MUTAGENIC EFFECT OF SOME TRANQUILIZERS IN DROSOPHILA

BY

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A thesis submitted in partial fulfillment

of

the requirements for the degree of

MASTER OF SCIENCE

In

Agriculture

(Genetics)

Department of Genetics

Faculty of Agriculture

Ain Shams University

(1989)

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APPROVAL SHEET

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Date of examination: 19/10/1989

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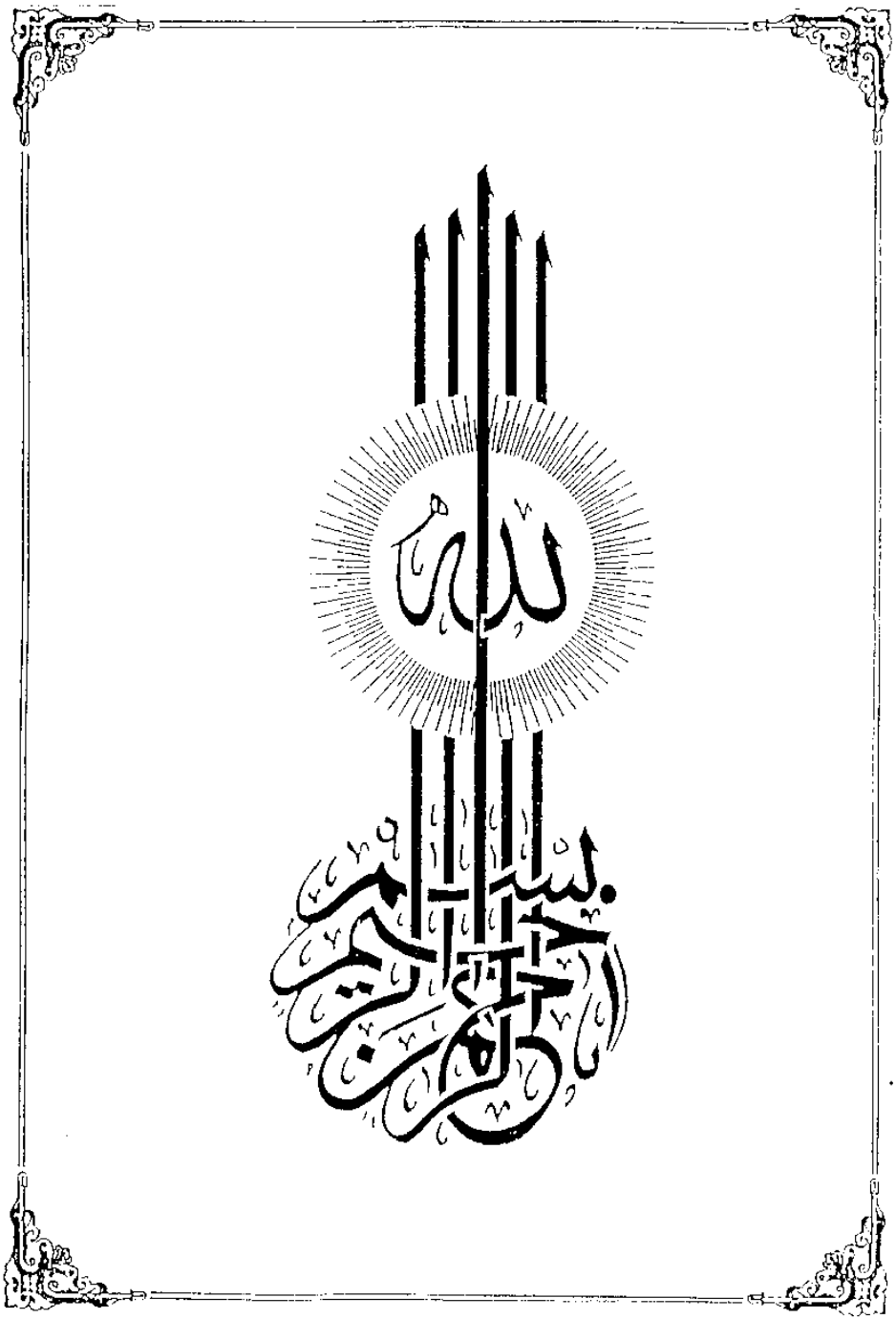

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B.Sc.1976

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ABSTRACT

The mutagenic potentialities of two benzodiazepine tranquilizers lorazepam and diazepam were tested in *D. melanogaster* using two test systems, the sex-linked recessive lethals test (SLRL) and the estimation of the activities of the two enzymes cholinesterase (ChE) and aliesterase (ALiE). Kaha male files of *Drosophila melanogaster* were reared on a medium containing two concentrations of each of the two drugs, 5 and 10 mg/100 ml medium, and screened for sex-linked recessive lethals.

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The results indicated that significant numbers of recessive lethals were induced in Drosophila in all stages of spermatogenesis except in spermatozoa stage at the two doses of each of the two drugs, indicating that lorazepam (ativan) and diazepam (valinil) are capable of inducins sex-linked recessive lethal mutations in Drosophila melanogaster. Meanwhile, the two drugs showed a mutagenic effect on the genetic background of each of ChE and AliE, which proves the mutagenic potentiality of the two drugs.

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ACKNOWLEDGEMENT

The writer wishes to express her sincere gratitude to Professor Dr. A.Z. EL ABIDIN SALAM, head of the Department of Genetics, Faculty of Agriculture, Ain Shams University, and Professor Dr. H.A. de-Hondt, Cell Biology Laboratory, National Research Centre, for supervising this work and for their constructive criticism during the progress of the study.

Thanks are also due to Dr. MARY THERASE IBRAHIM Lecturer of Genetics, Cell Biology Laboratory, National Research Centre, for her help offered during the progress of this study.

Thanks are also extended to the spirit of the late Lecturer of Genetics, Dr. ZENAB A. EL HADIDY, for her help throughout the experiments of this study.

Finally, the writer acknowledges the guidance by the staff members of the Genetics Department Faculty of Agric ulture, Ain Shams University, and the members of the Cell Biology Laboratory, National Research Centre.

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INTRODUCTION

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1. INTRODUCTION

Several reports indicate that many chemical pollutants which are widely spread in the environment, such as pesticides and drugs, are mutagenic in various test systems. These findings reflect an urgent need to draw more attention to the examination of the possible genetic hazards of such pollutants to public health and national biological resources. A number of psychoactive drugs are also suspected of inducing chromosome breakage (Morton et al., 1969).

Tranquilizers, a group of drugs introduced as psychotherapeutic agents, are being extensively used in human medicine to allay anxiety and muscle tension (Byck, 1974).

Since their introduction in medicine, a large number of individuals has been treated with these drugs. Some available reports reveal the mutagenic potential of these drugs. The extensive increase in the use of tranquilizers belonging to the benzodiazepine group, which includes diazepam and lorazepam, subjected these drugs to special attention concerning their mutagenic potential.

Diazepam, the active ingredient of valinil, produced isochromatid and chromatid breaks in human leucocytes

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(Morton et al., 1969) and sex-linked recessive lethals in Drosophila melanogaster (Susheela, 1975).

Lorazepam, the active ingredient of ativan, is useful in psychoneurotic states manifested by anxiety, tension, insomnia and fear. It was shown to have no toxic effect in human (McCurdy and Schatzberg, 1978).

The present study was carried out to evaluate the mutagenic response of ativan and valinil using two test system, the sex-linked recessive lethal test in Drosophila melanogaster which is known to be efficient in detecting chemical mutagens (Sobels and Vogel, 1976), and by estimating the effect of both drugs on the activity of cholinesterase and aliesterase, which is a recent tool in mutagenicity testing.

These two different mutagenicity tests were conducted in the present study to gain some insight into the genetic relation between the cholinesterase activity, aliesterase activity and the mutagenic effect of the benzodiazepine group, and also in order to compare the sensitivity of the two test systems.

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