Chapter 2

Objective and Plan of Work

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2.1 Objective

AD is a neurodegenerative disease which progresses into loss of the memory, cognition and thinking ability of a patient. The effects of disease lead to difficulty in performing activities of daily living and make the patient dependent on the caregiver. AI is rapidly transforming drug discovery, bringing speed and efficiency to the traditionally slow and expensive process. Here's how:

- Mining data mountains: AI excels at analyzing vast datasets of molecular structures, genetic information, and clinical trials, uncovering hidden patterns, and predicting drug properties [34].
- Designing new molecules: AI algorithms can design new drug candidates with desired properties, even suggesting novel scaffolds not found in nature [31].
- Repurposing existing drugs: AI can identify new uses for existing drugs, accelerating development and reducing costs [35].
- Optimizing clinical trials: AI can analyze patient data to design more efficient and targeted clinical trials, leading to faster drug approvals [36].

In the present research, efforts have been made to employ AI to find drugs for the treatment of AD.

2.2 Plan of work

2.2.1 Classification of BACE-1 inhibitors using machine learning

Plan of Work:

- Utilize existing datasets of BACE-1 inhibitors and their activity data.
- Extract various molecular descriptors such as Mordred descriptors and fingerprints.

- Apply and compare different machine learning algorithms, including Naïve Bayes, kNN, SVM, Random Forest, and XGBoost.
- Evaluate model performance using metrics like accuracy, precision, recall, and F1 score.
- Analyze the structural features of active and inactive compounds based on predicted classifications.

2.2.2 Machine learning-based screening of in-house database for BACE-1 inhibitors

Plan of Work:

- Build a robust ML model based on a suitable dataset of known BACE-1 inhibitors and their properties.
- Optimize the model for accurate prediction of inhibitor activity.
- Screen the in-house database using the developed model to identify promising candidates.
- Experimentally validate the activity of shortlisted compounds through assays like BACE-1 inhibitor activity evaluation.
- Perform docking studies to understand the binding interactions of identified hits.

2.2.3 Natural Language Processing (NLP) for deep learning-based prediction of BBB permeability

Plan of Work:

- Utilize public databases like B3DB containing molecules and their BBB permeability data.
- Generate SELFIES strings to represent molecular structures.

- Apply NLP techniques like word-level and N-gram tokenization to convert SELFIES into numerical vectors.
- Train and evaluate various deep learning models like ANN and LSTM using the extracted features.
- Optimize the model for accurate prediction of BBB permeability.

2.2.4 Design, synthesis and biological evaluation of *N-benzylpiperidines* as potential multitargeted ligands for the treatment of Alzheimer's disease

Plan of Work:

- Perform structure-based drug design (SBDD) to identify promising N-benzylpiperidine scaffolds.
- Synthesize N-benzylpiperidine derivatives with structural modifications predicted to enhance multi-target activity.
- Evaluate the *in-vitro* inhibitory activity of synthesized compounds against BACE-1, cholinesterases, and amyloid aggregation assays.
- Assess the *in-vivo* efficacy of promising candidates in relevant AD animal models.