TRADITIONAL AND INTEGRATIVE MEDICINE

Trad Integr Med, Volume 9, Issue 2, Spring 2024

Original Research

Comparability of Traditional Persian Medicine with the New Concepts of Personal and Precision Medicine: A Qualitative Study

Mojtaba Norouzi[1], Ali Akbar Haghdoost[2]*, Maryam Karimiafshar[3], Mohammad Setayesh[4]

[1]Department of Bio Statistics and Epidemiology, Faculty of Public Health, Kerman University of Medical Science, Kerman, Iran
[2]HIV/STI Surveillance Research Center, and WHO Collaborating Center for HIV Surveillance, Institute for Futures Studies in Health, Kerman University of Medical Sciences, Kerman, Iran
[3]Department of Persian Medicine, Faculty of Traditional Medicine, Kerman University of Medical Sciences, Kerman, Iran
[4]Department of Persian Medicine, Faculty of Traditional Medicine, Kerman University of Medical Sciences, Kerman, Iran

Received: 17 Jul 2023 **Revised:** 18 Feb 2024 **Accepted:** 27 Feb 2024

Abstract

Traditional Persian Medicine (TPM) has a thousand-year history and a holistic approach that respects personal characteristics in its diagnosis and management. The objective of this study was to explore the concepts of personal and precision medicine in traditional Persian and modern medicine. A qualitative study design with a content analysis approach was conducted. Purposive and snowball sampling approaches were used to select participants. Then, we approached experts in various fields, including TPM, genetics, epidemiology, physiology, pharmacy, and general medicine. In the beginning, we summarized the concept of personalized medicine (PM) and asked them how many similarities and differences they might find between TPM and PM. A semi-structured questionnaire with six parts was used to collect data. The duration of each interview varied from 30 to 65 min. The interviews and experts' viewpoints were recorded via an online platform and transcribed verbatim. The data analysis process involved several sequential steps: initial familiarization, coding, theme generation, theme review, theme definition and naming, and final writing. After coding all texts and extracting issues, categories and conceptual frameworks were created by interpreting the content. To analyze the data, the content analysis approach assisted by MAXQDA 2018 software was used. More than 70% of participants showed a favorable attitude in all evaluated parts. Approximately 80% of participants agreed that there are parallels between TPM and precision medicine; for example, in TPM and precision medicine, patients are treated with respect to their characteristics. More than 80% of participants thought temperamentology may help with patient diagnosis and treatment. They also suggested that TPM concepts could be used to improve and accelerate the implementation of precision medicine. The majority of participants acknowledged the use of phenotypes to reduce the reliance on genetics in precision medicine. However, several participants expressed skepticism. According to the participants, these concepts will not be beneficial unless TPM aligns with modern medicine. In addition, there must be scientific evidence confirming the association between different genes and temperaments. The advent of precision medicine does not mean disregarding TPM; rather, the concepts of TPM can be used in precision medicine. For example, phenotype can assist in reducing the reliance on genetics in precision medicine. Because phenotype, as an important concept in TPM, is the external manifestation of the genotype. In addition, like precision medicine, TPM can help to provide personalized medical treatment based on people's temperament.

Keywords: Traditional persian medicine; Precision medicine; Experts

http://doi.org/10.18502/tim.v9i2.15866

Citation: Norouzi M, Haghdoost AA, Karimiafshar M, Setayesh M. **Comparability of Traditional Persian Medicine with the New Concepts of Personal and Precision Medicine: A Qualitative Study**. Trad Integr Med 2024;9(2):128-135. http://doi.org/10.18502/tim.v9i2.15866

*Corresponding Author: Ali Akbar Haghdoost
HIV/STI Surveillance Research Center, and WHO Collaborating Center for HIV Surveillance, Institute for Futures Studies in Health, Kerman University of Medical Sciences, Kerman, Iran
Email: ahaghdoost@gmail.com

Introduction

The concept of personalized medicine (PM), which has been prevalent in Traditional Persian Medicine (TPM) for many years ago [1], has now become prominent globally and is recognized as a significant revolution in medical care [2,3]. Precision medicine is an advanced form of personalized medicine that is enhanced by the integration of technology [4]. Precision medicine, which has gained a lot of attention in the recent decade [5], refers to the use of individual data to improve prevention, diagnosis, and treatment [6]. PM, by considering individual characteristics [7], contributes to the advancement of medical research focused on inter-individual differences [8]. Advances in human genome research open a new window for precision medicine to develop individual treatments based on genetic profiles [9]. The rapid advancements in human genome sequencing and analytical methods have enabled clinical researchers to identify and understand various diseases. Also, genetic tests are used in clinical decision-making and have been made available to predict some diseases, such as cancer [10,11]. Precision medicine fills the gap between genomic knowledge and individualized care, thereby improving clinical care [12].

TPM has a thousand-year history with a holistic approach [13] and defines the concept of PM as mood or temperament [1]. Temperament is associated with an individual's physical and psychological characteristics, offering a holistic perspective on individuals and the factors that impact them [14]. According to the concepts of TPM, each individual has a unique temperament, and the maintenance of a balanced temperament is crucial for overall human health. Any disruption in temperament can potentially lead to illness [15]. Although the temperament of the body's organs may differ, their integration produces a person's overall temperament. The inherent temperament, known as "Mizaj e jebelli," can potentially transform into an "acquired temperament" over time due to the influence of various external factors [16]. As a result, each person has a distinct temperament, and each person's health state is determined independently of others. Moreover, the signs of a similar disease can vary among individuals, based on their temperaments [17]. Although there is an infinite range of temperaments, each individual possesses a unique temperament that distinguishes them from others [16]. Furthermore, everything ranging from food and medication to environmental factors such as climate and weather possesses its unique temperament that influences the temperament of individuals [18].

Research carried out on the genome reveals that numerous genes play a role in shaping an individual's temperament [19]. Exploring the molecular and hormonal evidence is crucial for identifying biomarkers and distinguishing between temperaments in humans [20]. The external manifestation of an individual's genetic makeup is referred to as their phenotype, which arises from the interplay of their genotype, environment, and genotype-environment interaction [21]. Consequently, the clinical classification of individuals based on differences and similarities in their phenotype, derived from variances in temperament, has a robust logical foundation that can be experimentally justified in the present era [22]. In line with this perspective, studies on TPM demonstrate that individuals with hot-natured temperaments exhibit a more active sympathetic nervous system compared to those with cold-natured temperaments [23]. Additionally, the body composition of individuals with hot temperaments significantly differs from those with cold temperaments, with higher levels of fat tissue observed in the cold group, while the hot group exhibits a higher percentage of skeletal muscle mass. Such findings validate the TPM viewpoint regarding temperaments [24]. Therefore, by considering temperaments, it becomes possible to categorize numerous physiological and pathological events, ultimately enabling the identification of distinct therapeutic strategies [25].

Personalizing patient care is a primary objective of contemporary medicine. Contemporary medicine is shifting away from a one-size-fits-all approach that applies the same treatment to all individuals. In contemporary medicine, the concept of precision medicine acknowledges that patients with the same disease can react differently to everything from pharmaceuticals to biological factors. As a result, the process of diagnosing and treating people is not entirely the same [26].

TPM and contemporary medicine appear to be different. The concept of personalized medicine within TPM is comparable to temperament and relies on phenotype. Personalized medicine is synonymous with precision medicine in contemporary medicine, emphasizing genetics. TPM and contemporary medicine may have certain concepts in common. However, there have been no studies conducted to compare TPM with the new concepts of personalized and precision medicine. This article attempted to investigate this issue using expert viewpoints.

Methods

A qualitative study was conducted to explore the concepts of precision medicine in TPM and contemporary medicine. We approached experts in this field to obtain more detailed information based on their opinions. The study, which involved recording participants' viewpoints, commenced in January 2022 and concluded in February 2022. The qualitative approach was chosen because it allows for the flexible study of the issue, including the respondents'

perspectives and experiences [27].

Population and sampling

Purposive and snowball selection approaches were used to select participants for this study based on predetermined criteria relating to the research issue. This sampling strategy is employed when it is difficult to find persons who possess the desired characteristics of the researcher [28]. Those who were interested in and conversant with the subject, such as experts in TPM, genetics, epidemiology, physiology, pharmacy, and general medicine, were considered for recruitment. To achieve maximum variation in sampling, we made efforts to include a wide variety of specializations and professional experiences in our sampling.

Data collection

A semi-structured questionnaire with six parts was used for the interview: 1) demographic information and the participant's field of study; 2) similarity between the concept of TPM and PM; 3) acceptability of the temperamentology view and temperament-based treatment; 4) the role of temperament in improving the diagnostic and therapeutic process of patients; 5) reducing PM's reliance on genetic and molecular concepts based on phenotypes; and 6) using concepts from traditional medicine to strengthen and accelerate the implementation of PM. In this study, the interviews were not face-to-face. To interview and complete the questionnaire, the Nazarejam system (https://Nazarejam.ir) was used. Nazarejam was an online platform that collected data electronically. The link to the Nazarejam system was sent via e-mail, social media, and short message service (SMS) to participants. At first, in both text and multimedia formats, the definition of TPM and PM was explained to respondents. Then, the system proposed the questions and allowed them to respond in either written or verbal form. Moreover, respondents had the option to feedback on their comments, questions, and suggestions, and obtained the research team's responses interactively. In addition, they could see the opinions of others. Also, after analyzing the opinions of the participants, if there were any questions, they were asked to explain their views. Interviews and experts' viewpoints, were recorded through the Nazarejam system, after obtaining informed consent. The duration of each interview varied from 30 to 65 min.

Data analysis

Following the record of each participant's interview, the output of the system was immediately provided and implemented in Microsoft Word 2016. In our study, the recruitment continued until the saturation was reached. Finally, 37 people were interviewed. In the 34th interview, data saturation was achieved. This was confirmed by the absence of any new themes emerging in further three interviews. The data analysis process involved several sequential steps: initial familiarization, coding, theme generation, theme review, theme definition and naming, and final writing. The content analysis approach, assisted by MAXQDA 2018 software, was used to analyze the data. After reading the text and reaching a general understanding of its content, primary codes were determined. Then, similar primary codes were categorized into classes (themes) and sub-classes. After coding all texts and extracting issues, categories and conceptual frameworks were created and content hidden in the data was extracted.

Four criteria of credibility, transferability, dependability, and confirmability were used to ensure the reliability of the data [29]. Prolonged engagement (immersion) with the subject matter was used to increase the credibility of the data. The opinions of the research team were used regarding questions, opinion recording process, participant selection, and data analysis. For dependability, the opinions of a researcher outside the research team who was familiar with qualitative studies were used regarding the classification of codes and conceptual framework. To ensure the confirmability of the findings, experts' perspectives about registered opinions, codings, and structural models were received and applied. To enhance transferability, the researchers meticulously documented all recorded opinions, allowing for traceability and follow-up at every stage. The process of data collection and analysis was conducted simultaneously.

Results

A total of 37 people with expertise in genetics, TPM, physiology, pharmacy, epidemiology, and general medicine registered their opinions. These participants were aged between 25 and 60 years and had been recruited from various cities of the country (Table 1).

The following categories and conceptual framework were created based on the content analysis (Table 2).

A thematic analysis of opinions revealed that the participants' overall attitude was positive. It was also disclosed that TPM experts expressed more supportive opinions than other groups (Chart 1).

Similarity between TPM and precision medicine

Most participants agreed with the conceptual similarities between TPM and precision medicine. Because both approaches focus on treating people based on their unique characteristics. However, there were a few participants who disagreed with this concept of similarity. Opinions on the presence or absence of similarities were varied and we mentioned some of them as follows:

Table 1. Demographic information of the participants for the comparability of Traditional Persian medicine with the new concepts of Personal and precision medicine

Variable		No. (%)
Gender		
	Female	12 (32)
	Male	25 (68)
Age		
	25-35	4 (11)
	36-46	14 (38)
	47-60	19 (51)
Work experience		
	10<	12 (32)
	10-20	14 (38)
	20>	11 (30)
Field of study		
	Genetics	9 (24)
	Traditional Persian Medicine	9 (24)
	Physiology	5 (14)
	Pharmacology	4 (11)
	Epidemiology	6 (16)
	General medicine	4 (11)
Service location		
	Kerman	13 (35)
	Tehran	5 (14)
	Mashhad	5 (14)
	Shiraz	3 (8)
	Sabzevar	3 (8)
	Golestan	2 (5)
	Qom	2 (5)
	Bam	1 (3)
	Zabol	1 (3)
	Sanandaj	1 (3)
	Borojerd	1 (3)

"TPM has been saying for many years that although the patient's main problem limits the range of measures and treatments to some extent, to make a better choice among various treatment options, each patient should be examined according to other symptoms and, of course, his inherent characteristics." (TPM expert, Pt. 22)
"TPM in Iran is practiced by those who are neither literate nor trying to improve it. It is just empty advertising and elementary studies on drugs. There should be a fundamental review by experts in this field." (Epidemiologist, Pt. 16)

The role of temperamentology in patients' diagnosis and treatment processes

Overall, participants' opinions on the influence of temperament on diagnosing and treating can be categorized into two main groups. The first group believed that temperamentology played a significant role in improving disease diagnosis and treatment. The second group acknowledged the potential usefulness of temperamentology but emphasized the need for scientific evidence.
"Of course, the temperament of people differs according to the type of immune response and genetics, so the level of performance differs also, which is completely obvious." (Geneticist, Pt. 7)
"If we acquire scientific discoveries and laboratory documents that substantiate this matter, such a perspective has the potential to significantly enhance the diagnosis and treatment of diseases. Also, it can address a crucial gap in contemporary medicine." (PhD in Physiology, Pt. 34)

Reducing precision medicine's reliance on

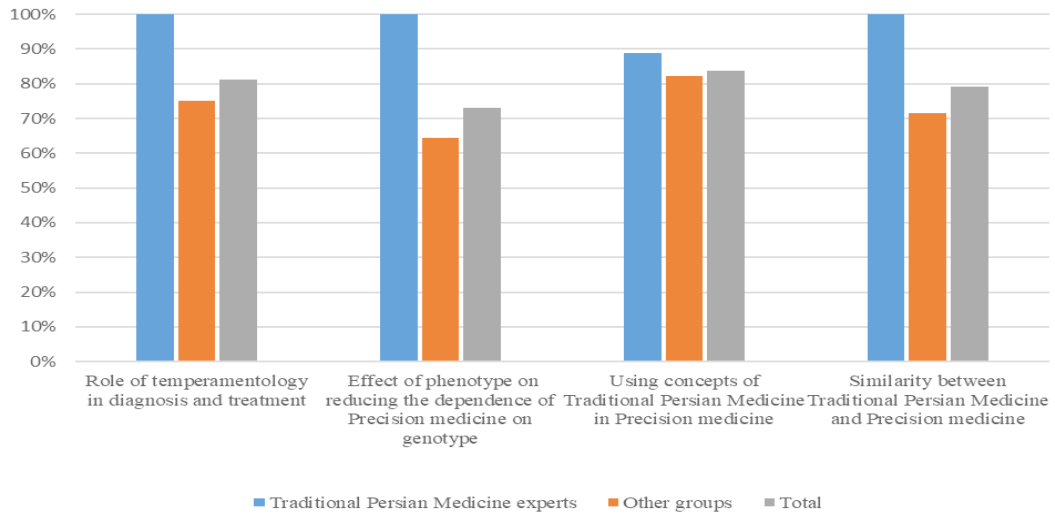

Chart 1. Comparability of Traditional Persian Medicine with the new concepts of personal and precision medicine: opinions of Traditional Persian Medicine experts and other medical groups.

Table 2. Thematic analysis of the data derived from expert comments about the comparability of Traditional Persian medicine with the new concepts of personal and precision medicine

The role of temperamentology in diagnosis and treatment	Supporters perspective	In different temperaments, genetics, the type of immune response, and function are different. It is effective in regulating immunological and inflammatory responses, as well as pain. It can increase the effectiveness of the drug. Before prescribing appropriate drugs, people's temperaments should be determined. It can help diagnose and treat patients by differentiating them and selecting better drugs.
	Hesitant perspective	If the evidence of modern science confirms it. It should be checked. First, be used in the diagnosis and, after confirming the evidence, in treatment. If temperamentology considered the concepts of phenotype, it would be helpful.
Reducing the dependency of precision medicine on genetic and molecular concepts with the help of phenotypes	Supporters perspective	The phenotype is based on genetics. Although genetics is more accurate, the phenotype cannot be ignored. A phenotype is cheaper and more available than a genotype. By maintaining genetic concepts, phenotypic concepts can be added.
	Hesitant perspective	It is necessary to conduct studies in this field. If traditional medicine approaches molecular and genetic findings. If a direct association between phenotype and genetics is found. Through evaluating the effect of the environment on the phenotype.
	Opponents perspective	Many diseases are genetic. Genetics cannot be changed.
Using concepts of Traditional Persian Medicine to strengthen and accelerate the implementation of Precision medicine	Hesitant perspective	If there is an association between different genes and temperaments. If the concepts of phenotype and genotype get close to each other. Rely on the commonalities of the two medicines. By confirming the association of different temperaments with the concepts of personalized medicine. If temperamental variations reflect genetic variations. Unless traditional medicine adapts to modern medicine.
	Opponents perspective	Traditional medicine's drugs are not specific. In traditional medicine, personalized treatment is not possible.
The similarity between Traditional Persian Medicine and Precision Medicine	Supporters perspective	The phenotype of traditional medicine is the result of the genotype of personalized medicine in a specific context. Both are preventive. Both rely on individual differences. Traditional medicine has been personalized based on people's temperaments.
	Opponents perspective	Temperaments are not personalized for people. Traditional medicine does not have a scientific basis.

genetic and molecular concepts based on phenotypes

Although the majority of participants had positive opinions about this section (ex: Pt. 22), some had doubts about it (ex: Pt. 23). Some believed that precision medicine would only be possible through genetics (ex: Pt. 8).

"The phenotype is the gene's final product." Many genes are not blocked, expressed, or mutated in any way. Finally, the physicochemical properties determine the patient's condition; however, not all of them fall under phenotype. For this term, some propose Clinomics (clinical symptoms). Using phenotype or Clinomics to classify patients, on the other hand, is more accessible, if not easier!" (TPM expert, Pt. 22)

"The phenotype does not express all genetics. Similarly, not all genes are expressed in phenotypic traits. Genetics appears to be more accurate. However, if we regard people's behaviors and lifestyle as part of the phenotype, then the phenotype is essential in

some respects, and we cannot focus only on genetics." (Pharmacist, Pt. 23)
"The personalization of treatment is a genetic work; for instance, genetic testing reveals a person's HLA and the desired HLA therapeutic vaccine is prepared based on how the antigen is supplied." (Geneticist, Pt. 8)

Using TPM approaches to strengthen and accelerate precision medicine implementation

Although the majority of participants had positive opinions on this issue, they expressed doubts. They believed that if TPM is adapted to modern medicine, traditional medicine notions can be used to enhance and accelerate the implementation of precision medicine. Furthermore, TPM concepts should be thoroughly evaluated. Also, investigations should be conducted to study the association between temperament and phenotype, as well as phenotype and genotype.
"Personally, and based on scientific evidence, I believe that people's genetics shape their immune and defensive responses to a variety of disorders, including cancer, autoimmunity, infection, and allergies. To prove or disprove the topic asked, investigations on the association between different temperaments from the perspective of traditional medicine or other TPM notions are required, and it is not possible to simply comment on this matter." (Geneticist, Pt. 10)

Discussion

This study utilized a qualitative approach and conducted interviews with experts to investigate the concepts of personal and precision medicine in TPM and modern medicine. The majority of participants expressed support for utilizing phenotype as a means to reduce the reliance on genetics in precision medicine. Moreover, most participants believed that temperament played a crucial role in the diagnosis and treatment of diseases, which can be highly useful with further research and the validation of evidence. Although most participants agreed that TPM and PM share some similarities, some of them were unsure of how to apply TPM's concepts to strengthen and hasten the implementation of PM. The participants emphasized that if TPM adapts to modern medicine and the association between various genes and temperaments is shown, then the concepts of TPM can be employed in PM.
Most of the participants agreed that using phenotype instead of genetics could reduce dependence on genetics for PM. However, some participants were skeptical and felt that more research in molecular and genetic fields should be conducted to determine the connection between phenotype and genetics. Studies conducted on the association between phenotype and genotype have shown that the concerns of these people are justified, and there is a need to conduct multi-centered studies with a larger sample size and extensive supervision to determine the association between genotype and phenotype [30-32]. It has long been understood that phenotype is influenced by a combination of genotype, environment, and their interaction [21]. Family history has been identified as the main factor influencing phenotype [33], suggesting that both genotype and phenotype can be inherited. If the link between genotype and phenotype in various diseases can be established, the identification of pathogenic phenotypes could enable early disease diagnosis [34]. Therefore, shifting from relying on genetics to utilizing phenotype, which is more easily accessible and cost-effective, would be possible.
The participants all agreed that identifying people's temperaments could lead to more effective diagnosis and treatment by prescribing suitable medications and improving medicine's effectiveness. Previous studies have found a link between temperament and diseases [35], but research in this field is still incomplete. The creation of temperaments is influenced by genetics, environment, and the interaction of them. Temperaments are thought to be the hereditary component of personality [36], and they are the same as phenotypes. As a result, certain temperaments can be inherited within families. To enhance the validity of temperamentology studies, issues such as multiple temperament classifications, different methodologies, the lack of standardized questionnaires, and the absence of expert involvement should be addressed [14]. By improving the reliability of temperamentology's findings, any doubts about its significance in diagnosing and treating diseases will be eliminated, and it can be effectively utilized.
The participants all agreed that there are significant similarities between PM and TPM, and considered the greatest similarity in treatment based on individual differences. A small percentage of participants disagreed with this resemblance and believed that, as temperaments are common to everyone, TPM cannot provide treatment based on personal distinctions. However, research has proven that in TPM each person has a distinct temperament, and each person's health situation is unrelated to the other's. Additionally, a comparable condition manifests differently in several individuals, based on their temperaments [17]. One of the critics argued that TPM lacked a precise scientific basis and had insufficient research conducted on it. Traditional medicine suffers from methodological shortcomings, and the methodological quality of conducted studies is also limited [37]. But TPM has been one of the most important schools of traditional medicine and an exporter of science, doctors, and medicine to different parts of the world [38]. Also, in recent years, the WHO has recommended traditional medicine as a complementary or alternative to

modern medicine [39]. If traditional medicine is connected with science, it will be very valuable [40]. Therefore, the potential capacities of TPM should not be ignored. TPM can gain more support by updating and standardizing its studies.

The participants noted that, if TPM's concepts are applied in modern medicine and the association between different genes and temperaments is confirmed, it could enhance and accelerate the implementation of PM. The scientific community understands the significance of integrating TPM with modern medicine to establish a comprehensive medical model [38]. Integrative medicine's growth fills in the weaknesses and enhances the strengths, which is crucial for the advancement of medical research. Therefore, it is important to understand the similarities and differences between TPM, modern medicine, and PM to develop integrated medicine. While Ayurveda studies have already examined the correlation between body types and genotypes and found it to be significant [41], more research is needed in TPM to investigate the connection between genotypes and temperaments. If significant associations are discovered, implementing TPM concepts in PM will become easier.

Limitations

The study's findings are based on expert opinions; thus, they may not be definitive.

Conclusion

Precision medicine can benefit from the concepts of personalized medicine found in TPM. Applying temperamentology will be useful in the prevention and treatment of diseases. It is feasible to reduce the dependency of precision medicine on genetics through phenotype. Furthermore, the concepts of TPM could be used to accelerate the implementation of precision medicine. However, several obstacles need to be overcome to achieve these goals. Some of these challenges, such as determining the correlation between temperament and genotype, require fundamental measures, such as providing appropriate infrastructure and conducting accurate and reliable studies. However, some challenges, such as the lack of valid studies on the association between temperaments and diseases as well as phenotype and genotype, can be addressed by updating and standardizing studies.

Suggestions

It is suggested to conduct accurate and trustworthy investigations on the associations between phenotype and genotype, temperament and disease, as well as genotype and temperament.

Conflict of interests

There is no conflict of interest between the authors.

Acknowledgments

This article is the result of a doctoral thesis that was reviewed and approved by Kerman University of Medical Sciences (ethical code: IR.KMU.REC.1401.569). Also, the authors acknowledge all the participants who participated in this study.

References

[1] Mojahedi M, Naseri M, Majdzadeh R, Keshavarz M, Ebadini M, et al. Reliability and validity assessment of Mizaj questionnaire: a novel self-report scale in Iranian traditional medicine. Iran Red Crescent Med J 2014;16:e15924.

[2] Carver RB, Castéra J, Gericke N, Evangelista NA, El-Hani CN. Young adults' belief in genetic determinism, and knowledge and attitudes towards modern genetics and genomics: the PUGGS questionnaire. PloS One 2017;12:e0169808.

[3] Marcon AR, Bieber M, Caulfield T. Representing a "revolution": how the popular press has portrayed personalized medicine. Genet Med 2018;20:950-956.

[4] Elemento O. The future of precision medicine: towards a more predictive personalized medicine. Emerg Top Life Sci 2020;4:175-177.

[5] König IR, Fuchs O, Hansen G, von Mutius E, Kopp MV. What is precision medicine? Eur Respir J 2017;50:25.

[6] Collins SC. Precision reproductive medicine: multigene panel testing for infertility risk assessment. J Assist Reprod Genet 2017;34:967-973.

[7] Wu X-Z. Traditional Chinese medicine should not be ignored during the development of precision medicine with Chinese characteristics. Trad Med Res 2016;1:105.

[8] Zhou X, Li Y, Peng Y, Hu J, Zhang R, et al. Clinical phenotype network: the underlying mechanism for personalized diagnosis and treatment of traditional Chinese medicine. Front Med 2014;8:337-346.

[9] Pirmohamed M. Personalized pharmacogenomics: predicting efficacy and adverse drug reactions. Annu Rev Genomics Hum Genet 2014;15:349-370.

[10] Schmidt KT, Chau CH, Price DK, Figg WD. Precision oncology medicine: the clinical relevance of patient-specific biomarkers used to optimize cancer treatment. J Clin Pharmacol 2016;56:1484-1499.

[11] Scheinfeldt LB, Schmidlen TJ, Gerry NP, Christman MF. Challenges in translating GWAS results to clinical care. Int J Mol Sci 2016;17:1267.

[12] Reardon S. Precision-medicine plan raises hopes: US initiative highlights growing focus on targeted therapies. Nature 2015;517:540-541.

[13] Zeinalian M, Eshaghi M, Naji H, Marandi SMM, Sharbafchi MR, et al. Iranian-Islamic traditional medicine: An ancient comprehensive personalized medicine. Adv Biomed Res 2015;4:12.

[14] Akhtari M, Moeini R, Mojahedi M, Gorji N. Assessment the studies on the concept of Mizaj (temperament) in Persian Medicine. J Complement Integr Med 2020;17:14.

[15] Yousefifard M, Parviz M, Hosseini M, Ebadiani M, Keshavarz M. Mizaj past, present and future. Physiol Pharmacol 2013;16:328-339.

[16] Jafari S, Abdollahi M, Saeidnia S. Personalized medicine: a

confluence of traditional and contemporary medicine. Altern Ther Health Med 2014;20:31-40.
[17] Nimrouzi M, Zare M. Principles of nutrition in Islamic and traditional Persian medicine. J Evid Based Complement Altern Med 2014;19:267-270.
[18] Shirbeigi L, Zarei A, Naghizadeh A, Alizadeh Vaghasloo M. The concept of temperaments in traditional Persian medicine. Trad Integr Med 2017;5:143-156.
[19] Rezaeizadeh H, Nikfar S, Rahimi R. Perspectives of personalized medicine in traditional Persian medicine. J Semnan Univ Med Sci 2022;7(3):12-25.
[20] Jafari M, Rezadoost H, Karimi M, Mirzaie M, Rezaie-Tavirani M, et al. Proteomics and traditional medicine: new aspect in explanation of temperaments. Res Complement Med 2014;21:250-253.
[21] Te Pas MF, Madsen O, Calus MP, Smits MA. The importance of endophenotypes to evaluate the relationship between genotype and external phenotype. Int J Mol Sci 2017;18:472.
[22] Naseri M, Rezaeiazdeh H, Taheripanah T, Naseri V. Temperament theory in the iranian traditional medicine and variation in therapeutic responsiveness, based on pharmacogenetics. J Islam Iran Trad Med 2010;1:237-242.
[23] Shahabi S, Hassan ZM, Mahdavi M, Dezfouli M, Rahvar MT, et al. Hot and cold natures and some parameters of neuroendocrine and immune systems in traditional Iranian medicine: a preliminary study. J Altern Complement Med 2008;14:147-156.
[24] Farsani GM, Naseri M, Hosseini S, Saboor-Yaraghi AA, Kamalinejad M, et al. The evaluation of basic and neurohormonal parameters in hot or cold temperament person proposed in iranian traditional medicine: an observational study. J Contemp Med Sci 2020;6:213.
[25] Rezadoost H, Karimi M, Jafari M. Proteomics of hot-wet and cold-dry temperaments proposed in Iranian traditional medicine: a Network-based Study. Sci Rep 2016;6:30133.
[26] Ho D, Quake SR, McCabe ER, Chng WJ, Chow EK, et al. Enabling technologies for personalized and precision medicine. Trend Biotechnol 2020;38:497-518.
[27] Grossoehme DH. Overview of qualitative research. J Health Care Chaplain 2014;20:109-122.
[28] Valerio MA, Rodriguez N, Winkler P, Lopez J, Dennison M, et al. Comparing two sampling methods to engage hard-to-reach communities in research priority setting. BMC Med Res Method 2016;16:1-11.
[29] Nowell LS, Norris JM, White DE, Moules NJ. Thematic analysis: Striving to meet the trustworthiness criteria. Int J Qual Methods 2017;16:160.
[30] Gana S, Serpieri V, Valente EM. Genotype–phenotype correlates in Joubert syndrome: A review. Am J Med Genet C Semin Med Genet 2022;4:72-88.
[31] Vasko A, Drivas TG, Schrier Vergano SA. Genotype-phenotype correlations in 208 individuals with coffin-siris syndrome. Genes 2021;12:937.
[32] Yang L, Shu X, Mao S, Wang Y, Du X, et al. Genotype–phenotype correlations in Angelman syndrome. Genes 2021;12:987.
[33] Casini A, De Moerloose P. Can the phenotype of inherited fibrinogen disorders be predicted? Haemophilia 2016;22:667-675.
[34] Zhang A, Sun H, Wang P, Han Y, Wang X. Future perspectives of personalized medicine in traditional Chinese medicine: a systems biology approach. Complement Ther Med 2012;20:93-99.
[35] Kamali MA, Khodadoost M, Tavakoli H, Kamalinejad M, Gachkar L, et al. The role of syndrome differentiation in the clinical efficacy of Punica granatum on patients with ulcerative colitis. Iran J Med Sci 2016;41:S15.
[36] Kőrösi B, Gyöngyösi H, Batta D, Laszlo A, Kovacs I, et al. Evaluation of affective temperaments and arterial stiffness in different hypertension phenotypes. Hypertens Res 2021;44:47-54.
[37] MacArtney JI, Wahlberg A. The problem of complementary and alternative medicine use today: eyes half closed? Qual Health Res 2014;24:114-123.
[38] Shirafkan H, Taghavi M, Mirzapor M. Investigating the difference between principals of Iranian traditional medicine and modern medicine for providing a model for integrated medicine. Islam Health J 2014;1:10-15.
[39] World Health Orgenization. WHO global report on traditional and complementary medicine 2019. Geneva: World Health Organization; 2019. https://apps.who.int/iris/handle/10665/312342
[40] Yuan H, Ma Q, Ye L, Piao G. The traditional medicine and modern medicine from natural products. Molecules 2016;21:559.
[41] Ghodke Y, Joshi K, Patwardhan B. Traditional medicine to modern pharmacogenomics: Ayurveda Prakriti type and CYP2C19 gene polymorphism associated with the metabolic variability. Evid Based Complement Altern Med 2011;2:4.