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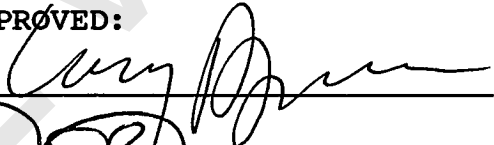

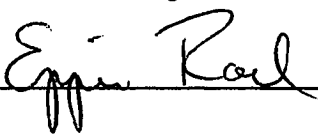
PREVIEW


SELECTIVE CHOLINESTERASE INHIBITORS

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BIOLOGY

APPROVED:


Dean of the Graduate School

SELECTIVE CHOLINESTERASE INHIBITORS

by

GEORGINA PACHECO, B.S.

THESIS

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ABSTRACT

One aspect of senile dementia of the Alzheimer's type (SDAT) is that the brain loses the ability to synthesize acetylcholine (ACh). One function of ACh within the central nervous system (CNS) is related to supporting memory functions. If cognitive impairment in SDAT is caused by inadequate amounts of ACh, treatment strategies can be designed to facilitate cholinergic activity. One strategy is to inhibit the breakdown of ACh produced in the brains of patients with SDAT. This can be accomplished by inhibiting acetylcholinesterase (AChE). In order to minimize toxicity, however, a cholinesterase inhibitor selective for only AChE would be an ideal treatment. The purpose of this study was to determine the selectivity of physostigmine, metrifonate, methanesulfonyl fluoride (MSF) and tetrahydroaminoacridine (THA), compounds being considered for the treatment of SDAT, for human brain AChE as compared to butyrylcholinesterase (BChE).

These experiments were conducted using human brain cortex. The results show that MSF is highly selective as an inhibitor of AChE as compared to BChE. Physostigmine inhibited AChE more than BChE. Metrifonate was found to inhibit BChE more than AChE. THA inhibited both enzymes in a complex way.

Table of Contents

	<u>Page</u>
Acknowledgements.....	iii
Abstract.....	iv
List of Figures.....	vii
Introduction.....	1
The Role of Cholinergic Function in Diseases Associated with Memory.....	1
The Role of Cholinergic Function in Normal Memory.....	3
Treatment Strategies Using Cholinesterase Inhibitors.....	5
Method.....	8
Tissue.....	8
Apparatus.....	8
Procedure.....	8
Tissue Preparation.....	8
Cholinesterase Assays.....	9
Experiments Measuring Inhibition.....	10
Irreversible Inhibition by Sulfonyl Fluorides, Carbamates, and Organophosphates.....	10
Reversible Inhibition by Tetrahydro- aminoacridine.....	12
Data Analysis.....	13

Results.....	15
Discussion.....	19
References.....	20
Appendix.....	26
Vita.....	27