



INTERNATIONAL JOURNAL OF PHARMA PROFESSIONAL'S RESEARCH



A Review on Personalized Medicine: A Medical Treatment to The Individual Characteristics of Each Patient

MOHAMMAD ASIF^{1*}, ANSHUMAN PANDEY², FARHEEN SANAD KHAN³, AYUSHI RAI⁴, NAJMUS SAQIB⁵,
QUMRE ALAM⁶, AKASH JOHRI⁷.

^{1,2,3,4,5}Student, Bachelor of Pharmacy, Innovative College Of Pharmacy, Greater Noida, U.P.

⁶Associate Professor, Department of Pharmacy, Innovative College Of Pharmacy, Greater Noida, U.P.

Keywords: Biomarker, Diagnostic Test (CDx), Genomics, Pharmacogenomics, Next-generation Sequencing, Stratification.

Corresponding Author-

Mohammad Asif,
Innovative College of Pharmacy,
Greater Noida, U.P-201308,
INDIA
Email: asif69439@gmail.com
Phone: +91-98717 95257

ABSTRACT:

The idea of Personalised Medicine is not new – Doctors have long recognised that different patients react differently to medical interventions because the goal of medicine has always been to treat each patient as an individual. What is new is that paradigmatic advances in science and technology hold out from hope for the creation of targeted therapeutics and tools for determining who will benefit from a medical treatment and who will have negative side effects. Personalised Medicine has made significant advancements in recent years, demonstrating the capability of science to radically advance medical practice. Despite this, the problems of understanding human health and disease remain sobering. The intricate interplay of environmental, genetic, social, and cultural factors affects not just “Who We Are..” but also “What Disease We Are Prone To.” Fundamental advancements in our comprehension of each of these characteristics, as well as how they interact, will be necessary to realize a genuinely individualized approach to patient-care. Personalised Medicine is something that concerns us all. Our unique viewpoints have an impact on how we interpret this area’s evolution. This section explains the idea of Personalised Medicine as well as various modern definitions and uses of the term.

Introduction:**History and Development:**

“It’s Far More Important To Know What Person The Disease Has Than What Disease The Person Has..”

- Hippocrates^[1]

Many hundreds of years ago, the idea of Personalised Medicine was first introduced. But, it wasn't until the 19th-century that advancements in Chemistry, Histochemistry and Microscopy enabled researchers to start understanding the fundamental causes of diseases. In the years afterwards, significant advances in Science and Technology have made it possible for healthcare judgements to become more precise. The 20th-century saw a development in Genetics, Imaging and Data Mining alongside the expansion of the Pharmaceutical and Medical Device sectors. The studies of individual variations in drug response led to a body of work aimed at identifying important enzymes that contribute to diversity in Drug Metabolism and response, which laid the groundwork for Pharmacogenetics. More recently, the decoding of the Human Genome at the beginning of the 21st-century stated the process of turning Personalised Medicine from a theory into a practice. Scientists now have the opportunity to build tools for genuinely Individualized Diagnosis and Therapy, thanks to the rapid advancements in Genomics and other fields, such as Regenerative Medicine.

We still have a long way to go in understanding why different people experience disease or respond to treatment in various ways, despite the amazing achievements made in the Medical Sciences so far. For the majority of diseases and ailments, we are currently unable to forecast a patient's response to treatment.

Therefore, Doctors are forced to use less-than optimal practices when prescribing medications and other forms of treatment.

e.g. a patient receiving treatment for High Blood Pressure, might be prescribed one of several Blood Pressure drugs.

Only general knowledge about what might genuinely help for that specific patient is used by the Patient's-Doctor when deciding what drug to prescribe. The patient may be moved to another drug if the first medications does not function after a few weeks. The Trial-and Error or “One Size Fits All” approach may result in Patient Dissatisfaction, Unfavorable Drug Reactions and Interactions, and poor Adherence to treatment regimens. By separating in advance those patients who are most likely to benefit from a given treatment from those who will incur expenditure and experience side effects without benefit, Personalised Medicine aims to simplify clinical decision-making.

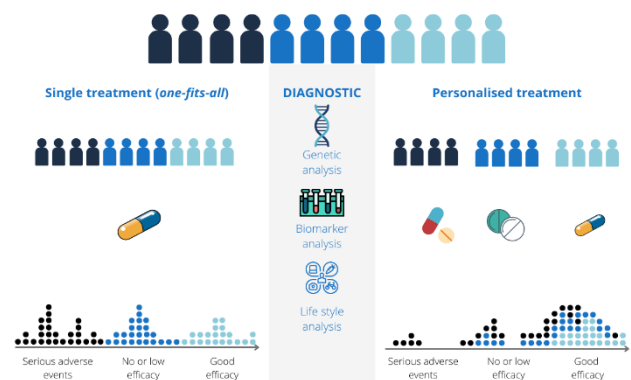


Fig.1 – “One Size Fits All” Approach V/s Personalised Medicine ^[2]

The Personalised Medicine:

The phrase “Personalised Medicine” is frequently defined as giving “Right Medicine To The Right Patient At The Right Time” ^[3]

IJPPR (2023), Vol. 14, Issue 2

A more general definition of Personalised Medicine is the customizing of Medical Care to a Patient's Unique Requirements, Preferences, and Traits throughout all phases of care including Preventions, Diagnosis, Treatment and follow-up. The National Academy of Sciences (NAS) has described "Precision Medicine" as the use of Genomics, Epigenomics exposure and other data to characterize individual patterns of disease, perhaps leading in improved Individual Therapy. Precision Medicine is most likely synonymous with "Personalised Medicine"^[4]

Stratification – This refers on the classification of patients with a given disease into subgroups based on a feature of some kinds, who respond. more frequently to a specific therapy, or alternatively are at lower risk of experiencing adverse effects as a result of a specific treatment.

Pharmacogenomics (PGx) -One of the most fascinating subfields of Personalised Medicine is the study of variations in DNA and RNA properties in relation to Drug Response^[5]. The area was created as a result of Pharmacology and Genetics advancements coming together (the study of Genes and their functions). Many of the medications that are currently available have variable responses from patients. It might be challenging to anticipate who will benefit from a medication, who won't respond at all, and who will experience negative effects. The goal of PGx is to comprehend how variations in Gene's expression impact how the body reacts to drugs. In more details, PGx makes up to Genetic Data (such DNA Sequences, Gene Expression, and Copy Number) to explain inter-individual variations in Drug Metabolism (Pharmacokinetics) and Physiological Drug Response (Pharmacodynamics), to identify responders and non-responders to a drug, and to forecast the efficacy

Review Article

and/or toxicity of a drug. New opportunities in Drug Discovery and Development have been made possible by advancements in PGx. With the help of PGx, a variety of health issues such as Cancer, HIV/AIDs and Cardiovascular disease, can now be treated more specifically. Since more than 10 years ago, the FDA's Centre for Drug Evaluation and Research (CDER) has supported Pharmacogenomics by offering regulatory guidance, examining applications and creating procedures and policies that are focused on Genomics and Personalised Medicine.

The creation of precise and trustworthy diagnostics, as well as, occasionally, the discovery of predictive Biomarkers is essential for the success of Personalised Medicine. In-vitro diagnostics, such as Electrocardiogram (EKG) Tracings, or Imaging Technologies are examples of diagnostics used in Personalised Medicine that are typically used to determine the existence, absence, or quantity of a Biomarker or to evaluate physiological or anatomical patient characteristics. The choice of treatment based on the results of the Diagnostic Test may not be the best one even, if it is accurate.

e.g. if a patient receives an inappropriate medication as a result of a poor diagnostic outcome, that patient may suffer injury or receive no benefit from the medication since it will either render the patient ineffective or induce adverse effects that could have been avoided.

TRADITIONAL "ONE SIZE FITS ALL" TREATMENT:

With Personalised Medicine, aims to deliver "The Right Medicine To The Right Patient At The Right Time"^[7]. Unlike the traditional "One Size Fits All" approach to Medical Research and Prescription, it

IJPPR (2023), Vol. 14, Issue 2

targeted to people who are most likely to benefit from them. In addition to improving Clinical Results and Patient Quality of Life, Personalised Medicine has enormous potential cost-benefits for our ailing Healthcare Systems.

But, we are only at the beginning of this journey.

The Promise Of Personalised Medicine:

The goal of Personalised Medicine is to provide “The Right Medicine To The Right Patient At The Right Time”.

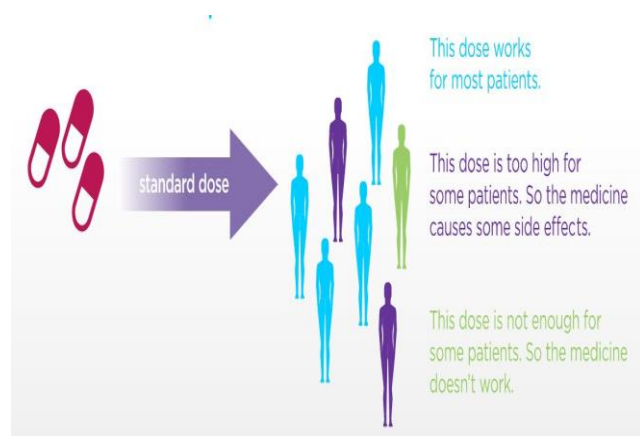


Fig.2 – Traditional “One Size Fits All” Treatment^[8]

An alternative to the traditional “One Size Fits All” approach of treatment is Personalised Medicine. We are now better able to categorize individuals into groups that benefit from a treatment since it is based on a Greater Understanding of the Molecular Mechanisms of Diseases. The common observation that patients with seemingly identical clinical diagnosis or symptoms frequently respond differently to the same medication is the first thing that Personalised Medicine attempts to address. As a result, Personalised Medicine has a significant potential to enhance the Clinical and Financial viability of treatments. This is particularly true for complex conditions like Cancer or Inflammatory diseases, where even in the best cases, a therapy frequently only benefits 30-50% of individuals receiving the treatment. Personalised Medicine also aids in lowering needless safety concern by only treating patients who are most likely to benefit or identifying those who are more likely to experience negative reactions. This raises safety and eases the Financial Strain on Healthcare Systems.

Biomarkers:

These characteristics of patients serve as indicators of disease processes or as indicators of therapy response, and they are crucial for the ability to individualize medications. These biological traits can be Hereditary, Blood Chemistry-related or Imaging-related, and they can all be objectively measured ^[9]. The Biomarker status of a patient is determined using Modern Diagnostic Techniques, particularly so-called Companion Diagnostic Procedures. These are used to identify patients who may either benefit from a particular medication or who may be vulnerable to side effects that could be very severe.

These crucial elements are essential for the successful implementation of Personalised Medicine –

- Our knowledge of diseases and relevance of Biomarkers,
- The precision and dependability of the corresponding Diagnostic Tools, and
- The individualized therapy.

Personalised Medicine has a lot of potential, and more accurate medical decisions may be made as a result of it. The inefficiencies brought on by Trial-and Error that currently endanger patient-care and drive-up Healthcare expenses may therefore be eliminated with the help of Personalised Medicine. Through the use of Personalised Medicine, doctors can recognize individuals who are most likely to benefit from a specific course of therapy or who are at a high risk of suffering serious adverse effects ^[10].

The goal of individualized treatment include –

- Increasing clinical results and predictability.
- Avoid side effects brought on by incorrect treatment.
- An improvement in the standard of living.

- Encourage patient co-operations since it produces greater results.
- Increase the efficiency with which healthcare resources are utilised.

“One Size Fits All” V/s Personalised Medicine:

One Size Fits All Traditional Medicine – Despite having various Biomarkers, Cancer patients for instance those with Colon Cancer, receives the same treatment.

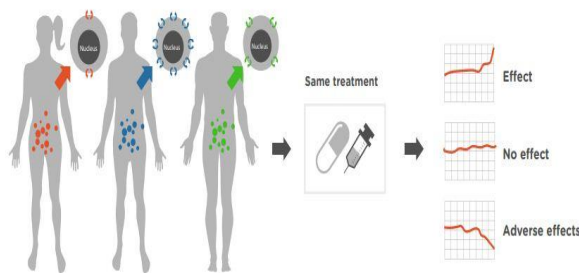


Fig.3 – “One Size Fits All” Traditional Treatment

“Right Medicine To The Right Patient At The Right Time” Personalised Medicine -Patient with Cancer, such as those with Colon Cancer receives a individualized treatment plan based on their Biomarkers.

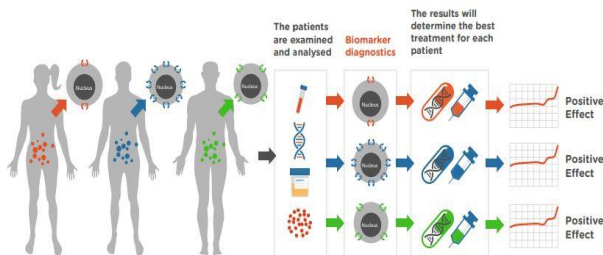


Fig.4 – “Right Medicine To The Right Patient At Right Time” Personalised Medicine

(The Impossibilities Of Personalised Medicine’s Promises):

A paradigm shift will be required to fully realise the potential of Personalised Medicine. It entails updating Disease Classifications, altering how Clinical Trials are conducted, establishing a suitable framework for Data Privacy and Protection, investing in Bioinformatics infrastructure for companion Diagnostic Tests, adapting Regulatory Processes for Personalised Medicine, Educating Healthcare Professionals and Patients, and making sure Pricing and Reimbursement Structures are in place for Personalised Medicine to live up to its potential.

The Scientific Basis For Personalised Medicine (New Molecular Understanding And Disease Classifications):

In the past, medical specializations were based on “Organ-and Systems” which helped on define how diseases were categorized. These disease definitions seem progressively less suitable in light of the scientific advancements brought on by Personalised Medicine.

e.g. Breast Cancer is a diagnostic that only refers to the location of the disease and ignores its Molecular and Genetic Aspects.

There isn’t one Breast Cancer drug that can effectively treat all patients – instead, many classes of Cancer drugs are used to treat different types of Breast Cancer as well as other types of Cancer, and are customized to particular underlying mechanisms. It is evident that the situation is the same for many diseases, including Schizophrenia, Diabetes and Rheumatoid Arthritis, where there are numerous causes of the same clinical symptoms. Therefore, in addition to the “Organ-and Systems”, the diagnosis of diseases must take into account Underlying Traits or Molecular Markers^[11].

Resources For Personalised Medicine – Bioinformatics, E-Health Records, Biobanks, And Data Sharing/Protections:

The greatest insights have been found through the Analysis, Linking and Comparison of numerous large datasets (Genomics, Clinical Outcomes, Bio-banks,

IMPLICATIONS OF PERSONALISED MEDICINE

Imaging etc) also known as “Big Data”. Although “Omics” datasets have provided remarkable insights, this is where the greatest insights have been found. The Collecting, Linking and Analysis of large datasets from patients participating in Clinical Trials and Routine Care are necessary for the advancement of Research and the Adoption of Personalised Medicine in National Health Systems. Complex Bioinformatics Systems and Analytical capabilities will also continue to be required. An important resource for the country is the magnitude of Biobanks that exists in various Academic Institutions or at the National Level. Ability to identify potential Biomarkers in Patient Tissue and Blood Samples is crucial for Research on Personalised Medicine. Linking clinical data to Biobank samples for the same patient is a very effective strategy, and collaboration across Biobanks (inside and across National boundaries) as well as the connection of Biobank sample data to clinical information should both be promoted to support advancements in Personalised Medicine. To maintain and speed up progress in this area, the capacity to perform additional research on such novel Biomarkers in current sample sets is crucial. Therefore, uniform processes for obtaining consent for research should be used to approve additional studies using Biobank specimens already in existence.

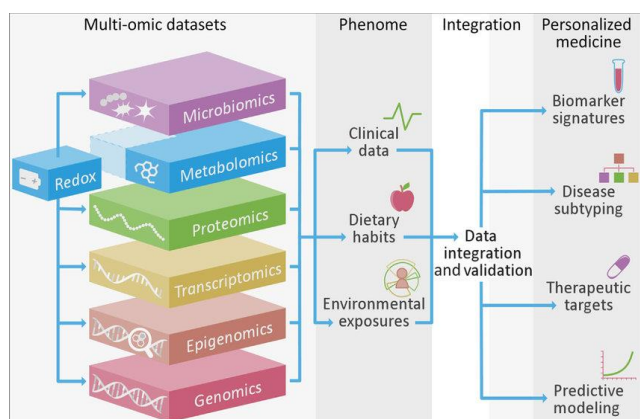


Fig.5 – “Omics” Dataset^[12]

It is crucial to have High-quality Sample Preparation and Storage Procedures in a Biobanks. Research’s high calibre and dependability are ensured by standardizing methods and sharing best practices among Biobanks. As was previously said, many common diseases are now more precisely classified

into smaller groups with comparable underlying molecular problems. So, it becomes crucial to gather and analyze clinical data and samples from other Nations.

Utilizing Personalised Medicine To Increase The Speed And Effectiveness Of Clinical Trials:

The effectiveness and safety of a new drug are currently assessed in several Clinical Trials by examining the effects of treatment in patient groups that are generally unselected. Therefore, to find relatively modest advantages, massive studies are used. A major contributing cause to the high failure rates in Drug Development is this method of conducting Clinical Trials, which is manifestly ineffective. Such Clinical Trials might show no overall benefit from a treatment yet ‘miss’ a significant benefit for a small sub-group of patients. Even when these trials are successful, approx. 30-50% of the people who are treated will typically benefit, and other patients will not improve at all but may still experience major adverse events. A Personalised Medicine strategy helps to identify the patients most likely to respond to the test treatment and enables smaller, more individualized Clinical Trials by pre-selecting patients based on Biomarkers. But, when Biomarkers are discovered retroactively, after a Phase-III Clinical Trial has been completed, or even after a drug has been approved, problems can occur. Re-analyzing the data in these situations in light of the newly identified Biomarker is advantageous, if not critical. It would therefore be significant progress to standardize methods for obtaining consent and approval for extra and retrospective analysis (as well as the use of tissue samples).

It should be possible to quickly identify patients qualified to participate in Clinical Trials of new

IJPPR (2023), Vol. 14, Issue 2

medicines using Electronic Health Information System as Genomic information becomes more frequently available to patients as part of Traditional Clinical-care. The use of Genomics, e-Health and other Clinical data for Health and Research requires, consistent Datasets, Interoperability of e-Health Records across the country, effective and secure e-Health data software/hardware and suitably flexible privacy legislations.

A Regulatory Environment That Will Support And Encourage Personalised Medicine:

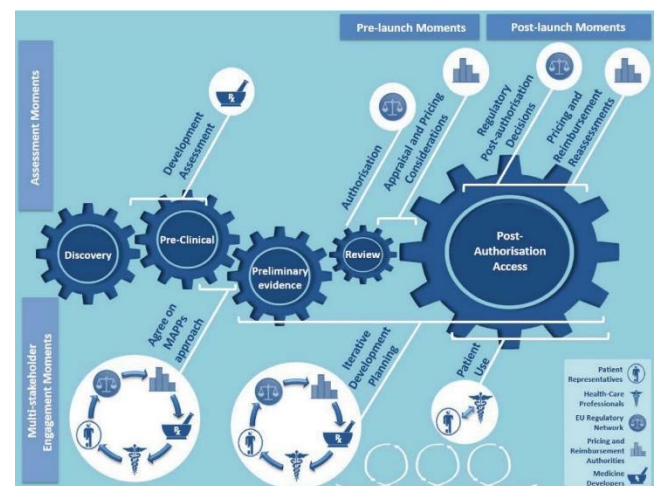
The development of Personalised Medicine differs significantly from that of Traditional Medicine in a number of significant ways, not the least of which is the requirement for patients to be identified through Diagnostic Tests (CDx) as having the necessary Biomarker [13]. Because smaller, Biomarker-identifiable populations can be studied in more limited Clinical Studies and used to identify patients for Efficacy and Safety Surveillance in Post-marketing Surveillance after Initial Licensing Approval, the Adaptive Pathways approach may be particularly well suited for Personalised Medicine Therapies. Once more, e-Health Records play a significant role in the collecting of ‘Real World’ data for ongoing Efficacy and Safety Data Analysis to enable Adaptive Pathways. Continuous Safety and Efficacy monitoring for Adaptive Pathways would be significantly easier to carry-out if High-quality reliable e-Health Data could be collected effectively. The creation of new adaptable routes and their testing in pilot programmes should go on in order to increase early patient access to Personalised Medicine. Regulators must to actively promote the use of currently available flexible licensing strategies, such as conditional marketing authorizations subject to conditions (such as post authorization safety and efficacy studies) [14]. Another feasible strategy that would be easy to implement is

Review Article

“Orphan Indications” in the orphan products legislation driven by Biomarkers.

Fig.6 – Medicine Adaptive Pathways To The Patient [15]

Making Clinical Decisions And Improving Patient-care By Developing Diagnostics Test For



Personalised Medicine:

The supplementary Diagnostic Test (CDx) is an essential element of Personalised Medicine. The entire idea will fall flat in the absence of an Accurate, Dependable and Quick Diagnosis. Technology in the medical field is developing quickly. As a result of both Molecular Biology advancements and the emergence of new Novel Technology Platforms for Diagnostic Procedures, such Next-generation Sequencing, which enables the simultaneous investigation of numerous Genetic Indicators. As a result, “One Size Fits All” approach is undergoing change, and many markers will dictate how and when to utilize medications. The difficulties presented by the diagnostic aspect of Personalised Medicine will grow as more test panels are regulated and compensated. It’s important to keep in mind that efforts are being made to integrate clinical, “Omics” and e-Health datasets in order to give Healthcare practitioners Clinical Decision

support. This is due to the rapid expansion of these datasets.

These Bioinformatics technologies, while not exactly ‘Diagnostics’, will increasingly direct Clinical Judgments and Patient Treatment Regimens. Regulators, Payers and Healthcare Systems will face new obstacles in Developing, putting these systems into use, and evaluating their Efficacy. In this field of Bioinformatics and Decision Assistance, Patient and Healthcare Education is necessary. The growing innovation in this field will complicate matters even more by putting more pressure on the Testing Facilities. Personnel must be trained to conduct the tests and interpret the results in addition to being provided with up-to date Diagnostic Instruments that provide results quickly.

As a last point, there is insufficient innovation protection in the market for diagnostics. To drive CDx development and promotion, the right incentives are required.

CURRENT RESEARCH (Gene Therapy Treatment For Haemophilia-B):

It’s been more than 20-years since Gene Therapy for Haemophilia-B first became a possibility. Despite improvements in Haemophilia-B treatment, Peter Marks, M.D. Ph.D. Director Of The FDA’s Centre for Biologics Evaluation and Research, warned that the prevention and treatment of Bleeding Episodes can negatively affect people’s “Quality Of Life”. “Today’s approval provides a new treatment option for Haemophilia-B patients and represents significant advancement in the Development of Novel Medicines for people dealing with a high burden of Disease associated with this form of Haemophilia-B”, said the FDA^[17-30].

A Genetic Bleeding illness called Haemophilia-B is caused by low or absent amounts of the Blood Clotting

Protein Factor-IX, which is necessary to form Blood Clots to halt Bleeding. In severe circumstances, Bleeding Episodes can happen spontaneously without a known cause. Symptoms can include significant or persistent bleeding after an Injury, Surgery or Dental procedure. Prolonged Bleeding Episodes can cause major issues such bleeding into Muscles, Joints or Internal Organs like the Brain. In order to strengthen the body’s capacity to stop bleeding and encourage healing, the Clotting Factor that is inadequate or lacking is routinely replaced. In order to maintain enough amounts of Clotting Factor to stop Bleeding Episodes, patients with severe Haemophilia-B often need a routine treatment programme that include Intravenous (IV) Infusion of Factor-IX Replacement Medicines.

Genetic Alterations That Result In Disease Are Fixed By Gene Therapy:

A viral vector encoding the Clotting Factor-IX, Gene makes-up the one-time Gene Therapy drug Hemgenix, which is administered Intravenously in a single-dose.

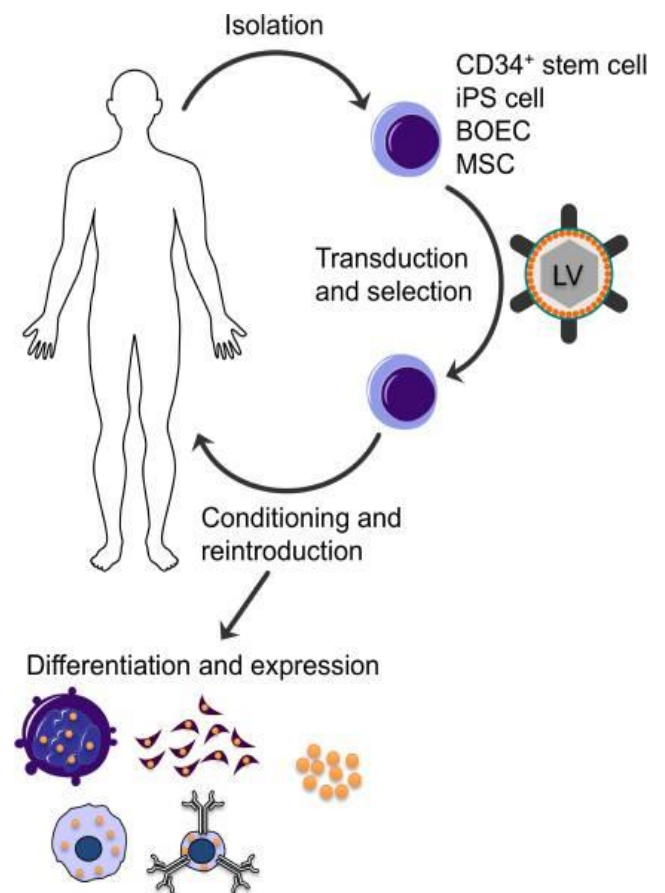


Fig.7 – Gene Therapy Treatment For Haemophilia-B^[18]

IJPPR (2023), Vol. 14, Issue 2

In this course of treatment, a Doctor injects Healthy Genes into your body's cells using a modified Virus. Additionally, they might eliminate or deactivate problematic Genes, by replacing Faulty F9-Gene with a Non-faulty Gene, effective Gene Therapy for Haemophilia-B may offer long-term or even permanent benefits. This would enable your body to create enough Factor-IX on its own, leading to fewer or no Factor-IX infections. Numerous Gene Therapy strategies have been investigated by Researchers to treat Haemophilia-B. In Clinical Trials, several of these strategies have showed promise.

e.g., for at least 3-years, Researchers discovered that Gene Therapy elevated Blood Levels of Factor-IX to 1-6% of the baseline level. The greatest dose of the medication resulted in more than 90% fewer Bleeding Episodes in the patients. A lesser number of Factor-IX concentrate treatments were also necessary. ^[31-32]

CONFLICT OF INTEREST

The authors declare that the review do not have any conflict of interest.

ACKNOWLEDGEMENT

The authors are very thankful to the Mr. QUMRE ALAM, Associate Professor (Department of Pharmacy) at INNOVATIVE COLLEGE OF PHARMACY, Greater Noida, U.P for his continuous guidance throughout the session in the successful completion of this manuscript. Also, our teamwork has helped us a lot in the proper compilation of this manuscript and improvement of individual skills.

REFERENCES

1. Abrahams, E. & Silver, M. (2010). The History Of Personalized Medicine. In E. Gordon and S. Koslow (Eds.), *Integrative Neuroscience And Personalized Medicine* (3-16). New York, NY: Oxford University Press.

Review Article

2. https://www.genosalut.com/wp-content/uploads/2022/05/Genosalut_Personalised_medicine.png
3. Sadee, W. and Z. Dai, "Pharmacogenetics/Genomics And Personalised Medicine", *Human Molecular Genetics*, 2005, Vol.14, Review Issue (2) R207-R214.
4. National Research Council: Committee On A Framework For Developing A New Taxonomy Of Disease (2011). *Toward Precision Medicine: Building A Knowledge Network For Biomedical Research And A New Taxonomy Of Disease*. Washington, DC: The National Academies Press.
5. FDA, Guidance For Industry: E15 Definitions For Genomic Biomarkers, Pharmacogenomics, Pharmacogenetics, Genomic Data And Sample Coding Categories, April 2008.
6. *Paving The Way For Personalised Medicine: FDA's Role In A New Era Of Medical Product Development*, October 2013.
7. European Alliance For Personalised Medicine (2013) *Report On Innovation And Patient Access To Personalised Medicine*.
8. <https://researchbank.kaiserpermanente.org/wp-content/uploads/2019/12/newsletter-2019-chart-prescription-medicine.svg>
9. WHO International Programme On Chemical Safety Biomarkers In Risk Assessment: *Validity And Validation* (2001). Retrieved From: <http://www.inchem.org/documents/ehc/ehc/ehc222.htm>
10. The Personalized Medicine Coalition (2014), *The Case For Personalized Medicine*, 4th Ed.

11. National Academies Press (2011) Toward Precision Medicine: Building A Knowledge Network For Biomedical Research And A New Taxonomy Of Disease.
12. https://www.researchgate.net/figure/Integration-of-Multi-Omics-Biological-Datasets-and-Phenotypic-Data-Is-Key-to-the_fig2_342575338 (Accessed 17 Dec, 2022).
13. http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000601.jsp (2015/03/02).
14. European Science Foundation (2012) ESF Forward Look: Personalised medicine for the European citizen.
15. Seamless Process And Decision Points Of An Adaptive Pathway Retrieved From: http://adaptsmart.eu/wp-content/uploads/2017/06/ADAPT-SMART-seamless-pathway_final_website.pdf (Accessed 28 March 2018)
16. EBE A Specialized Group Of European Federation Of Pharmaceutical Industries And Associations, EFPIA: White Paper On Personalised Medicine, September 2015.
17. <https://www.fda.gov/news-events/press-announcements/fda-approves-first-gene-therapy-treat-adults-hemophilia-b>
18. https://www.ncbi.nlm.nih.gov/core/lw/2.0/html/tileshop_pmc/tileshop_pmc_inline.html?title=Click%20on%20image%20to%20zoom&p=PMC3&id=4476626_nihms-699885-f0005.jpg
19. Pal N, Mandal S, Shiva K, Kumar B. Pharmacognostical, Phytochemical and Pharmacological Evaluation of *Mallotus philippensis*. *Journal of Drug Delivery and Therapeutics*. 2022 Sep 20;12(5):175-81.
20. Singh A, Mandal S. Ajwain (*Trachyspermum ammi* Linn): A review on Tremendous Herbal Plant with Various Pharmacological Activity. *International Journal of Recent Advances in Multidisciplinary Topics*. 2021 Jun 9;2(6):36-8.
21. Mandal S, Jaiswal V, Sagar MK, Kumar S. Formulation and evaluation of carica papaya nanoemulsion for treatment of dengue and thrombocytopenia. *Plant Arch*. 2021;21:1345-54.
22. Mandal S, Shiva K, Kumar KP, Goel S, Patel RK, Sharma S, Chaudhary R, Bhati A, Pal N, Dixit AK. Ocular drug delivery system (ODDS): Exploration the challenges and approaches to improve ODDS. *Journal of Pharmaceutical and Biological Sciences*. 2021 Jul 1;9(2):88-94.
23. Ali SA, Pathak D, Mandal S. A REVIEW OF CURRENT KNOWLEDGE ON AIRBORNE TRANSMISSION OF COVID-19 AND THEIR RELATIONSHIP WITH ENVIRONMENT. *International Journal of Pharma Professional's Research (IJPPR)*. 2023;14(1):1-5.
24. Shiva K, Mandal S, Kumar S. Formulation and evaluation of topical antifungal gel of fluconazole using aloe vera gel. *Int J Sci Res Develop*. 2021;1:187-93.
25. Vishvakarma P, Mandal S, Verma A. A REVIEW ON CURRENT ASPECTS OF NUTRACEUTICALS AND DIETARY SUPPLEMENTS. *International Journal of Pharma Professional's Research (IJPPR)*. 2023;14(1):78-91.
26. Ali S, Farooqui NA, Ahmad S, Salman M, Mandal S. CATHARANTHUS ROSEUS (SADABAHAR): A BRIEF STUDY ON MEDICINAL PLANT HAVING DIFFERENT PHARMACOLOGICAL ACTIVITIES. *Plant Archives*. 2021;21(2):556-9.
27. MANDAL S, JAISWAL DV, SHIVA K. A review on marketed Carica papaya leaf extract (CPLE) supplements for the treatment of dengue fever with thrombocytopenia and its drawback. *International Journal of Pharmaceutical Research*. 2020 Jul;12(3).

28. Mandal S, Vishvakarma P, Verma M, Alam MS, Agrawal A, Mishra A. Solanum Nigrum Linn: An Analysis Of The Medicinal Properties Of The Plant. *Journal of Pharmaceutical Negative Results*. 2023 Jan 1:1595-600.
29. Vishvakarma P, Mandal S, Pandey J, Bhatt AK, Banerjee VB, Gupta JK. An Analysis Of The Most Recent Trends In Flavoring Herbal Medicines In Today's Market. *Journal of Pharmaceutical Negative Results*. 2022 Dec 31:9189-98.
30. Mandal S, Pathak D, Rajput K, Khan S, Shiva K. THROMBOPHOB-INDUCED ACUTE URTICARIA: A CASE REPORT AND DISCUSSION OF THE CASE. *International Journal of Pharma Professional's Research (IJPPR)*. 2022;13(4):1-4.
31. Mandal S, Shiva K, Yadav R, Sen J, Kori R. LEIOMYOSARCOMA: A CASE REPORT ON THE PREOPERATIVE DIAGNOSTIC CRITERIA. *International Journal of Pharma Professional's Research (IJPPR)*. 2022;13(4):1-4.
1. Mandal S, Vishvakarma P, Mandal S. Future Aspects And Applications Of Nanoemulgel Formulation For Topical Lipophilic Drug Delivery. *European Journal of Molecular & Clinical Medicine*.;10(01):2023.