

Chapter III

Results

1. Median effective dose of VHA with anticonvulsant activity against MES in rats.

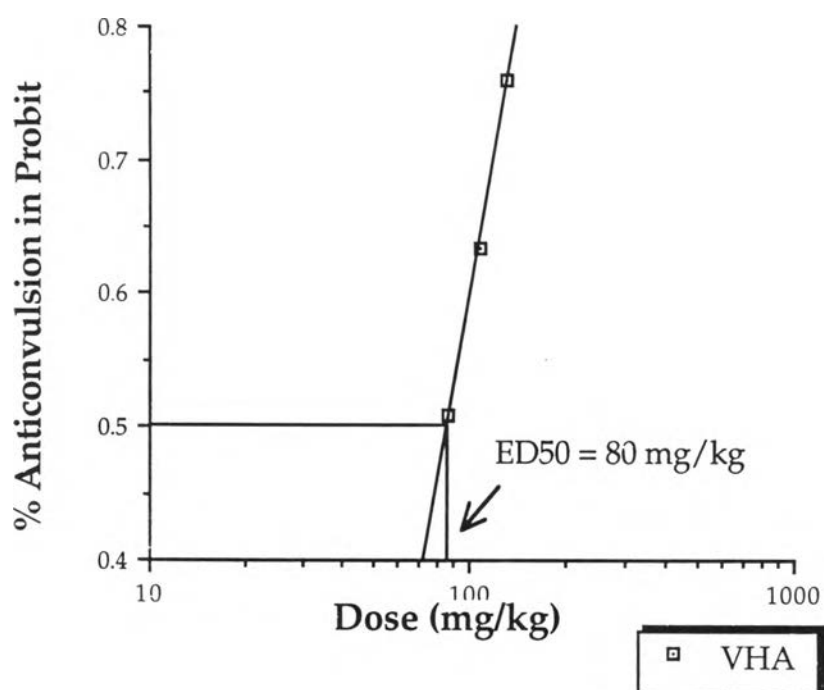
The optimal pretreated time defined as the minimal time for the tested substance to exert its highest anticonvulsant activity was noted. The result of anticonvulsant activity of VHA was also demonstrated in rats (Fig 5) in which the ED₅₀ was 80 (51-124) mg/kg B.W. in optimal pretreated time at 15 min.

2. Effects on some cortical amino acid neurotransmitter levels in freely moving rats.

The excitatory neurotransmitters in question are glutamate and aspartate whereas GABA and glycine are the ones with inhibitory effect. Alteration of amino acid neurotransmitter's levels was expressed as percentage of change from basal value which was determined from three consecutive samples before the administration of the tested substances. Qualitative and quantitative determination of the amount of the amino acids were accomplished by HPLC as exemplified by HPLC chromatogram in Figure 6.

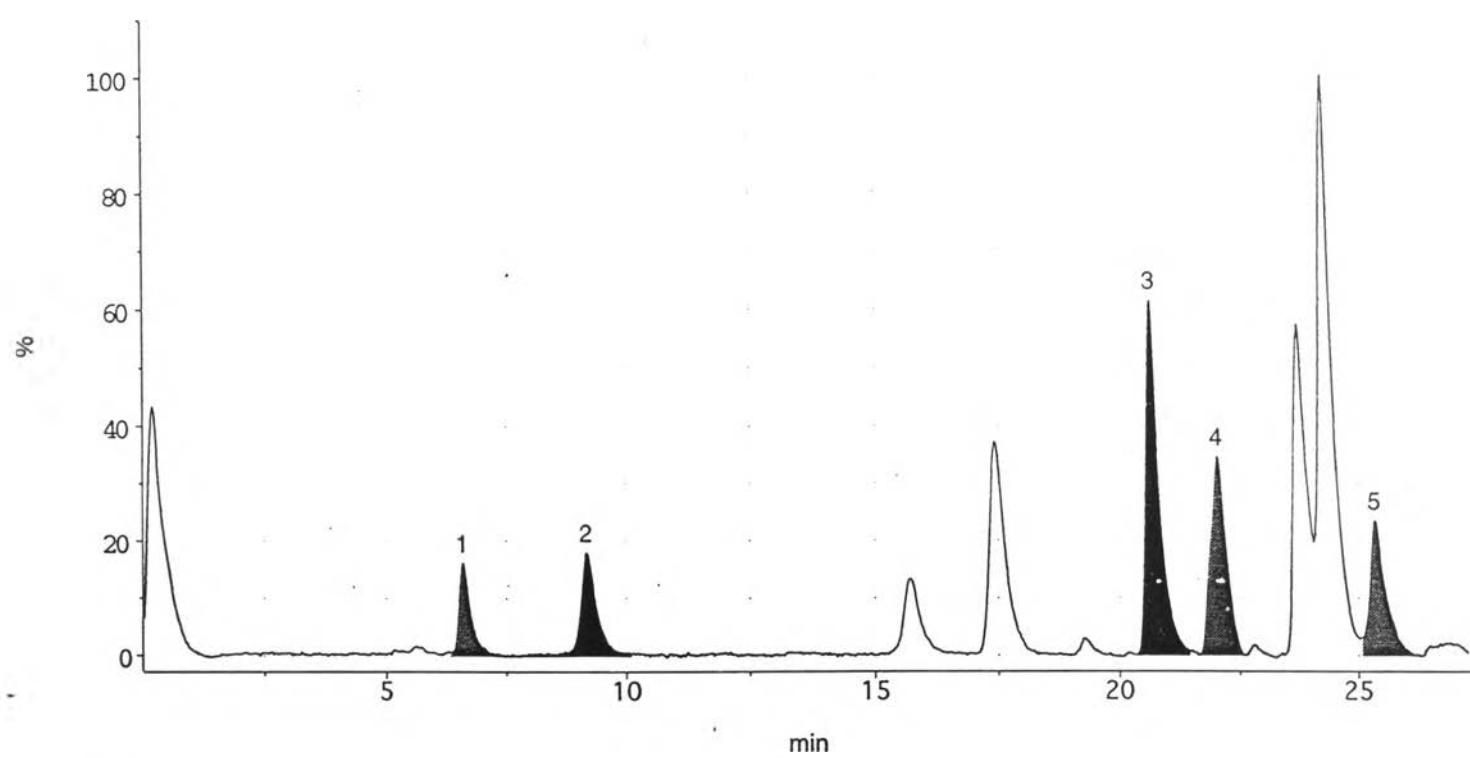
In control groups, the effect of PEG400 on cortical aspartate, glutamate, glycine and GABA level was not statistically different from those of NSS (Fig 7,8,9 and 10). VPA in the dose of 200 mg/kg B.W. did not exert any significant effect on the levels of aspartate, glutamate, glycine and GABA. Nevertheless, in higher dose (400 mg/kg B.W.), VPA did reduce glutamate but not aspartate level (Fig 11, 12, 15 and 16). No significant effect of high dose of VPA (400 mg/kg B.W.) was noted on the levels of inhibitory amino acids, glycine and GABA (Fig 13, 14, 17 and 18).

VHA in the dose of 100 and 200 mg/kg B.W. significantly increased the level of glycine (Fig 13 and 17). A marked increase in the level of GABA was elicited exclusively by VHA in the dose of 200 mg/kg B.W. (Fig 14 and 18). On the contrary, VHA did not exerted any major effect on either aspartate or glutamate level (Fig 11, 12, 15 and 16).



$$\text{Probit of VHA} = -2.1965 + 1.4149 \cdot \text{LOG}(\text{dose}) \quad R^2 = 0.997$$

Figure 5. Log dose response curve of VHA (i.p.) against MES in rat at 15 min pretreated times (n = 5).



Peak	↓	Name	t_R (min)	Start (min)	End (min)	Area	Height (%)	Norm (%)	Peak Type	Amount	F
1		ASP	6.600	6.350	7.275	4.277	7.439	8.30	DD		
2		GLU	9.175	7.275	10.100	7.12	8.324	13.81	DB		
3		HOMO	20.650	20.350	21.450	19.601	28.300	38.05	BB		
4		GLY	22.025	21.650	22.575	12.257	15.914	23.79	BB		
5		GABA	25.350	25.075	26.150	8.266	10.800	16.04	BB		
						51.52	70.777	100.00			

Figure 6. HPLC chromatogram of OPA derivatized amino acid from the rat cerebral cortex.

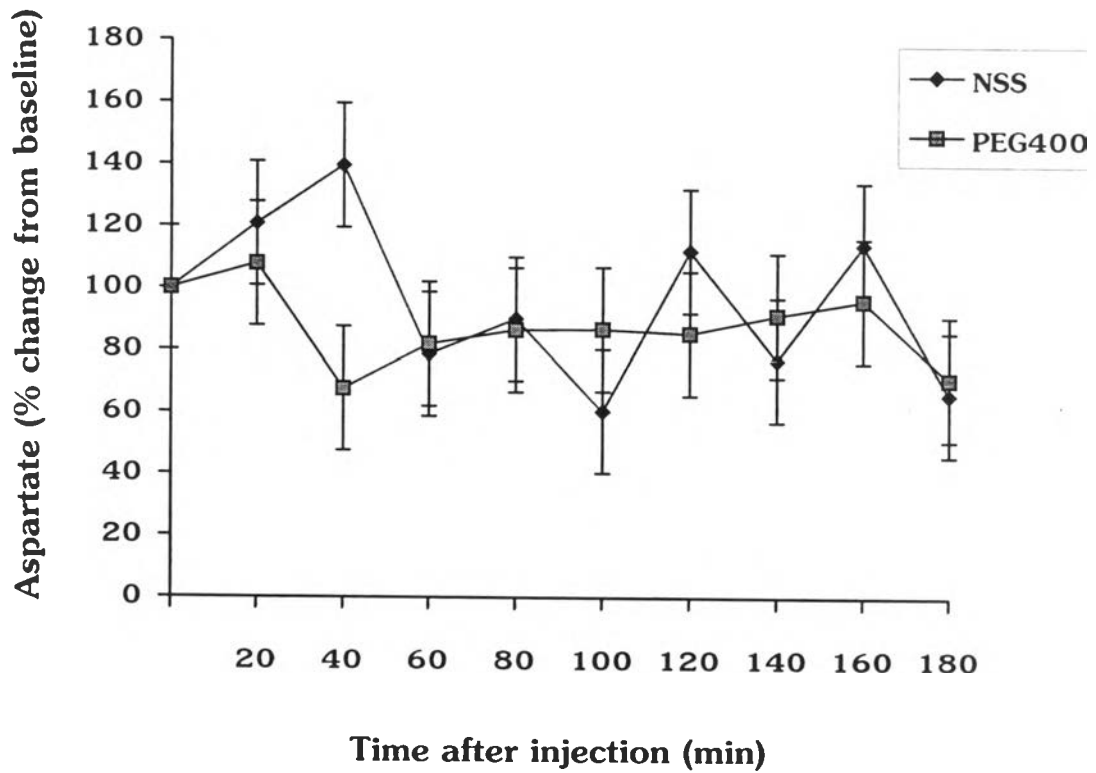


Figure 7. Change in the rat cortical aspartate levels at various times after an intraperitoneal administration of NSS and PEG400 (n = 5)

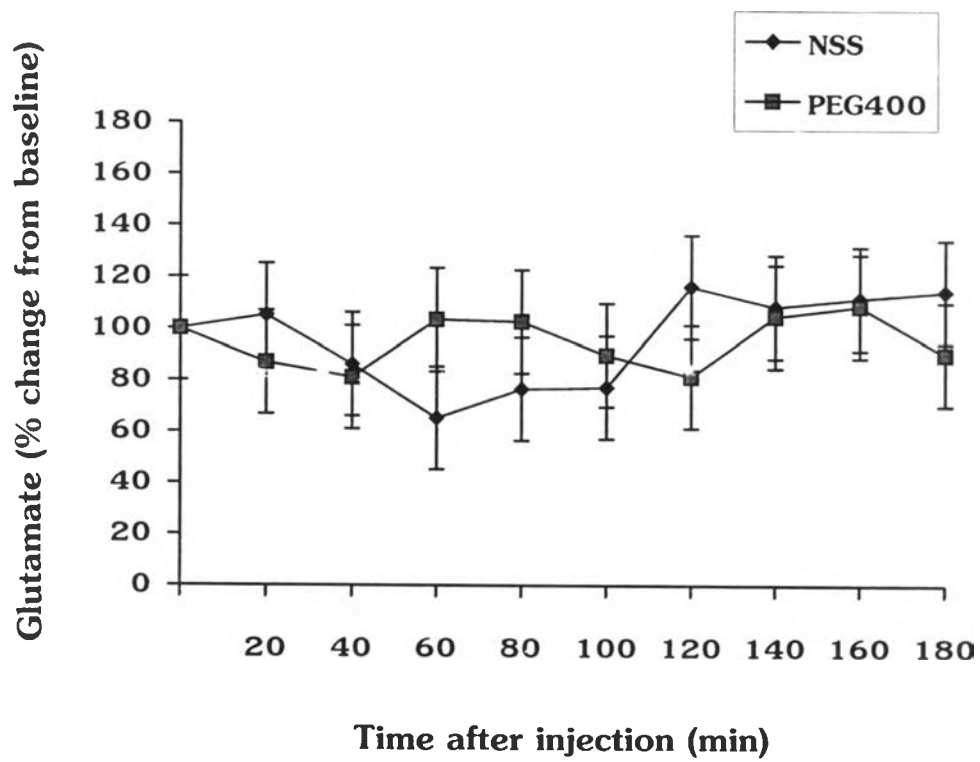


Figure 8. Change in the rat cortical glutamate levels at various times after an intraperitoneal administration of NSS and PEG400 (n = 5)

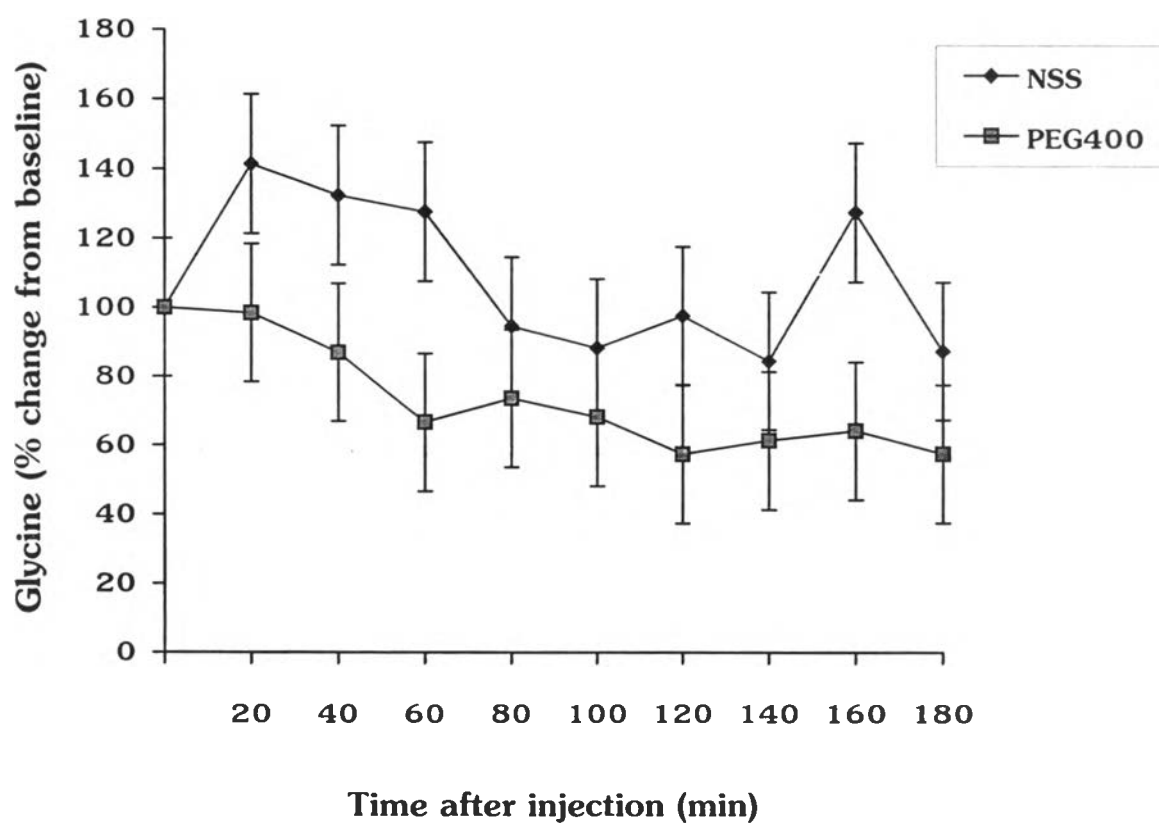


Figure 9. Change in the rat cortical glycine levels at various times after an intraperitoneal administration of NSS and PEG400 (n = 5)

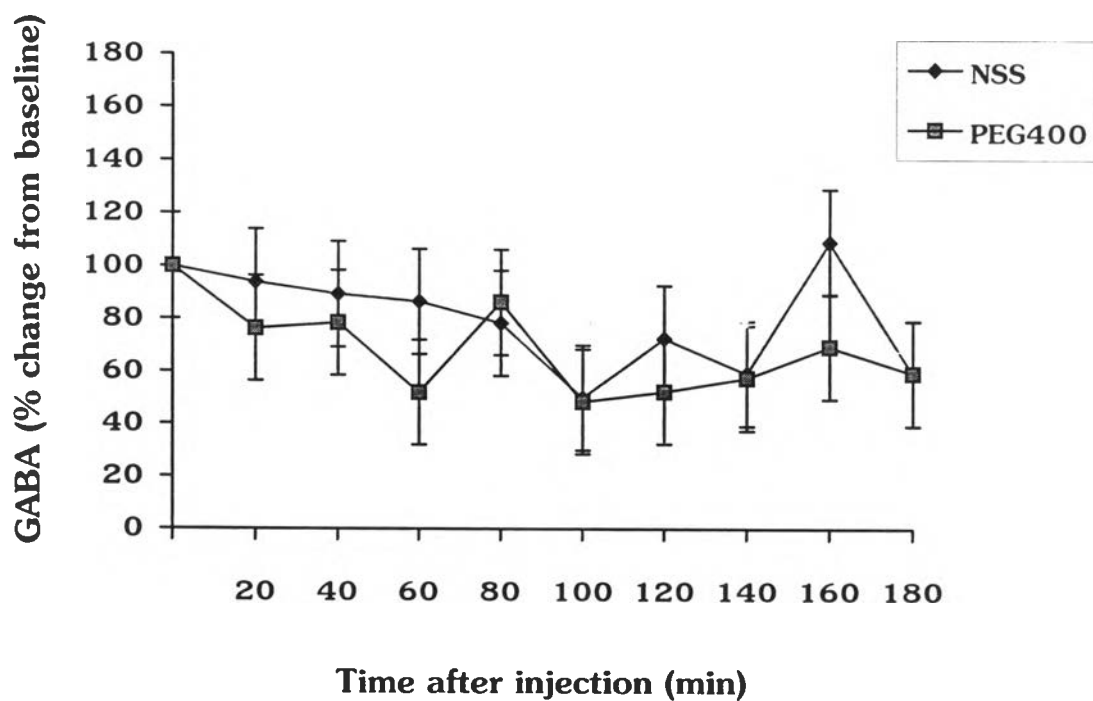


Figure 10. Change in the rat cortical GABA levels at various times after an intraperitoneal administration of NSS and PEG400 (n = 5)

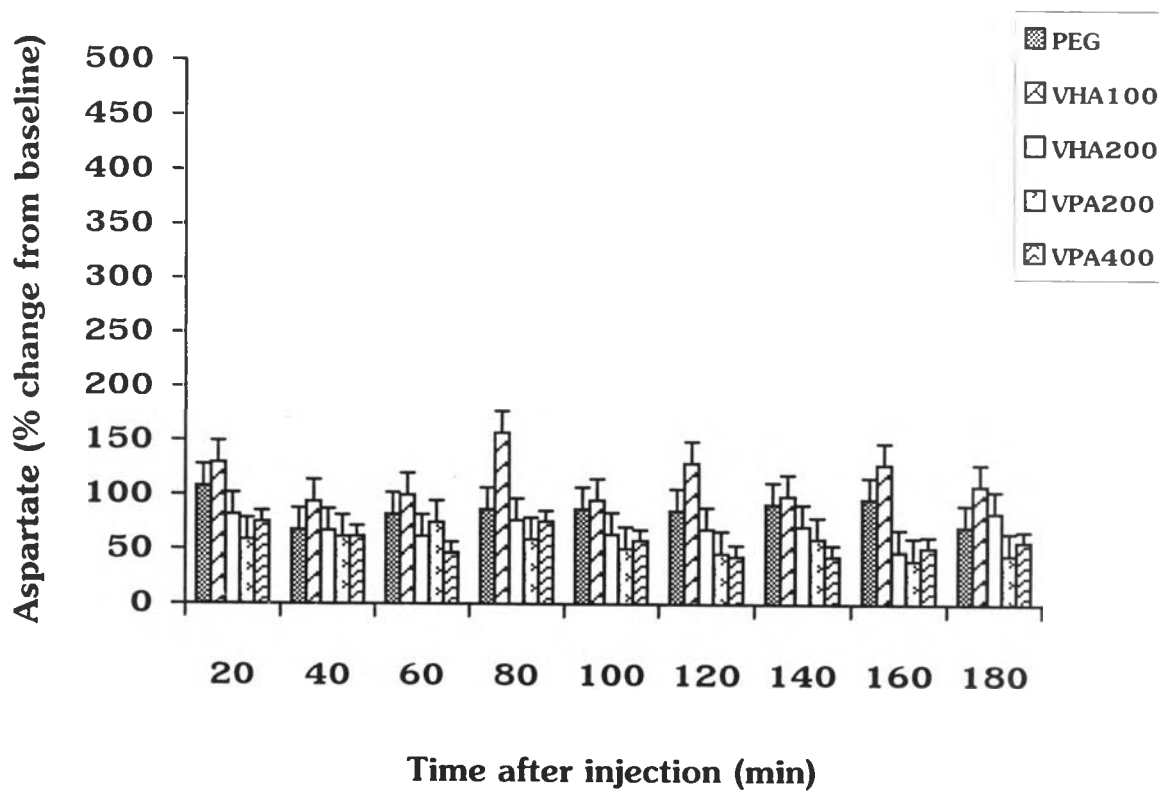
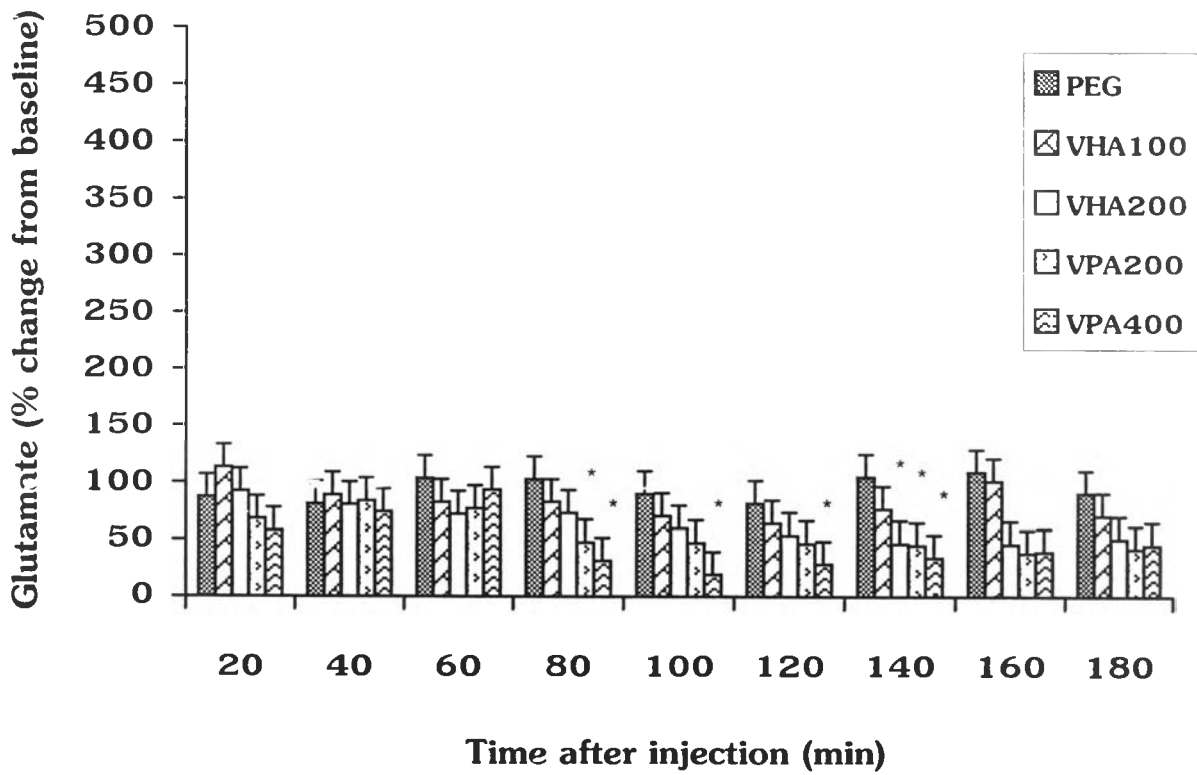
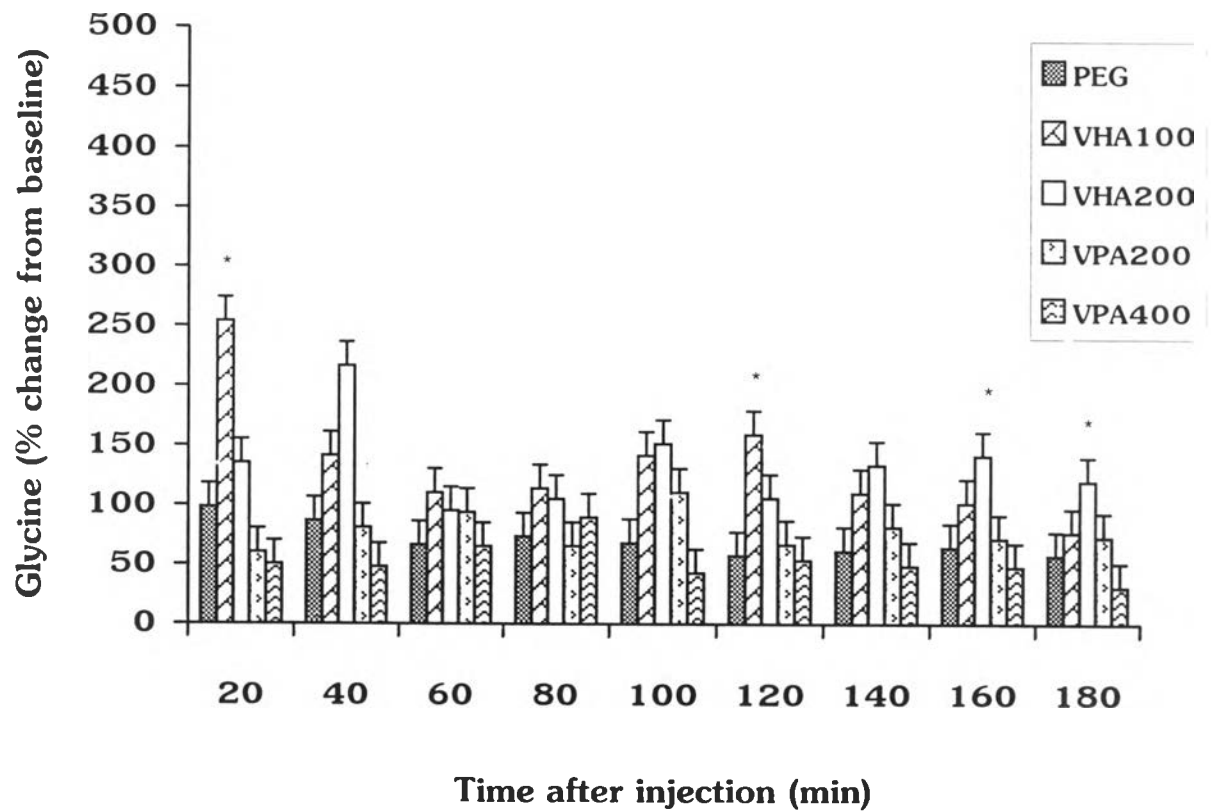


Figure 11. Effects of an intraperitoneal administration of VPA and VHA on the rat cortical aspartate levels at various times.



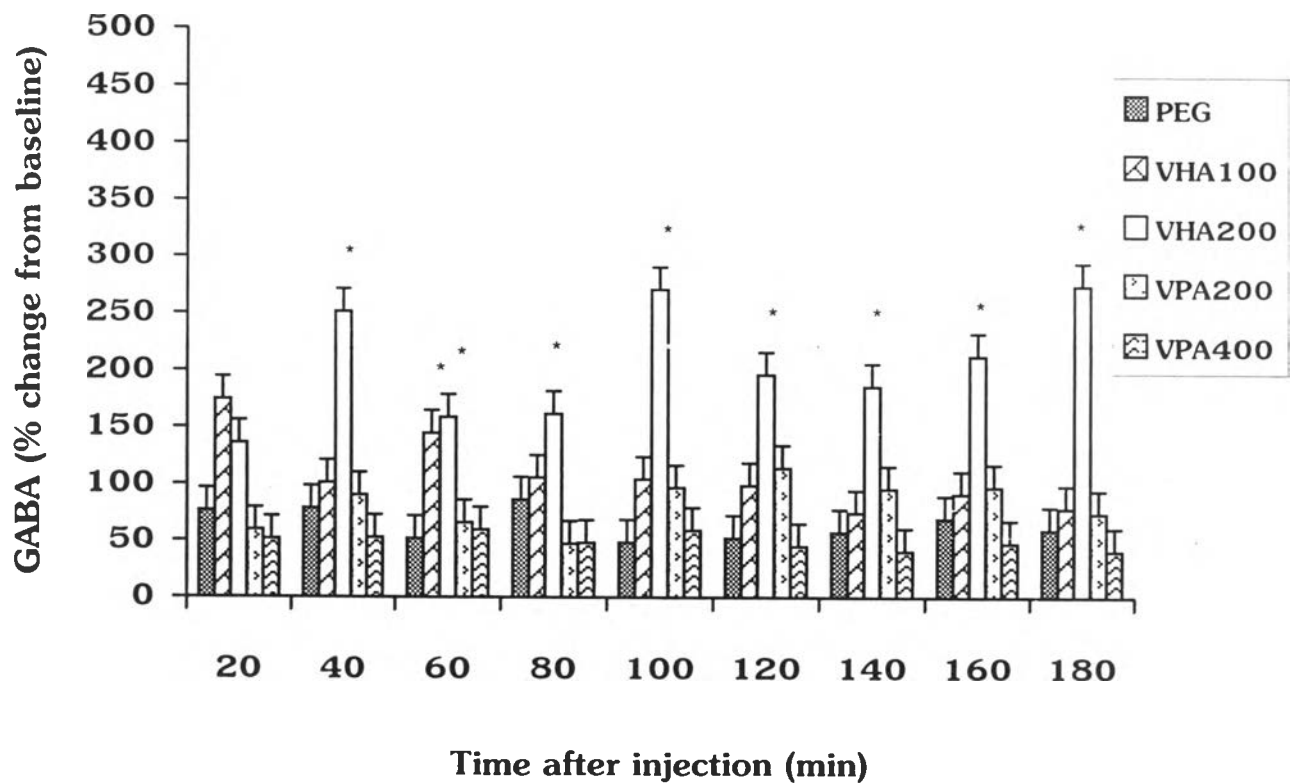
* $p < 0.05$ denotes statistically significant difference from PEG400

Figure 12. Effects of an intraperitoneal administration of VPA and VHA on the rat cortical glutamate levels at various times.



* $p < 0.05$ denotes statistically significant difference from PEG400

Figure 13. Effects of an intraperitoneal administration of VPA and VHA on the rat cortical glycine levels at various times.



* $p < 0.05$ denotes statistically significant difference from PEG400

Figure 14. Effects of an intraperitoneal administration of VPA and VHA on the rat cortical GABA levels at various times.

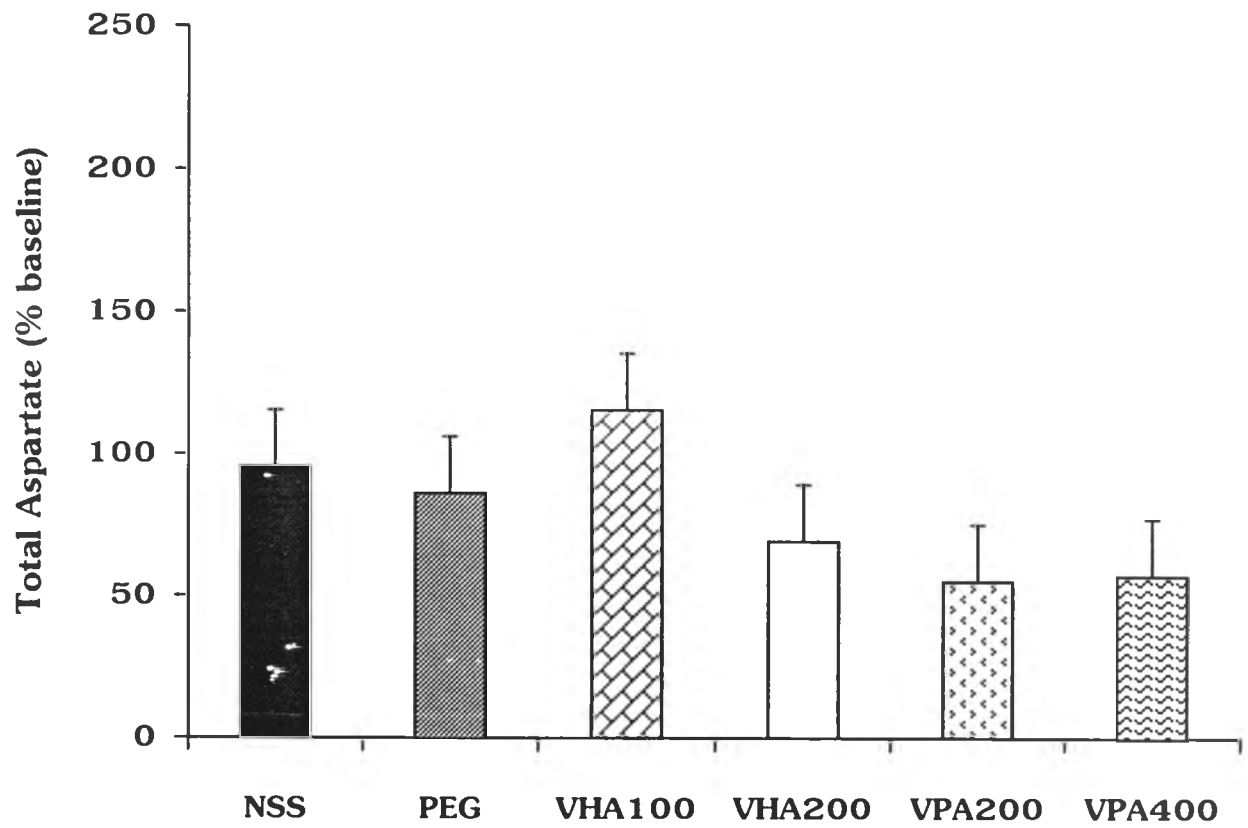
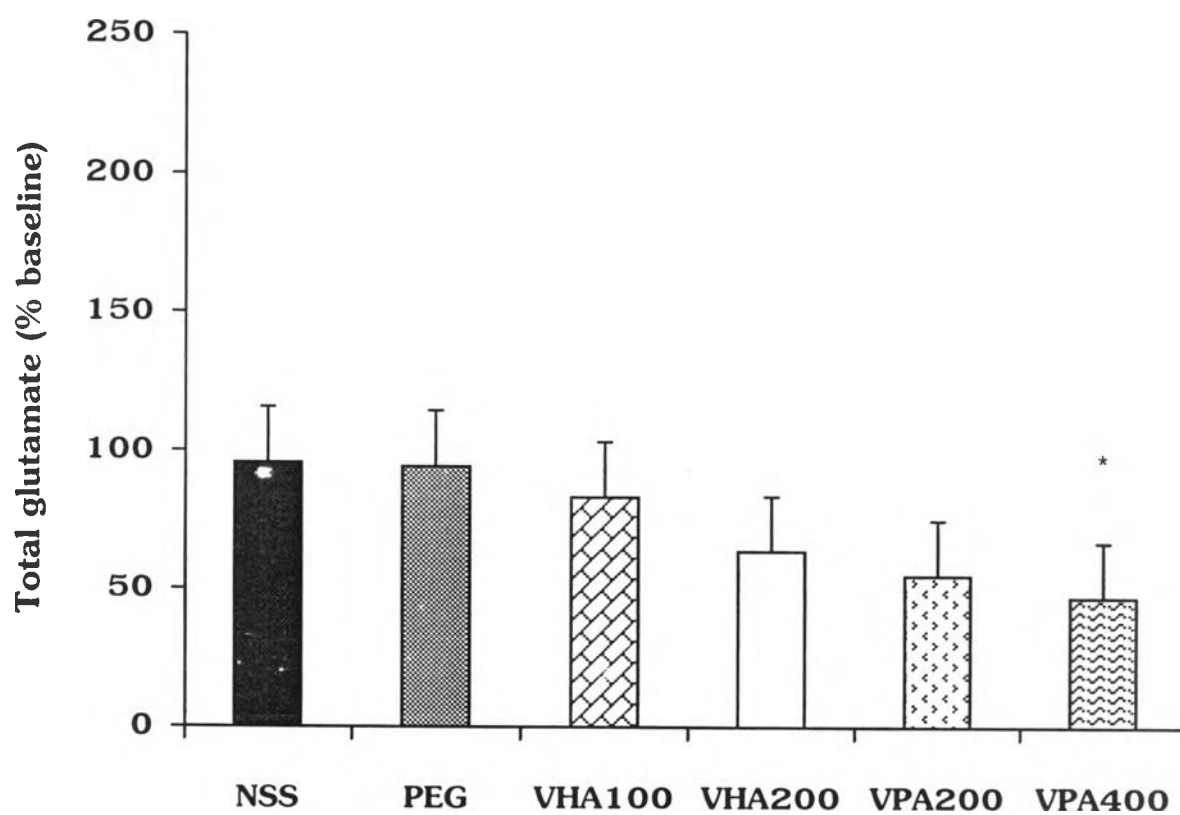
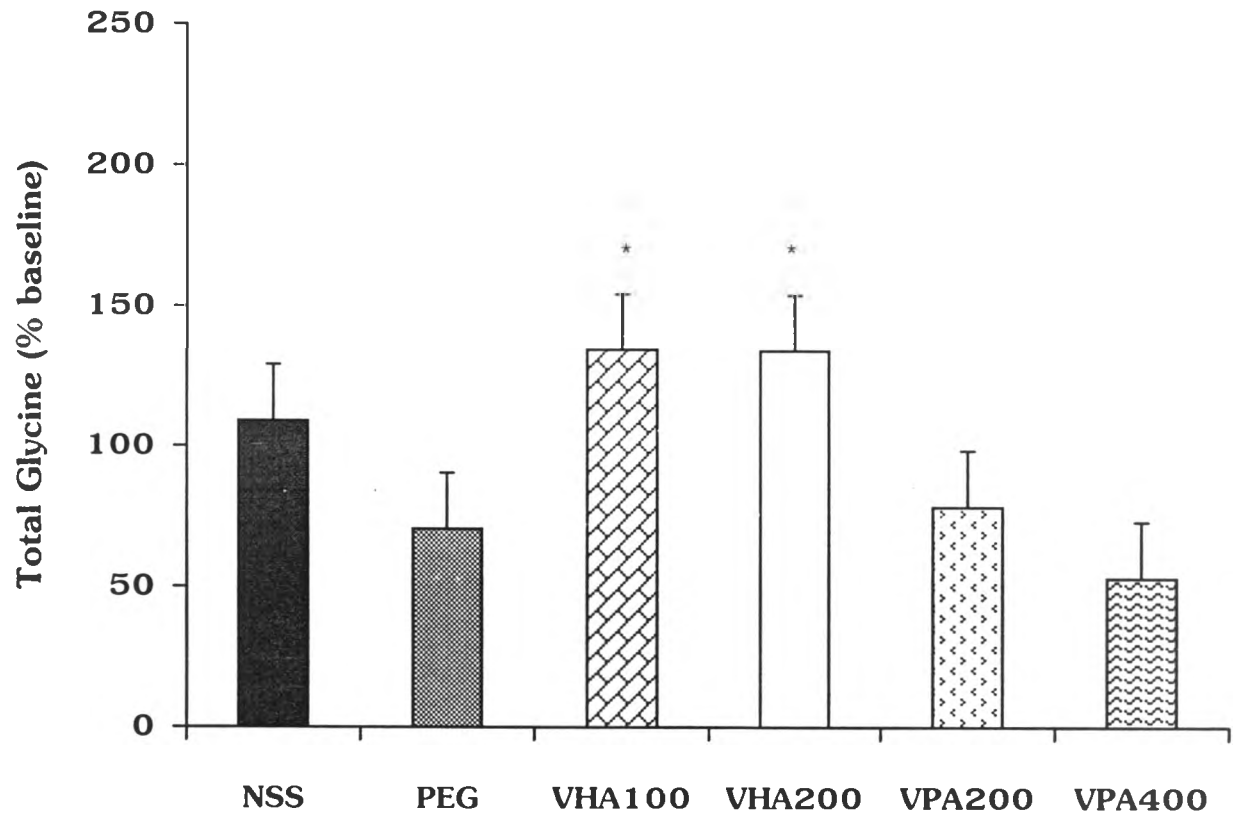


Figure 15. Effects of VPA and VHA on the total amount of the rat cortical aspartate in the dialysate collected for 3 hours after an intraperitoneal administration of the tested substances.



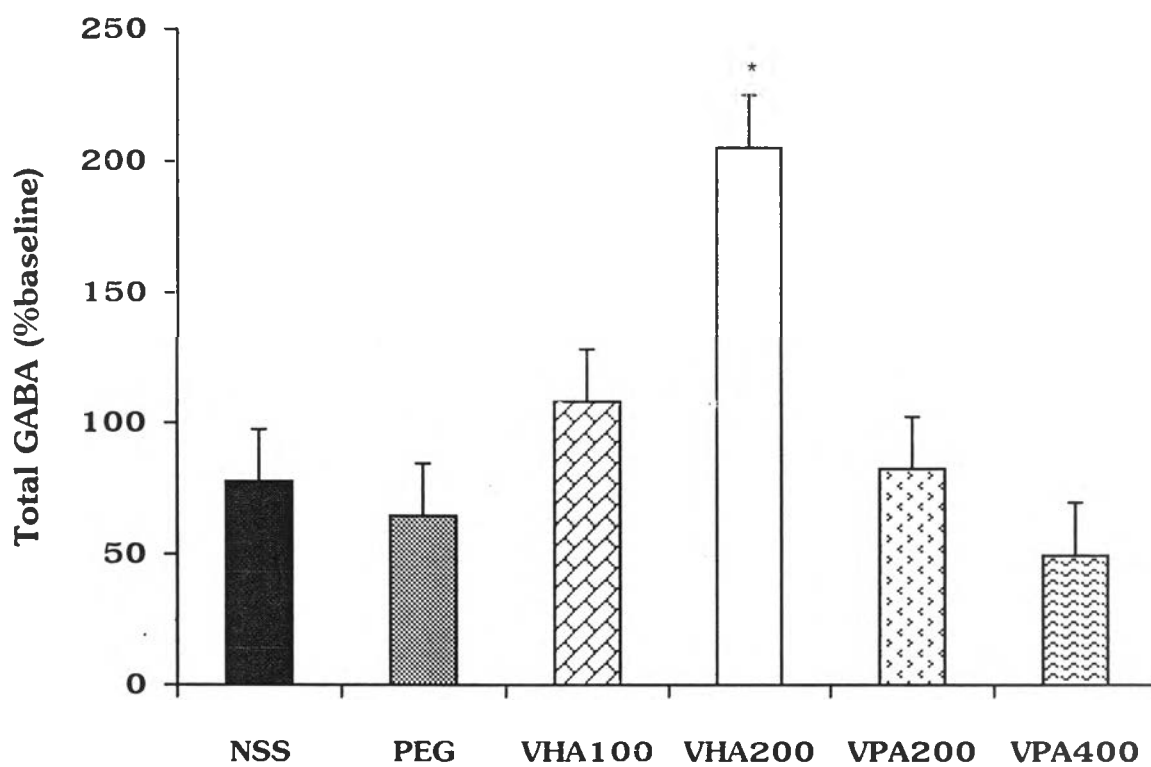
* $p < 0.05$ denotes statistically significant difference from PEG400

Figure 16. Effects of VPA and VHA on the total amount of the rat cortical glutamate in the dialysate collected for 3 hours after an intraperitoneal administration of the tested substances.



* $p < 0.05$ denotes statistically significant difference from PEG400

Figure 17. Effects of VPA and VHA on the total amount of the rat cortical glycine in the dialysate collected for 3 hours after an intraperitoneal administration of the tested substances.



* $p < 0.05$ denotes statistically significant difference from PEG400

Figure 18. Effects of VPA and VHA on the total amount of the rat cortical GABA in the dialysate collected for 3 hours after an intraperitoneal administration of the tested substances