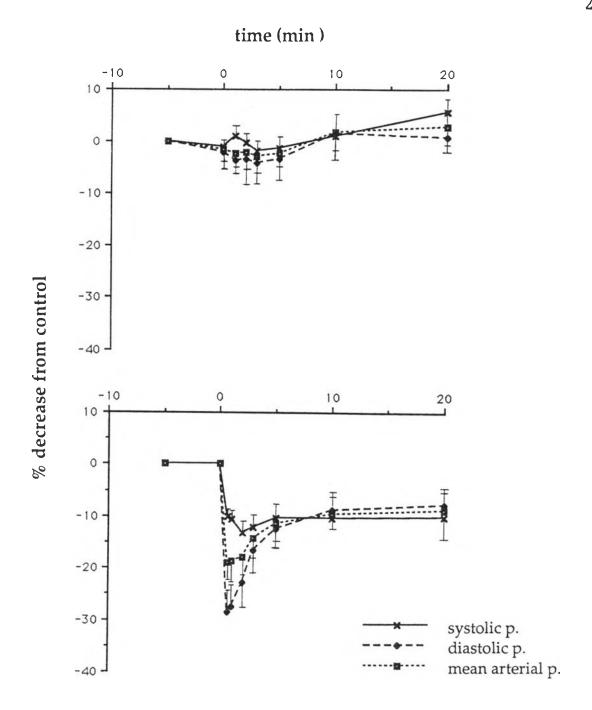


Figure 8. Representative experiment depicting the changes in systolic, diastolic and mean arterial pressure at base line (< 0 min) and for 0-20 min after intravenous 10%PEG (top panel) and ALK  $3.2\,\mathrm{mg/kg}$  in 10% PEG (bottom panel) administration. Values represent the mean  $\pm$  S.E.M.

observed. However, the statistically significant decreased was found in the dose 3.2 and 6.4 mg/kg at initially hypotensive effect. Where as at the higher dose, 16.0 mg/kg, the heart rate increased significantly from control (student's paired  $\ell$ - test, p<0.05).



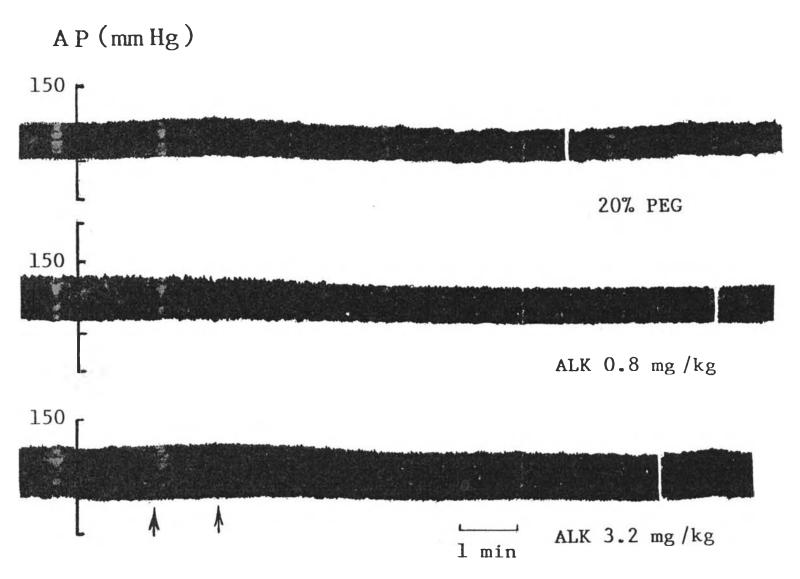
DOSE OF	HEART RATE (BEATS/MIN)							
ALK (mg/kg)	CONTROL	INITIAL	%CHANGE	MAXIMUM	%CHANGE			
20%PEG	315.00 ± 10.25	312.00 ± 14.69	-1.08 ± 1.81	329.50 ± 20.65	5.05 ± 3.28			
0.8	370.00 ± 50.00	358.50 ± 43.50	-2.95 ± 1.35	372.00 ± 42.00	0.87 ± 2.27			
1.6	301.50 ± 13.50	293.50 ± 11.50	-2.65 ± 0.55	299.00 ± 11.00	-0.79 ± 0.79			
3.2	292.86 ± 24.46	284.57 ± 24.56	-2.97 ± 0.68 *	297.43 ± 24.73	2.27 ± 0.97 *			
6.4	370.00 ± 28.57	361.20 ± 27.52	-2.33 ± 0.96 *	362.40 ± 22.01	-1.15 ± 2.57			
16.0	402.00 ± 36.49	412.00 ± 36.72	2.53 ± 0.57 *	422.00 ± 34.87	5.14 ± 0.96 *			
24.0	388.00 ± 26.46	398.00 ± 26.00	2.62 ± 1.08	413.00 ± 21.17	6.46 ± 2. 82			

Table 5. The effect of intravenous ALK in various doses on heart rate in anaesthetized tree shrews. Values represent the mean  $\pm$  S.E.M. Significant symbol: \*p< 0.05, Student's paired t-test INITIAL = at initial hypotensive effect of ALK MAXIMUM = maximum hypotensive effect of ALK

The Effect of Intracerebroventricular ALK. 3α - dihydrocadambine , on Systemic Blood Pressure and Heart Rate.

The effects of intracerebroventricular ALK ( $3\alpha$ -dihydrocadambine) in various doses 0.4, 0.8, 1.6 and 3.2 mg/kg B.W. on AP were shown in Figures 9 and 10. The decreasing effect was observed in both systolic and diastolic blood pressure. Nearly about 20 minutes after injection is the time at which the peak effect of ALK was observed following VENT administration (Figure 9.11 and Table 9). The corresponding values of the decreasing effect at each dose in percentage averaged were 28.30 ± 4.99,  $23.94 \pm 5.93$ ,  $26.44 \pm 3.77$  and  $24.82 \pm 4.06$  for systolic blood pressure; in case of the diastolic blood pressure values attained were  $29.62 \pm 8.33$ ,  $23.96 \pm 6.27$ ,  $26.52 \pm 4.21$  and  $26.78 \pm 4.14$  in doses ranging from 0.4 to 3.2 mg/kg B.W.(Table 6.7 and Figure 10). When comparing these data to those base-line measurements, significant reduction in systolic, diastolic and also MAP were observed in every doses (Table 6,7,8 and Figure 10)(paired t -test). However, in Figure 10 and Tables 6,7, it was also found that the placebo injection of 20% PEG aCSF intraventricularly itself evoked significant systemic change, as well as systolic and diastolic blood pressure (p < 0.005, paired t-test). While the peak effect was observed about 10 minutes after injection(Table 9, Figure 11).

The effect of VENT doses of ALK on heart rate was shown in Table 10. The decreasing effect was observed and the peak were reached about 10 minutes in the placebo group, while, in doses of ALK its were reached about 20 minutes after injection. When these data were analyzed by using the student's paired t- test, significant reduction (p< 0.05) in heart rate were observed almost in every doses except the dose of 1.6 mg/kg B.W..



<u>Figure 9.</u> Changes of arterial pressure at base line after intraventricular administration of ALK in doses 0.0 (20% PEG), 0.8 and 3.2 mg/kg.

DOSE	NUMBER	SYSTOLIC BLOOD PRESSURE						
OF ALK	OF		(mn	nHg)				
(mg/kg)	ANIMAL	BEFORE ALK	AFTER ALK	DECREASE	%DECREASE			
20%PEG	5	94.60 ± 20.05	75.80 ± 17.24	18.80 ± 3.87	20.66 ± 2.58****			
0.4	5	125.20 ± 15.15	89.40 ± 11.17	35.80 ± 7.89	28.30 ± 4.99****			
0.8	5	145.80 ± 16.39	110.60 ± 13.26	35.20 ± 10.23	23.94 ± 5.93***			
1.6	5	117.40 ± 11.97	85.00 ± 6.24	32.40 ± 6.65	26.44 ± 3.77****			
3.2	5	129.20 ± 10.83	97.20 ± 9.97	32.00 ± 6.36	24.82 ± 4.06****			

<u>Table 6.</u> Decreasing effect of intraventricular ALK on systolic blood pressure in anaesthetized tree shrews. Values represent the mean  $\pm$  S.E.M. Significant symbols: \*\*\* p < 0.01; \*\*\*\* p < 0.005, Student's paired  $\ell$ - test.

DOSE	NUMBER	DIASTOLIC BLOOD PRESSURE						
OFALK	OF		(min	nHg)				
(rng/kg)	ANIMAL	BEFORE ALK	AFTER ALK	DECREASE	%DECREASE			
20%PEG	5	42.40 ± 6.37	31.00 ± 6.39	11.40 ± 2.25	28.34 ± 6.20***			
0.4	5	66.60 ± 10.70	49.00 ±10.77	17.60 ± 3.20	29.62 ± 8.33**			
0.8	5	64.00 ± 6.72	49.20 ± 6.94	14.80 ± 3.95	23.96 ± 6.27***			
1.6	5	57.40 ± 6.57	42.20 ±5.47	15.20 ± 2.48	26.52 ± 4.21****			
3.2	5	74.40 ± 9.39	55.60 ± 9.06	18.80 ± 2.63	26.78 ± 4.14****			

<u>Table 7.</u> Decreasing effect of intraventricular ALK on diastolic blood pressure in anaesthetized tree shrews. Values represent the mean  $\pm$  S.E.M. Significant symbols: \*\* p < 0.025; \*\*\* p < 0.01; \*\*\*\* p < 0.005, Student's paired f- test.

DOSE	NUMBER	MEAN ARTERIAL PRESSURE						
OF ALK	OF		(mn	nH <b>g</b> )				
(mg/kg)	ANIMAL	BEFOREALK	AFTER ALK	DECREASE	%DECREASE			
20%PEG	5	59.80±11.11	45.94±9.87	13.86±2.46	24.36 ± 4.12****			
0.4	5	86.12±12.01	62.46±10.83	23.66±4.49	28.64 ± 6.17****			
0.8	5	91.26±9.69	69.68±8.69	21.58±5.99	23.86± 6.01***			
1.6	5	77.42±7.65	56.46±5.34	20.96±3.71	26.50 ± 3.85****			
3.2	5	92.66±9.41						

<u>Table 8.</u> Decreasing effect of intraventricular ALK on mean arterial pressure in anaesthetized tree shrews. Values represent the mean  $\pm$  S.E.M. Significant symbols: \*\*\* p < 0.01;\*\*\*\* p < 0.005; Student's paired t- test.



## ALK concentration (mg/kg)

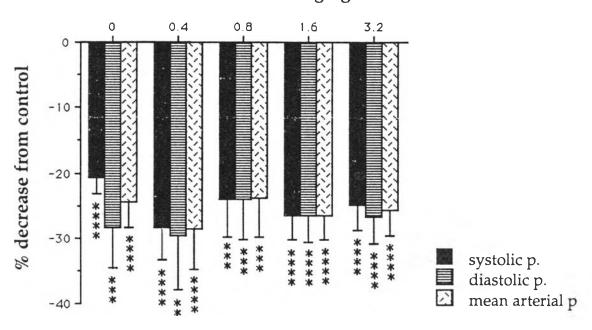


Figure 10. The mean of percent decreases in systolic, diastolic and mean arterial pressure produced by intraventricular administration of ALK. The ordinate scale is percent decrease in arterial pressure; the abscissa scale is dose of ALK in mg/kg B.W. Standard errors of the mean are indicated on each histogram.

Significant symbols: \*\*\* p < 0.025 : \*\*\* p < 0.01

: \*\*\*\* p< 0.005, Student's paired t-test

DOSEOFALK	%CH/	ANGE IN A	RTERIAL PR	ESSURE AF	TER ALK A	DMINISTRA	TION
(mg/kg)	0 min	1 min	3 min	5 min	10 min	20 min	30 min
0.0 (10% PEG)					<b>,</b> —————		
SYSTOLIC P.	0.00	3.20 ±0.46	11.60 ±3.46	14.35 ±2.81	18.06 ±2.92	13.40 ±4.30	7.23 ±3.62
DIASTOLIC P.	0.00	8.97 ±2.51	18.47 ±10.23	20.58 ±8.29	20.50 ±7.16	15.05 ±6.40	5.33 ±3.00
МАР	0.00	5.93 ±1.03	14.90 ±6.69	17.33 ±5.43	19.22 ±4.67	14.28 ±4.02	6.43 ±0.57
3.2			·		7	<b></b>	
SYSTOLIC P.	0.53 ±0.53	1.38 ±0.49	7.90 ±1.71	17.95 ±3.07	28.70 ±2.23	31.80 ±3.65	26.37 ±1.62
DIASTOLIC P.	1.73 ±1.73	3.73 ±2.28	9.45 ±1.63	20.33 ±3.62	30.40 ±3.42	35.87 ±5.25	28.53 ±3.61
MAP	1.08 ±1.08	2.53 ±1.33	8.68 ±1.17	19.18 ±3.13	29.57 ±2.23	34.06 ±4.44	27.50 ±2.73

Table 9. Comparison of the percent changes in arterial pressure produced by intraventricular ALK 0.0 (20% PEG) and  $3.2 \, \text{mg/kg}$  as function of the time. Values represent the mean  $\pm$  S.E.M.

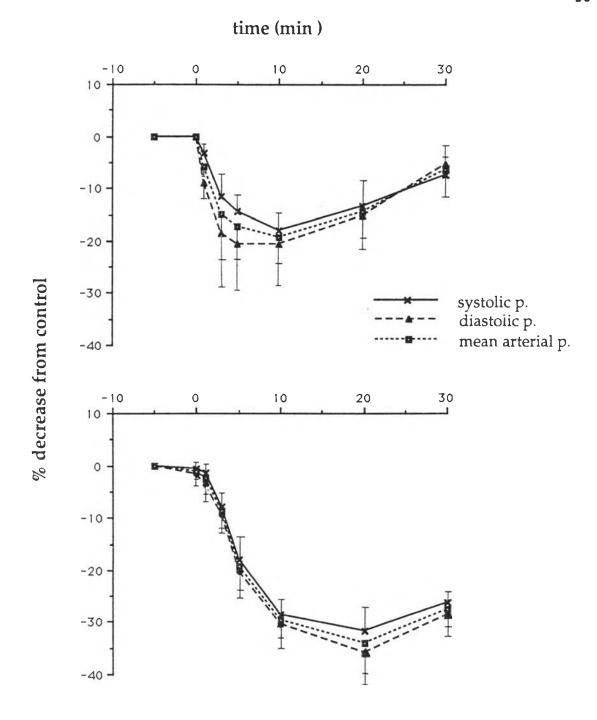


Figure 11. Representative experiment depicting the changes in systolic, diastolic and mean arterial pressure at base line ( $< 0 \, \text{min}$ ) and for 0-30 min after intraventricular 20%PEG (top panel) and ALK 3.2 mg/kg in 20% PEG (bottom panel) administration. Values represent the mean  $\pm$  S.E.M.

DOSE OF		Н	EART RATE	(BEATS/MI	N)		
ALK (mg/kg)	CONTROL	5 min	%CHANGE	15 min	%CHANGE	25 min	%CHANGE
20%PEG	326.66 ±17.64	318.00±9.17	-2.29±3.96	332.00±1.73	2.33±6.49	344.00±4.00	10.47±2.83*
0.4	368.00± 26.23	336.00±30.19	-8.88±2.49 *	324.00±30.19	-12.22± 1.83*	328.67±28.39	-10.87±1.50*
0.8	392.00± 32.00	350.67±18.52	-10.06±3.64	324.00±6.93	-16.54±4.98*	327.33±16.34	-15.16±9.14
1.6	365.00± 5.00	329.00±19.00	-9.76±6.46	297.00±27.00	-18.52± 8.52	302.00±22.00	-17.16±7.16
3.2	380.00 ±10.00	320.00±10.00	-15.80±0.42*	285.00±15.00	-25.06±1.98*	305.00±25.00	-19.85±4.47*

<u>Table 10.</u> The absolute values and the percent changes of heart rate before and after intraventricular administration in various doses of ALK. Values represent the mean  $\pm$  S.E.M. Significant symbol: \*p< 0.05, Student's paired  $\ell$ - test.

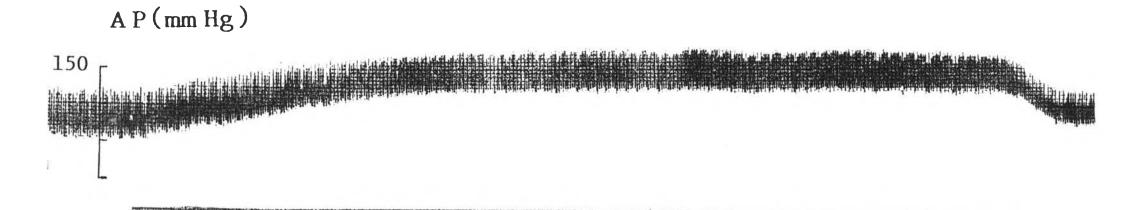
The Hypotensive Effect of Intravenous ALK. 3α-dihydrocadambine.

during FN Stimulation.

Figure 12. shows the fastigial pressor response during FN stimulation with the exploratory stimulus consisting of 0.1 mS in duration, at a frequency of 50 Hz and stimulus current of 0.15 mA. It resulted in significant increase in both systolic and diastolic blood pressure (Table 11) which began to elevate within 2-3 seconds of the onset of the stimulus, and then rised rapidly to a peak. During the stimulation continued, the AP was sustained and rapidly declined to control level after the stimulation was terminated.

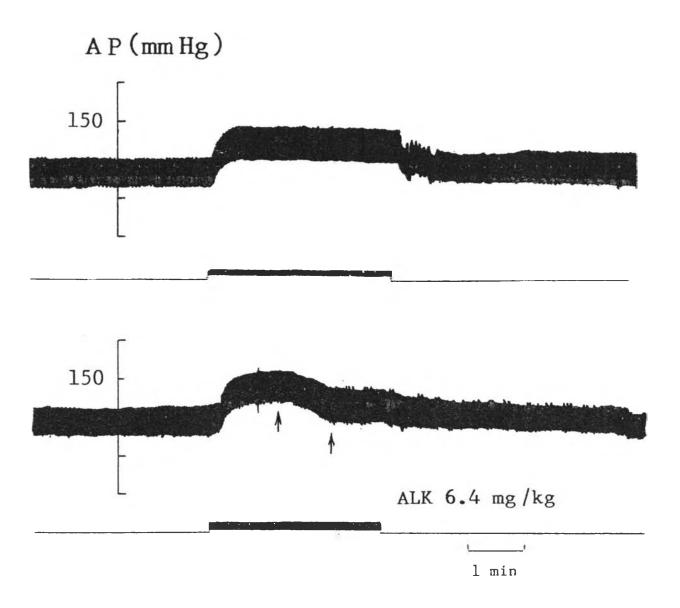
The effect of ALK,  $3\alpha$ -dihydrocadambine, on FPR when the AP was sustained during FN stimulation were shown in Figure 13 and Table 11. It was found that after ALK injection, the AP decreased immediately. There were statistically significant decreases after the dose of ALK 3.2 mg/kg and also the most effective dose 6.4 mg/kg were administered, when the changeable values of AP were compared to the AP during FN stimulation before administration of ALK (p<0.05) (Table 11).

Furthermore, when compared the hypotensive effect of the ALK during basal AP to during FPR at the same dose, there were no significant systemic change between them. Except in systolic blood pressure of the dose 3.2 mg/kg (p< 0.05, unpaired t-test) (Figure 14 and Table 12, 13, 14).



10 sec

Figure 12. Fastigial pressor responses during FN stimulation. The exploratory stimulus consist of duration 0.1 mS, frequency 50 Hz and stimulus current 0.15 mA.



 $\frac{Figure~13.}{Figure~13.}~Records~showing~fastigial~pressor~response~in~anaesthetized~tree~shrews~(~top~panel)~and~its~attenuation~by~intravenous~ALK~6.4~mg/kg~(~bottom~panel).$ 

DOSE OF	NUMBEROF		ARTERIAL	PRESSURE (mm	Hg)			<del></del>
ALK (mg/kg)	ANIMAL	CONTROL	STIMULATE	INCREASE	%INCREASE	AFTERALK	DECREASE	%DECREASE
SYSTOLIC P.								
3.2	5	113.60 ± 14.55	142.00 ± 17.65	28.40 ± 8.19	27.68 ± 9.98*	128.80±15.00	13.20±2.71	8.98±0.75*****
6.4	5	124.00±8.67	156.60±4.28	32.60±6.12	27.96±6.68***	130.20±7.78	24.60±4.63	17.06±3.27****
DIASTOLICP.								
3.2	5	70.60±10.13	93.00±6.59	22.40±4.15	42.40±19.21*	72.60±6.73	20.40±2.01	22.34±2.48****
6.4	5	77.40±2.42	108.40±5.66	31.00±7.61	41.02±10.38***	70.20±9.55	38.20±5.67	36.08±6.08****
MAP								
3.2	5	84.94±11.35	109.32±9.79	24.38±4.91	35.18±14.05*	91.34±9.14	17.98±1.45	16.70±1.34****
6.4	5	92.96±4.35	124.46±3.75	31.50±6.78	35.32±8.84***	90.20±8.16	34.26±5.30	27.94±4.82****

<u>Table 11.</u> Comparison of the effect of FN stimulation on arterial pressure and the effect of intravenous ALK 3.2 and 6.4 mg/kg during FPR. Values represent the mean  $\pm$  S.E.M. Significant symbols

: \* p < 0.5; \*\*\* p < 0.01, significant increase from normal control : \*\*\*\* p < 0.005, \*\*\*\*\* p < 0.0005, significant decrease from stimulate control

	NUMBER	SYSTOLIC BL	OOD PRESSU	JRE (mmHg)
TREATMENT	OF	BEFORE	AFTER	%
1	ANIMAL	ALK	ALK	DECREASE
ALK 3.2 mg/kg	10	111.50±6.50	92.60±5.75	17.06±1.52
ALK 3.2 mg/kg	5	142.00±17.65	128.80±15.00	8.98±0.75*
DURING		(113.60±14.55)		
FN STIMULATION				
ALK 6.4 mg/kg	8	103.63±7.08	76.00±5.49	26.46±2.82
ALK 6.4 mg/kg	5	156.60±4.28	130.20±7.78	17.06±3.27
DURING		(124.00±8.67)		
FN STIMULATION				

Table 12. Comparison of the effect of intravenous ALK on basal systolic blood pressure and during FN stimulation at doses 3.2 and 6.4 mg/kg (mean  $\pm$ S.E.M.). Numbers in parentheses represent systolic blood pressure before FN stimulation. \* = significantly different (p < 0.05) from basal blood pressure group, Student's unpaired  $\ell$ -test.

	NUMBER	DIASTOLIC PRESSURE (mmHg)		
TREATMENT	OF	BEFORE	AFTER	U)
	ANIMAL	ALK	ALK	DECREASE
ALK 32 mg/kg	10	74.70±7.84	58.20±7.42	25.76±1.05
ALK 3.2 mg/kg	5	93.00±6.59	72.60±6.73	22.34±2.48
DURING		(70.60±10.13)		
FN STIMULATION				
ALK 6.4 mg/kg	8	51.38±5.97	29.25±3.71	43.19±3.32
ALK 6.4 mg/kg	5	108.40±5.66	70.20±9.55	36.08±6.08
DURING		(77.40±2.42)		
FN STIMULATION				

<u>Table 13.</u> Comparison of the effect of intravenous ALK on basal diastolic blood pressure and during FPR at doses 3.2 and 6.4 mg/kg (mean  $\pm$ S.E.M.). Numbers in parentheses represent diastolic blood pressure before FN stimulation.



	NUMBER	DIASTOLIC PRESSURE (mmHg)		
TREATMENT	OF	BEFORE	AFTER	%
	ANIMAL	ALK	ALK	DECREASE
ALK 32 mg/kg	10	81.69± 5.91	66.66±5.44	18.97±1.15
ALK 32 mg/kg	5	109.32± 9.79	91.34± 9.14	16.70±1.34
DURING		(84.94 ±11.35)		
FN STIMULATION				
ALK 6.4 mg/kg	8	68.79±5.98	44.83±3.99	34.46±2.86
ALK 6.4 mg/kg	5	124.46±3.75	90.20±8.16	27.94±4.82
DURING		(92.96±4.35)	- 11	
FN STIMULATION				

Table 14. Comparison of the effect of intravenous ALK on basal mean arterial pressure and during FPR at doses 3.2 and 6.4 mg/kg (mean  $\pm$ S.E.M.). Numbers in parentheses represent mean arterial pressure before FN stimulation.

### ALK 3.2 mg/kg

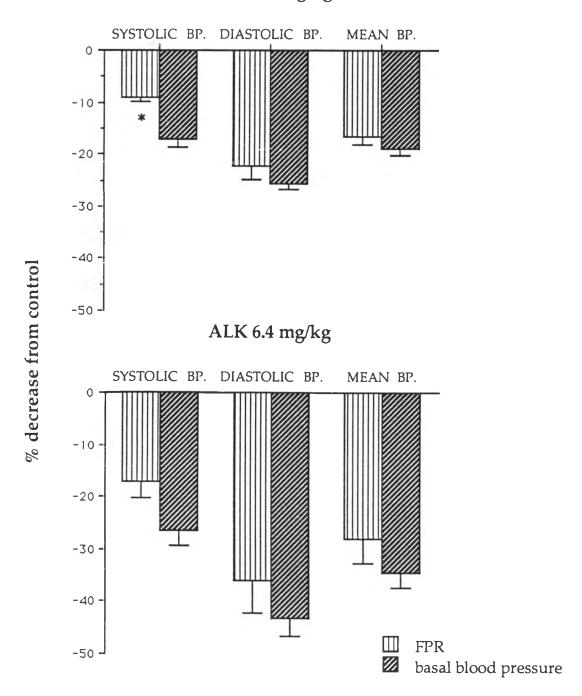


Figure 14. Comparison of the effect of intravenous ALK on basal blood pressure and during FPR at doses  $3.2\,\mathrm{mg/kg}$  (top panel) and  $6.4\,\mathrm{mg/kg}$  (bottom panel). Standard errors of the mean are indicated on each histogram. \* : Significant difference (p < 0.05)