

Pharmacogenomics in Drug Safety: Role in Preventing Adverse Drug Reactions

Mangesh Yadav Kolnure, Kartik Ashok Dongarkar, Ankosh Wanole

Dr. Shivshankar Mhaske, Vivek villas Rathod

Satyajeet College of Pharmacy, Mehkar, Buldhana. Maharashtra

Abstract: Adverse drug reactions (ADRs) are a major challenge in clinical practice, contributing significantly to patient morbidity, mortality, and healthcare costs worldwide. Pharmacogenomics—the study of how genetic variations influence drug response—offers a promising approach to predict, prevent, and manage ADRs through individualized therapy. Genetic polymorphisms in drug-metabolizing enzymes, transporters, receptors, and human leukocyte antigens (HLAs) can alter drug absorption, distribution, metabolism, and elimination, resulting in variable efficacy and toxicity among individuals. This project provides a comprehensive review of the growing role of pharmacogenomics in enhancing drug safety. Key genes linked to ADRs, such as CYP450 isoenzymes (CYP2D6, CYP2C9, CYP2C19), TPMT, UGT1A1, VKORC1, and HLA-B alleles, are discussed with examples of drugs affected by these genetic differences. Clinical implementation strategies, available FDA pharmacogenomic biomarkers, and global guidelines from CPIC and DPWG are summarized. Despite challenges such as high testing costs, lack of clinician awareness, and ethical concerns, pharmacogenomics holds significant promise in transitioning from the traditional “one-size-fits-all” approach to truly personalized medicine. Incorporating pharmacogenomic testing into routine healthcare can minimize ADRs, optimize drug dosing, and improve therapeutic outcomes. This project concludes that pharmacogenomics is a key component of future precision medicine and must be integrated into pharmacy education and clinical decision-making to enhance drug safety.

Keywords: Adverse Drug Reactions”, “CYP450”, “Drug Safety”, “Genomics”, “Personalized Medicine, Pharmacogenomics

I. INTRODUCTION

Pharmacogenomics is an important and rapidly evolving branch of pharmacology that rigorously examines how genetic variations among individuals can significantly influence their responses to various forms of drug therapy. This specialized field intricately integrates several scientific disciplines, including genomics, which focuses on the study of an organism's complete set of DNA, molecular biology, which explores the molecular mechanisms of biological processes, and clinical pharmacology, which assesses how drugs interact with biological systems in a clinical setting. By synthesizing knowledge from these areas, pharmacogenomics aims to optimize the effectiveness of drug therapies while simultaneously minimizing the potential for adverse drug reactions and toxicity. This personalized approach to medicine takes into account the unique genetic makeup of each patient, thereby allowing healthcare providers to tailor medication regimens that are most appropriate and beneficial for individual patients, ultimately leading to improved health outcomes and enhanced patient safety.

Pharmacogenomics is a branch of pharmacology that studies how genetic variations influence a patient's response to drug therapy. It integrates genomics, molecular biology, and clinical pharmacology to optimize drug efficacy while minimizing toxicity.

Pharmacogenomics is a specialized branch of pharmacology that focuses on understanding how genetic variations influence an individual's response to drug therapy. Every person's genome contains unique genetic polymorphisms that may alter drug absorption, distribution, metabolism, and excretion, ultimately affecting therapeutic outcomes. These



variations can lead to differences in drug efficacy, treatment failure, or the development of adverse drug reactions (ADRs).

The field integrates concepts from genomics, molecular biology, biotechnology, and clinical pharmacology to predict drug behavior at the genetic level. Unlike traditional “one-size-fits-all” therapy, pharmacogenomics supports a personalized or precision medicine approach, where treatments are tailored based on a patient’s genetic makeup.

Genetic polymorphisms in drug-metabolizing enzymes such as CYP450 isoenzymes (CYP2D6, CYP2C19, CYP2C9), drug transporters like ABCB1, and drug targets including VKORC1 or HLA alleles, play a significant role in inter-individual variability. These variations can convert a normally safe drug into a harmful one by causing toxicity or therapeutic failure.

With the increasing prevalence of ADRs contributing to hospitalizations and mortality, pharmacogenomics has emerged as a crucial tool for enhancing drug safety. Regulatory bodies such as the U.S. FDA, CPIC, and EMA now recommend or mandate pharmacogenomic testing for several medications to prevent serious ADRs.

1.1 What are Adverse Drug Reactions (ADRs)?

ADRs are unwanted or harmful effects caused by medications given in standard doses. They contribute to hospitalization, treatment failure, and even death.

Adverse Drug Reactions (ADRs) are detrimental side effects that occur because of medications being administered at their usual recommended doses. These reactions can have serious implications and are documented contributors to prolonged hospital stays, treatment ineffectiveness, and in severe cases, fatality. It is alarming to note that a significant proportion, estimated at approximately 6-10%, of hospital admissions are directly linked to the occurrence of ADRs, shedding light on the pervasive impact they can have on healthcare systems and patient well-being.

Moreover, within hospital settings, between 3 to 7% of patients experience severe ADRs, further underscoring the prevalence and severity of these drug-induced complications. These statistics emphasize the imperative nature of pharmacovigilance and ensuring patient safety in the administration of medications, advocating for careful monitoring, proper dosage management, and a thorough understanding of potential adverse effects. The fact that such a substantial number of hospitalizations and negative outcomes can be attributed to ADRs exemplifies the need for enhanced awareness, rigorous reporting systems, and continual research and improvement in drug development and administration practices. Ultimately, addressing and mitigating the risks associated with ADRs plays a crucial role in safeguarding patient health and minimizing avoidable harm in medical care.

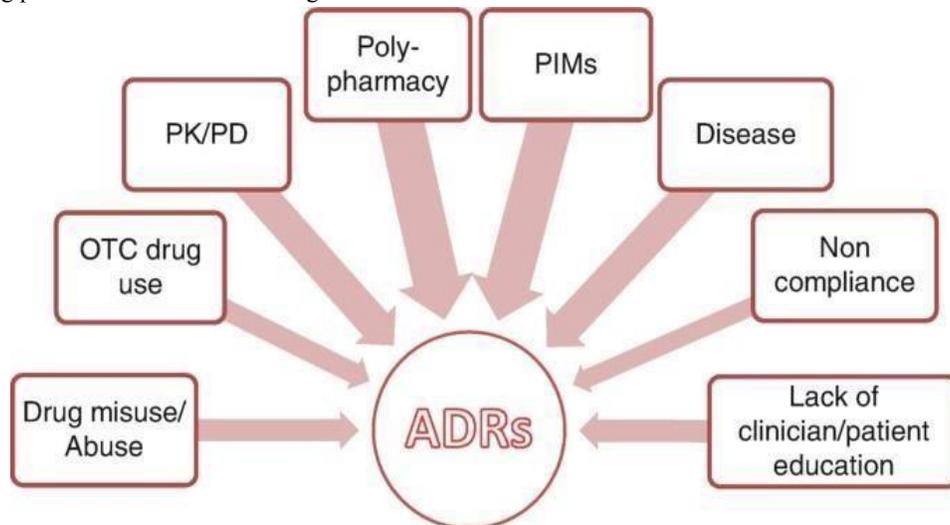


Fig.1: Diagram Adverse Drug Reactions (ADRs)



1.2 Importance of Pharmacogenomics

Pharmacogenomics is changing the way we approach treatment. At its core, it looks at how your genes shape the way you respond to medication. People process drugs differently—some get great results, others face nasty side effects, and a few see no change at all. This field gives doctors the tools to move beyond guesswork and match the right medication and dose to each person.

Personalized Drug Therapy

Genes like CYP450, TPMT, UGT, and NAT play a big role in how your body handles medicine. With pharmacogenomic testing, doctors can spot these differences early. Instead of relying on trial and error, they pick drugs and doses that work for you. That means better results and fewer wasted months on the wrong medication.

Fewer Adverse Drug Reactions (ADRs)

Nobody wants to end up in the hospital because of a prescription. But ADRs are still a leading cause of serious health problems. Pharmacogenomics helps flag patients who metabolize drugs unusually fast or slow. That way, doctors can avoid medicines that would either do nothing or cause harm.

Better Drug Efficacy

Some gene variants—like HLA-B*1502 with carbamazepine or VKORC1 with warfarin—can make or break treatment. Genetic profiling makes it possible to spot these markers and choose drugs that actually work, boosting success rates.

Smarter Drug Dosing

Lots of drugs have a very tight safety window. Go too low, and nothing happens. Too high, and things get dangerous. Genetic info helps doctors tweak doses to keep drug levels just right. This is especially important for tricky meds like warfarin, 6-mercaptopurine, and certain epilepsy drugs.

Targeted Therapy Development Pharmacogenomics doesn't just help patients—it speeds up drug research too. By focusing on genetic pathways, researchers can create therapies that hit the problem directly. This has already led to breakthroughs in cancer and immune diseases, like HER2 inhibitors and EGFR-targeted treatments.

Safer Treatment and Better Compliance

When side effects drop and drugs work better, people stick to their treatment plans. Pharmacogenomics gives patients a smoother experience, which leads to higher satisfaction and fewer missed doses.

Cost Savings Over Time

Genetic testing isn't free, but it pays off. By cutting down on bad reactions, failed treatments, and unnecessary hospital stays, the overall cost of care drops. In the end, everyone wins—patients, doctors, and the healthcare system.

The Backbone of Precision Medicine

Pharmacogenomics is at the heart of precision medicine. It brings together your unique genetic profile with your doctor's expertise to create a treatment plan that's truly tailored to you. This isn't just the future—it's happening now.

II. LITERATURE REVIEW

2.1 Genetic Influence on Drug Response

Genetics really shapes how people react to medications. We're not all built the same, and those little differences—genetic polymorphisms—can change how our bodies absorb, break down, and get rid of drugs. This ends up impacting how well a drug works for you and how safe it is. The big players here are drug-metabolizing enzymes, drug transporters, drug targets, and certain HLA variants.

Drug-Metabolizing Enzymes (CYP450 Family)

The CYP450 enzymes handle the metabolism of about 70–80% of the drugs people take. Changes in genes like CYP2D6, CYP2C9, CYP2C19, CYP3A4, and CYP1A2 mean some people process drugs slower or faster than others. Here's what that looks like in real life:



Poor metabolizers: They break down drugs slowly, which can make the drug toxic.

Intermediate metabolizers: They clear drugs a bit better, but not perfectly—doses might need tweaking.

Extensive metabolizers: This is the standard—normal processing.

Ultra-rapid metabolizers: They clear drugs so fast that the medicine barely has a chance to work.

CYP2D6 changes mess with how people respond to antidepressants, opioids, and beta-blockers. CYP2C9 variants affect how you handle warfarin, so doctors often have to adjust doses. CYP2C19 variants change how well clopidogrel works and mess with proton pump inhibitors too.

Drug Transporters (P-gp, OATP, BCRP)

Drug transporters decide how much of a drug gets into your cells. If you have certain genetic variants, these transporters can either let in too much or keep too much out.

P-glycoprotein (P-gp, ABCB1): This one pushes drugs like digoxin, antiepileptics, antiretrovirals, and chemo drugs out of cells. The C3435T variant here changes how well your body absorbs these drugs.

OATP (SLCO1B1): If you have the SLCO1B1*5 variant, you're more likely to get muscle problems (myopathy) from statins.

BCRP (ABCG2): The Q141K variant affects how your body handles certain cancer drugs and allopurinol.

Drug Targets (Receptors and Enzymes)

The actual target of a drug—like a receptor or enzyme—can also be different from person to person. These genetic tweaks can change how well a drug does its job.

β 1-adrenergic receptor changes affect how people with high blood pressure respond to betablockers.

VKORC1 variants change how sensitive you are to warfarin, so the dose has to be adjusted.

EGFR mutations can predict how well certain cancer drugs (tyrosine kinase inhibitors) will work.

OPRM1 (A118G) changes how people feel pain relief from morphine.

HLA Variants (Immune-Mediated Drug Reactions)

Some HLA genes are linked to bad, sometimes life-threatening, reactions to medications. Here's what matters:

HLA-B*1502: Linked to severe skin reactions (Stevens–Johnson syndrome) from carbamazepine.

HLA-B*5801: Raises the risk of allopurinol hypersensitivity.

HLA-A*3101: Connected to carbamazepine reactions, especially in Europeans.

HLA-B*5701: If you've got this, abacavir can trigger a dangerous allergic reaction.

Because of these risks, genetic testing before starting some drugs is now the norm. It helps doctors avoid serious side effects and find safer, more effective treatments for each person. Drug response variability is caused by genetic polymorphisms in:

Drug-metabolizing enzymes (CYP450 family)

Drug transporters (P-gp, OATP)

Drug targets (receptors, enzymes)

•HLA variants

2.2 Historical Development

Pharmacogenomics didn't just pop up overnight—it's the result of decades of work in genetics, biochemistry, and clinical medicine. The story is basically one of scientists slowly realizing that our genes play a huge role in how we react to drugs. Here's how it all unfolded:

1950s: The First Clues

Back in the '50s, doctors started noticing something odd: some people had really strange reactions to common drugs. In 1957, researchers figured out why some folks processed isoniazid much slower than others—it came down to differences in the NAT2 gene. Around the same time, they also linked unusual responses to succinylcholine to genetic



quirks in pseudocholinesterase. Suddenly, it was clear: our genes can seriously change the way we metabolize medicine. That idea kicked off the whole field of pharmacogenetics.

1970s–1980s: Digging Deeper

By the '70s and '80s, scientists had their sights set on the cytochrome P450 (CYP450) enzyme system. They found major genetic differences in enzymes like CYP2D6, CYP2C9, and CYP2C19. These differences explained why two people might respond totally differently to the same drug—or why one person might have side effects while another doesn't.

1990–2003: The Human Genome Project

Then came the Human Genome Project. Starting in 1990 and wrapping up in 2003, this effort mapped all three billion base pairs in human DNA. Suddenly, scientists could pinpoint exactly which genes were responsible for drug metabolism, targets, and transporters. This took the field from simply focusing on single genes (pharmacogenetics) to looking at the whole genome (pharmacogenomics).

2000s: Spotting Genetic Markers

The 2000s brought a wave of discoveries. Researchers identified HLA alleles like HLA-B*1502, which can predict severe reactions to drugs like carbamazepine. They built huge SNP databases and developed high-throughput genotyping tools. Suddenly, it was possible to scan for genetic markers much more quickly and on a much larger scale.

2010s: Making It Real in the Clinic

Fast forward to the 2010s—pharmacogenomics started making its way into everyday medical practice. Groups like CPIC, the FDA, and the EMA began publishing official guidelines for using genetic information to tailor drug prescriptions. Now, doctors had evidence-based recommendations for dosing warfarin (CYP2C9, VKORC1), clopidogrel (CYP2C19), carbamazepine (HLA-B*1502), and thiopurines (TPMT, NUDT15). Hospitals started adding genetic test results directly into electronic health records. Across the world, precision medicine initiatives picked up speed, and more patients began getting treatments matched to their DNA.

2020s: Whole-Genome Sequencing and AI

These days, whole-genome sequencing is faster and cheaper than ever. Machine learning models are jumping in to help predict how people will react to medications. Researchers are linking up genomics with data from proteomics and metabolomics, building even bigger pharmacogenomic databases like PharmGKB and gnomAD.

So now, pharmacogenomics is right at the heart of precision medicine. It's changing the way we prescribe drugs, making treatments safer and more effective for each person.

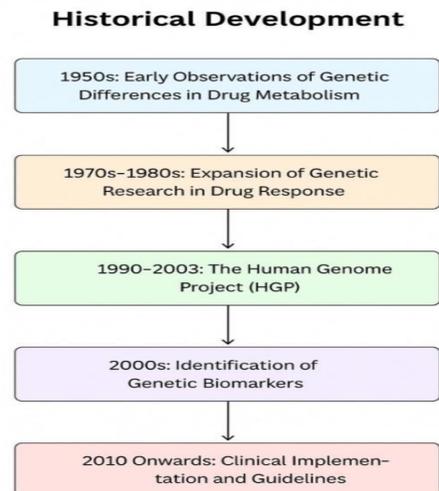


Fig.2: Diagram Historical Development



III. TYPES OF GENETIC VARIATIONS AFFECTING DRUG RESPONSE

- Single Nucleotide Polymorphisms (SNPs)
- Insertions/Deletions (Indels)
- Copy Number Variations (CNVs)
- Gene duplications/amplifications

These variations alter enzyme levels and activity.

Genetic differences shape how our bodies handle medications—everything from how we absorb a drug to how we break it down and get rid of it. These differences can change the way enzymes, transporters, or even drug targets work, which means some people end up needing a different dose or might react badly to a medicine that works fine for someone else. Here’s a quick rundown of the main types of genetic variations that matter for drug response:

Single Nucleotide Polymorphisms (SNPs)

Basically, a SNP happens when a single letter in your DNA—A, T, C, or G—gets swapped for another at a specific spot. These are super common, popping up every few hundred base pairs. They can do things like tweak how well your enzymes work (like the CYP2D6 1846G>A change that slows down drug metabolism), mess with drug transporters (for example, ABCB1 C3435T affects how drugs get pumped out of cells), or even change the drug’s target (VKORC1 variants mean you might need a different warfarin dose). Medications influenced by SNPs include warfarin, clopidogrel, codeine, and statins.

Insertions/Deletions (Indels)

Sometimes, DNA gains or loses a few letters—these are called indels. They can shift the reading frame, leading to proteins that just don’t work right or at all. Enzyme activity can drop off a cliff. In the real world, this shows up when a UGT1A1 TA-repeat insertion slows down bilirubin breakdown, making irinotecan more toxic. Or, if you’re missing GSTT1 or GSTM1 genes, your body struggles to detoxify certain chemo drugs.

Copy Number Variations (CNVs)

Here, it’s about how many copies of a gene you have. You might have extra copies, or not enough, because of DNA mix-ups or bigger structural changes in your chromosomes. More copies of a gene usually means you process drugs faster; fewer copies mean you’re slower. For example, people with more copies of CYP2D6 can be ultra-rapid metabolizers—they burn through codeine into morphine quickly, which can be dangerous. On the flip side, fewer copies mean drugs hang around longer. CNVs in transporter genes like SLC can change how statins work in your body.

Gene Duplications / Amplifications

This is a special type of CNV where a gene gets copied multiple times. The result? Ultra-rapid metabolism or an outsized response to a drug. You see this a lot with enzymes that process drugs. For instance, if you have extra CYP2D6 genes, you’ll metabolize antidepressants, opioids, or betablockers way faster than most people. In cancer, HER2 gene amplification makes tumors more sensitive to drugs like trastuzumab

Genetic Variation Type	Effect on Drug-Metabolizing Enzymes	Clinical Consequence
SNPs	Change activity (increase/decrease), alter protein structure	Variable dosing, toxicity risk
Indels	Loss of function or reduced enzyme activity	Overdose risk, therapeutic failure
CNVs	Increased or decreased enzyme quantity	Ultra-fast or poor metabolism
Gene duplications	Major increase in enzyme expression	Ultra-rapid metabolism, dose adjustment needed

Table. 1: TYPES OF GENETIC VARIATIONS AFFECTING DRUG RESPONSE



IV. KEY PHARMACOGENOMIC GENES & ASSOCIATED ADRs

Pharmacogenomic differences in key genes shape how our bodies handle drugs—everything from how fast we break them down to whether they work safely or not. Cytochrome P450 enzymes, or CYP450s, really stand out here. They’re behind the metabolism of about 70–80% of all drugs doctors prescribe. Depending on which versions of these genes you have, you might process medicine too slowly, too quickly, or just right, and that directly changes drug levels in your blood and how likely you are to get side effects.

4.1 Cytochrome P450 Enzymes

Think of the CYP450 family as the body’s main drug-processing crew. These enzymes handle oxidation, which helps clear out all sorts of medications. But not everyone’s enzymes work the same way. Thanks to genetic differences, people respond differently to the same pills.

CYP2D6

This one’s a big deal—it helps break down about a quarter of all drugs out there. The gene is super variable, with over 100 versions floating around. Some people have extra copies, some have none at all. How does that play out? Well, if you’re a poor metabolizer, you barely process certain drugs, so they build up and can become toxic. On the other end, ultra-rapid metabolizers zip through medications so fast, they barely have any effect.

Drugs heavily influenced by CYP2D6 include codeine (where ultra-rapid folks can actually overdose), tricyclic antidepressants, SSRIs, beta-blockers like metoprolol, and antipsychotics. Watch out for side effects like breathing problems with codeine, serious drowsiness, dangerously low blood pressure with beta-blockers, and central nervous system toxicity from some antidepressants.

CYP2C9

This enzyme manages several crucial drugs, including warfarin, NSAIDs, and sulfonylureas. Certain variants—CYP2C9*2 and *3, for example slow things down a lot.

When metabolism drops, drug levels skyrocket. That’s why people with these variants run a higher risk of bleeding on warfarin, need smaller doses, and must get their INR checked more often. NSAIDs can cause more gut problems, and sulfonylureas can push blood sugar too low. Key drugs affected: warfarin, phenytoin, NSAIDs like diclofenac and ibuprofen, and diabetes meds like glipizide and glimepiride.

CYP2C19

CYP2C19 handles drugs like proton pump inhibitors, certain antidepressants, and it activates clopidogrel, which is a blood thinner. Not everyone has the same version of this gene. Some people are poor metabolizers, some are ultra-rapid, and others fall in between.

When it comes to clopidogrel, this matters a lot. Poor metabolizers can’t turn it into its active form, so their blood doesn’t thin like it should. That means a higher risk for heart attacks or strokes after a stent. Ultra-rapid metabolizers, on the other hand, might process it too quickly and face bleeding problems.

Side effects here include failed treatment in heart patients, stent clots, or bleeding in ultra-rapid folks.

Drugs most impacted: clopidogrel, omeprazole, pantoprazole, citalopram, and escitalopram.

Gene	Role	Effect of Polymorphism	Drugs Affected	Major ADRs
CYP2D6	Metabolizes 25% of drugs	PM → toxicity; UM → treatment failure	Codeine, antidepressants, βblockers	Opioid toxicity, CNS effects, hypotension



CYP2C9	Metabolizes warfarin/NSAIDs	Reduced metabolism → accumulation	drug Warfarin, NSAIDs, sulfonyleureas	Bleeding, GI toxicity, hypoglycemia
CYP2C19	Clopidogrel activation	PMs → no activation of drug	Clopidogrel, PPIs, SSRIs	Cardiovascular events, stent thrombosis

Table.2:KEY PHARMACOGENOMIC GENES & ASSOCIATED ADRs

4.2 Thiopurine S-Methyltransferase (TPMT)

Thiopurine S-Methyltransferase, or TPMT, plays a big role in breaking down thiopurine drugs like azathioprine, 6-mercaptopurine (6-MP), and 6-thioguanine (6-TG). The way your body handles these drugs hinges on your TPMT gene. Some people have genetic differences that change how active this enzyme is, which can really affect how you respond to the medication— and how likely you are to run into side effects. What does TPMT actually do? It adds a methyl group to thiopurine drugs. That’s a fancy way of saying it turns these drugs off, so you don’t end up with a dangerous build-up of toxic byproducts. But if your TPMT activity is low, your body can’t deactivate the drugs efficiently. Active thioguanine nucleotides (TGNs) start piling up, and that’s where trouble begins.

There’s more than one version of the TPMT gene out there. The most common, TPMT*1, works as expected. Then there are the troublemakers—TPMT*2, *3A, *3B, and *3C. These variants slow the enzyme down, so patients with them face a higher risk of drug toxicity.

- Clinical Significance

- Thiopurines are widely used in:

- Acute lymphoblastic leukemia (ALL)

- Inflammatory bowel disease (IBD)

- Autoimmune disorders

- Organ transplantation

Doctors use thiopurines to treat all kinds of conditions—acute lymphoblastic leukemia, inflammatory bowel disease, autoimmune disorders, even after organ transplants. They’re pretty common in the clinic. But there’s a catch. If someone has low TPMT activity, those drugs can build up in the body. Suddenly, you’re looking at sky-high levels of TGNs, which is a recipe for serious side effects.

- Associated Adverse Drug Reactions (ADRs)

- Patients with low TPMT activity are at high risk for:

- Life-threatening bone marrow suppression

- Severe myelosuppression

- Leukopenia/neutropenia

- Hepatotoxicity doctors check your TPMT either by looking at your genes or testing your enzyme levels—before

- starting thiopurines. This isn’t just a suggestion; big organizations like CPIC back up this approach.

- Clinical Recommendations

- Normal metabolizers: Standard starting doses -

- Intermediate metabolizers: **Reduce dose by 30–70%**



-Poor metabolizers:

Start with drastically reduced doses (10% of normal)

Or choose alternative therapy

4.3 UDP-Glucuronosyltransferase (UGT1A1)

UGT1A1 is a phase II drug-metabolizing enzyme that handles glucuronidation—basically, it tags things like bilirubin and various drugs, including some cancer meds, so your body can get rid of them. This enzyme plays a big role when it comes to irinotecan, a common drug for colorectal cancer.

Here's how it goes: Irinotecan turns into its active form, SN-38. UGT1A1 then steps in to detoxify SN-38 through glucuronidation. When UGT1A1 doesn't work well, SN-38 builds up, which makes toxic side effects more likely. Now, there's a genetic twist. People with the UGT1A1*28 variant—where there's an extra TA repeat in the gene's promoter—end up with less enzyme. If someone has two copies of this variant, they can't clear SN-38 efficiently. That puts them at serious risk for dangerous neutropenia and intense diarrhea while taking irinotecan.

4.4 Vitamin K Epoxide Reductase (VKORC1)

Vitamin K epoxide reductase complex subunit 1 (VKORC1) is the molecular target of warfarin, an oral anticoagulant widely prescribed for thromboembolic disorders. VKORC1 plays a critical role in the vitamin K cycle, which is essential for the activation of clotting factors II, VII, IX, and X.

Warfarin sensitivity

Genetic variations in VKORC1 significantly influence patient sensitivity to warfarin. Polymorphisms in the VKORC1 promoter region (e.g., *-1639G>A*) reduce gene expression, leading to lower enzyme activity. As a result, patients require lower warfarin doses to achieve therapeutic anticoagulation.

Genetic mutations → excessive bleeding

Individuals carrying VKORC1 variants associated with reduced enzyme activity are at increased risk of over-anticoagulation. This predisposes them to excessive bleeding, especially if standard warfarin doses are administered without genetic-guided adjustment. Pharmacogenomic testing helps identify such patients and tailor dosing to improve safety.

4.5 HLA Variants

Human leukocyte antigen (HLA) variants play a critical role in predicting severe immunemediated adverse drug reactions. Pharmacogenomic screening for specific alleles has become a cornerstone of personalized medicine, particularly in preventing life-threatening hypersensitivity syndromes.

HLA-B*15:02 → Carbamazepine-induced Stevens-Johnson syndrome (SJS) The HLA-B15:02* allele is strongly associated with carbamazepine-induced Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN), especially in individuals of Asian ancestry. Genetic testing prior to carbamazepine initiation is recommended in high-risk populations to prevent these severe cutaneous adverse reactions.

HLA-B*57:01 →

Abacavir hypersensitivity The HLA-B57:01* allele predicts abacavir hypersensitivity reaction (HSR), a potentially fatal immune-mediated response. Screening for HLA-B57:01* before prescribing abacavir is now standard clinical practice, significantly reducing the incidence of HSR and improving patient safety.

V. ROLE OF PHARMACOGENOMICS IN PREVENTING ADRs

5.1 Predicting Drug Toxicity

Pharmacogenomics is changing the way we approach drug therapy. By looking at a person's genetic makeup, we can tailor treatments to lower the risk of bad reactions. Adverse drug reactions—those unexpected side effects—send a lot



of people to the hospital, cause treatments to fail, and even lead to death. When doctors use pharmacogenomic testing in everyday practice, patients get safer, more effective treatments, and better results overall.

Genes can make a huge difference in how someone processes medicine. Some people break down drugs too slowly or too quickly, which can ramp up the risk of serious side effects. Pharmacogenomic testing spots these people before the doctor even writes the prescription.

What's the payoff?

It flags poor metabolizers like CYP2D6, CYP2C9, CYP2C19 so doctors know who might be at risk. It stops drugs from building up to toxic levels in the body.

It helps doctors steer clear of medicines that could really hurt someone with certain genes. A few real-life cases:

People with CYP2D6 poor metabolizer status can have severe problems with some antidepressants or opioids. CYP2C9 variants can make warfarin downright dangerous, causing excessive bleeding.

A lack of TPMT activity puts people at risk for bone marrow suppression when using thiopurines.

6.2 Individualizing Drug Dosing (Precision Dosing)

Genetic info isn't just good for picking drugs—it's key for finding the right dose, too. This is precision dosing, and it's already making a difference

Warfarin Dosing (CYP2C9 & VKORC1)

If someone has CYP2C9 variants, they don't process warfarin as fast, so the drug can build up.

VKORC1 variants make people extra sensitive to warfarin, so they need a lower dose. With the right dose for their genes, patients bleed less and keep their INR more stable.

Thiopurine Dosing (TPMT)

Low TPMT activity? That means toxic levels of thioguanine nucleotides unless you cut the dose—sometimes by as much as 90%.

Dose adjustments like this prevent life-threatening myelosuppression.

Patients respond better, have fewer bad reactions, and reach stable drug levels faster.

Avoiding Hypersensitivity Reactions

Certain genes can predict when drugs will trigger dangerous immune reactions. Screening for these genes before starting treatment saves lives.

Key HLA markers:

HLA-B*57:01: Linked to abacavir hypersensitivity.

HLA-B*15:02: Raises risk of Stevens–Johnson syndrome with carbamazepine.

HLA-A*31:01: Associated with drug rash and eosinophilia (DRESS).

Why do HLA screens matter? They prevent severe skin reactions, keep people out of the hospital, and help doctors choose safer meds.

Improving Efficacy of Essential Drugs

Pharmacogenomic testing doesn't just make drugs safer—it helps make sure they actually work.

Take clopidogrel, for example. It needs to be activated by CYP2C19. If someone's a poor metabolizer, the drug just doesn't work, so they're at higher risk for things like stent thrombosis, heart attacks, or strokes. Genetic testing guides doctors to pick alternatives, like prasugrel or ticagrelor, so the patient gets proper antiplatelet therapy.

A few more examples:

EGFR mutations: These mean better responses to tyrosine kinase inhibitors in lung cancer.

HER2 amplification: Predicts if trastuzumab will work.

DPYD testing: Prevents fluorouracil toxicity and makes sure patients get the right dose. Pharmacogenomics isn't just a buzzword. It's making medicine smarter, safer, and more personal—one patient at a time.



VI. PHARMACOGENOMIC TESTING METHODS

Pharmacogenomics, a field that investigates how an individual's genetic makeup influences their response to drugs, heavily relies on various molecular and genomic technologies to identify genetic variations that impact drug metabolism, efficacy, and toxicity. Among these technologies, PCRbased testing (Polymerase Chain Reaction) stands out as a foundational and widely utilized method in both clinical and research settings.

PCR's key features make it a valuable tool for identifying pharmacogenetically relevant genetic variants. Through targeted amplification, PCR can selectively amplify specific DNA regions containing genetic variants of interest, enabling the detection of small variants such as single nucleotide polymorphisms (SNPs), small insertions/deletions, and allele-specific variants. This precision is crucial for understanding how genetic variations may affect an individual's response to medication.

One of PCR's strengths lies in its clinical utility. It is known for being fast, cost-effective, and well-suited for routine clinical testing, making it practical for widespread use in healthcare settings. Moreover, PCR's versatility allows it to be combined with other techniques like real-time PCR or allele-specific PCR to enhance specificity and quantification, further improving its accuracy and reliability in detecting genetic variations.

In the realm of Pharmacogenomics, PCR plays a critical role in various applications. It is instrumental in detecting variants in genes that encode drug-metabolizing enzymes such as CYP2C9 and CYP2D6, which are crucial for drug metabolism. Additionally, PCR-based genotyping is used for predicting the risk of adverse drug reactions and optimizing personalized drug doses, especially for medications with narrow therapeutic windows. By leveraging PCR technology in these applications, healthcare providers can tailor drug therapies to individual patients based on their genetic profiles, ultimately improving treatment outcomes and minimizing the risk of adverse reactions.

PCR-based testing

Microarray analysis

Whole genome sequencing

Next-generation sequencing (NGS)

Targeted genotyping panels

Shortens trial-and-error prescribing

Improves drug effectiveness

Reduces hospitalizations

Enhances patient safety

VII. FUTURE PROSPECTS

1.Integration of AI with Pharmacogenomics

Artificial intelligence and machine learning algorithms can analyze large genomic datasets to predict individual drug responses, optimize dosing, and minimize adverse drug reactions (ADRs).

AI-driven models can also identify new drug targets based on genetic variations, accelerating drug discovery.

2.Personalized Drug Design

Leveraging pharmacogenomic data, drugs can be tailored to a patient's genetic profile, enhancing efficacy and reducing side effects.

This approach may lead to "precision therapeutics," where treatments are highly specific to individual genetic variants.

3.Pharmacogenomic Cards for Patients

Patient-specific genomic information can be stored in a card or digital format, providing healthcare providers with instant access to drug response profiles.

This can guide clinicians in selecting safe and effective medications, avoiding trialand-error prescribing.

4.Population-Wide Screening

Implementing genomic screening at a population level can identify individuals at risk for severe ADRs or poor drug response.



Such proactive measures can improve public health outcomes, reduce hospitalizations, and optimize healthcare costs.

5. Routine Genomic Testing Before Drug Prescription

In the future, genomic testing may become a standard pre-prescription step, especially for high-risk or critical medications (e.g., chemotherapy, anticoagulants).

Routine testing ensures that therapy is tailored from the outset, improving treatment outcomes and minimizing adverse effect

VIII. CONCLUSION

Pharmacogenomics, the study of how genetic variations influence an individual's response to drugs, has emerged as a potent tool in the realm of healthcare. By predicting and preventing adverse drug reactions (ADRs), pharmacogenomics contributes significantly to enhancing drug safety. This field focuses on understanding how genetic differences impact drug metabolism and responses, enabling healthcare providers to make informed decisions about drug selection and dosage.

Pharmacogenomic testing, once considered a niche practice, is now becoming more affordable and accessible. This accessibility is poised to revolutionize the landscape of medicine by facilitating personalized treatment plans tailored to individuals' genetic profiles. As a result, pharmacogenomics is set to play a pivotal role in the advancement of precision medicine, where treatment strategies are customized based on genetic information to optimize therapeutic outcomes.

In this era of precision medicine, pharmacists are positioned as key players in implementing pharmacogenomic principles in clinical settings. By utilizing genetic data to guide medication decisions, pharmacists can significantly improve patient care by reducing the incidence of ADRs and enhancing treatment efficacy. Through their expertise in medication management and their direct interactions with patients, pharmacists are well-equipped to leverage pharmacogenomic information to tailor drug therapies for optimal results.

REFERENCES

- [1]. Ingelman-Sundberg, M., Nebert, D. W., & Lauschke, V. M. (2023). Emerging trends in pharmacogenomics: from common variant associations toward comprehensive genomic profiling. *Human Genomics*, 17, 105. <https://doi.org/10.1186/s40246-023-00554-9> (SpringerLink)
- [2]. Qahwaji, R., Ashankyty, I., Sannan, N. S., Hazzazi, M. S., Basabrain, A. A., & Mobashir, M. (2024). Pharmacogenomics: A Genetic Approach to Drug Development and Therapy. *Pharmaceuticals*, 17(7), 940. <https://doi.org/10.3390/ph17070940> (MDPI)
- [3]. Soria-Chacartegui, P., Cendoya-Ramiro, P., González-Iglesias, E., Martín-Vílchez, S., Rodríguez-Lopez, A., Mejía-Abril, G., Román, M., Luquero-Bueno, S., Ochoa, D., & AbadSantos, F. (2024). Genetic Variation in CYP2D6, UGT1A4, SLC6A2 and SLCO1B1 Alters the Pharmacokinetics and Safety of Mirabegron. *Pharmaceutics*, 16(8), 1077. <https://doi.org/10.3390/pharmaceutics16081077> (MDPI)
- [4]. Mosch, R., van der Lee, M., Guchelaar, H. J., & Swen, J. J. (2025). Pharmacogenetic Panel Testing: A Review of Current Practice and Potential for Clinical Implementation. *Annual Review of Pharmacology and Toxicology*, 65, 91–109. <https://doi.org/10.1146/annurevpharmtox-061724-080935> (Annual Reviews)
- [5]. Hertz, D. L., Bousman, C. A., et al. (2024). Recommendations for pharmacogenetic testing in clinical practice guidelines in the US. *American Journal of Health-System Pharmacy*, 81(16), 672–683. <https://doi.org/10.1093/ajhp/zxae110> (OUP Academic)
- [6]. Spahn, C., Toda, N., Groat, B., Aimer, O., Rogers, S., Oni-Orisan, A., Monte, A., Hakooz, N., & the Pharmacogenomics Global Research Network (2025). Transforming Pharmacovigilance With Pharmacogenomics: Toward Personalized Risk Management. *Clinical Pharmacology & Therapeutics*. <https://doi.org/10.1002/cpt.70095> (PMC)



- [7]. Callister, M. (2025). Pharmacogenomics in Adverse Drug Reaction Prediction. *Journal of Pharmacovigilance*, 13:506. <https://doi.org/10.35248/2329-6887.25.13.506> (@WalshMedical)
- [8]. Roncato, R., et al. (2024). Clinical Benefits and Utility of Pretherapeutic DPYD and UGT1A1 Testing in Gastrointestinal Cancer: A Secondary Analysis of the PREPARE Randomized Clinical Trial. *JAMA Network Open*. <https://doi.org/10.1001/jamanetworkopen.2024.49441> (JAMA Network)
- [9]. (2022). Pharmacogenomics in adverse drug reactions. *IJBPR (International Journal of Basic & Pharmaceutical Research)*, 11(2). <https://doi.org/10.35248/2287-6898.22.11.2720-2721> (Bio-Pharma Research Journal)
- [10]. Amstutz, U. (2025). Preventing adverse drug reactions and more: current clinical use of pharmacogenetic testing. *Med Genet*. <https://doi.org/10.1515/medgen-2025-2019> (PMC)
- [11]. (2024). Pharmacogenomics: Challenges and Future. *Genes*, 15(6), 714. <https://doi.org/10.3390/genes15060714> (MDPI)
- [12]. (2024). Frontiers: Editorial: Insights in pharmacogenetics and pharmacogenomics: 2023.
- [13]. *Frontiers in Pharmacology*, 15:1540478. <https://doi.org/10.3389/fphar.2024.1540478> (Frontiers)
- [14]. (2024). Development and validation of a pharmacogenomics reporting workflow based on the Illumina Global Screening Array chip. *Frontiers in Pharmacology*, 15:1349203. <https://doi.org/10.3389/fphar.2024.1349203> (Frontiers)
- [15]. (2024). Systematic analysis of the pharmacogenomics landscape towards clinical implementation of precision therapeutics in Greece. *Human Genomics*. <https://doi.org/10.1186/s40246-025-00720-1> (SpringerLink)
- [16]. (2024). A systematic review and meta-analysis of the impacts of germline pharmacogenomics on severe toxicity and symptom burden in adult patients with cancer. *Clinical and Translational Science*. (from 2024 systematic review) (PubMed)

