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# Computational Approaches for Identifying Drugs Against Alzheimer's Disease



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## PREFACE

Alzheimer's disease is the most common cause of dementia that leads to problems with memory, thinking and behavior. Alzheimer's disease is named after the Scientist Alois Alzheimer, who described it as a physical disease that affects the brain. During the course of the disease, proteins build up in the brain to form structures called plaques. This leads to the loss of connection between the nerve cells and eventually leads to the death of the nerve cells and loss of the brain tissues. People with Alzheimer's also have a shortage of some important chemicals in the brain by which the signals are not transmitted effectively. So far there is no cure for Alzheimer's disease. In this study, 3D QSAR and pharmacophore mapping studies were carried out using Accelrys Discovery Studio 2.1. Quantitative Structure–Activity Relationship models (QSAR models) are classification models used in the chemical and biological sciences.  $\beta$ -Secretase is an important protease in the pathogenesis of Alzheimer's disease. Some statine-based peptidomimetics show inhibitory activities to  $\beta$ -secretase. To explore the inhibitory mechanism, molecular docking and three-dimensional quantitative structure–activity relationship (3D-QSAR) studies on these analogues were performed. This study was useful in identifying the involvement of statine-based peptidomimetics and their analogues in the treatment of Alzheimer's disease. Further in vitro studies could be carried out to find a potent target in curing Alzheimer's disease.

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**Dr. Radha Mahendran**

## **DEDICATION**

This work is dedicated to my *Guru, Dr.G.JAYARAMAN* (Late) *Professor & co-ordinator, Molecular biology program, Department of Genetics, DR.ALM.PG. Institute of Basic Medical Sciences, Taramani, University of Madras*, Chennai, India.

I thank him for being my *MENTOR, LEADER, INSTRUCTOR, GUIDE AND INSPIRATION.*

**Dr. Radha Mahendran**

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## **ABSTRACT**

Alzheimer's disease is the most common form of dementia which is incurable. Although some kinds of memory loss are normal during aging, the changes due to aging are not severe enough to interfere with the level of function.  $\beta$ -Secretase is an important protease in the pathogenesis of Alzheimer's disease. Some statine-based peptidomimetics show inhibitory activities to  $\beta$ -secretase. To explore the inhibitory mechanism, Molecular docking and three-dimensional quantitative structure–activity relationship (3D-QSAR) studies on these analogues were performed. Quantitative structure-activity relationship (QSAR) modeling pertains to the construction of predictive models of biological activities as a function of structural and molecular information of a compound library. The concept of QSAR has typically been used for drug discovery and development and has gained wide applicability for correlating molecular information with not only biological activities but also with other physicochemical properties, which has therefore been termed quantitative structure-property relationship (QSPR). In this study, 3D QSAR and pharmacophore mapping studies were carried out using Accelrys Discovery Studio 2.1. Nine best drugs were selected out of the 16 ligands and pharmacophore features were generated. Further hypothesis was done using Hypogen and out of 3 molecules selected one molecule produced the highest fit value of 3.473 from the test set. Hence, it could be one of the best drugs in the treatment of Alzheimer's disease.