
I. Introduction

According to the FDA, drugs are defined as substances intended to diagnose, cure, alleviate, treat, or prevent diseases. They also include products (excluding food) that affect the structure or function of the human or animal body [1]. Over recent decades, significant scientific advancements have driven the development of innovative drugs [2]. However, despite the rigorous process of clinical trials, it is important to recognize the potential risks associated with adverse side effects that may harm patients. Adverse drug reactions (ADRs) rank among the top 10 leading causes of death in some countries [3]. The Uppsala Monitoring Center, an international ADR database, has collected nearly 4.7 million case reports from national centers, estimating that ADRs account for approximately 6–10% of these cases [3]. Accurate and efficient identification of adverse events is essential for the early detection and management of these risks.

Conventional methods in new drug research involved both in vivo and in vitro testing for safety, side effects, and toxicity [4]. However, these methods require significant time, effort, and resources [4]. Pharmacologists are exploring other methodologies, such as computer-aided drug design (CADD), due to constraints [5]. CADD is known as "in silico" in biological terminology [5]. Early prediction of toxicity using in silico methods allows for early identification of possible adverse effects [6]. In 2022, annual revenues from in silico drug development reached \$8.3 billion [6], with growth expected as machine learning and data analysis advance.

In silico research has predicted pharmacological side effects in numerous disorders. Karimah et al. used SMILES2Vec, a vector representation of pharmacological compounds, to study hepatobiliary disorders in 2023 [7]. Because this research uses text-based material, it uses Long Short-Term Memory (LSTM) [7]. The best model had an F1-Score of 70.78% and an accuracy of 67.98% [7]. Nevertheless, their complex model architecture (CONV + 2-layer LSTM + DENSE) faced overfitting issues and generalization constraints [7]. In the same year, Afinda et al. also conducted research using SMILES2Vec to predict drug side effects in hepatobiliary disorders with datasets from the Side Effect Resource (SIDER) version 4.1 [8]. The research of the Gated Recurrent Unit (GRU) model revealed an optimum architecture with an accuracy of 64.39% and an F1-Score of 67.39%, and the Adagrad optimizer can boost it to 68.62% [8]. Despite these results, the study faced limitations in learning long-term dependencies and model training stability [8].

M.R. Wiliatama and R.R. Septiawan developed a drug development prediction model for hepatobiliary disorders in the same year, using the Gravitational Search Algorithm (GSA) for feature selection and ensemble approaches [9]. The researchers used Random Forest (RF), Adaptive Boosting (AdaBoost), and Extreme Gradient Boosting (XGBoost) [9]. RF had the highest accuracy and F1-Score (0.68 and 0.77), though the study faced challenges with complex data distribution patterns [9]. In 2023, D.R. Ahmad and Jondri also used the ensemble method approach [10]. They conducted a study on metabolic and nutritional disorders using SIDER datasets [10]. The research results show that XGBoost has the highest accuracy of 0.74 and an F1-Score of 0.81 in predicting drug side effects, but encountered data imbalance issues that required Random Oversampler implementation [10].

In 2022, M.K. Keleş and Ü. Kiliç employed the binary Artificial Bee Colony Algorithm (ABC) to classify volumetric brain data for Alzheimer's disease [11]. The online system volBrain processed volumetric and statistical MRI brain scans from the Alzheimer's Disease Neuroimaging Initiative (ADNI) [11]. Binary Grey Wolf Optimization (BGWO) using Random Forest as the classifier had the highest average accuracy of 0.905, while ABC had the lowest standard deviation and the best stability [11]. A notable limitation was the small sample size affecting result generalization [11].

From these studies, several limitations have been identified as factors affecting optimal research outcomes. This research aims to evaluate the effectiveness of feature selection using Artificial Bee Colony-Ensemble algorithm, assess the impact of hyperparameter tuning, and analyze the model's performance in predicting drug side effects on reproductive system and breast disorders. The feature selection process will utilize the Artificial Bee Colony (ABC) algorithm, which is inspired by intelligent honeybee swarm behavior divided into three groups: worker bees, observer bees, and scout bees [12]. The combination of ABC and ensemble methods is expected to provide optimal results in accurately identifying drug side effects, thus contributing to developing safer and more effective drugs.