

AI-DRIVEN DRUG SIDE EFFECT ANALYSIS USING DNA PROFILES: A SYSTEMATIC REVIEW

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Abstract: Adverse drug reactions (ADRs) are a major global cause of hospital admissions and preventable medical issues. Traditional drug prescriptions that follow a “one-size-fits-all” approach overlook genetic differences between individuals, resulting in variable drug responses. **Pharmacogenomics** combines genetic information with pharmacological insights to support personalized treatment strategies. With the rapid growth of genomic data and drug–target databases, **artificial intelligence (AI)** now plays a crucial role in modeling the complex interactions between genetic variations, drug structures, and potential side effects. This paper reviews recent **machine learning** and **deep learning** techniques for predicting ADRs, including Random Forest, XGBoost, convolutional neural networks, graph neural networks, and multimodal fusion frameworks. Studies show that integrating genetic information with molecular drug features markedly enhances prediction performance compared to models using only drug characteristics. Despite this progress, key challenges persist, such as limited labeled data, lack of interpretability, and reduced model transferability across populations. Finally, we propose a high-level AI-driven framework that links patient genotype data with pharmacogenomic databases to estimate individual side-effect risks. This review emphasizes the potential of combining DNA-based personalization with advanced AI models to achieve safer and more precise medical treatments.

Keywords: Adverse Drug Reactions (ADRs), Pharmacogenomics, Artificial Intelligence (AI), Machine Learning, Deep Learning, Personalized Medicine

I. INTRODUCTION

Adverse drug reactions (ADRs) continue to pose a significant challenge in clinical medicine, contributing to hospital admissions, therapy interruption, and increased patient morbidity[1]. Conventional prescribing practices often rely on a “one-size-fits-all” model, assuming uniform drug response among individuals. In practice, however, drug efficacy and toxicity vary widely due to genetic diversity[2]. Genetic variants such as single-nucleotide polymorphisms (SNPs) in genes encoding metabolic enzymes, receptors, and transporters can substantially influence pharmacokinetic and pharmacodynamic outcomes[3].

Pharmacogenomics, which explores how genetic variation affects drug response, underpins precision medicine initiatives [4]. Advances in genome sequencing and the availability of large-scale public repositories—such as the **1000 Genomes Project**, **DrugBank**, **SIDER**, and **FAERS**—have enabled data-driven modeling of ADRs [5][6]. While classical **machine-learning** algorithms such as Random Forest and XGBoost have been applied for ADR prediction, their performance remains limited for complex, high-dimensional biological datasets[7].

Recent developments in **deep learning**, including convolutional neural networks (CNNs), Transformers, and graph neural networks (GNNs), allow modeling of intricate, multimodal biomedical relationships[8]. Fusion-based architectures combining drug molecular fingerprints with genomic variants have achieved improved ADR-prediction accuracy[9]. Moreover, pharmacogenomics-aware networks such as **DGANet** highlight the potential of integrating gene–drug interactions for personalized ADR risk estimation[10].

This review summarizes current **AI-based** strategies for predicting drug side effects using genomic profiles, evaluating datasets, architectures, and methodological limitations. It also proposes a conceptual AI framework that integrates patient genotype information with molecular drug features to estimate individualized ADR risks, supporting safer and more personalized therapy decisions.

II. PHARMACOGENOMICS BACKGROUND:

Pharmacogenomics explores the influence of genetic diversity on how individuals respond to medications. One of

the most common genetic differences is the **single-nucleotide polymorphism (SNP)** a change in a single DNA base that can vary among people. When such polymorphisms occur in genes responsible for **drug-metabolizing enzymes** (such as members of the CYP450 family), **transport proteins**, or **drug-binding receptors**, they can alter the way drugs are absorbed, processed, and cleared from the body, sometimes affecting both effectiveness and toxicity.

Key genes like **CYP2D6**, **CYP2C9**, and **TPMT** are particularly important because they determine the rate at which many drugs are metabolized. Individuals carrying **loss-of-function variants** in these genes may accumulate higher concentrations of medication in their bloodstream, which increases the risk of adverse side effects even at standard dosages. This genetic variability explains why a treatment that works safely for one person may produce harmful outcomes in another.

Conventional prescribing approaches generally overlook such genetic factors. With the rise of publicly accessible genomic resources—such as the **1000 Genomes Project**—and specialized databases like **PharmGKB**, **DrugBank**, and **PubChem**, researchers can now merge **genetic** and **chemical** information to enhance precision therapy. Moreover, recent studies indicate that integrating **multi-omics datasets** (including genomic, chemical, and clinical information) within **deep-learning frameworks** substantially improves the accuracy of predicting drug responses and potential adverse effects.

III. EXISTING AI MODELS FOR ADR PREDICTION:

A. Traditional Machine Learning Models:

Early computational approaches for adverse drug reaction (ADR) prediction relied on classical **machine learning algorithms** such as **Random Forest (RF)** and **Extreme Gradient Boosting (XGBoost)**. These models primarily utilize **drug-related chemical descriptors**—including molecular fingerprints, structural features, and physicochemical properties—to identify potential side-effect patterns.

IV. COMPARATIVE ANALYSIS:

Table I. Comparison of existing AI-based studies on adverse drug reaction (ADR) prediction using pharmacogenomic and drug data.

This table compares recent studies that apply machine learning and deep learning approaches for adverse drug reaction prediction, highlighting their data sources, models, and outcomes.

Their main advantage lies in their **robust performance with structured, tabular datasets** and their **interpretability**, which allows researchers to understand key molecular predictors.

However, such models have limited ability to capture **complex biological interactions** and **nonlinear genomic dependencies**, making them less suitable for high-dimensional **DNA or multi-omics data** where feature relationships are interdependent and non-linear.

B. Deep Learning on Drug Data:

With the advent of deep learning, models such as **Convolutional Neural Networks (CNNs)** have been applied to extract spatial and structural patterns directly from **drug molecular representations**. These networks can automatically learn hierarchical chemical features without requiring extensive manual feature engineering. In addition, **Graph Neural Networks (GNNs)** have emerged as a powerful framework for representing **drugs as molecular graphs**, where nodes correspond to atoms and edges represent chemical bonds. This representation enables the model to better capture **topological and relational properties** of molecules, thereby improving accuracy in **drug–target and ADR prediction tasks**.

C. Deep Learning in Pharmacogenomics:

Recent studies have begun integrating **pharmacogenomic data** with drug structure information to achieve more personalized ADR predictions. These **multi-modal deep learning models** combine **drug molecular descriptors** with **genomic profiles**, such as **single-nucleotide polymorphisms (SNPs)** or **gene expression data**, to model individual differences in drug response. Such approaches enable the prediction of patient-specific side-effect risks by leveraging both **chemical** and **genetic** features. Frameworks using **graph-based learning**, **attention mechanisms**, and **fusion neural networks** have demonstrated improved predictive performance compared to models relying solely on chemical data. These developments mark a shift from general drug safety modeling to **precision pharmacogenomic prediction**, where AI systems aim to tailor medication safety to each patient’s genetic makeup.

Author/Year	Data Used	Model Used	Key Contribution	Result
Ou et al., 2021	DrugBank + SIDER	Fusion DL Model	Combines drug features & omics for ADR	Improved AUROC ↑
He et al., 2025	Pharmacogenomics + CTD	DGANet (CNN + graph features)	Gene–drug–ADR interaction learning	AUROC 92.76%
Lin et al., 2021	Genomic + Clinical	ML + DL Fusion	Patient stratification for treatment outcomes	Increased accuracy in response prediction

V. PROPOSED SYSTEM ARCHITECTURE:

Table 2. Proposed AI-based Framework for Adverse Drug Reaction (ADR) Prediction

The proposed system integrates pharmacogenomic and molecular data to predict adverse drug reactions. It combines patient-specific SNP profiles and drug molecular features through separate encoding modules, followed by a fusion and classification layer that outputs the likelihood of side-effect occurrence.

Component	Input	Processing
DNA SNP Encoder	Patient SNPs (VCF from 1000 Genomes)	Encoded into numerical genomic embeddings (One-hot / k-mer / BERT-based encoding)
Drug Molecular Encoder	Drug SMILES (from DrugBank/PubChem)	Converted to molecular fingerprints using RDKit and/or processed via GNN
Feature Fusion Layer	Genomic Embeddings + Drug Features	Concatenation or cross-attention layer
ADR Classifier	Fused Representation	Predicts probability of specific adverse effect

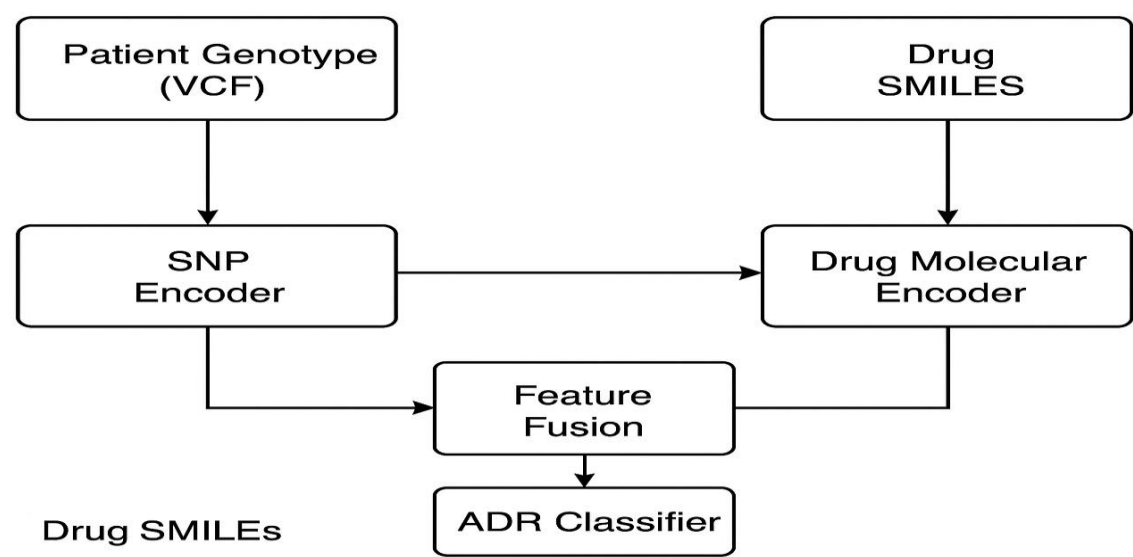


Fig. 1 Block diagram of the proposed method

VI. LITERATURE REVIEW:

Recent progress in pharmacogenomics has driven efforts to merge diverse biomedical data sources—such as **single-nucleotide polymorphism (SNP) profiles**, **drug molecular structures**, and **clinical adverse drug event records**—to

enhance precision in **adverse drug reaction (ADR)** prediction. Earlier computer-aided drug analysis techniques mainly depended on **molecular descriptors** and **chemical similarity scores**, which were effective for identifying general drug behavior but inadequate for explaining **patient-specific differences** in side-effect susceptibility.

Modern **AI-driven approaches** have transformed this space by adopting **multi-modal data fusion**, enabling algorithms to model complex **gene–drug–phenotype** interactions more comprehensively. For instance, **Ou et al. (2021)** introduced a **deep learning fusion model** that jointly represents drug fingerprints and omics-level biological signals to predict ADRs. Their work showed that integrating multiple data types consistently yields better predictive accuracy than single-source inputs, though reliance on **cell-line expression data** restricts its clinical applicability to genetically diverse populations.

Similarly, **Lin et al. (2021)** explored the integration of **machine learning** and **deep neural architectures** within pharmacogenomic studies of antidepressants. Their research demonstrated that **SNP-based patient stratification**, when combined with layered neural modeling, improves the prediction of therapeutic outcomes and highlights the importance of genetic variation in treatment response.

In another notable contribution, **He et al. (2025)** proposed **DGANet**, a cross-feature **deep graph neural network** designed to learn hidden **gene–drug interactions** from pharmacogenomic datasets. By integrating **gene–disease** and **chemical–gene** association matrices, DGANet significantly outperformed traditional compound-based ADR prediction systems.

Taken together, existing research underscores that **multi-source representation learning** and **deep fusion architectures** provide superior predictive performance in ADR modeling—particularly when **genomic information** is included. However, applying these models to **real-world patient populations** remains difficult due to limited labeled data and inconsistent annotation standards across databases such as **FAERS**, **SIDER**, and **electronic health records (EHRs)**.

VII. PROPOSED METHOD:

The proposed framework is designed to predict **multiple potential adverse drug reactions (ADRs)** for an individual patient by integrating **genomic SNP profiles** with the **molecular representation** of the administered drug. Unlike traditional binary classifiers that assess a single ADR at a time, this system employs a **multi-label classification strategy**, allowing simultaneous prediction of several possible side effects associated with a specific drug–patient combination.

A. Input Data:

Genotype Data (VCF – Variant Call Format): Genetic information is sourced from publicly available repositories such as the **1000 Genomes Project**. SNPs associated with genes involved in **drug metabolism**—including *CYP450*, *SLCO1B1*, *TPMT*, and *UGT1A1*—are identified and filtered using established pharmacogenomic

resources such as **dbSNP** and **PharmGKB**. These filtered variants serve as the genomic input for model training.

Drug	Molecular	Data:
Drug chemical structures are represented using SMILES strings , obtained from databases such as DrugBank and PubChem . These representations are processed through RDKit to generate molecular fingerprints (e.g., ECFP or Morgan fingerprints). Alternatively, the molecular structures can be modeled as graphs , where atoms and bonds are treated as nodes and edges for further processing using Graph Neural Networks (GNNs) .		

B. SNP Encoding:

The **SNP Encoder** module transforms patient genotypes into numerical feature vectors suitable for machine learning models.

Each SNP is encoded based on genotype states (e.g., 0, 1, 2 representing allele variations). To manage the high dimensionality of genomic data, **dimensionality reduction** is performed using an **autoencoder** or **Transformer-based encoder layers**.

The final output is a **dense, low-dimensional genomic embedding** that preserves key genetic variation patterns relevant to drug response.

C. Drug Molecular Encoder:

Two encoding strategies are considered for representing drug features:

- 1) Fingerprint-Based Encoder:
 - a) Converts **SMILES strings** into **ECFP fingerprint vectors** using **RDKit**.
 - b) The fingerprint vector passes through a **dense layer** to generate a **drug embedding**.
- 2) Graph Neural Network (GNN) Encoder:
 - a) Represents molecules as **graphs**, with atoms as nodes and bonds as edges.
 - b) Through **message-passing** operations, the GNN learns **structural and relational features** of the compound.
 - c) The resulting output is a **continuous drug embedding vector** capturing molecular behavior and chemical interactions.

D. Feature Fusion Layer:

In this stage, **genomic embeddings** and **drug embeddings** are combined to model the interaction between patient-specific variations and drug chemical properties. Fusion can be performed through **simple concatenation** or via an **attention-based mechanism**, which dynamically emphasizes the most relevant features contributing to ADR risk.

This integration allows the model to capture **cross-domain relationships** between genetic variants and molecular behavior that influence side-effect manifestation.

E. Multi-Label ADR Classifier:

The fused feature representation is fed into a **multi-label classification network**, enabling the prediction of multiple ADRs simultaneously.

A **Sigmoid activation function** is used in the output layer—unlike Softmax—to assign independent probability scores to each potential side effect. Training utilizes the **Binary Cross-Entropy (BCE)** loss function, with adjustments for **class imbalance** to handle uneven distribution across ADR categories.

VIII. CONCLUSION AND FUTURE SCOPE:

The integration of **artificial intelligence (AI)** with **pharmacogenomics** is transforming how adverse drug reactions (ADRs) are predicted and understood. By combining **patient-specific genetic information** with **drug molecular characteristics**, AI models can uncover complex biological patterns that traditional analytical methods often overlook. This review highlights that **multi-modal feature fusion**, which integrates genomic and chemical data, substantially improves prediction accuracy compared to single-source models. Despite these advancements, challenges such as limited annotated genomic datasets, population-level genetic variability, and the need for greater model transparency still constrain clinical translation.

The proposed framework contributes to overcoming these limitations by **jointly modeling SNP-level genetic variations and molecular drug representations**, allowing the prediction of **multiple ADR outcomes simultaneously**. This multi-label prediction capability supports **personalized and safer prescribing decisions**, moving closer to the goal of precision medicine.

Future extensions of this work could focus on:

- Integrating **real-world electronic health record (EHR)** datasets to enhance clinical applicability.
- Enhancing **model interpretability** through visualization of attention weights or feature importance scores.
- Deploying the framework as a **clinical decision support system (CDSS)** to assist healthcare professionals in personalized drug selection and dosage optimization.

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