

Pharmacogenomics: How to select right drug to right patient

MR. PAGAR ANIKET¹, MR. RAUT KRUSHNA², MS SALVE SONAL³, MR. WADHAVE AMOL⁴

^{1,2} Student of Diploma in Pharmacy, 2nd year Chh Sambhajinagar

³ Lecturer of Diploma in Pharmacy, 2nd year Chh Sambhajinagar

⁴ Principal of Diploma in Pharmacy, 2nd year Chh Sambhajinagar

Abstract—Pharmacogenomics plays a crucial role in understanding how different people respond to medications, which helps improve treatment and drug development. It focuses on how our genes and complex genetic systems influence the way our bodies react to drugs. Recent advances in clinical research have led to the discovery of new biomarkers that can predict which patients are more or less likely to benefit from specific medications. The ultimate goal is to personalize treatment by giving the right drug, at the right dose, at the right time. This field considers not just genetics, but also environmental and personal factors that affect how drugs work in different individuals. Pharmacogenomics has the potential to revolutionize drug development, improve treatment effectiveness, and identify disease risks. This review aims to provide a foundation for developing new tools, strategies, and applications in pharmacogenomics.

Index Terms—Pharmacogenomics, Genetic testing, Personalised medicine

I. INTRODUCTION

Pharmacogenomics is an emerging field of science that explores how an individual's genetic makeup influences their response to medications. By applying genomic tools and techniques, researchers can better understand how drugs are processed in the body (drug disposition), how they function (drug action), and why some individuals experience side effects or do not respond to certain treatments. This growing knowledge is paving the way for a more tailored approach to healthcare, commonly known as personalized medicine.

Personalized medicine aims to move away from the traditional "one-size-fits-all" method of prescribing drugs. Instead, it focuses on giving the right medication, at the right dose, to the right patient, based

on their unique genetic profile. This can increase treatment effectiveness, reduce the risk of adverse drug reactions, and potentially lower healthcare costs by avoiding ineffective treatments.

In addition to the concept of personalized medicine, a newer term stratified medicine has also gained attention. While personalized medicine focuses on individual-level differences, stratified medicine aims to group patients into subcategories based on their likely response to a particular drug. This helps healthcare professionals predict outcomes more accurately and make better-informed treatment decisions for specific patient groups.

Pharmacogenomics is advancing rapidly, and with it, the terminology and definitions used in the field are still being shaped. As a result, it is critical for researchers, clinicians, and pharmaceutical developers involved in global drug development projects to have a clear understanding of the commonly used scientific terms and regulatory language. This ensures effective communication and proper integration of pharmacogenomic data into clinical and research settings.

Moreover, public interest in pharmacogenomics and personalized medicine has been increasing significantly. Media coverage, along with education campaigns and scientific publications, has helped raise awareness among both healthcare providers and the general population. People are now more informed about the possibilities of receiving treatments based on their genetics, leading to higher expectations for customized and more effective healthcare options.

In summary, pharmacogenomics holds great promise for transforming modern medicine. By better understanding how genetics influences drug response, we are moving closer to a future where treatments are not only more effective but also safer and more

precisely targeted to each individual or subgroup of patients. [1,2]

The basis of pharmacogenomics: The first example of a drug developed using a pharmacogenomic approach was for alkaptonuria, a rare metabolic disorder. As early as 1902, researchers suspected that this condition was caused by a genetic mutation, making it one of the first diseases linked to a genetic basis. [3] During World War II, doctors noticed that some African-American soldiers experienced severe breakdown of red blood cells (hemolysis) after being treated with antimalarial drugs. This led scientists to discover that the cause was a genetic difference involving a specific enzyme, marking an important step in understanding how genetics can affect drug response. [4]

Pharmacogenetics focuses on how differences in our genes affect the way individuals respond to the same drug. This idea is often summed up as “many genomes, one drug,” meaning that people with different genetic makeups may react differently to the same medication. On the other hand, pharmacogenomics takes a broader approach. It involves adjusting or developing different drugs to match a specific genetic profile. This is known as “many drugs, one genome,” where the goal is to find or design the best drug for a particular genetic type [5].

II. SHORT TERM BENEFITS

Out of the 3 billion prescriptions written each year in the United States, it's estimated that about 3 million of them are either wrong or don't work as intended. This leads to over 100,000 deaths every year caused by adverse drug reactions (ADRs) when a medication harms the patient instead of helping [8,9]. Adverse drug reactions (ADRs) are so serious that they rank between the fourth and sixth leading causes of death in the United States. Right now, medications are usually prescribed based on a person's illness, without knowing how well the drug will actually work for them. This means anyone with a certain condition might be given the same drug, even though their response can vary widely. In fact, even the most popular and widely used drugs often called blockbuster drugs are only effective for about 40% to 60% of the people who take them [10].

Long term benefits: One of the expected benefits of pharmacogenomics is a more efficient and effective healthcare system. By combining a patient's medical

history with their genetic information, doctors will be able to make more accurate and personalized treatment decisions. When patients feel confident in their treatment and trust the healthcare system, they are more likely to take better care of their health. Right now, because so many prescriptions don't work as expected, about half of all patients stop taking their medications for chronic illnesses within a year. Pharmacogenomics could help change that by ensuring patients receive treatments that are more likely to work for them [11].

Pharmacogenomics: Pharmacogenomics is an important tool now being used in the pharmaceutical industry, and it represents a major breakthrough in the field of medicine. Its key goals include identifying new drug targets, making medications more effective, reducing harmful side effects, linking a person's genetic makeup (genotype) with their medical condition, and creating genetic profiles to help predict how someone will respond to certain drugs or their risk of developing specific diseases. In the past, most drugs were designed for the general population, without considering individual differences. Pharmacogenomics challenges that approach by aiming to create safer, more effective treatments that are tailored to each person's unique genetic makeup. Instead of just treating the visible symptoms of a disease (the phenotype), pharmacogenomic treatments go deeper by focusing on the underlying genetic causes (the genotype). Over time, this approach will become a regular part of how new drugs are discovered and developed, potentially making the process faster, more efficient, and more affordable. [12,13,14]

The main goal of personalized medicine is to treat each patient as a unique individual and to predict how different treatments will work for different people. Pharmacogenomics plays a key role in making this possible. The basic idea is that many factors like a person's age, gender, other medications they're taking, lifestyle, environment, genetics, and even how their genes are regulated (epigenomics) can all influence how someone responds to a particular drug. Understanding these differences helps doctors choose the most effective and safest treatment for each individual [15].

Recent advances in pharmacogenomics, often referred to as “omics” technologies, have completely changed

how we understand the causes of diseases and why some people are more likely to develop certain conditions. These advancements also offer exciting new possibilities for developing better treatments. For example, the drug Ivacaftor is specifically approved to treat cystic fibrosis in patients who carry a particular genetic mutation called G551D in the CFTR gene. This gene produces a protein that helps regulate the movement of water and chloride in and out of cells. In people with cystic fibrosis, this protein doesn't function properly, leading to thick mucus buildup, especially in the lungs. Ivacaftor works by activating the faulty CFTR protein, helping it function more normally. This leads to better water and salt balance in the lungs, which in turn improves breathing and overall lung function in patients with the G551D mutation [16].

Implications of genetic testing: In pharmacogenomics, genetic testing can serve several important purposes. One major application is to understand how a person's body processes medications this includes how a drug is absorbed, distributed, broken down (metabolized), and eventually eliminated. Another key use of genetic testing is to help match individuals with the medications that are most likely to be effective for them, ensuring a better treatment outcome. Additionally, genetic testing can be used to identify people who may be at higher risk for developing certain health conditions, allowing for earlier monitoring or preventive care [17].

Genetic testing gives people access to information about their health and their chances of developing certain diseases or conditions in the future. By analyzing specific parts of a person's DNA that are linked to known health risks, it's possible to estimate how likely they are to develop a particular illness. However, this kind of information can affect people in different ways. For some, it may encourage healthier lifestyle choices, while for others, it might lead to anxiety or a sense of helplessness especially if the risk isn't something they can control through their environment or behavior. Because of this, there are concerns about how genetic testing should be shared and explained to ensure it's helpful and not harmful [18]. When people receive their genetic test results, there's a risk that the information could be misunderstood or misinterpreted. For example, if the results highlight a genetic predisposition to a disease

without clearly explaining how common that risk is in the general population, the person might overreact or worry more than necessary.

On the other hand, if someone expects to see certain risks in their results based on family history but those risks don't appear in the test, they might feel relieved, but more often they may doubt the accuracy of the test. This shows how important it is to communicate genetic information clearly and responsibly, so people can understand their results in the right context [19,20].

III. IMPACT ON THE PHARMACEUTICAL INDUSTRY

The traditional blockbuster drug model focuses on developing just a few highly profitable medications each year, aiming to create drugs that can earn billions of dollars by being used widely across the general population [21]. Because pharmaceutical companies rely heavily on a small number of high-earning drugs, they tend to focus on creating medications that can be used by large groups of people, especially those meant for long-term treatment. This approach is driven by the need to maximize profits. The figure below illustrates the typical drug development process and the time it usually takes from start to finish.

The process of developing a new drug starts with around 10,000 potential compounds. Through a long and careful process of testing and evaluation, only one strong and effective compound usually makes it to the end. This final compound becomes the patented active ingredient used in the actual medication [22]. With the help of advanced technologies like high throughput screening and microarrays, scientists can now identify promising drug candidates more quickly and efficiently than ever before. However, the preclinical stage where drugs are tested in lab settings and on animals to assess safety and toxicity is still one of the slowest and most critical parts of the drug development process. Only compounds that pass this stage safely can move on to human testing.

During Phase 2 clinical trials, the drug is tested on a carefully selected group of volunteers, often excluding children, the elderly, and people with other health conditions. The goal here is to find out how well the drug actually works. If pharmacogenetics is included in this phase, researchers can begin to see how a person's genes affect the drug's safety and

effectiveness. This can help identify specific biomarkers linked to how well the drug works or doesn't for different individuals. This information can then be used to either refine the drug or focus future trials on those more likely to benefit from it.

Phase 3 trials are the most extensive and involve a much larger and more diverse group of participants. But by using pharmacogenomics, researchers can often reduce the trial size earlier by identifying and removing non-responders' people who aren't likely to benefit from the drug.

Once the drug reaches the market, pharmacogenomics can continue to play a role by helping doctors identify patients who experience severe side effects, and then tracing those reactions back to specific genetic causes. This ongoing learning helps improve drug safety and guide better treatment decisions in the future [23].

Reconfiguring the pharmaceutical business model: Pharmacogenomics is expected to become a core part of everyday medical practice within the next decade. In this evolving field, smaller biotech companies aren't competing directly with large pharmaceutical firms. Instead, they often work together. The smaller companies typically focus on early-stage research and discovery, while the larger pharmaceutical companies, which have more resources and experience with large-scale clinical trials, step in later to handle advanced testing and marketing. This kind of partnership allows both sides to combine their strengths and move new drugs forward more efficiently [24].

Pharmaceutical companies see pharmacogenomics as a valuable addition to their traditional drug development process because it helps them identify and eliminate drugs that are unlikely to succeed much earlier. This saves time, money, and resources by allowing them to focus only on the most promising candidates [25].

Pharmacogenomics offers a promising way to give older or previously unsuccessful drugs a second chance. By using genetic information, researchers can identify specific groups of people who are more likely to benefit from these drugs. This approach can turn past commercial or scientific failures into successful treatments when targeted to the right patients [26]

IV. ADVANTAGES OF PHARMACOGENOMICS

- Drugs are more effective and safer when they are designed to match a person's unique genetic makeup including their proteins, RNA, and enzymes. This personalized approach allows the medication to target specific diseases more precisely, leading to better results and fewer side effects compared to traditional treatments.
- Vaccines are becoming more effective thanks to the use of DNA and RNA technologies. These advanced vaccines help boost the immune system safely, without exposing the body to the actual infection.
- With the help of genetic testing, drugs can be matched to a person's unique genetic makeup. This means doctors can prescribe the right medication from the start, reducing or even eliminating side effects unlike the old trial-and-error method, where patients often had to try multiple drugs before finding one that worked.
- Patients recover faster because they receive the right medication from the beginning, tailored to their specific needs.

V. DISADVANTAGES OF PHARMACOGENOMICS

Complexities of finding gene variations that affect drug response: Finding the specific genetic variations (SNPs) that affect how people respond to drugs is extremely challenging it's like looking for a needle in a stack of needles while blindfolded. Since we still don't fully understand which genes are involved in drug response, the search for the right SNPs is often very costly and time consuming. This complexity can slow down the progress of pharmacogenomics research and drug development.

Educating Health Care professionals: One challenge with pharmacogenomics is that it could lead to the development of hundreds or even thousands of very similar drugs, each slightly adjusted for different genetic profiles. This could make it much more complicated for doctors and pharmacists to choose the right prescription for each patient and manage treatments effectively

Ethical Issues: There are several ethical concerns surrounding pharmacogenomics. One major issue is

the risk of creating “designer drugs” that are tailored to individual genetic profiles. While this sounds promising, it may lead to inequality in healthcare, as poorer individuals and countries might not be able to afford these advanced treatments. This could widen the gap between the rich and the poor, making top-quality healthcare accessible only to the wealthy unless major pharmaceutical companies commit to making pharmacogenomics affordable and widely available.

Another ethical concern involves the use of genetically modified animals to produce human drugs, a process known as “pharming.” This could require the use of domestic animals on an unprecedented scale, raising serious questions about animal welfare. With ongoing debates and opposition to animal testing, pharming could spark even more controversy over the humane treatment of animals in medical research and production.

REFERENCES

- [1] Mincer, Jilian, “Genetic Testing Guidance,” Wall Street Journal, July 13, 2008
- [2] Pollack, Andrew, “A Special Drug Just for You, At the End of a Long Pipeline,” The New York Times, November 5, 2005
- [3] Personalized Medicine and the Practice of Medicine in the 21st Century; Amalia M. Issa; McGill Journal of Medicine; 2007
- [4] Pharmacogenomics: Social, Ethical and Clinical Dimensions, Edited by Mark A. Rothstein, Wiley-Liss Publication, Hoboken, NJ, 2003.
- [5] Lindpaintner, Klaus, “The role of pharmacogenomics in drug discovery and therapeutics,” in Pharmacogenomics: The Search for Individualized Therapies, Edited by Julio Licinio and Ma-Li Wong, Wiley-VCH, 2002.
- [6] NCBI, A Science Primer; www.ncbi.nlm.nih.gov/about/primer/pharm.html; Observed June 14, 2008
- [7] Peterson-Iyer, Karen, “Pharmacogenomics, Ethics, and Public Policy,” Kennedy Institute of Ethics Journal, Vol. 18, No. 1, 2008, Johns Hopkins University Press; PROJECT MUSE
- [8] “Personalized Medicine: The Emerging Pharmacogenomics Revolution”, PricewaterhouseCoopers, Global Technology Centre, Health Research Institute, Feb. 2005
- [9] Teutsch, Steven M. and Marc L. Berger, “Misaligned Incentives in America’s Health: Who’s Minding the Store?” Annals of Family Medicine, 2005; editorial
- [10] Arendt, D.; Musser, J.M.; Baker, C.V.H.; Bergman, A.; Cepko, C.; Erwin, D.H.; Pavlicev, M.; Schlosser, G.; Widder, S.; Laubichler, M.D.; et al. The origin and evolution of cell types. Nat. Rev. Genet. 2016, 17, 744–757.
- [11] Wang,L.; McLeod, H.L.; Weinshilboum, R.M. Genomics and Drug Response. N. Engl. J. Med. 2011, 364, 1144–1153.
- [12] Mansoori, B.; Mohammadi, A.; Davudian, S.; Shirjang, S.; Baradaran, B. The Different Mechanisms of Cancer Drug Resistance: A Brief Review. Adv. Pharm. Bull. 2017, 7, 339–348.
- [13] Sweegers, M.G.; Depenbusch, J.; Kampshoff, C.S.; Aaronson, N.K.; Hiensch, A.; Wengström, Y.; Backman, M.; Gunasekara, N.; Clauss, D.; Pelaez, M.; et al. Perspectives of patients with metastatic breast cancer on physical exercise programs: Results from a survey in five European countries. Support. Care Cancer 2023, 31, 694.
- [14] Aavikko, M.; Kaasinen, E.; Andersson, N.; Penttinen, N.; Sulo, P.; Donner, I.; Pihlajamaa, P.; Kuosmanen, A.; Bramante, S.; Katainen, R.; et al. WNT2 activation through proximal germline deletion predisposes to small intestinal neuroendocrine tumors and intestinal adenocarcinomas. Hum. Mol. Genet. 2021, 30, 2429–2440.
- [15] Melzer, Raven, Ling, Detmer, and Zimmern, “Pharmacogenetics: policy needs for personal prescribing,” Journal of Health Services Research & Policy, Vol. 10, No.1, January 2005.
- [16] DNAPolicy.org, Genetic Perspectives on Policy Seminar, 2008
- [17] Highleyman, Liz, “HLA B*5701 Genetic Test Predicts Abacavir Hypersensitivity in Black as well as White HIV Patients,” HIVandHepatitis.com, May 2, 2008.
- [18] “Personalized Medicine: The Emerging Pharmacogenomics Revolution”, PricewaterhouseCoopers, Global Technology Centre, Health Research Institute, Feb. 2005
- [19] Furness, Mike L., “Genomics Applications that facilitate the understanding of drug action and toxicity,” in Pharmacogenomics: The Search for

Individualized Therapies, Ed. By Julio Licinio and Ma-Li Wong, Wiley-VCH,2002.

- [20] Mullin, Rick, "Drug Development Costs About \$1.7 billion," Chemical & Engineering News, December 15, 2003, Vol. 81, No. 50, p. 8
- [21] Miller, Paul, "Role of Pharmacoeconomic Analysis in R&D Decision Making: When, Where, how?" *Pharmaeconomics*, 2005; 23(1): 1-12.
- [22] Vernon, John A., Scott J. Johnson, W. Keener HUghen, and Antonio Trujillo, "Economic and Development Considerations for Pharmacogenomic Technology," *Pharmaeconomics*, 2006; 24(4); 335-343.
- [23] Nunally, Allen C., Scott A. Brown and Gary Cohen, "Intellectual Property and Commercial Aspects of Pharmacogenomics," in *Pharmacogenomics: Social, Ethical, and Clinical Dimensions*, Edited by Mark A. Rothstein, Wiley-Liss Publication, Hoboken, NJ, 2003.
- [24] FaizKermani (2007, October). "The future is pharmacogenomic," *Pharmaceutical Technology Europe*, 19(10), 17-18.