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Electronic description for ANN-QSAR model building as new approach for the optimal design of new inhibitors of GSK3-β in the context of Alzheimer's disease

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Alzheimer's disease (AD) is the leading cause of dementia worldwide, currently affecting approximately 55 million people, with an estimated increase to 131.5 million cases by 2050. Given its significant impact, effective treatment is urgently needed. Consequently, numerous studies and strategies are being developed, drawing upon various theories regarding its etiology, which remains incompletely understood. One promising treatment approach involves the inhibition of the GSK-3β enzyme. Research indicates that the hyperphosphorylation of tau protein, facilitated by GSK-3β, is directly associated with the formation of neurofibrillary tangles, a hallmark pathological feature of AD. Moreover, GSK-3β is also involved in regulating the production and deposition of beta-amyloid, another crucial component of the plaques found in the brains of Alzheimer's patients. This suggests that inhibiting GSK-3β could be a promising solution for the treatment of AD. To address this challenge, our research explored a promising avenue in drug discovery for AD, employing Artificial Neural Networks - Quantitative Structure Activity Relationship (ANN-QSAR) models. These models have demonstrated great potential in predicting the biological activity of compounds based on their molecular structures. By harnessing the capabilities of machine learning and computational chemistry, we aimed to create a systematic approach for analyzing and forecasting the activity of potential drug candidates, thus streamlining the drug discovery process. We assembled a diverse set of compounds targeting this receptor and utilized Density Functional Theory (DFT) calculations to extract essential electronic descriptors, effectively representing the structural features of the compounds. Subsequently, these molecular descriptors served as input for training the ANN-QSAR models alongside corresponding biological activity data, enabling us to predict the potential efficacy of novel compounds as GSK-3β inhibitors. Through comprehensive analysis and validation of the ANN-QSAR models, we successfully identified several promising compounds with potential therapeutic activity against AD.

References

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