THE SCIENCE WORLD
A Monthly e Magazine
ISSN:2583-2212
March, 2025 Vol.5(3), 6591-6595

Popular Article

Pharmacogenomics and personalized diabetology

B. Dhanvandhini[1] and M. Sakthi Priya[2]
[1]PG Scholar, [2]Assistant Professor
Department of Veterinary Pharmacology and Toxicology
Veterinary College and Research Institute, Namakkal
DOI:10.5281/ScienceWorld.15132489

Introduction

Pharmacogenomics refers to the study of how genes affect a person's response to drugs. This field combines pharmacology (the science of drugs) and genomics (the study of genes and their functions) to develop effective, safe medications and doses tailored to a person's genetic makeup.

In the context of diabetes, traditional treatments often rely on a homogeneous therapeutic algorithm, which frequently leads to therapeutic failure and various diabetic complications due to the complex and heterogeneous nature of the disease. The advancement of high-throughput sequencing technologies and the integration of "omics" data enable a comprehensive global profiling of health and disease states.

History of Pharmacogenomics

- **Early Seeds (1950s-1970s):**

-1950s: The discovery of the double helix structure of DNA by Watson and Crick laid the foundation for understanding genetics.

-1959: The term pharmacogenetics was coined by Friedrich Vogel in Heidelberg, Germany.

-1960s-70s: The development of techniques like electrophoresis and restriction enzyme digestion made it possible to study DNA variations and their impact on disease.

- **Birth of Pharmacogenomics (1980s-1990s):**

-1980s: The Human Genome Project was launched with the ambitious goal of mapping the entire human genome. This spurred massive advances in DNA sequencing technology.

Official Website
www.thescienceworld.net
thescienceworldmagazine@gmail.com
Published 31/03/2025

-1990s: The first genetic markers associated with drug response were identified. Early examples include the CYP2D6 gene's role in metabolizing codeine and the HLA-B*1502 gene's association with Stevens-Johnson syndrome caused by certain medications.

• Pharmacogenomics Takes Off (2000s-Present):

-2000s: The completion of the Human Genome Project provided a comprehensive map of human genes, opening the door to large-scale pharmacogenomic studies. Clinical pharmacogenomic tests started appearing in the market, primarily focused on drug metabolism and response.

-2010s-Present: The development of next-generation sequencing (NGS) made genetic testing more affordable and accessible, fueling the growth of pharmacogenomics. We've seen the expansion of pharmacogenomic testing for various diseases, including cancer, cardiovascular disease and diabetes.

Integration of Pharmacogenomics and Personalized Medicine

- **Pharmacogenomics in Pharmacokinetics**

Genetic Variability in Metabolizing Enzymes- CYP450 Enzymes: Variants in genes encoding cytochrome P450 enzymes (e.g., CYP2C9, CYP2D6) can lead to different metabolic rates (e.g., poor, intermediate, extensive, and ultra-rapid metabolizers).

Transporter Proteins- SLCO1B1: Variants in the SLCO1B1 gene affect the transport of drugs like statins into liver cells, impacting drug distribution and efficacy.

- **Pharmacogenomics in Pharmacodynamics**

Drug Targets- Receptor Variants: Genetic variations in drug targets (e.g., receptors) can alter drug binding and response. For Example., Variants in the KCNJ11 gene, which encodes the Kir6.2 subunit of the KATP channel, affect the response to sulfonylureas in patients with neonatal diabetes.

Signal Transduction Pathways- TCF7L2 Gene: Variants in TCF7L2 affect insulin secretion and action, influencing the efficacy of diabetes medications.

- **Personalized Medicine through Pharmacokinetics**

Dose Adjustments- Individuals with CYP2C9 variants may require lower doses of sulfonylureas to avoid hypoglycaemia.

Drug Selection- Patients with certain SLCO1B1 variants might be prescribed alternative medications to statins to prevent myopathy.

- **Personalized Medicine through Pharmacodynamics**

Targeted Therapies- Patients with KCNJ11 mutations may benefit more from sulfonylureas than insulin, as the former directly targets the affected pathway.

Official Website
www.thescienceworld.net
thescienceworldmagazine@gmail.com
Published 31/03/2025

Optimizing Drug Efficacy: Adjusting treatment plans based on TCF7L2 variants to ensure optimal insulin secretion and action.

Diabetes Mellitus

Diabetes mellitus, more simply called diabetes, is a serious, long-term (or "chronic") condition that occurs when raised levels of blood glucose occur because the body cannot produce any or enough of the hormone insulin or cannot effectively use the insulin it produces.

Current Treatment Paradigms in Treating Diabetes Mellitus

Metformin is a first-line drug that is recommended. If the HbA1c target is not met, any other anti-diabetic agents can be added sequentially as second- and third-line drugs. However, this strategy has changed in recent years.

The management of T2DM has evolved from a glucose-centered approach, which focuses solely on controlling blood glucose levels, to an individual approach that accounts for the unique characteristics and needs of each patient, including specific blood glucose and weight goals, the potential effect on weight, the risk of hypoglycaemia and prevention of cardiovascular and kidney complications. The accessibility, cost and availability of medications are also important.

A sequential approach uses an initial single oral glucose-lowering medication and then other medications are added over time if the treatment fails. This approach has limitations because many patients do not quickly achieve glycaemic targets and the risk of complications increases over time. A more recent recommendation is to provide an early combination of two or more agents to achieve glycaemic targets more quickly and reduce the risk of complications.

Recent few combinations include glycomet trio (Metformin, glimepiride & voglibose), Diared-MPZ (Glimepiride, pioglitazone & metformin), Kombiglyze (Saxagliptin & metformin extended release). Mostly metformin is used for combination along with Dipeptidyl peptidase 4 inhibitors, Thiazolidinediones and α-Glucosidase inhibitors.

Does one Size Fits All Approach?

The one-size-fits-all approach in diabetes treatment often fails to account for the significant variability in patients' genetic backgrounds, disease progression, and individual responses to medications. This approach can lead to suboptimal glycaemic control and increased risk of side effects. For instance, standard therapies like sulfonylureas may cause hypoglycaemia in some patients, while others may experience gastrointestinal discomfort from alpha-glucosidase inhibitors. Moreover, combination therapies, although more effective than monotherapy, can result in complex regimens that challenge patient adherence.

Official Website
www.thescienceworld.net
thescienceworldmagazine@gmail.com
Published 31/03/2025

These limitations highlight the necessity for personalized medicine, which tailors' treatment based on genetic testing and individual patient characteristics, thereby improving efficacy, reducing adverse effects, and enhancing the overall quality of life for patients with diabetes.

Personalized Treatment Approach

In personalized diabetes care, pharmacogenomic testing analyses key genes such as CYP2C9 (affecting drug metabolism), SLC22A1 (influencing metformin response), and TCF7L2 (linked to insulin secretion). By combining these genetic insights with the patient's medical history, clinicians can optimize medication choices, avoiding ineffective or harmful drugs and provide tailored lifestyle recommendations. This precision approach moves beyond the traditional 'one-size-fits-all' model, ensuring treatments are as unique as the patient's genetic makeup.

Conclusion

The integration of pharmacogenomics into diabetes management represents a paradigm shift from empirical therapy to genetically-guided precision medicine. This evidence-based approach minimizes adverse drug reactions while maximizing its therapeutic efficacy.

References

Ali, O. (2013). Genetics of type 2 diabetes. World journal of diabetes, 4(4), 114.

Singh, S., Sarma, D. K., Verma, V., Nagpal, R., & Kumar, M. (2023). Unveiling the future of metabolic medicine: omics technologies driving personalized solutions for precision treatment of metabolic disorders. *Biochemical and Biophysical Research Communications*.

Tiwari, P. (2015). Recent trends in therapeutic approaches for diabetes management: a comprehensive update. *Journal of diabetes research*, 2015(1), 340838.

Venkatachalapathy, P., Padhilahouse, S., Sellappan, M., Subramanian, T., Kurian, S. J., Miraj, S. S., & Munisamy, M. (2021). Pharmacogenomics and personalized medicine in type 2 diabetes mellitus: potential implications for clinical practice. *Pharmacogenomics and Personalized Medicine*, 1441-1455.

White Jr, J. R. (2014). A brief history of the development of diabetes medications. Diabetes spectrum: a publication of the *American Diabetes Association*, 27(2), 82.

World Health Organization. (2019). Classification of diabetes mellitus.

Official Website
www.thescienceworld.net
thescienceworldmagazine@gmail.com
Published 31/03/2025