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CARDIOVASCULAR PHARMACOLOGY OF  
 $\Delta^9$ -TETRAHYDROCANNABINOL

BY

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CHAPTER 6

SUMMARY

Using one solvent system, Bovine albumin, and one species and strain of animals, Harlan Wistar rats, a series of experiments were conducted to determine the cardiovascular and respiratory effects of an intravenously administered, 97% pure natural  $\Delta^9$ -Tetrahydrocannabinol. A dose-dependent decrease in heart rate, respiration rate, diastolic, systolic and mean blood pressure was observed, as well as a decrease in internal body temperature. These responses are consistent with the possibility of hypothalamic stimulation in the central nervous system.

Later investigations showed that pretreating the animals with atropine inhibited the effect of THC on heart rate, and to a lesser degree on blood pressure. No effect on the respiration rate response to THC was noted by prior atropinization of the experimental animal.

Bilateral vagotomy abolished the negative chronotropic response to the administration of THC, thus showing that the effect of THC on heart rate was not a result of a direct action on the heart, but rather an action mediated through the vagus. Bilateral

vagotomy inhibited the fall in blood pressure and the respiratory rate depression that occurs after the administration of THC.

Inhibition of the response to bilateral carotid occlusion was observed as the result of the administration of THC. Thus it appears that there is a malfunction in at least one cardiovascular reflex controlling blood pressure in the intact rat.

Further studies were conducted to try to determine where in the bilateral carotid occlusion reflex THC was having its effect. These studies, in which norepinephrine was administered to animals pretreated with THC, showed that the inhibition of the bilateral carotid occlusion reflex was not the result of the ineffectiveness of norepinephrine. Moreover, the studies showed that the effect of norepinephrine was increased if the animal was pretreated with THC.

Using a ganglionic stimulating agent, dimethylphenylpiperazinium, experiments were devised to determine if THC was interfering with the bilateral carotid occlusion reflex before or after the ganglia in the reflex arc. The effect of DMPP was not diminished, and was in fact increased after the administration of THC. This demonstrated that the inhibition of the bilateral carotid occlusion reflex was taking place prior to the

ganglia in the reflex arc.

The studies presented in this dissertation describe the cardiovascular and respiration rate effects of THC in the rat. Depression of heart rate was seen to be the result of a non-direct action on the heart. The changes in heart rate, blood pressure, and internal body temperature appear to be the result of an interaction between THC and the central nervous system, or more specifically the hypothalamus; though the possibility of some degree of peripheral cholinergic involvement cannot be disregarded.

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