REVIEW ARTICLE

Application of computer on Pharmacogenomics

Muhammed Amanat [1], Randhir Singh[2]*

ABSTRACT

Background

Pharmacogenomics is an emerging field that explores the relationship between a person's genetic makeup and their response to drugs.

Objectives

Computer applications have been instrumental in advancing pharmacogenomics research and facilitating personalized medicine. In this abstract, we review some of the key computer applications used in pharmacogenomics research, including bioinformatics tools for analyzing genetic data, machine learning algorithms for predicting drug response, and clinical decision support systems for guiding drug selection and dosing. We also highlight the challenges and opportunities in the field of pharmacogenomics, including the need for large-scale, multi-omics datasets, and the importance of developing robust and interpretable machine learning models. Overall, computer applications have played a critical role in enabling pharmacogenomics research and have the potential to revolutionize the practice of medicine by facilitating the development of more personalized and effective drug therapies.

Keywords:

Pharmacogenomics; computer; bioinformatics; challenges.

INTRODUCTION

The focus of pharmacogenomics (PGx) research is to improve the effectiveness and safety of existing medical therapies by revealing the impression of individual genetic dissimilarity on drug response. Its ultimate goal is to promote a shift from the existing prescription paradigm based on empirical trial and error towards one more stratified and accurate[1]. Pharmacogenomics, which integrates pharmacology and genomics elements, has been overgrown over the last decade. The Pharmacogenomics field has advanced in the past 20 years, and new tools for detecting genetic variations have emerged[2]. Exploring the complex relationships between genes, medications, interpretations, and phenotypes is now feasible using high-throughput computer technology.

Furthermore, pharmacogenomics is an integral part of patient treatment. It's an enormous sector that exists worldwide. Large-scale administration and personnel are essential for the smooth operation of the Pharmacogenomics area. However, advancements in computer technology have significantly decreased the need for human labor and time in the pharmacogenomics sector. Virtually every facet of genomics relies on computers in some way. These are used for pharmacogenomics research, computer-assisted learning in hospitals and clinics, medication storage and inventory management, and the creation of new medicines. The role of pharmacogenomics in different sectors is depicted in Fig 1. As a subfield of pharmacy, pharmacogenomics is a growing field of study. Around 1980, computers began to be widely used in the

1. Muhammed Amanat, Department of Pharmacology, Central University of Punjab, Ghudda, Bathinda-151401, India.
2. Randhir Singh, Department of Pharmacology, Central University of Punjab, Ghudda, Bathinda-151401, India.

Correspondence

Randhir Singh, PhD, Department of Pharmacology, Central University of Punjab, Ghudda, Bathinda-151401, India. Email: randhir.singh@cup.edu.in. Randhir Singh: 0000-0003-0183-0797

Bangladesh Journal of Medical Science Vol. 23 No. 02 April'24

DOI: https://doi.org/10.3329/bjms.v23i2.72092

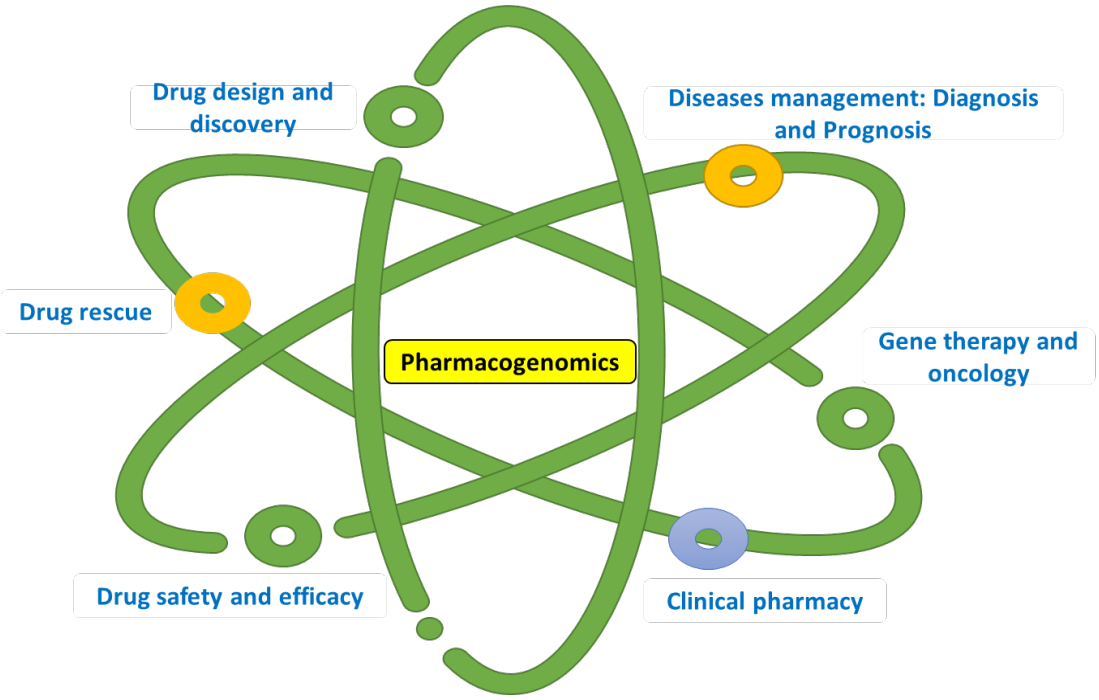

Fig 1. Role of Pharmacogenomics

pharmacy industry. Since then, the pharmaceutical industry has shown a significant interest in computing. Computers provide several benefits, including the ability to do more in less time, more accuracy, fewer mistakes, less need for human labor, more incredible speed, less fatigue, more memory, and greater storage capacity[3]. Computer applications play a crucial role in pharmacogenomics research by providing tools to analyze and interpret genomic data, predict drug responses, and develop personalized treatment plans. This paper discusses the applications of computer technology in pharmacogenomics, its benefits, and challenges.

METHODOLOGY:

A systematic search was conducted using electronic databases, including Google Scholar, PubMed, Medline, and Web of Science. The search terms used were "pharmacogenomics" AND "computer application." The search was limited to articles published in English between 1988 and 2023 (Fig 2).

Ethical Clearance:

Pharmacogenomics data are sensitive, and there are ethical and legal issues surrounding their use and storage. To address these issues, researchers and developers must adhere to ethical guidelines and data protection regulations.

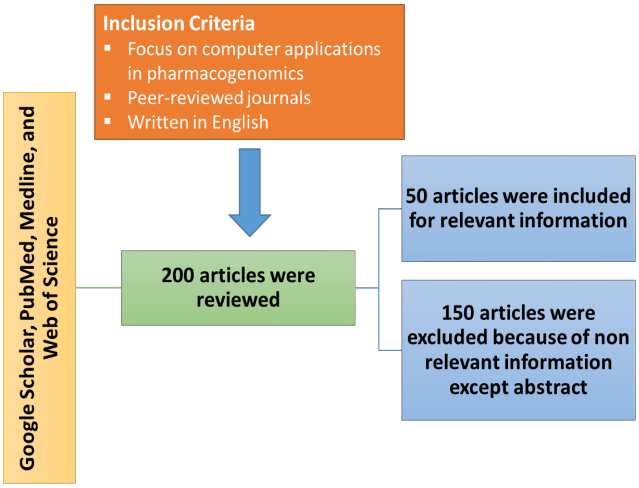

Fig 2. Methodology for article search protocol

Results and discussion

Application of computers in pharmacogenomics

E-learning

The term "e-learning" has come to refer to the

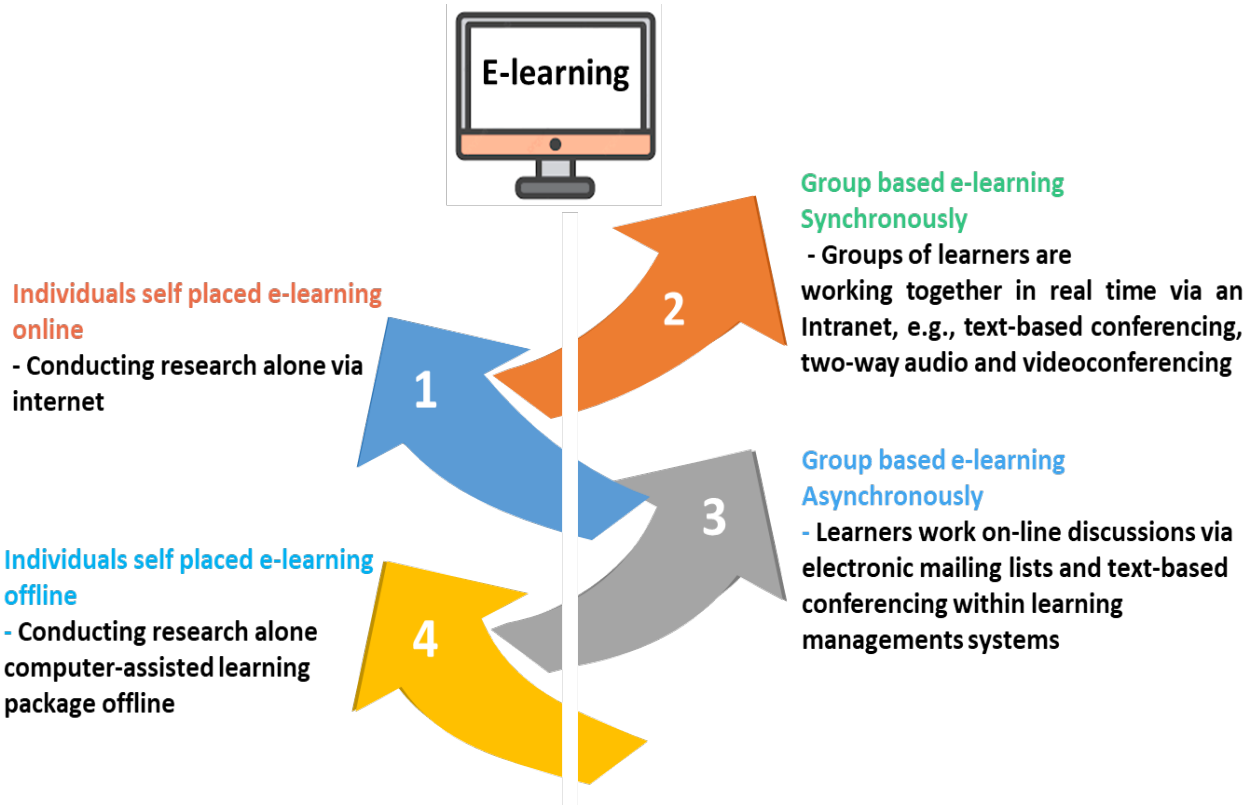

Fig 3. E-learning platforms for the study of pharmacogenomics through computer

educational practice of using digital media and the Internet for educational purposes. E-learning is also known as online, virtual, distributed, network-based, and web-based learning[4]. Pharmacists and other healthcare graduates may find the Online Program in Pharmacogenomics very useful. Issues related to health pharmacogenomics are covered in depth throughout the e-learning program. In addition, it emphasizes the development and administration of quality initiatives. It also provides a well-regarded academic education. There is no prerequisite for participants to have any knowledge of pharmacogenomics. The computer plays a crucial part in this form of E-learning program, with examples including text-based conferencing under learning management systems and online conversations through electronic mailing (Fig 3).

Digital libraries

A digital library is an online or offline collection of electronic documents, images, audio, video, and other materials. The ability to access digital knowledge from any location in the world is one of the main reasons why digital libraries have gained so much attention in recent years. Educators, scientists, and professionals now commonly rely on them as well as prefer them to other sources of knowledge. The rapid growth of the Internet and the growing interest in developing computer have both aided in the rapid digitalization of printed texts in past years. Moreover, lots of pharmacogenomics data including gene and genome information are stored in digital libraries[5, 6]. However, digital libraries provide several benefits, including the ability to store more information in a smaller footprint, reduce library maintenance costs, speed up the search process, and more.

Entity recognition (identifying genes, drugs, variants & phenotypes)

Recognition of biological entities such as genes, medicines, and variations in text has also made great strides. The usage of everyday English terms as gene names, among other concerns [7], makes it very challenging to automatically detect genes. Good progress was made on the problem of recognizing genes in text due to the

Critical Assessment of Information Extraction systems in Biology[8]. ABNER[9], LingPipe[10], and BANNER[11] are just a few of the computer-based tools that may be used to annotate genes in text. Furthermore, a number of programs, such as MutationFinder[12], MarkerInfoFinder[13], MuteXT[14], and Pharmspresso[15], can recognize genetic variants in written form (such as C3435T). With this context of view, application of computer in genomic field is vast.

Genomic Databases

Genomic databases play a vital role in pharmacogenomics research. They provide researchers with access to a vast amount of genomic data that can be analyzed to identify genetic variations that are associated with drug responses. One of the most widely used genomic databases is the National Center for Biotechnology Information's (NCBI) GenBank[16]. This database contains DNA sequences for a wide range of organisms, including humans. Researchers can use GenBank to search for specific genes or genetic variations that are associated with drug responses. Another popular genomic database is the Pharmacogenomics Knowledge Base (PharmGKB)[17]. This database contains information on how genetic variations affect drug responses, including data on drug interactions, adverse drug reactions, and drug efficacy. Researchers can use PharmGKB to identify genetic variations that are associated with drug responses and to develop personalized drug therapies[18].

One of the challenges in pharmacogenomics is integrating data from different sources. This requires the use of data integration tools such as BioMart[19] and InterMine[20]. These tools allow researchers to query multiple databases simultaneously and integrate the results.

Genomic Data Analysis

One of the most important applications of computer technology in pharmacogenomics is data analysis. Pharmacogenomics involves analyzing vast amounts of genomic data to identify genetic variations that affect drug response. The analysis requires the use of high-performance computing (HPC) systems, which can handle large datasets, complex algorithms, and parallel processing[21-23]. HPC systems enable researchers to process genomic data faster, accurately, and efficiently. The use of HPC has led to the discovery of new drug targets and biomarkers for personalized medicine.

Furthermore, there are several computational tools available for data analysis in pharmacogenomics. These tools include bioinformatics software for sequence alignment, variant calling, and annotation. They also include statistical packages for data normalization, hypothesis testing, and machine learning algorithms for classification and prediction. Popular genomic data analysis software includes GATK[24], Samtools[25], BWA[26], and VarScan[27, 28].

Drug Discovery

The traditional approach to drug discovery involves synthesizing compounds, testing them in vitro and vivo, and optimizing them for efficacy and safety. However, this approach is time-consuming, expensive, and often yields limited success. The integration of computer technology in drug discovery has led to the development of *in silico* methods that accelerate the process of drug discovery. *In silico* methods involve using computational models to predict the efficacy and toxicity of drugs, optimizing the drug structure, and identifying potential drug targets. Moreover, the use of *in silico* methods reduces the time and cost of drug discovery and increases the success rate[29].

Bioinformatics Tools

Bioinformatics tools are computer applications that are used to analyze genomic data. These tools may be used to uncover genetic variants linked to medication responses and generate customized pharmacological therapy[30]. In pharmacogenomics research, some of the most used bioinformatics tools include (Fig 4)-

Genome-Wide Association Studies (GWAS)

GWAS is a bioinformatics tool that is used to identify genetic variations that are associated with disease or drug responses[31, 32]. In a GWAS, researchers compare the DNA of individuals who have a particular disease or who respond differently to a drug to the DNA of individuals who do not have the disease or who respond differently to the drug. By comparing these two groups, researchers can identify genetic variations that are more common in the group that has the disease or that responds differently to the drug.

Next Generation Sequencing (NGS)

NGS is a bioinformatics tool that is used to sequence entire genomes or specific genes[33]. NGS may be used to discover genomic variants linked to drug reactions. For example, NGS can be used to identify mutations in the

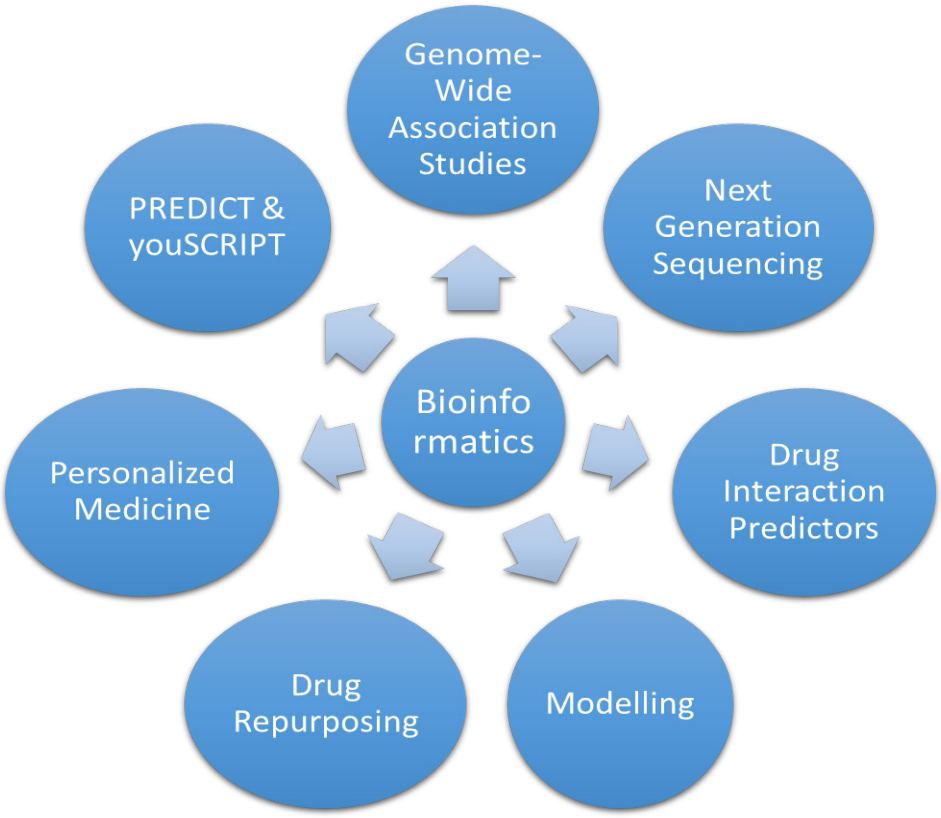

Fig 4. Different bioinformatics tools possibly used in pharmacogenomics

CYP2D6 gene, which is responsible for metabolizing many commonly used drugs. Mutations in this gene can affect how quickly or how slowly a person metabolizes a drug, which can affect the drug's efficacy and toxicity.

Drug Interaction Predictors

Bioinformatics techniques known as "drug interaction predictors" try to guess how two medications will react to one another, or to things like food or alcohol. These tools can be used to develop personalized drug therapies that minimize the risk of adverse drug reactions. For example, a drug interaction predictor could be used to identify drugs that should not be taken together because they can cause a dangerous drop in blood pressure. KGNN[34], and DPDDI[35] are two examples of computational methods that can predict drug interactions.

Modeling

Another important application of computer technology in pharmacogenomics is modeling. Modeling involves the use of mathematical and statistical models to predict drug response based on genetic variations. These models can aid drug development and personalized medicine by identifying genetic markers that are associated with drug efficacy, toxicity, and pharmacokinetics. There are several modeling techniques available in pharmacogenomics including linkage analysis[36], and machine learning algorithms[37]. Linkage analysis involves the analysis of familial data to identify genetic markers that are linked to drug response while machine learning algorithms involve the use of statistical models to predict drug response based on genetic variations. Machine learning methods notably decision trees[38], random forests[39], and neural networks are all employed in pharmacogenomics. Moreover, the PREDICT-1 study is a large-scale clinical trial that aims to develop and validate a pharmacogenomics model for warfarin dosing[40]. The study involves the use of machine learning algorithms to predict the optimal warfarin dose based on genetic variations, clinical factors, and demographic data[41]. Similarly, Pharmacokinetic modeling is a technique used to predict how drugs will be absorbed, distributed, metabolized, and excreted in the body. Computer applications have made it possible

to develop complex pharmacokinetic models that can predict drug responses accurately. SwissADME[42], PreADMET[43], and Simcyp Simulator[44] are three examples of pharmacokinetic models. These models can be used to optimize drug dosing and minimize side effects. In addition, these tools can aid drug development and personalized medicine by predicting drug concentrations in different populations and identifying factors that affect drug metabolism and excretion.

Drug Repurposing

Drug repurposing involves identifying new uses for existing drugs. It is a cost-effective approach to drug discovery since the drugs have already undergone clinical trials and are known to be safe. Computer technology has revolutionized drug repurposing by enabling researchers to analyze vast amounts of genomic and clinical data to identify drugs that can be used to treat different diseases. The use of computer technology has led to the discovery of new uses for drugs, such as the use of metformin, an antidiabetic drug, in cancer treatment[45-47].

Personalized Medicine

Customizing a patient's medical care to their unique DNA is at the heart of personalized medicine. Computer technology plays a crucial role in personalized medicine by enabling the analysis of an individual's genome and identifying genetic variations that affect drug response. The use of computer technology in personalized medicine has led to the development of pharmacogenomics tests that can predict an individual's response to medication. The tests let doctors prescribe the safest possible dosage of a medicine, decreasing the possibility of side effects and toxicity.

Decision Support Systems

Decision support systems are computer programs that provide clinicians with evidence-based recommendations for drug dosing and selection based on the patient's genetic profile. These systems use algorithms to analyze patient data and provide personalized treatment plans. Examples of decision support systems include PREDICT[48] and YouScript[49].

Future directions and challenges

Computer applications will continue to play a critical role in the development of pharmacogenomics. As technology continues to advance, we can expect to see more personalized medicine, machine learning algorithms, data analytics tools, genomic sequencing, and integration with electronic health records. These developments will ultimately lead to better patient outcomes and more effective treatment options. Computer applications can play a crucial role in pharmacogenomics by facilitating the analysis of large volumes of genomic data and supporting the discovery of new drug targets. However, there are also several challenges associated with the use of computer applications in pharmacogenomics. In the present study, we have addressed some challenges with potential solutions regarding computer applications in pharmacogenomics.

Data integration

Pharmacogenomics involves the analysis of large amounts of genomic, clinical, and drug-related data. The integration of these different data sources can be challenging, as they may be stored in different formats and structures. Potential solutions to this challenge include developing standard data formats and ontologies, and using data integration tools and algorithms to automate the process.

Data Quality

The quality of the genomic data used in pharmacogenomics can be affected by factors such as sample collection, storage, and processing. There are a few possible approaches to resolving this difficulty, including the creation of quality control measures and standards for genomic data and the use of machine learning algorithms for mistake detection and correction.

Data Privacy

Genomic data is sensitive and confidential information that must be protected to avoid illegal access and usage. Using safe data-sharing platforms that are in accordance with applicable privacy requirements, such as the General Data Protection Regulation (GDPR)[50], is one potential approach to resolving this issue.

Interpretation of Results

Interpreting the massive volumes of complicated data produced by genetic data analysis could be challenging. The use of machine learning algorithms to predict drug response based on genetic data and the development of algorithms that prioritize genetic variations based on their functional relevance are two possible approaches to fixing this problem.

Clinical Implementation

The integration of pharmacogenomics into clinical practice can be challenging due to factors such as lack of standardization, limited clinical evidence, and the need for specialized expertise. Creating pharmacogenomics clinical standards, educating healthcare professionals, and integrating pharmacogenomics into electronic health records are a few possible solutions to this problem.

Computational infrastructure

Pharmacogenomics data are often large and complex, and require significant computational resources for analysis. Cloud computing and distributed computing can be used to address this challenge.

Conclusion

In conclusion, computer technology has revolutionized the field of pharmacogenomics, allowing for the analysis of large datasets and the prediction of drug response based on genetic variations. Data analysis, modeling, and simulation are important applications of computer technology in pharmacogenomics, aiding drug development and personalized medicine. As the field continues to evolve, it is expected that more sophisticated computational tools will be developed, leading to the discovery of drugs.

Acknowledgement

Central University of Punjab has our deepest appreciation for allowing us to write this review.

Source of fund

This article receives no funding

Conflict of interest

None

Ethical clearance

Not applicable

Authors's contribution

Data gathering and idea owner of this study: Muhammed Amanat

Study design: Muhammed Amanat, Randhir Singh

Data gathering: Muhammed Amanat

Writing and submitting manuscript: Muhammed Amanat

Editing and approval of final draft: Randhir Singh

References

1. Evans WE, McLeod HLJNEJoM. Pharmacogenomics—drug disposition, drug targets, and side effects. *N Engl J Med* 2003;**348**(6):538-49.
2. Garten Y, Altman RBJP. Teaching computers to read the pharmacogenomics literature… so you don't have to. *Pharmacogenomics* 2010;**11**(4):515-8.
3. Wang B. Computer applications in pharmaceutical research and development. Canada: John Wiley & Sons; 2006.
4. Kumar V, Sharma DJIJoW-BL, Technologies T. E-learning theories, components, and cloud computing-based learning platforms. *Int J Web-Based Learn Teach Technol* 2021;**16**(3):1-16.
5. Ambati V, Balakrishnan N, Reddy R, Pratha L, Jawahar C, editors. The digital library of india project: Process, policies and architecture. *2nd Int Conf on Digital Lib* (ICDL); 2006: Citeseer.
6. Sood A, Chandrasekharan UJArcbEDC. Digital libraries in India-A baseline Study. *Report Commiss Edu Dev Center* (EDC) 2004;**3**(10).
7. Chang JT, Altman RBJP, Genomics. Extracting and characterizing gene–drug relationships from the literature. *Pharmacogenet Genom* 2004;**14**(9):577-86.
8. Hirschman L, Yeh A, Blaschke C, Valencia AJBb. Overview of BioCreAtIvE: critical assessment of information extraction for biology. *BioMed Central* 2005. p. 1-10.
9. Settles BJB. ABNER: an open source tool for automatically tagging genes, proteins and other entity names in text. *Bioinformatics* 2005;**21**(14):3191-2.
10. Alias-i:. Alias-i: LingPipe 3.9.0. 2023 [Available from: http://alias-i.com/lingpipe].
11. Leaman R, Gonzalez G. BANNER: an executable survey of advances in biomedical named entity recognition. *Biocomputing* 2008. p. 652-63.
12. Caporaso JG, Baumgartner Jr WA, Randolph DA, Cohen KB, Hunter LJB. MutationFinder: a high-performance system for extracting point mutation mentions from text. *Bioinformatics* 2007;**23**(14):1862-5.
13. Xuan W, Wang P, Watson SJ, Meng FJB. Medline search engine for finding genetic markers with biological significance. *Bioinformatics* 2007;**23**(18):2477-84.
14. Horn F, Lau AL, Cohen FEJB. Automated extraction of mutation data from the literature: application of MuteXt to G protein-coupled receptors and nuclear hormone receptors. *Bioinformatics* 2004;**20**(4):557-68.
15. Garten Y, Altman RB, editors. Pharmspresso: a text mining tool for extraction of pharmacogenomic concepts and relationships from full text. *BMC bioinformatics*; 2009: Springer.
16. Attimonelli M, Lanave C, Liuni S, Pesole GJNar. MERGE: a software package for generating a single data-base starting from EMBL and GenBank collections. *Nucleic Acids Res* 1988;**16**(5 Pt A):1681.
17. Hewett M, Oliver DE, Rubin DL, Easton KL, Stuart JM, Altman RB, et al. PharmGKB: the pharmacogenetics knowledge base. *Nucleic Acids Res* 2002;**30**(1):163-5.
18. Barbarino JM, Whirl-Carrillo M, Altman RB, Klein TEJWIRSB, Medicine. PharmGKB: a worldwide resource for pharmacogenomic information. *Wiley Interdiscip Rev Syst Biol Med* 2018;**10**(4):e1417.
19. Triplet T, Butler GJBiB. A review of genomic data warehousing systems. *Brief Bioinform* 2014;**15**(4):471-83.
20. Carlson J, Goodstein D, Rokhsar D. InterMine Webservices for Phytozome (Rev2). 2014.
21. Thakre V, Vedpathak S, Sawarkar S. Genomics, High Performance Computing and Machine Learning. *United Int J Res Technol* 2021; **2**(8):149-155
22. Liu T, Lu D, Zhang H, Zheng M, Yang H, Xu Y, et al. Applying high-performance computing in drug discovery and molecular simulation. *Natl Sci Rev* 2016;**3**(1):49-63.
23. Mohandas B, Vennila JJ, Ruban NJBJoMS. Gene co-expression analysis and Network biology studies in Indian population reveals functional similarities between Gastric cancer and other metabolic disorders. *Bangladesh J Medical Sci* 2022;**21**(3):688-93.
24. Brouard J-S, Schenkel F, Marete A, Bissonnette NJJoas, biotechnology. The GATK joint genotyping workflow is appropriate for calling variants in RNA-seq experiments. *J Anim Sci Biotechnol* 2019;**10**(1):1-6.
25. Danecek P, Bonfield JK, Liddle J, Marshall J, Ohan V, Pollard MO, et al. Twelve years of SAMtools and BCFtools. *Gigascience* 2021;**10**(2):giab008.
26. Jung Y, Han DJB. BWA-MEME: BWA-MEM emulated with a machine learning approach. *Bioinformatics* 2022;**38**(9):2404-13.
27. Koboldt DC, Chen K, Wylie T, Larson DE, McLellan MD, Mardis ER, et al. VarScan: variant detection in massively parallel sequencing of individual and pooled samples. *Bioinformatics* 2009;**25**(17):2283-5.

28. Koboldt DC, Zhang Q, Larson DE, Shen D, McLellan MD, Lin L, et al. VarScan 2: somatic mutation and copy number alteration discovery in cancer by exome sequencing. *Genome Res* 2012;**22**(3):568-76.
29. Shaker B, Ahmad S, Lee J, Jung C, Na DJCib, medicine. In silico methods and tools for drug discovery. *Comput Biol Med* 2021;**137:**104851.
30. Yusof AMJBJoMS. Bioinformatics Applications on Cryptosporidium Research: A Review. *Bangladesh J Medical Sci* 2022;**21**(1):8-18.
31. Tam V, Patel N, Turcotte M, Bossé Y, Paré G, Meyre DJNRG. Benefits and limitations of genome-wide association studies. *Nat Rev Genet* 2019;**20**(8):467-84.
32. Uffelmann E, Huang QQ, Munung NS, De Vries J, Okada Y, Martin AR, et al. Genome-wide association studies. *Nat Rev Methods Primers* 2021;**1**(1):59.
33. Slatko BE, Gardner AF, Ausubel FMJCpimb. Overview of next-generation sequencing technologies. *Curr Protoc Mol Biol* 2018;**122**(1):e59.
34. Lin X, Quan Z, Wang Z-J, Ma T, Zeng X, editors. KGNN: Knowledge Graph Neural Network for Drug-Drug Interaction Prediction. *Int Jt Conf AI* 2020.
35. Feng Y-H, Zhang S-W, Shi J-YJBb. DPDDI: a deep predictor for drug-drug interactions. *BMC Bioinformatics* 2020;**21**(1):1-15.
36. Pulst SMJAon. Genetic linkage analysis. 1999;56(6):667-72.
37. Lin E, Lin C-H, Lane H-YJCP, Neuroscience. Machine learning and deep learning for the pharmacogenomics of antidepressant treatments. *Clin Psychopharmacol Neurosci* 2021;**19**(4):557.
38. Podgorelec V, Kokol P, Stiglic B, Rozman IJJoms. Decision trees: an overview and their use in medicine. *J Med Syst* 2002;**26**:445-63.
39. Qi Y. Random forest for bioinformatics. Ensemble machine learning: Methods and applications: Springer; 2012. p. 307-23.
40. Drozda K, Pacanowski MAJPTJoHP, Therapy D. Clinical trial designs to support clinical utility of pharmacogenomic testing. *J Human Pharmacol Drug Ther* 2017;**37**(9):1000-4.
41. Wu AHJTL. Pharmacogenomic testing and response to warfarin. *Lancet* 2015;**385**(9984):2231-2.
42. Daina A, Michielin O, Zoete VJSr. SwissADME: a free web tool to evaluate pharmacokinetics, drug-likeness and medicinal chemistry friendliness of small molecules. *Sci Rep* 2017;**7**(1):42717.
43. Amanat M, Reza MS, Shuvo MSR, Ahmed KS, Hossain H, Tawhid M, et al. Zingiber roseum Rosc. rhizome: A rich source of hepatoprotective polyphenols. *Biomed Pharmacother* 2021;**139:**111673.
44. Jamei M, Marciniak S, Feng K, Barnett A, Tucker G, Rostami-Hodjegan AJEoodm, et al. The Simcyp® population-based ADME simulator. *Expert Opin Drug Metab Toxicol* 2009;**5**(2):211-23.
45. Chai AWY, Tan AC, Cheong SCJSR. Uncovering drug repurposing candidates for head and neck cancers: insights from systematic pharmacogenomics data analysis. *Sci Rep* 2021;**11**(1):1-15.
46. Wang L, Liu H, Chute CG, Zhu QJBm. Cancer based pharmacogenomics network supported with scientific evidences: from the view of drug repurposing. *BioData Min* 2015;**8**(1):1-14.
47. Saengboonmee C, Sanlung T, Wongkham SJAR. Repurposing metformin for cancer treatment: A great challenge of a promising drug. *Anticancer Res* 2021;**41**(12):5913-8.
48. Kadri F, Chaabane S, Tahon CJSMP, Theory. A simulation-based decision support system to prevent and predict strain situations in emergency department systems. *Simul Model Pract Theory* 2014;**42**:32-52.
49. Hinderer M, Boeker M, Wagner SA, Lablans M, Newe S, Hülsemann JL, et al. Integrating clinical decision support systems for pharmacogenomic testing into clinical routine-a scoping review of designs of user-system interactions in recent system development. *BMC Med Inform Decis Mak* 2017;**17:**1-14.
50. Regulation PJI. General data protection regulation. 2018;**25**:1-5.