Drugs Toxicity Prediction: A Review

Kamal[1], Devender Kumar[2], Anuj Kumar Sharma[3]

Dept. of Computer Science Engineering, Baba Mastnath University, Rohtak, India[1,2], Dept. of Computer Science Engineering, BRCM College of Engineering, Bahal, India[3]

Corresponding author: Kamal, Email: kamaldhanda05@gmail.com

Various possible anti-addiction treatments are concerned about drug toxicity, which additionally greatly raises that price of drug research. Drug toxicity can be extremely harmful to the body, resulting in a wide range of diseases such as memory loss, blurriness, liver damage, and so on. Machine learning is an important aspect of drug toxicity; this method helps generate data for many drug candidates. Machine learning also helps in the pharmaceutical industry with quick decisions and critical analyses. Predicting drug toxicity at an early stage has the potential to change people's lives. During the development of any prediction, safety is critical, as is measuring all effects. We review the various predictive models for predicting the toxicity level, as well as other machine learning techniques that aid in the efficient construction of the predictive model, such as feature selection, balancing, dealing with missing values, and so on, in this paper. Machine learning models along with their approaches such as predictive modeling, ensembling, feature selection, missing values and balancing are used for prediction, This paper focuses on all of the techniques required for predictive modelling.

Keywords: Drugs Toxicity, Prediction Model, Feature Selection.

2023. In Satyasai Jagannath Nanda & Rajendra Prasad Yadav (eds.), *Data Science and Intelligent Computing Techniques*, 235–243. Computing & Intelligent Systems, SCRS, India. https://doi.org/10.56155/978-81-955020-2-8-20

1. Introduction

Toxicity refers to all dangerous components and is also concerned with a variety of negative effects that may occur when too much of a medicine is used. This is where the liver and kidneys are located, and they will be unable to remove medications from the blood. There is some physical and mental immaturity in the aquatic system that needs to be addressed. Drug toxicity refers to how dangerous a substance can be to humans, and a wide range of medications can cause a wide range of deadly diseases. Drug toxicity can happen by chance, but drug overdose can happen on purpose. Drug toxicity, on the other hand, can occur over decades, whereas drug overdose can happen quickly.

There are various signs that a person has been affected by drug toxicity; for example, diarrhoea, vomiting, weakness, ataxia, and other symptoms are common in lithium poisoning. Carbamazepine is a toxic variant that causes symptoms like difficulty walking, disorientation, and, in rare cases, coma and seizures. Drugs are mostly used to treat or prevent diseases, but they can also be used to relieve symptoms temporarily. Drugs have the ability to alter how the brain functions as well as moods and feelings. Depressants, which slow down the body and the brain, such as alcohol, GHB, and heroin, are examples of drugs that influence the body. Another type is hallucinogens, such as LSD and PCP, which cause people to become confused and see or taste different things. Stimulants, such as caffeine and nicotine, are another type of medication that speeds up the brain and body. To get high, people use a variety of drugs, including MDMA, cocaine, and marijuana.

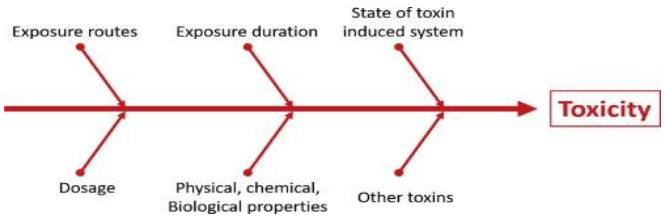

Fig 1. Major influencing factors of toxicity.

2. Characteristics of Drug toxicity

Drug poisoning is characterised by insecurity, self-centeredness, dominance, and control. The problem of drug toxicity has been identified through the use of easily identifiable parts and symptoms, which will be followed by various types of medicine administration. It's important to educate the prototype on a database with roughly the similar number of samples when using a machine learning methodology. Researchers want equitable classes in order to educate a model, although if these are n't, we'll need to use a class balancing strategy before running a machine learning techniques. As part of the feature, various types of symptoms are also shown, which are caused by accepting the drug that is being used as part of the medical therapy. One of the main causes of unsuccessful drug production and research is toxicity (R&D). Experimental evaluation for pharmacological toxicity profiles is a costly and time process. So it becomes sense to create reliable and efficient choices, like in silico prediction frameworks. various methods for predicting acute toxicity, cancer causing effects, and human ether restriction, three toxicity outcome. [1]. Drug toxicity can be avoided by paying attention to both the administration and the stage of the medication. Various methods for treating drug toxicity are also presented in the characteristic section, with the end result being an overdose. Because activated charcoal prevents it from being absorbed into the bloodstream, this component of the medication can provide an antidote. The reliability, selectivity, accuracy, and clarity of machine learning techniques centered on decision trees, machine support vector machines (SVM), neural networks, and Bayesian networks served as the inspiration for this research.

3. Impact of Drug toxicity

Drug toxicity, that happens where someone gets more of the drug in his body instantly, may result from taking excessively medication. These days, there's a lot of talk about 'smart' or 'intelligent' cities. The rate at which your body clears a medication from your system is affected by age, kidney function, and hydration. For the reason, blood quantities for medications like lithium must be regularly checked by blood testing. Three factors influence whether a poison or prescription medication is harmful: Chemical composition, How much the body is capable of absorbing, the ability of the body to detoxify and eliminate the substance. In the field of drug toxicity, there are numerous transport proteins that are compressed with various types of things that will be sent in both the maternal and foetal directions [2]. The transformer will allow us to keep all of the barriers in place while also reducing some of the impacts. The influence of drug toxicity may be a factor in the failure of the pregnancy, which will also be exposed to various therapeutic medicines. This medicine component will be more dangerous for individual patients, and those components will be determined by a variety of criteria related to age, condition, and administration.

In the area of drug toxicity, the application of machine learning is usually used for the part of the estimation just to understand the level of toxicity of the drug candidates and try to reduce the ethical concern as well as the cost, time, and others that are attached in the drug development part. Machine learning has techniques that can improve the part of the decision to measure the safety assessment. Moreover, that goal will fall short outwardly the need of data-focused mechanisms (such machine learning and big data analytics), which may serve as facilitator for delivering early diagnosis and therapy of individuals especially absence referral to clinics. Machine learning can also help to understand the effect of drug toxicity[3]. This section is used to develop a computational method in drug toxicity for prediction purposes, and it is capable of developing variation toxicity prediction that will be more effective in cooperation using machine learning. Additionally, machine learning is used to understand the accuracy, safety, and sensitivity in order to highlight the issue of drug toxicity. To maintain the prediction part, some models are presented in the algorithm section, which can help to make the prediction part of the drug taxonomy more effective.

4. Predictive Modelling Structure

Toxicity has been identified as a responsible component of drugs, with the high cost of drug development playing a significant role. The cause of drug toxicity can be classified as mechanism-based toxicity or the immune component of hypersensitivity. Drugs will also be extremely difficult to obtain [4].

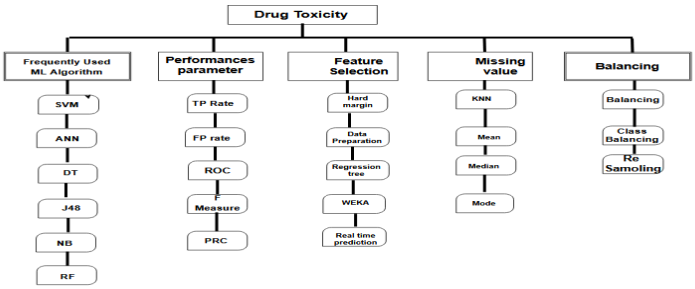

Fig 2. Prediction Model

Drug toxicity is an evaluation component that is an important part of the drug development process and is thought to be the cause of attrition. The initial step of drug evolution, that has been made conceivable by machine learning techniques, will greatly benefit from the model's

current state of development. Toxicity can be measured by the affected target, which could be an organism, organ, tissue, or cell. After the matter of acute and try to expose in the area of the

biological entity, the direct pathway will be ensured up with various types of biological functions downstream. Predictive modelling is defined in machine learning as the statistical techniques used by machine learning and the part of the data that will be predicted, as well as the part of the forecasting such as the outcome using historical and existing data. In the field of machine learning, this protection model can analyse recent data generated as a result of forecasting. The experimental protection and analysis component of the newer pharmaceuticals which may be employed straight in people heartiness, and also the great level of the drugs, are viewed as being most crucial by the toxicity analysis. While working with imbalanced data sets, there is no another method for increasing the forecast model 's performance[5].

Historically, in vitro and in vitro analysis toxicity of the test has been associated with the time consuming, high part of the expenses the prediction part has been considered the most useful part for drug development. The machine learning overview is based on drug toxicity prediction and is capable of highlighting all issues. Based on the knowledge obtained, the machine learning method can construct a classification or regression model to explain the complex relationship between the structure of the chemical of the drug part and their drug toxicity. The machine learning process can be used to create a drug toxicity prediction model. To deliver helpful and individualised care to patients, health care ecosystems are incorporating cutting-edge technologies[6]. Machine learning techniques of various types are presented, including filter methods, wrapper methods, embedded methods, and hybrid methods.

Aside from that, all relevant features can be easily increased using supervise and unsupervised techniques. The parameter, on the other hand, is used to free the model with the help of the unsupervised model. Aside from all of the parts, some algorithms are also used, such as logistic regression, linear regression, SVM, KNN, K-means, and others. The drug toxicity problem was easily solved with the help of the algorithm. Decision Tree as well as Logistic Regression are two common classification methods that prioritize classes with many repetitions. Typically, they can effectively predict data from the vast number of categories. Usually, the traits of the minority class are overlooked and discarded as noise. The minority class is therefore more likely to be incorrectly classified as the dominant class. Machine learning techniques frequently create subpar classifiers while given uneven datasets.

If indeed the occurrence to be predicted comes to the minority class, it is typically stated to as an exceptional occasion in any biased data set. Through the use of just valuable data and the eradication of distortion, feature selection is a strategy for reducing the incoming variable to your model. It is the process of deciding the traits your machine learning model should have dependent on the kind of situation you're trying to solve efficiently. We achieve this by keeping or getting rid of crucial characteristics without changing them. Both the quantity of our input data and the amount of disturbance in our data are reduced with its help. The input parameters having the closest correlation to the targeted variable are chosen after every input variable's connection to the goal variable has been statistically analysed. These techniques can be fast and effective, albeit the selection of quantitative measurements depending on the database table of both the input and output variables. The next phase is to assess the model's performance using experimental samples depending on certain metric after the usual Feature Extraction, Evaluation, and obviously, construction of a model and producing certain result in the type of a probability Several effectiveness measures are used to assess machine learning techniques. We'll focus on such for the time being because they are utilized in categorization problems. We can use metrics like Log-Loss, Accuracy, and AUC (Area Under Curve), among others, as classification efficiency measures. Some other type of statistic for assessing machine learning techniques is accuracy and remember, that can be applied for ranking techniques heavily used by search engines..

5. Analysis of Literature Review

This section focuses on the prominent work done in this domain by various researchers, and they have focused on the machine learning technique used to predict the toxicity level in a drug, as well as the features, data set balancing, and performance evaluation parameters. This may happen if the medication is either too high or too low compared to what is advised. IoT is remaking and reinventing the country through technological advancement, with all of the benefits and drawbacks that go along with that. Based on the nature of the unbalanced data set, several strategies will be most beneficial[7,12]. During the model comparison, relevant evaluation parameters should be taken into account. For improved conclusions, scientists also focused on incomplete data procedures, that may need the employment of many ways to identify the most appropriate sampling approaches for the dataset.

Table 1. Algorithm, techniques and Approaches

					SVM	RF	KNN	NB	NN	DT	ANN	J48	MLP	BN	LR	Others			
1	Li Zhang et al.	Application of machine learning methods in drug toxicity prediction	Current topics in medicinal chemistry (2018)	Tradtional toxicity evaluation methods are laborious, time consuming and highly expensive	√	√	√	√	√								R-Tool , Weka, Python	Computational prediction model developed based on machine learning methods	More interpretive molecular features and effective feature selection algorithm can be used for best prediction.
2	Anna O. Basile et al.	Artificial intelligence for drug toxicity and Safety	Trends in Pharmalogical Sciences-2019	Toxicity and Safety Challenges	√	√	√	√									QSAR	Explored recent advances as applied to preclinical drug safety with specific focus on ML and deep learning approaches	Expected that use of AI will extend to drug development and safety to the future.
3	Borrero et al.	Predicting Toxicity properties through Machine	Procedia Computer Science - 2020	Ignorance of Absorption, distributio	√	√	√	√		√	√						R	Analyze the best ML techniques for predicting toxicity as an ADME-Tox property	Prediction accuracy can be improved
4	Nishtha Hooda et al.	B^{3}SFE Framework for high dimensional imbalanced data A case	Neuro Computing - 2017	To develop an efficient model for prediction of drug toxicity to improve	√	√						√				√	R "Caret"	Better balanced feature selection. Ensemble framework for classification of toxicity molecules, carried out on imbalanced and high dimensional complex	To enhance the B^{3}FSE Framework by implementing it on top of modern big data techniques like Hadoop , Spark etc.
5	Amanda C Schirez	Virtual Screening of bioassay Data	Bio med central Journal of cheminformatics.-2009	Freely – available curated data, Number of false properties,	√	√		√				√					Weka	For virtual screening of bioassay data, it is recommended that primary and corresponding confirmatory screening data are used.	Extend the work for curated data and no. of false positives.
6	Lin Liu et al.	In Silico prediction of chemical aquatic	Press -2018	Production of chemical aquatic toxicity in marine	√	√	√	√			√	√					Orange, Python Scripting LIBSVM package	Models were built by using machine learning algorithm for prediction of chemical toxicity.	It would be helpful in gaining further insights into prediction of chemical aquatic toxicity.
7	Agnieszka et al.	Generating accurate in silico predictions of acute	Chemosphere -2021	Heterogeneity of datasets in predictions of aquatic			√									√	Dragon-7 R-Software	Two Similarity based ML methods in predicting the acute aquatic toxicity of diverse organic	Models can be developed with other approaches for good overall performance.
8	Haixin Ali	QSAR modeling study of bio concentration factor and toxicity of	Ecotoxicology and Environmental Safety - 2019	To develop a model for chemical toxicity production	√	√										√	R package Caret	Developed a Regression Model using Recursive feature Elimination (RFE) method combined with SVM. Built 3 ensemble models by using 3 ML algorithms in classification	New models can be developed via ensembling for prediction.
9	Pathak et al.	Protein structure prediction using machine learning models	International Journal Data Mining and Bioinformatics -2016	To have a predictive model which can tell us how far a structure is from the native in absence of		√			√	√						√	AMBER 12, R Software	Explore ML models to predict RMSD of protein structure in absence of its true native state.	If more physical and chemical properties and other computational methods are combined with ML methods, it may produce even better results.
10	Sonal Mishra et al.	Comparative study of ML models in protein structure prediction	International Journal of computer Science & Information Technologies	To develop a Model for protein structure prediction		√			√	√						√	R	Comparative study of models based on ML for protein structure prediction.	Ensembling of other ML models can be done and evaluated with performance.

11	Sharma et al.	Optimized ensemble machine learning framework for high	Revue d' Intelligence Artificielle -2019	To study activity of bio active compounds and drugs with	√	√			√			√		√	√	√	R	Design an efficient and accurate method to assess the activity of bioactive compounds & drugs.	The ML frameworks will be enhanced by applying it to various big data techniques like Hadloop etc.
12	Zhi-hua Zhou	Ensemble learning	AI Communications -2009	Prediction of weak learners		√										√	R	Ensembling of ML algorithms.	ML is future for predictions so more work can be done on it.
13	Niculescu	Optical method for improving the accuracy of Bio chemical assays	6th IEEE International Conference on E- Health and Bio engineering -2017	How to improve the accuracy of assays												√	EXL 200 Analyzer	Described an automated optical method to improve the accuracy of assays.	To develop model for fastest, cheapest and easiest way to provide a correct diagnostic.
14	Marwala et al.	Electricity load forecasting using an ensemble of	9th IEEE-GCC Conference and Exhibition -2017	Unable to predict the demand for electricity consumption	√				√							√	R	Developed non-linear ensemble model for forecasting and their performance is measured and compared.	Ensembling can be done with other classifiers to check the results for accuracy.
15	Hooda et al.	Optimizing fraudulent firm prediction using ensemble	Taylor and Francis Applied Artificial Intelligence -2019	Unfair practices without fear of legal repercussio n i.e.	√	√		√	√	√			√			√	Python, R Script, R Caret	Developed a decision making system for auditors before initializing the audit field work of public firms.	Ensemble of other classifiers is advised.

Below is a graphical analysis of the table, which includes algorithm analysis, evaluation parameters, and approaches. In algorithm analysis, the most frequently used algorithms are given, as well as which algorithm is used the most based on its usability. As we can see, the most commonly used algorithms are SVM, NN, and J48. A biopsy is a medical procedure in which a patient's condition is checked for progression by a surgeon. A simple filter called Class Balancer can be used to assign that importance to each instance on a class, giving each instance in the dataset the appropriate value and maintaining the dataset's total instance count[8].

Multilayer Perceptron, Bagging, Random Committee, and J48 are four machine learning techniques that were used. Class Balancer is a simple filter that applies that weightage to every instance in the dataset, ensuring that the sum of all instances in the dataset remains unchanged. Then we used many parameters that provide more value and usability in research; as we can see, some parameters are more usable than others; this does not mean that others are not useful. Numerous machine learning techniques has been used to train the database, and the results have been examined considering the parameters[9]. Many approaches are used by researchers for their research. As we can see, classification is the most useful approach for daa analysis. The air quality monitoring system measures the concentration of a certain pollutant in the surrounding and outside environment to systematically monitor the level of pollutants in the air[10]. The classification approach is very useful and adds more value to data. Other approaches include feature selection. A feature selection approach aids in correlating data values; some feature selection techniques are commonly used. As a result, we have examined numerous techniques.

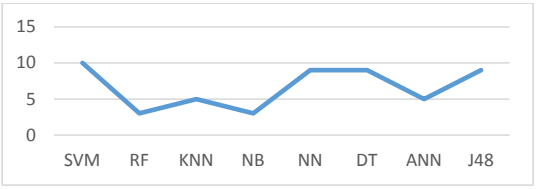

Fig 3. Algorithm analysis

Classification is the process of dividing a set of data into categories. It can be done on both structured and unstructured data. Naive Bayes is a classification algorithm that assumes independent predictors in a dataset. A Decision Tree is a visual representation of decision-making using an algorithm. The K-Nearest Neighbor technique divides data into classes based on the distance between data points and is used for classification and prediction. We'll need some accuracy measurements to evaluate the accuracy of our classifier model. The gap between our actual and expected numbers is known as bias.

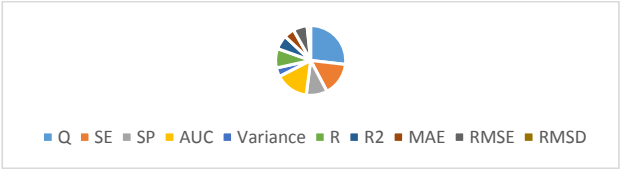

Fig 4. Evaluation parameter

Any machine learning model's goal is to analyse and learn patterns from data, which may then be used to create predictions, answer queries, or just understand the underlying pattern that isn't readily apparent.

The standard deviation (SD) is a measurement of a set of values' variance or dispersion. R-squared (R2) is a statistical measure that quantifies the amount of variation explained by an independent variable or variables in a regression model for a dependent variable.

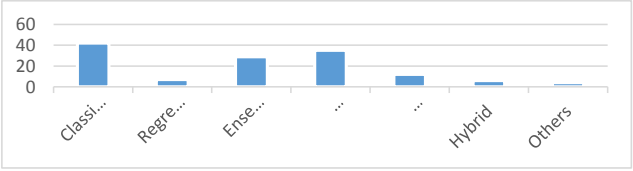

Fig 5. Approaches

A quantifiable property of a process or item that is being observed is defined as a feature. It can also be referred to as an attribute, component, variable, column, or dimension. The training dataset is utilised to provide better border conditions that may be used to define each target class; after these boundary criteria are established, the next goal is to predict the target class. The forecasts of many different models are combined in ensemble learning, a generalized meta method to machine learning, to increase forecast effectiveness. [11]

6. Observation

Toxics that can be harmful if they enter the body through the oral cavity, such as drinking any type of water. This drug disrupts and destroys blood tissues, making recovery difficult. Many toxins have been discovered by scientists to have a very dangerous quick effect in the human

body, and that even if the smallest amount of these components enters the body, the recovery rate from this toxin is unlikely. The pathological effects of the four classes of drug toxicity can be classified. The majority of drug toxicity is classified as on target, off target, hypersensitivity, and others. It will also be stated during the observation stage that drug toxicity can easily affect the nervous system, and this part can be linked to the availability of the drugs as well as the occupational part. There are various types of neurological symptoms that are occupied by various types of toxin. Overall, the high quality of drugs consumed is a reason for future attacks on various types of nervous systems, which will be affected as a negative part of the human body. We used machine learning algorithms to accurately predict failures, which will help in the medical field. To predict chemical toxicity in class imbalance datasets, many effective FS methods are used. Effective FS methods increased accuracy and improved understanding of the learning model.

7. Summary

Toxins and drugs frequently target the body's nervous system; there are numerous side effects of drugs such as anxiety, sobriety, and mental trauma; some of the effects of these toxic drugs can last for generations; and they are not only harmful to humans but also to the entire ecosystem; and the most encouraging sources of such acts are nuclear power plants, large agricultural factories, and numerous unrecognised companies. Numerous Machine learning (ML) methods has been applied recently to diabetes predictions. Under the use of conditioned data capture, a creative prediction strategy using deep modelling is frequently suggested to forecast the intensity and specific risk factor of diabetics[13].In summary, the term drug toxicity refers to the various levels of damage that can be caused to the organism.[14-16] This toxic component, along with the dose, can be affected by a drug, which can affect the entire system, including the liver, among other things.[17-20] Aside from this section, predictions are also presented; one of the most important for public health is the toxic prediction section. Various types of applications are also presented in terms of prediction, which aid in understanding the part of prediction. By incorporating innovative methods for producing innovative attributes, classification is utilised to boost feature field efficiency and improve model correctness[21]. There are numerous ways to select features[22]. Finally, we examined algorithms, evaluation parameters, and approaches. The most frequently used algorithms are given in algorithm analysis, as well as which algorithm is used the most based on its usability. SVM, NN, and J48 are the most commonly used algorithms, as we can see.[23-25] An ensemble framework for classification of toxicity molecules was applied to imbalanced and high-dimensional complex drug data to develop a superior model. For their research, researchers employ a variety of approaches. As we can see, classification is the most effective method of analysis. The classification approach is extremely beneficial and adds value to data. Feature selection is another approach. Finding a collection of input variables that may correctly characterise the data by minimising the impact of disturbance or unnecessary factors while yet producing high predicted outcomes is the aim of feature extraction. Several distinctive elements that hold the maximum class-specific material can be used to extract the overall information content. As a conclusion, the volume of information can be decreased by deleting the relying variables, potentially improving classification performance.Although we have reviewed a number of articles by different authors worked on different problem statements like balancing, ensembling, optimising the problem and feature selection. Different scenarios have different effects that are considered and we can improve the performance of our model.

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