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A Review On Pharmacogenomics In Pharmacognosy

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ABSTRACT

Pharmacogenomics is the area of pharmacology that examines how genetic variation affects a patient's reaction to medication by linking a drug's toxicity or efficacy to changes in gene expression or single-nucleotide polymorphisms. It seeks to create logical methods for tailoring medication regimens to patients' genotypes in order to maximize benefits and minimize side effects. These methods herald the arrival of "personalized medicine," in which medications and treatment combinations are tailored to the specific genetic composition of each patient. The whole genome application of pharmacogenetics, which studies the relationships between single genes and medications, is called pharmacogenomics.[1]

KEYWORDS

Phamarmacogenomic,pharmacogenetics, pharmacognosy,polymorphism,omics,therapy,medicines,

INTRODUCTION

Pharmacogenomics refers to the study of genetic polymorphisms in drug response.1 It is a rapidly developing research fielddue to the newer technologies like next generation sequencing (NGS) to scan the genome with precision.2 The potential areas of importance are the prediction of personalized medicine, Tailor made individual drug prescriptions and reducing the potential adverse drug reaction[3]

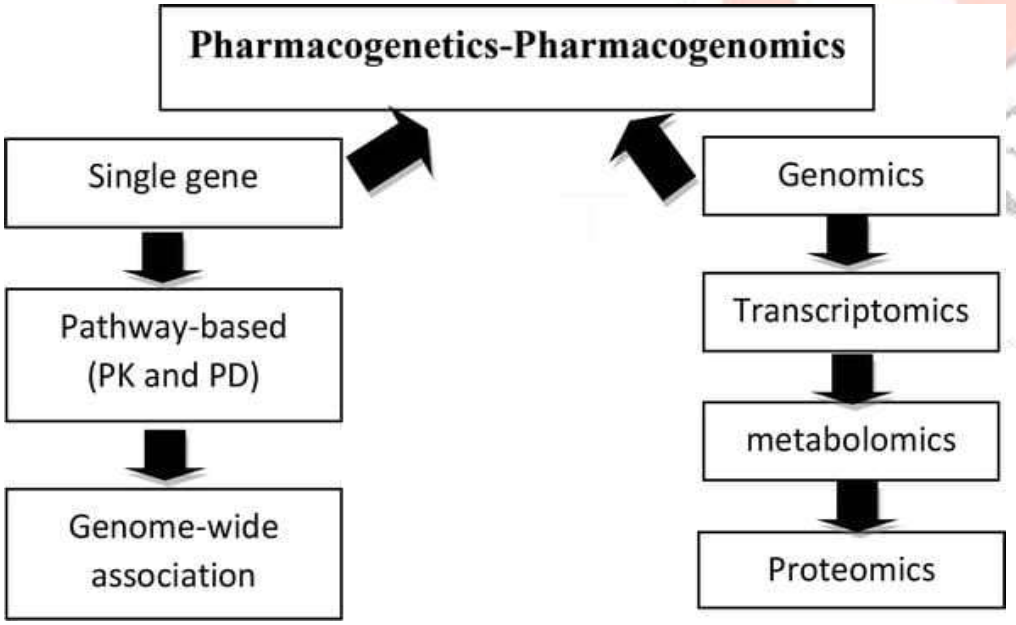
Pharmacogenomics and pharmacogenetics are related terms commonly used in drug development and therapy. Pharmacogenomics is the study of gene components to identify factors influencing medication responses. . Cancer chemotherapy and oral anticoagulants are now administered based on a patient's pharmacogenetic condition to reduce toxicity and failure rates. . The pharmacogenetic technique is currently replacing traditional medication and dose form selection methods.[2]

The new field of pharmacogenomics, which is based on gene-drug interactions, has the potential to improve resource utilization while speeding up the process of finding novel, more effective drug formulations for existing medications and uncovering new drug molecules for diseases that are currently untreated [6, 7]. Pharmacogenomics was initially developed as the study of genetic variations in defined populations, such as particular ethnic groups, and changes in the way that drugs responded to them.

The study of genetic variants in defined populations, such as certain ethnic groups, and variations in medication response has led to the development of pharmacogenomics. But as research has progressed, it has evolved into the study of genetic variants on an individual basis, independent of race or other racial differential systems (Fig. 1). Based on the human genome, gene polymorphism, or genetic variability, is studied to understand why drug responses vary. This information is then used to construct disease-gene, drug-drug, and drug-effect correlations(.3)

Pharmacogenomics is the investigation of the commitment Of genomics and of other "omics" to individual variety In drug reaction aggregates. This variation can include Serious, potentially fatal adverse drug reactions as well As inadequate therapeutic efficacy. Electronic health Records are increasingly incorporating pharmacogenomics Data, which is rapidly becoming an essential part of the "therapeutic encounter." Consequently, pharmacogenomics

Is the component of clinical genomics that will almost Certainly see the earliest and broadest clinical application-Possibly affecting the treatment of every patient worldwide At some point (Allen JD et al., 2019). In the paragraphs That follow, we will briefly discuss the origins and Development of this significant component of "rational Therapeutics," briefly discuss the science that underpins Pharmacogenomics, address the difficulties associated With the clinical application of this component of genomic Science, and, finally, present a vision for the future in which "pharmacogenomics" will have evolved into "pharmacoOmics" and will be an essential component of every medical Decision regarding a therapeutic drug (Altieri AH et al., 2015).Genomics is the study of an organism's DNA sequence and How its variations affect its traits and phenotype. The study Of the genomics of drug response aims to identify genetic Variants that influence how individuals respond to different Drugs. The current standard approach to drug development And prescribing is based on the assumption that most people Will respond similarly to a given medication (Anderson CR et al., 2009). However, this is not always the case, as Individuals can differ in their response to drugs due to Genetic variations that affect the way the body metabolizes And responds to them. Genetic variations can be inherited or acquired, and they[4]



- **HISTORY:**

Friedrich Vogel initially used the term "pharmacogenetics" in 1959 to characterize the features of phenotypic variability that lead to a non-constant metabolic rate and a variable response to particular drugs.1. Since the Human Genome Project was completed in 2003, the medical applications of genomics, such as pharmacogenetics and pharmacogenomics (PGx), have expanded to new heights, underscoring the significance of genetic research at all levels of the health care industry.2-4 PGx is a vast area that unifies the study of medications (pharmacology)

and genes, their interactions, and how they work in the unique environment (genomics) under a single umbrella word. Middle Eastern and Arab doctors' and pharmacists' attitudes toward and knowledge of pharmacogenetics In order to give readers and local researchers in this region a synopsis of some of the trends and distribution of the results throughout these countries, we attempted to compile the few published studies undertaken throughout the Arab Region into one review.[4]

Fred Sanger pioneered genomics by sequencing the genomes of viruses and mitochondria. In the 1970s and 1980s, his group pioneered procedures for sequencing, genomic mapping, data storage, and bioinformatics. Dr. Tom Roderick, a geneticist at the Jackson Laboratory in Bar Harbor, ME, is claimed to have originated the term 'genomics' during a beer-fueled meeting in Maryland to map the human genome.[5]

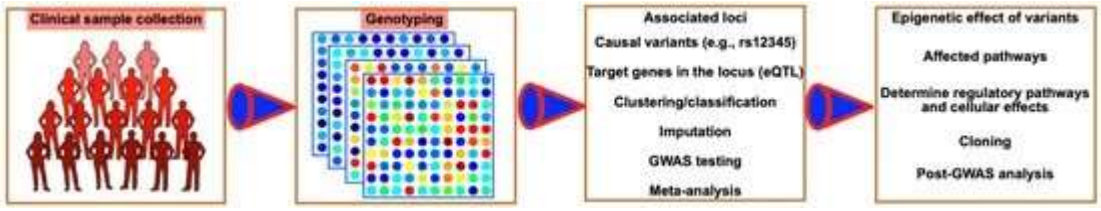
METHODOLOGY

The 127 medications used to treat patients in many medical specialties demonstrate the rapid advancement of clinically relevant pharmacogenomics knowledge. Implementing pharmacogenomics presents hurdles, including making knowledge accessible to practitioners in a useable and understandable format (Bell PRF et al., 1999). Developing objective, evidence-based guidelines and investing in infrastructure to make pharmacogenomics data accessible to physicians are key steps towards achieving this goal. Most institutions focus on drug-gene interactions as doctors provide pharmaceuticals rather than genes (Bernardi-Aubry F et al., 2004). The use of Electronic Health Records (EHRs)

Pharmacogenomics testing is increasingly using "pharmacognosy" panels, which test multiple genes that affect response to commonly prescribed medications and have therapeutic value. Some organizations utilize computer-based alarms to notify caregivers when a drug is administered. A pharmacogenomics test may provide important information (Boynton WR et al., 1995). At the Mayo Clinic, notifications for 17 drug-gene combinations are activated when a prescription is written for that medication. A subcommittee of the Formulary Committee oversees and approves execution.

The deployment of pharmacogenomics across a big university medical centre necessitates a significant investment of time and money, which is self-evident. This is why we emphasised that while NIH funding from the PGRN and eMERGE grants served as an important "catalyst" to bring this aspect of genomic science to the bedside, this process requires collaboration with hospitals and medical centres (Karia R et al., 2020). This starts with committed institutional leadership, engagement across multiple medical staffs, including physicians, nurses, allied health professionals, and chemists, with significant investments needed for the process. The discovery and application of genomes and other "omics" approaches to improve drug therapy may seem ambitious, but as will be shown below, we are only at the beginning of this process.[12]

Genetic Causes of Individual Variability in Drug Response



Summary of the steps taken in pharmacogenomics therapeutics. It starts from the integration of multi-omics data (the generation and analysis of large data sets by different high-throughput approaches) and proceeds through pathway-level understanding, pathway–pathway interactions (pathway crosstalk), and network-level understanding, unraveling the integrated mechanisms and predicting the optimal putative biomarkers in the case of cancer. The implementation of precision medicine may be contingent upon next-generation sequencing methodology and technology .

Pharmacogenetics :

Pharmacogenetic research over a long period of time has demonstrated how genetic variants affect drug response in a broad way [1,2,3,4,5].

The notion that genetic variants might modulate variability in drug actions, was first proposed by the English physiologist Garrod[3]. He suggestedthat enzymatic defects not only lead to aggregation of endogenous substrates in"in-born errors of metabolism", but also to aggregation of exogenously administered substrates, such as food, toxin and drugs, with clinical concerns. The word 'pharmacogenetics' was first used by Vogel of Heidelberg, Germany in 1959[3]. The science that analyzes individuals' responses to therapeutic agents and their genetic

inheritance is called pharmacogenetics[8]. Pharmacogenetics can thus be defined as the science of determining the genetic differences on metabolic pathways which can affect individual responses to drugs, both therapeutically and adversely[8]. The term has been coined together from the words pharmacology (the study of action of drugs in the human body) and genetics

Current Challenges and Limitations in Pharmacogenomics

While there is no doubt that the applications of pharmacogenomics have great potential in personalized medicine, it is important to critically examine its challenges and limitations from the standpoint of science, policy, and education.

To begin with, although the research conducted by Chan et al2 on tamoxifen is significant and comprehensive in terms of conveying the importance of taking patients' race and ethnicity into consideration when studying and developing genetic-based drugs, it should be noted that they only used CYP2D6 as one of the many enzymes for therapeutic target. In reality, there are a plethora of enzymes and their corresponding isoforms that present in different racial and ethnic groups. Next

Pharmacogenomics: a key component of personalized therapy

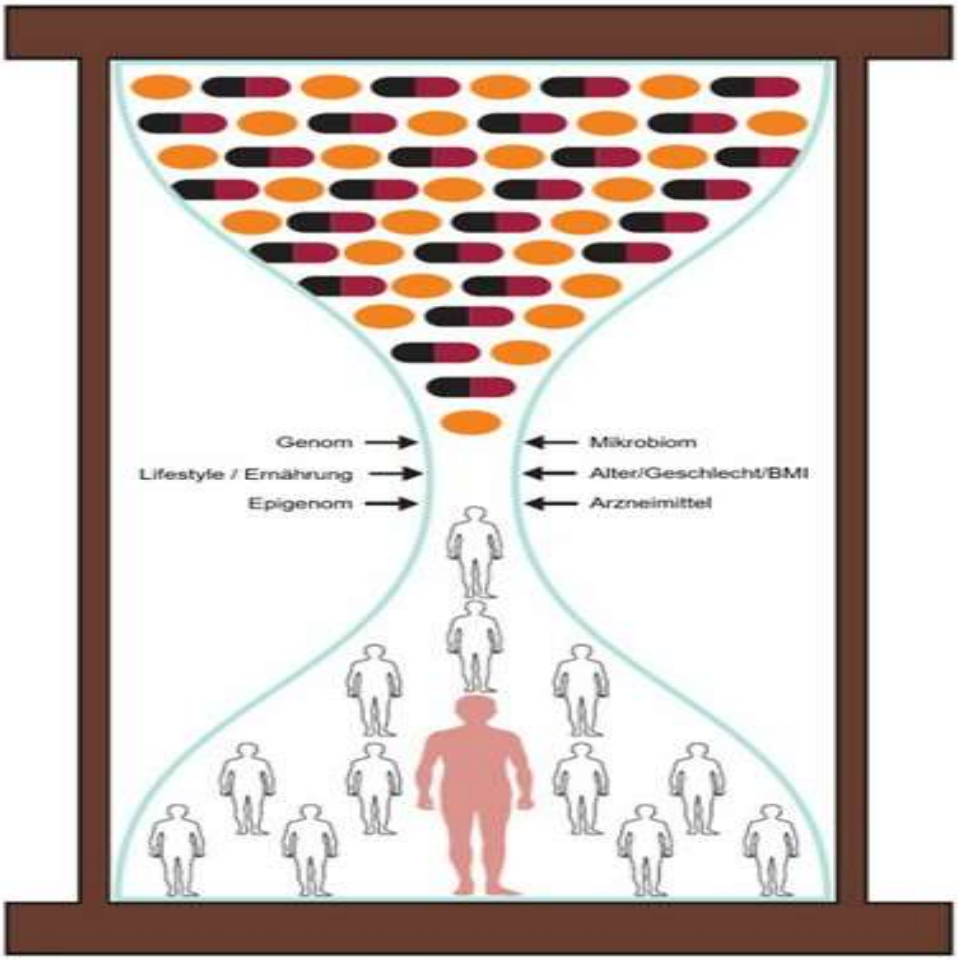
Personalized medicine aims to deliver tailored treatment and forecast clinical outcomes for individual patients. Personalized medicine relies heavily on pharmacogenomics. Drug response varies amongst individuals due to factors such as genetics, epigenomics, environment, and patient characteristics (e.g. gender, age, concomitant medications) [1]. Genetic polymorphisms in drug-metabolizing enzymes, such as cytochrome P450 2D6 and thiopurine S-methyltransferase, have been found to affect drug response over a decade ago [2]. However, valid and predictive biomarkers for therapeutic effects and avoiding severe side effects are still lacking for over 90% of patients.

There is reasonable hope that pharmacogenomic research will benefi t from a combination of different omics technologies. Recently, multi-omics studies have shown their use in discovering potential novel therapeutic targets [1]. For instance, in one multi-omics study the integrative personal omics profi le (iPOP), which combines genomic information with additional dynamic omics activities (that is, transcriptomic, proteomic, metabolomic and autoantibody profi les), from a single individual over a 14-month period demonstrated that iPOP data can be used to interpret healthy and diseased states, and can be helpful in the diagnostics, monitoring and treatment of diseased states .

The main problem is accurately analyzing and interpreting massive multi-omics data sets using bioinformatics. According to a recent National Institutes of Health White Paper by the Quantitative and Systems Pharmacology Workshop Group [5], genomics alone is insufficient to develop and study drugs. Biological networks are influenced by changes in coding sequence and gene expression, as well as transient responses to external signals at the level of protein activity, posttranslational modification, and stochasticity. We used an integrative systems pharmacology technique to analyze numerous one-dimensional biomolecular-omics as well as patient history, can be linked together to achieve a better understanding of the biology behind diseases as well as drug-response phenotypes. Such a strategy should ultimately result in the identification of novel drug targets.

Over the last decade, there has been significant study into pharmaco-genomics. Functional genomics is expected to be a valuable resource for predicting clinical outcomes in the future. However, bringing pharmacogenomics knowledge to the bedside as part of individualized care poses a significant difficulty. EMRs and EHRs may be important in this setting. EMRs can enhance information management and clinical relevance

analysis for pharmacogenomics [10]. EMRs may compare treatment and outcomes for thousands of patients in a clinical context, integrating genetic and multi-omics data. Integrating EMRs/EHRs into a dynamic, verified framework.[11]



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CLINICAL IMPLICATIONS OF PHARMACOGENOMICS

- **Adverse Drug Reactions**

One benefit of understanding pharmacogenomics is the possibility of a decrease in the number of ADRs. The CYPP450
enzymes in families 1 to 3 mediate 78% to 80% of all phase I dependent metabolism of clinically used drugs (Spatzenegger
& Jaeger, 1995). The polymorphic forms of CYPP450s are responsible for the development of idiosyncratic ADRs
(Kalgutkar, Obach, & Maurer, 2007). According to Phillipsand Van Bebber (2005), 56% of drugs cited in ADR studies
are metabolized by polymorphic phase I enzymes, of which 86% are p450s .[8]

- **CLINICAL UTILITY OF PHARMACOGENOMICS**

Strong evidence indicates that variants in about 20 genes affecting more than 60 drugs could affect one's response to these medications. Evidence-based, peer-reviewed guidelines are available from the Clinical Pharmacogenetics Implementation Consortium (CPIC) (www.cpicpgx.org), an initiative funded by the US National Institutes of Health to help clinicians interpret the results of genomic tests and apply them to patient care.5 Table 1 lists the
currently recognized gene-drug pairs for which clinical guidelines are available.

Numerous examples for implementing pharmacogenomic testing have been published, with strategies ranging from preemptively testing everyone with panels of genes to testing single genes before prescribing certain

drugs.6–9 But regardless of the implementation model, clinicians face challenges in deciphering the clinical evidence, and institutions face the challenge of creating the infrastructure to store genomic information that may be relevant throughout a patient's life.[9]

Clinical Implementation of Pharmacogenomics forPersonalized Precision Medicine: Barriers and Solutions■

Clinical implementation of pharmacogenomics (PGx) leads to personalized medicine, which improves The efficacy, safety, and cost-effectiveness of treatments. Although PGx-based research has been con Ducted for more than a decade, several barriers have slowed down its widespread implementation inCClinica practice. Globally, there is an imbalance in programs and solutions required to empower the Clinical implementation of PG between countries. Therefore, we aimed to review these issue Comprehensively, determine the major barriers, and find the best solutions. Through an extensive review Of ongoing clinical implementation programs, scientific, educational, ethical, legal, and social issues, Information technology, and reimbursement were identified as the key barriers. The pace of globa Implementation of genomic medicine coincided with the resource limitations of each country. The key Solutions identified for the earlier mentioned barriers are as follows: building of secure and suitable Information technology infrastructure with integrated clinical decision support systems along wit Increasing PGx evidence, more regulations, reimbursement strategies for stakeholder's acceptance,Incorporation of PGx education in all institutions and clinics, and PGx promotion to all health care Professionals and patients. In conclusion, this review will be helpful for the better understanding ofCommon barriers and solutions pertaining to the clinical application of PGx.

DEVELOPING PHARMACOGENOMIC SERVICES

A few organizations are working to incorporate predictive pharmacogenomics testing so that it can be used as a model. In a sizable healthcare system, Hicks et al.8 detailed the application of clinical pharmacogenomic testing of three gene-drug combinations (HLA-B*57:01-abacavir, HLA-B*15:02-carbamazepine, and TPMT-thiopurines). Specialized guidelines and notifications were created and incorporated into the electronic health record to facilitate point-of-care decision-making. Incorporating panel genotyping and initiating clinical decision support alerts for individuals who possess an actionable genotype without requiring additional testing might potentially be included in the design of such a system. Additionally, a pharmacogenomics clinic was established, with medical geneticists, genetic counselors, and a pharmacist with specific expertise in pharmacogenomics working together to determine whether particular patients needed pharmacogenomic testing and to give Surgical services are conducting pilot studies to evaluate preemptive pharmacogenomic testing to better manage acute postoperative pain, reduce opioid consumption, and minimize recovery time after surgery. Senagore et al45 compared overall benefi t of analgesia scores and narcotic consumption in 2 groups: 50 patients who received pharmacogenomic-guided pain management after colorectal resection or major ventral hernia repair and a historical control group managed by an enhanced recov-ery protocol. The pharmacogenomic-guided group had signifi cantly lower scores (indicating better pain control) and consumed 50% less narcotics compared with the control group.45Given that poor analgesia and adverse effects from medications may result in an unplanned admission to intensive care or lengthier hospital stays, preemptive pharmacogenomic testing could help minimize such events.[10]

Conclusion

Pharmacogenomics, a branch of precision medicine, is the analy-sis of how an individual's response to a particular drug is based on his or her genes. Nurses best care for patients with a foundation about pharmacogenomics and an understanding of genetic differences, tumor markers, and types of testing. This article provides educational and clinical resources so nurses can expand their pharmacogenomics expertise. This knowledge will cultivate a holistic plan of care. As the focus of healtcare remains on reducing costs and improving morbidity and mortality rates, the reduction of ADRs will continue to highlighted. Tailoring medications based on individual responses will not only help to improve patient outcomes, but potentially affect the cost of health care as these genetic tests become a standard of care.

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