CHAPTER 1

INTRODUCTION

Drug–drug interactions (DDIs) occur during the co-administration of medications. They are a common cause of adverse drug reactions (ADRs) and lead to increasing healthcare costs.

Drug-drug interactions occur when a drug interacts, or interferes, with another drug. This can alter the way one or both of the drugs act in the body or cause unexpected side effects. The drugs involved can be prescription medications, over-the-counter medicines and even vitamins and herbal products.

Drug-drug interactions (DDIs) are an important consideration in both development and clinical application, especially for co-administered medications. While it is necessary to identify all possible DDIs during clinical trials, DDIs are frequently reported after the drugs are approved for clinical use and they are a common cause of adverse drug reactions (ADR) and increasing healthcare costs. Computational prediction may assist in identifying potential DDIs during clinical trials.

We propose a heterogeneous network- assisted inference (HNAI) framework to assist with the prediction of DDIs for Amyotrophic Lateral Sclerosis (ALS) disease.

First, we constructed a comprehensive DDI network that contained 6946 unique DDI pairs connecting 721 approved drugs based on Drug Bank data. Next, we calculated drug–drug pair similarities using four features: phenotypic similarity based on a comprehensive drug–ADR network, therapeutic, chemical and genomic properties.

These things are done by the use of SMILES data and the genomic similarity based on a large drug-target interaction network built using the DrugBank and the therapeutic target database.

In-vivo clinical trials involved administering drugs into a person which was socially and economically not viable. The co-administration of medications leads to DDIs which may result in Adverse Drug Reaction(ADR) and is a major healthcare issue. There is an immediate need to detect and determine DDIs before medications are approved in order to reduce patient mortality.

There is a lack of comprehensive experimental data and high study costs are incurred in the experimental approaches to identify DDIs. The limited ability to identify DDIs using experimental approaches is a major obstacle during drug development for ALS.

During the past decade, several methods have been designed and made available for the prediction of potential DDIs but none of which involve Machine-Learning. Therefore the development of a machine learning based model using multidimensional drug properties must be a promising strategy to predict unknown DDIs of ALS.

We propose a Heterogeneous Network-Assisted Inference(HNAI) framework for large-scale prediction of DDIs. The HNAI model hypothesis for ALS asserts that if two drugs have similar chemical structures, share a similar target protein and similar ADRs and have similar therapeutic purposes, they have a high probability of DDIs.

Several predictive models are implemented by HNAI using supervised learning techniques such as Naive Bayes, Decision tree etc.. By this the drug-drug interactions can be predicted and its adverse drug affects can be mitigated accordingly.

Therefore, by implementing machine learning-based model using multi-dimensional drug properties might be a best suitable way to predict unknown of DDIs for ALS.

1.1 DEFINITION AND ACRONYM

HNAI- Heterogeneous Network Assisted Inference.

DDIs- Drug-Drug Interactions.

ADR- Adverse Drug Reactions.

MetaADEDB- Comprehensive database of ADR.

ATC- Anatomical Therapeutic Chemical.

SVM- Support Vector Machine.

Machine learning is a scientific discipline that explores the construction and study of algorithms that can learn from data.

A **Drug interaction** is a situation in which a substance (usually another drug) affects the activity of a drug when both are administered together.

Heterogeneous Network Assisted Inference is a comprehensive term used to denote the different drug properties being used and the network models used for predicting the interactions.