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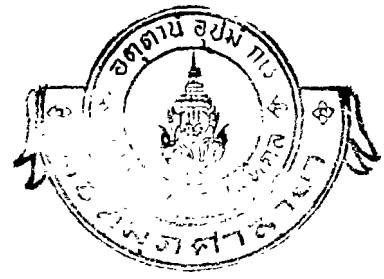

COMPARATIVE EFFECTS OF ALLOXAN AND STREPTOZOTOCIN ON HEPATIC DRUG METABOLISM

BY

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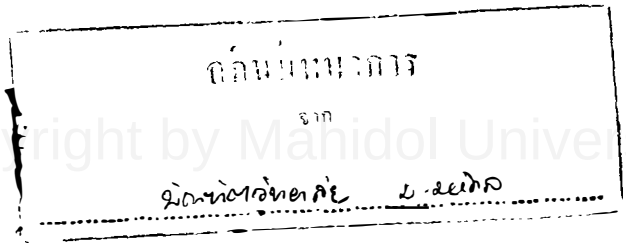

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Abstract

The acute and chronic effects of alloxan (120mg/kg,sc) and streptozotocin (55mg/kg,ip) on the activities of four hepatic drug-metabolizing enzymes in male Wistar rats were compared over a period of 2 weeks(1,4,7,11 and 14 days). The optimum condition for the induction of hyperglycemia in rats was found by fasting the animals for 24 hours before and 6 hours after either diabetogen. When compared with control, a significant decrease by 10-40% in the activity of aminopyrine N-demethylase was seen both in alloxan and in streptozotocin diabetes. Aniline hydroxylase activity was increased by about 20% at day 7th after alloxan and by about 80% at day 4th after streptozotocin. In contrast, a 15-40% reduction in this enzymatic activity was found in these two groups of diabetic animals at the remaining days. p-Chloro-N-methylaniline N-demethylase activity was decreased by 17% in alloxan but increased by 17% in streptozotocin induced diabetes. Furthermore,p-nitroanisole O-demethylase activity was increased in both groups of the animals, 42% in alloxan and

62% in streptozotocin, respectively. Kinetic studies using Lineweaver-Burk plots have suggested that the enhanced aniline hydroxylase activity from streptozotocin -treated rats was due to a quantitative change in the enzyme. Such observed alterations in the activities of hepatic drug-metabolizing enzymes could not be mediated by a change in the circulating testosterone level, which was found to be unaffected by either alloxan or streptozotocin. In agreement with the findings of previous investigators, the microsome was most likely to be the major site of action of these two drugs, since SDS polyacrylamide gel electrophoresis protein profile of microsomes from chemical diabetic rats exhibited a marked difference from that of normal microsome.