

Pharmacogenomic: A Genetic Approach To Drug Development And Therapy.

Miss. Pooja. M. Amte¹, Miss Snehal Dhewale², Mr. Dr. D. K Vir³, Mr. Akash. S. Aher⁴,

Miss. Deepali. P. Dangode⁵.

1.(Student), 2. (Associate Professor), 3. (Principal), 4. (Student),5. (Student)

Department of Pharmaceutical Science and Technology.

Shree Goraksha College of Pharmacy and Research Center, Khamgaon, Chhatrapati Sambhaji Nagar.
India

Abstract: Pharmacogenomics is an emerging field that deepens our understanding of how medications interact with the human body. It plays a vital role in improving treatment strategies and supporting the development of safer and more effective drugs. The central focus of pharmacogenomics is to explore how genes and complex genetic networks influence individual responses to medications. Drug response often varies among patients due to genetic factors, environmental influences, and personal characteristics that shape pharmacokinetic and pharmacodynamic processes. As research progresses, pharmacogenomics has become important for predicting disease risk, guiding personalized therapies, and enhancing overall treatment outcomes. Advances made through human genome sequencing have further strengthened this field by enabling early identification of genetic disorders, supporting gene therapy initiatives, and improving the understanding of genetic variations involved in drug metabolism. This review aims to provide a clear overview of key pharmacogenomic concepts, including genetic polymorphisms, mutations, variations, and alleles. By highlighting how these factors influence drug action, the review offers a foundation for developing new approaches, techniques, and applications in personalized medicine and modern drug development.

Keyword: pharmacogenomics, genetic approach, drug therapy, drug development, personalized medicine or therapy, human diseases.

1.Introduction:

Pharmacogenetics examines how individuals differ in their responses to medications and has rapidly grown within molecular biology and clinical practice.[2] Pharmacogenomics builds on this by combining pharmacology with genomics to develop safer, more effective drugs and determine appropriate dosages based on a patient's genetic profile. Research over the years has shown that genetic variations strongly influence drug response. The identification of functional polymorphisms and detailed SNP maps has strengthened the role of pharmacogenetics in personalizing therapy. With continuing advances in genomic and other omics-based technologies, pharmacogenomics has evolved as a key approach for improving drug development and individualized treatment. Pharmacogenomics includes several key components such as genetic variations, drug metabolism, drug response, adverse reactions, personalized medicine, dosing optimisation, and its influence on drug development. Traditional "one-size-fits-all" treatments often overlook genetic diversity, resulting in inconsistent therapeutic outcomes and unwanted effects. In contrast, pharmacogenomic approaches help design safer, more effective, and individualized therapies. This genetic-guided method improves clinical efficacy, reduces trial-and-error prescribing, accelerates drug discovery, and supports the growth of precision medicine.

Although first introduced in the 1930s, pharmacogenetics gained renewed importance with advances in genetic testing. Both genetic and environmental factors shape drug response, with genetic variations accounting for up to 95% of treatment differences.[2] Pharmacogenomics has become an important tool in modern pharmaceutical science, aiming to identify new drug targets, improve treatment outcomes, minimize adverse reactions, and link genetic variations to clinical responses. Unlike traditional drug development, which targets broad populations, pharmacogenomics focuses on personalized therapy guided by genetic information to enhance safety and effectiveness.

2. History of Pharmacogenomic

Pharmacogenomics examines how genetic differences influence individual responses to medications. The earlier concept of pharmacogenetics was introduced by Friedrich Vogel in 1959, while the broader term pharmacogenomics emerged in the late 1990s with advances in DNA and genomic technologies. Historical observations also contributed to this field. As early as 510 BC, Pythagoras noted that certain individuals from Mediterranean regions developed hemolytic anemia and jaundice after eating fava beans—later identified as favism, caused by inherited G6PD deficiency.[3]

Pharmacogenetics developed from the union of pharmacology and genetics, two disciplines that became scientifically established in the eighteenth century. Their connection was foreshadowed by Sir Archibald Garrod in 1931 and later supported by J.B.S. Haldane, who suggested that biochemical differences might explain unusual drug reactions.[5] The first pharmacogenetics textbook appeared in 1962, well before DNA sequencing was possible. As genomic science advanced, the term pharmacogenomics was adopted to reflect that drug responses result from multiple genetic variants. Research has expanded from studying non-synonymous variants to recognizing the roles of non-coding variations, epigenetic modifications, and small RNA molecules in shaping individual differences in drug response.[6]

3. Role Of Pharmacogenomic

Pharmacogenomics studies how genetic variations influence individual drug responses. The concept began with pharmacogenetics, introduced by Friedrich Vogel in 1959, and expanded into pharmacogenomics in the late 1990s as genomic technologies advanced. Early observations also shaped the field; in 510 BC, Pythagoras reported severe reactions such as hemolytic anemia after fava bean consumption, later linked to inherited G6PD deficiency.[3]

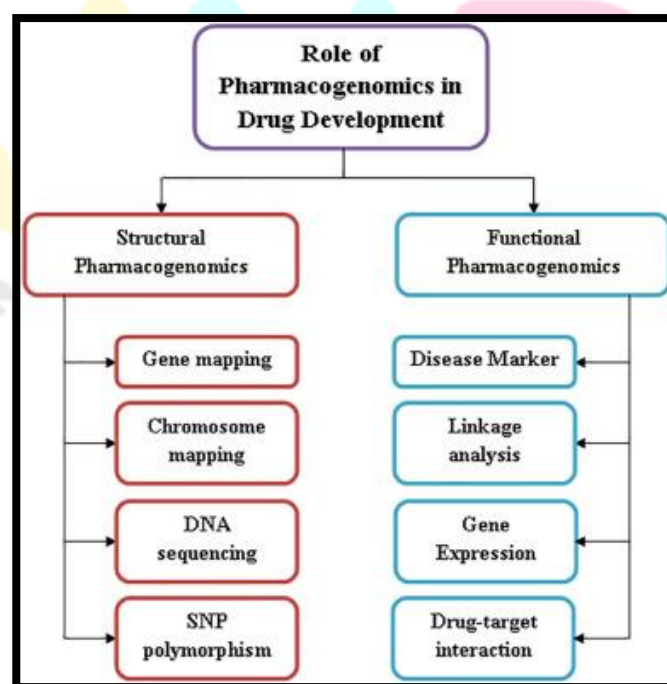


Fig No .1: Role of Pharmacogenomic

Pharmacogenetics grew from the integration of pharmacology and genetics; disciplines formally developed in the eighteenth century. Their connection was anticipated by Sir Archibald Garrod in 1931 and later reinforced by J.B.S. Haldane, who proposed that biochemical differences could explain unusual drug reactions.[5] By 1962, the first pharmacogenetics textbook had appeared, preceding modern sequencing tools. With progress in genomics, the term pharmacogenomics was adopted to reflect the influence of multiple genetic variants on drug response. Current research highlights not only non-synonymous variants but also non-coding changes, epigenetic modifications, and small RNA molecules as key contributors to variability in drug effects.[6]

4. Advantage Of Pharmacogenomic

- A. Improves drug effectiveness by matching treatments to a patient's genetics.
- B. Reduces adverse drug reactions and increases safety.
- C. Supports personalized and precision medicine.
- D. Helps determine accurate drug dosing.
- E. Speeds up drug development and reduces trial failures.
- F. Identifies new drug targets through genomic insights.
- G. Enhances patient compliance with safer, more effective therapies.
- H. Lowers healthcare costs by avoiding ineffective treatments.

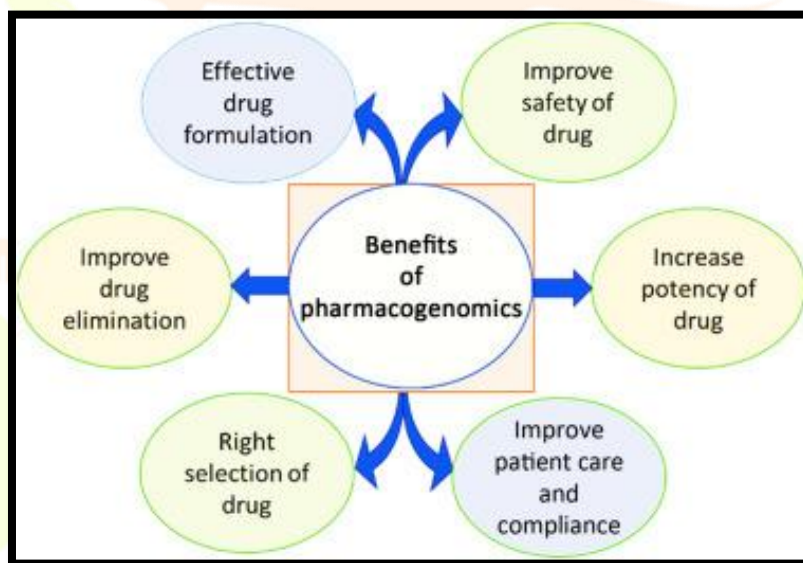


Fig. No 2: Benefits of Pharmacogenomic

5. Principal of Pharmacogenomic and Pharmacogenetic.

Pharmacogenomics studies how a person's genetic makeup affects their response to medications. Its core idea is that genetic variations—including SNPs, insertions, deletions, and copy number changes—can influence drug absorption, distribution, metabolism, and excretion, thereby impacting both efficacy and toxicity. These genetic insights help clinicians choose suitable drugs, determine proper doses, and set appropriate treatment durations while reducing the risk of adverse reactions. Pharmacogenetic research also contributes to the development of new therapeutic agents. Despite medical progress, only 30–60% of treatments achieve the intended outcomes, and about 7% of hospital admissions are associated with

adverse drug reactions.[7] The underlying principle of pharmacogenetics is that genetic differences explain why individuals respond differently to the same medication, supporting the goal of personalized therapy with better effectiveness and fewer side effects.

5.1: Pharmacokinetic and Pharmacodynamic Relationship

A strong understanding of pharmacokinetics (PK) and pharmacodynamics (PD) is essential for explaining how drugs function under different disease conditions.[8] Pharmacodynamics describes how drug concentrations produce biological effects through mechanisms such as presynaptic binding and activation of postsynaptic receptors.[9],[10] In clinical practice, PK and PD are closely linked: PK defines the concentration–time profile of a drug, while PD reflects the resulting therapeutic effect. Therefore, both must be evaluated together to achieve optimal treatment outcomes, and a solid grasp of these principles is necessary before progressing to pharmacogenomic (PGx) studies.[11]

6.Genetic Based of Drug Response

Family-based research has helped identify genetic contributions to diseases such as myocardial infarction and sudden cardiac death, but collecting consistent drug-response data from related patients remains difficult. To estimate heritability of drug effects, lymphoblastoid cell lines from family members have been exposed to anticancer agents, revealing heritability estimates for drug-induced cytotoxicity between 0.25 and 0.65 and identifying genomic regions linked to this toxicity.[12]

Genetic variations—including SNPs, indels, and CNVs—play a major role in shaping individual drug responses. These differences affect genes responsible for drug-metabolizing enzymes, transporters, and targets, influencing drug absorption, distribution, metabolism, excretion, and pharmacodynamic effects. Variants in enzymes such as CYP450 contribute to poor, intermediate, extensive, or ultra-rapid metabolizer phenotypes, leading to toxicity or reduced efficacy. Changes in drug transporters and targets further modify drug levels and sensitivity, while HLA gene variants can trigger severe hypersensitivity reactions such as those seen with abacavir.

Understanding these genetic influences supports personalized therapy, minimizes adverse reactions, and improves treatment outcomes. Pharmacogenomic testing enables clinicians to select appropriate medications and dosages based on each patient’s genetic profile.

7. Pharmacogenomic Drug Response.

Pharmacogenomics is increasingly important in modern drug development because it uses genetic information to enhance drug safety, efficacy, and precision. By examining how genetic variations affect drug response, it supports the creation of targeted therapies and more individualized treatment strategies. Although pharmacogenomic data are expected to transform both drug development and clinical practice, limited empirical analysis has evaluated how these insights influence real-world processes.[13]

Pharmaceutical companies must submit pharmacogenetic data to the U.S. FDA during drug development, but many submissions lack sufficient clarity for regulatory use. Separate FDA guidelines also apply to pharmacogenetic information submitted for IND applications and for unapproved or approved products.[5]

In early drug discovery, pharmacogenomics helps identify genetic targets linked to disease or drug response, improving the selection of promising compounds and predicting responders and non-

responders. Retrospective studies show that patient genotypes significantly affect drug efficacy and safety, supporting broader use of genomic data in future drug development. A Phase IIa study demonstrated that early pharmacogenetic analysis can strengthen decisions about advancing drug candidates. Modern genomic mapping techniques also aid in detecting adverse drug reactions during trials and aftermarket release.[24]

8. Pharmacogenomic in Clinical Practices.

Pharmacogenomics is increasingly used in clinical practice to guide drug therapy according to an individual's genetic profile. Its main goal is to personalize treatment so patients receive the most effective drug at the safest dose. By detecting genetic variations that influence drug metabolism, transport, and targets, clinicians can anticipate patient responses before starting therapy. Despite major progress in biomedical research, many patients still do not respond adequately to medications, and FDA data show that about 38–75% of common drug treatments may be ineffective, increasing healthcare costs [14].

However, several barriers limit widespread adoption. Fragmented healthcare systems and limited use of electronic medical records make it difficult to link genetic results with future treatments. Preventive care and adverse-reaction reduction also receive minimal incentives. Many clinicians lack sufficient genomic training, and because pharmacogenetic tests are rarely performed early, results often arrive too late for treatment decisions [15]. To support clinicians, the FDA provides two online databases with reviewed pharmacogenetic information [16], including a table listing biomarkers and the corresponding drug-label sections where they are discussed [17]. Organizations such as the FDA and CPIC have also developed guidelines and drug-label recommendations, and electronic health records now allow pharmacogenomic data to be integrated into prescribing workflows.

Despite these improvements, challenges remain, including high testing costs, limited clinician education, and ethical issues related to genetic-data privacy. Even so, growing research efforts, supportive policies, and precision-medicine initiatives are steadily advancing the adoption of pharmacogenomics as a routine part of patient care. Pharmacogenomics continues to expand in clinical use by enabling prediction of drug responses based on genetic variation, ensuring safer and more effective personalized therapy [18].



Table No.1: Clinical Application of Pharmacogenomic

Sr. No	Clinical Area	Biomarker	Drug involved	Clinical Application Benefit
1.	Personalized medicine	Various (e.g. CYP2D6, CYP2C19)	Antidepressants, opioids	Tailors therapy based on individual genetic profile to improve efficacy and reduce side effects.
2.	Adverse Drug Reaction	HLA-B, TPMT, NUDT15	Abacavir, Azathioprine	Prevents severe hypersensitivity or toxicity before drug administration.
3.	Clinical Decision Support	FDA-Approved Pgx Biomarker	Multiple Drug	Incorporates genetic data into EHR systems for real-time dosing and drug selection guidance
4.	Dose Optimization	CYP2C9, VKORC1	Warfarin	Enables safe and effective dosing by predicting metabolism and sensitivity.
5.	Cancer therapy	HER2, KRAS, EGFR	Trastuzumab, cetuximab	Gefitinib Guides targeted therapy by matching drugs to tumor gene mutations.
6.	Psychiatric Disorder	CYP2D6, CYP2C1	SSRI, TCAs, Antipsychotics	Antipsychotics Helps select and dose psychiatric drugs to minimize adverse effects.
7.	Cardiovascular Diseases	CYP2C19, SLCO1B1	Clopidogrel, Statins	Predicts drug response and risk of statin-induced myopathy
8.	Infection Diseases	HLA-B	Abacavir (HIV Therapy)	Prevents severe hypersensitivity or toxicity before drug administration.
9.	Pain Management	CYP2D6	Codeine, Tramadol	Tramadol Determines opioid metabolism rate

				to ensure proper pain control
10.	Transplant medicine	CYP3A5	Tacrolimus	Optimizes immunosuppressant dosing and prevents organ rejection.

9.Genetic Expression and Epigenetic.

Epigenetics involves heritable changes in gene activity that occur without altering the DNA sequence. These modifications control how genes are switched on or off and are essential for normal cell function and development. Key mechanisms—such as DNA methylation, histone modification, and non-coding RNA activity—regulate gene expression and allow cells to respond to environmental signals. Disruptions in these processes are linked to diseases including cancer and neurological disorders.

Gene expression regulation is central to how cells with identical DNA develop different structures and functions. During transcription and translation, genetic information flows from stable DNA to mRNA and then to proteins, and these expression patterns are maintained through mitosis once established [19].

Epigenetic changes influence chromatin structure and DNA accessibility, shaping transcriptional activity. The major mechanisms include DNA methylation and histone protein modifications, which operate through coordinated pathways. These regulatory systems are vital for differentiation, development, and cellular activation, and growing evidence connects epigenetic alterations to cancer and inflammatory diseases [20].

10.Challenge and Limitation.

Modern pharmacogenomics now includes a broad range of molecular features beyond germline variants, influencing both pharmacokinetics and pharmacodynamics. This expanding knowledge requires advanced diagnostic tools, new drug-design strategies, improved data-analysis systems, and updated global regulatory frameworks [21].

Despite its promise in cancer therapy, major barriers remain, including limited strong clinical evidence, non-standardized testing methods, and challenges in integrating genomic information into health records and decision-support systems [22]. A key difficulty in clinical use is the lack of clear dosing algorithms. Although the FDA recommends genetic testing for certain drugs, specific dose-adjustment guidelines are often unavailable. For instance, no defined dose-reduction advice exists for irinotecan in patients homozygous for certain polymorphisms [23]. Pharmacogenomics still needs stronger clinical validation, uniform testing standards, and better incorporation of genetic data into healthcare systems [15].

Genetic variation significantly affects drug metabolism and response, shaping efficacy and toxicity. Pharmacogenomic testing can anticipate a patient’s drug response before treatment, particularly for genes such as CYP2D6, CYP2C19, VKORC1, CYP2C9, and SLCO1B1. These variations determine whether a person is a poor, intermediate, extensive, or ultrarapid metabolizer, guiding dose adjustments and drug selection. Overall, pharmacogenomic testing supports personalized therapy, reduces adverse effects, optimizes dosing, and avoids trial-and-error prescribing.

11.Future Perspective:

Pharmacogenomics is expected to further advance drug discovery and personalized medicine by enabling safer and more precise therapies. Future progress will rely on advanced technologies and large-scale data integration. Multi-omics approaches will link genomics with transcriptomics, proteomics, metabolomics, and epigenomics for a deeper understanding of drug response. AI and machine learning will help analyze genomic data, predict drug effects, and improve trial design. Expanding global databases such as Pharm, CPIC, and the FDA PGx Biomarker Table will strengthen evidence-based practice.

Gene-editing tools like CRISPR may correct harmful variants and support personalized therapeutic strategies. More population-based genomic studies will improve knowledge of genetic diversity across global groups. Integrating pharmacogenomic information into electronic health records will support real-time drug and dose selection. Genetic profiling in clinical trials will help identify responders earlier and improve development success. International ethical and regulatory guidelines will promote safe use of genomic data. Pharmacogenomic tools will also support personalized polypharmacy management, especially in elderly patients. Finally, greater education and clinical implementation will help translate research findings into everyday healthcare.

Conclusion:

Pharmacogenomics provides key insights into how genetic differences shape individual drug responses, supporting safer and more effective personalized therapies. By incorporating genetic data across drug development—from target identification to clinical use—it improves drug selection, dosing, and the prediction of adverse reactions. Future progress will rely on integrating multi-omics data, artificial intelligence, and real-world clinical evidence to advance precision-guided drug discovery. Although obstacles such as high testing costs, limited awareness, and regulatory issues persist, ongoing genomic innovations are making individualized treatment more accessible. Overall, pharmacogenomics aims to deliver the right drug to the right patient at the right dose, driving a new era of precision healthcare.

Reference:

- 1.Rowaid Qahwaji, Pharmacogenomics: A Genetic Approach to Drug Development and Therapy, Pharmaceuticals, MDPI, 2024; 17: 940.
- 2.J.T. Oates, D. Lopez, Pharmacogenetics: An Important Part of Drug Development with a Focus on Its Application, International Journal of Biomedical Investigation, SciRes Literature, 2018; 1(2): 1–28.
- 3.Jurgen Brockmöller, Mladen V. Tzvetkov, Pharmacogenetics: Data, Concepts and Tools to Improve Drug Discovery and Drug Treatment, European Journal of Clinical Pharmacology, Springer, 2008; 64: 133–157.
- 4.A. Surendiran, Role of Pharmacogenomics in Drug Discovery and Development, Indian Journal of Pharmacology, Medknow/Wolters Kluwer, 2008; 40(4): 137–143.
- 5.Werner Kalow, Human Pharmacogenomics: The Development of a Science, Human Genomics, Henry Stewart Publications, 2004; 1(5): 375–380.
- 6.Dan M. Roden, Pharmacogenomics: The Genetics of Variable Drug Responses, NIH Public Access / Circulation (American Heart Association), 2011; 123(15): 1661–1670.

7. Bagher Larijani, Principles of Precision Medicine, Springer Nature, 2022. DOI: 10.1007/978-981-19-5082-7_1.
8. van den Anker J, Reed MD, Allegaert K, Kearns GL, Developmental Changes in Pharmacokinetics and Pharmacodynamics, Journal of Clinical Pharmacology, Wiley, 2018; 58.
9. Currie G.M., Pharmacology Part 1: Introduction to Pharmacology and Pharmacodynamics, Journal of Nuclear Medicine Technology, Society of Nuclear Medicine, 2018; 46(2): 81–86.
10. Lista A.D., Sirimatuross M., Pharmacokinetic and Pharmacodynamic Principles for Toxicology, Critical Care Clinics, Elsevier, 2021; 37(3): 475–486.
11. Derendorf H., Lesko L.J., Chaikin P., Colburn W.A., Lee P., Miller R., et al., Pharmacokinetic/Pharmacodynamic Modeling in Drug Research and Development, Journal of Clinical Pharmacology, Wiley, 2000; 40(12 Pt 2): 1399–1418.
12. Dan M. Roden, Pharmacogenomics: The Genetics of Variable Drug Responses, Circulation, American Heart Association, 2011; 123: 1661–1670.
13. Yingying Guo, Pharmacogenomics and Drug Development, Pharmacogenomics, Future Medicine Ltd., 2005; 6(8): 857–864.
14. Indu Passi, US-FDA Approved Drugs in 2020–2021: A Review, Mini-Reviews in Medicinal Chemistry, Bentham Science, 2023; 23(12): 1273–1297.
15. M.V. Relling, CPIC: Clinical Pharmacogenetics Implementation Consortium of the Pharmacogenomics Research Network, Clinical Pharmacology & Therapeutics, Wiley, 2011; 89(3): 464–467.
16. Mehta D., Uber R., Ingle T., Li C., Liu Z., Thakkar S., et al., Study of Pharmacogenomic Information in FDA-Approved Drug Labeling..., Drug Discovery Today, Elsevier, 2020; 25(5): 813–820.
17. M. Cheng, Thomas W. Jeff L., Characterization of Information in Food and Drug Administration Drug Labeling, Clinical Pharmacology & Therapeutics, Wiley, 2020; 55(10).
18. Mustafa Adnan Malki, Drug–Drug–Gene Interaction and Adverse Drug Reaction, The Pharmacogenomics Journal, Nature Publishing Group, 2020; 20: 355–366.
19. F. Perri, Epigenetic Control of Gene Expression: Potential Implication for Cancer Treatment, Critical Reviews in Oncology/Hematology, Elsevier, 2017; 111: 166–172.
20. E.R. Gibney, Epigenetics and Gene Expression, Heredity, Nature Publishing Group, 2010; 105: 4–13.
21. Ann K. Daly, Opportunities and Limitations: The Value of Pharmacogenetics in Clinical Practice, British Journal of Clinical Pharmacology, Wiley-Blackwell, 2014; 77(4): 583–586.

22.Karra Geetha, Pharmacogenomics in Healthcare: Applications, Challenges, and Future Directions with a Focus on Oncology, International Journal of Health Sciences and Research, IJHSR Publications, 2024; 14(6).

23.Sharon Marsh, Tibor Van Rooij, Challenges of Incorporating Pharmacogenomics into Clinical Practice, Pharmacogenomics, Future Medicine Ltd., 2009; 3(S): 206–207.

24.Geoffrey S. Ginsburg, Richard P. Konstance, Jennifer S. Allsbrook, Implications of Pharmacogenomics for Drug Development and Clinical Practice, JAMA, American Medical Association, 2005; 165(20): 2331–2336.

