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ALTERATIONS OF CARDIAC CHOLINOCEPTOR AND  
ADRENOCEPTOR RESPONSES DURING BENZODIAZEPINES  
TREATMENT AND TERMINATION

BY

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A THESIS SUBMITTED IN PARTIAL FULFILLMENT OF  
THE REQUIREMENTS FOR THE DEGREE OF  
MASTER OF SCIENCE  
(TOXICOLOGY)

IN THE  
FACULTY OF GRADUATE STUDIES  
OF  
MAHIDOL UNIVERSITY

1986

อภินันท์นากการ

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### Summary

The results of this study can be summarized as follow :

1. The intraperitoneal injection of a rather high dose (20 mg/kg) of diazepam twice daily for 7 days produced the reduction in sleeping times which can be observed clearly on day 2 to 4. The body weights of BZP-treated rats remained the same throughout the test period. At the end of the BZP treatment, a significant lower body weight was observed in BZP-treated group as compared to the control group.
2. The low dose (2 mg/kg) of diazepam Ip., twice daily for 1,2,3 and 4 weeks did not significantly alter the rat atria response to pilocarpine.
3. The potency of the negative chronotropic action of the tested cholinergic agonist is carbachol > methacholine > pilocarpine.
4. In the BZP-treated rats (20 mg/kg, Ip., twice daily for 7 days), the increases in negative chronotropic action of pilocarpine was more markedly than methacholine. At low doses of carbachol there were no significant alterations as compared to the control, except at a very high dose the increase in negative chronotropic effect was observed.

5. The increase in the negative chronotropic action of pilocarpine in the BZP-treated group was clearly observed on day 1 of termination. The increased sensitivity to pilocarpine was gradually diminished and reach normal on day 5.
6. In the diazepam-treated rats (20 mg/kg, Ip., twice daily for 7 days), the effect of norepinephrine and isoproterenol were not significantly different from control when tested on day 7 of diazepam treatment. However, the significant reduction on the effect of these adrenoceptor agonists were observed on day 3 following diazepam termination, and gradually returned to normal on day 5.
7. The rather high doses (20-50 times of therapeutic range) of several benzodiazepines; clonazepam, midazolam, triazolam given intraperitoneally or orally twice daily for 7 days to each group of rats slightly but not significant increased the responses of rat atria to pilocarpine.
8. Triazolam 0.25 mg/kg given orally twice daily for 15 days to the rats significantly increased the responses of rat atria to pilocarpine on day 15 of treatment and day 1 of termination.

9. The negative chronotropic actions of pilocarpine and methacholine were significantly increased in right atria of thiamine-deficient rats as compared to the control groups.
10. The positive chronotropic actions of norepinephrine and isoproterenol were significantly decreased in right atria of thiamine-deficient rats as compared to the control groups.

