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Computational Approaches for Identifying Drugs Against Alzheimer's Disease

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Mahendran, Radha, Jeyabaskar, Suganya, Francis, Astral Gabriella: Computational Approaches for Identifying Drugs Against Alzheimer's Disease, Hamburg, Anchor Academic Publishing 2017

PDF-eBook-ISBN: 978-3-96067-638-6
Druck/Herstellung: Anchor Academic Publishing, Hamburg, 2017

Bibliografische Information der Deutschen Nationalbibliothek:
Die Deutsche Nationalbibliothek verzeichnet diese Publikation in der Deutschen Nationalbibliografie; detaillierte bibliografische Daten sind im Internet über http://dnb.d-nb.de abrufbar.

Bibliographical Information of the German National Library:
The German National Library lists this publication in the German National Bibliography. Detailed bibliographic data can be found at: http://dnb.d-nb.de

Hermannstal 119k, 22119 Hamburg
http://www.diplomica-verlag.de, Hamburg 2017
Printed in Germany

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. β-Secretase is an important protease in the pathogenesis of Alzheimer's disease. Some statine-based peptidomimetics show inhibitory activities to β-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.

ACKNOWLEDGEMENTS

First and foremost, I thank **God** for enabling me to complete this project.

I would like to express my sincere gratitude to our Management, especially ***Dr.Ishari k.Ganesh, Chancellor, Vels University***, Founder-Chairman, Vels group of Institutions, for giving us a platform to prove ourselves in the field of Bioinformatics and constantly motivating us in all our endeavours.

Dr.A.Jothi Murugan, Vice-President (P&D), Vels University deserves a big word of thanks from me since he was a silent motivator for all our academic achievements.

I would like to thank ***Dr.V. Thamizh Arasan, Vice-Chancellor, Vels University*** for always motivating us.

I would also like to thank ***Dr.S.Sivasubramaniam, Advisor-Research &Development, Vels University*** for always encouraging us.

I record my sincere gratitude to the ***Registrar, Dr. A. R.Veeramani*** and the ***Controller of Examinations***, ***Dr. A. Joseph Durai*** for their support.

I am Very thankful to ***Dr.DinakaranMichael, Dean, School of Life sciences,*** for his constant help and support in all our endevours.

I thank the editorial team of *publishing*, for taking effort in editing this project and constantly giving their opinions during the course of time.

I wish to express my sincere and warm Acknowledgements to my ***Family members*** for their encouragement and support.

THANKS TO ALL

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

Index

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. β-Secretase is an important protease in the pathogenesis of Alzheimer's disease. Some statine-based peptidomimetics show inhibitory activities to β-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.