

THE METHODOLOGY OF FOOD DESIGN.

PART 1. THE INDIVIDUAL ASPECT

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Abstract

Innovative technologies for food raw material processing and food production are becoming globally important within the framework of modern biotechnology. The need to create a universal methodology for food design and the importance of its implementation in different lines of human life activity are obvious. Within the paradigm of modern biotechnology, personalized diets that take into consideration the genetic characteristics of consumers are becoming more and more popular. Nutrition science deals with the development of this direction. It is divided into nutrigenetics and nutrigenomics. Nutrigenetics investigates an effect of modifications in genes on absorption of metabolites, nutrigenomics investigates how food components affect the work of genes. In this work, we consider mutations that influence the assimilation of metabolites and contribute to nutrigenetic research. The work is aimed at finding and studying genes responsible for eating behavior. Methods of analysis of genetic polymorphisms and modern achievements of nutrigenetics in the development of personalized nutrition are considered. The review allowed us to find and describe the genes that influenced human eating behavior: the role of genes, their localization, polymorphisms affecting the metabolism of nutrients and food preferences are indicated. Thirty four genes that influence eating behavior were identified, and significant shortcomings of current methods / programs for developing personalized diets were indicated. Weaknesses in the development of nutrigenetics were identified (inconsistency of data on SNP genes, ignoring population genetics data, information that is hard for consumers to understand, etc.). Taking into consideration all shortcomings, an approximate model for selecting a personalized diet is proposed. In the future, it is planned to develop the proposed model for making up individual diets.

Introduction

Interrelation between nutrition and health is a cornerstone of human life. Questions of nutrient interaction and their effect on the human body allow the complex study of regularities of biophysical, biochemical and energy mechanisms ensuring life activity.

Nutrition is one of the most important factors of health support. Medical data indicate interrelation between nutrition and the most common noncommunicable diseases. Many cardiovascular diseases, different cancers, diabetes, gout, obesity are directly linked with excess intake of calories due to fats, simple carbohydrates, table salt, diets with reduced content of vitamins and dietary fibers.

Innovative technologies of food raw material processing and food production are becoming globally important within the framework of modern biotechnology [1]. At the current stage of the biotechnology development, nutrition science is not only the topical interdisciplinary research direction, but also rapidly developing. Personalized nutrition is individually adapted nutrition. With this approach, the gender, age, level of physical activity, presence of different chronic diseases and personal food preferences are taken into account. Individually tailored nutrition is aimed at prevention and treatment of different diseases, reduction of a negative effect of harmful environmental factors, support of healthy lifestyle. It is impossible to choose a diet without relying on achievements of modern genetics and nutrition science.

The paper is devoted to the study of food design principles. A necessity to create a universal methodology for food design, an importance of its realization in different directions of human life activity are obvious. The presented problem has different history of highlighting questions about methods for food design. There is a certain tradition of studying theoretical foundations and specific methods for using principles of balanced food design. Traditionally, food design is linked with formalization of qualitative and quantitative concepts about the rational use of food products [2]. The nutritional value of one or another product (proteins, fats, carbohydrates and their ratio) is placed in the center of the traditional design methods. At present, not only nutritional and biological value, but also a variety of medical, technological, economic, social and many other factors are taken into account when designing food products. The center of the modern biotechnological research is an individual [3, 4].

We presume that there is a relation between biotechnological, nutrition factors and a human diet. For complex examination of eating behavior and prescription of a corresponding diet with consideration for personal preferences of consumers, it is necessary to study methods for food design, including complete analysis of the human genome for polymorphisms in different gene groups. The scientific novelty of this work resides in the fact that there are no available studies that examine systemically and in detail genes and their polymorphisms influencing human eating behavior.

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In our previous studies, we have already dealt with the indicated problem [5, 6, 7]. Principles and regularities of formation of dispersed food systems with functional properties are demonstrated from the current viewpoint. The peculiarities that should be taken into account in the development of functional food recipes are shown in [6, 7, 8]. This paper will actualize specific methodological aspects of the product design process in the personalized aspect.

The aim of this study is to assess the effectiveness of food design methods and detect genes influencing food preferences by analysis of publications on the indicated theme. In particular, our research focus includes the genes that are responsible for fat and carbohydrate assimilation, food intolerance, vitamin metabolism, taste sensation, oxidation of xenobiotics, food preferences and food addiction.

Materials and methods

The search of the literature carried out in November 2019 and updated in September 2020 considered papers published from January 1, 2015 up to now. For cross-validation, we used databases of papers from Scopus, Web of Sciences, Google Scholar, PubMed, LitVar, GeneCards, SNPedia, 1000 genomes (1KGP), Russian scientific electronic libraries (<https://www.elibrary.ru>; <https://cyberleninka.ru>). Search queries were formed by key words 'genes', 'gene polymorphism', 'genetic diseases', 'eating habits' and so on.

Results and discussion

In the national research, the development of functional products is based on the principles of food combinatorics (exclusion, fortification, replacement of a certain nutrient according to a human health state). A food product itself, its nutritional value, different recipe modifications are in the center of the traditional methodology. Modern methods for food product design have the anthropocentric direction. They are guided by requirements of individuals, their social-economic status, place of residence, peculiarities of the life activity of the body and genetic "memory" in general. The improvement of recipe design of multi-component food products is largely linked with the use of one or another method of linear, experimental-statistical programming or the object-oriented approach.

For example, A. B. Lisitsyn and colleagues proposed a system modeling methodology for multi-component food products [9]. The essence of such tasks is selection of an optimal option from multiple possible recipe options by a targeted feature. O. N. Krasulya et al. (2015) examined the question of designing multi-component food products with consideration for information about actual values of functional-technological properties (FTP) of main raw materials and ingredients, kinetics of biochemical and colloid processes, analytical and empirical dependencies [10]. The study [11] proposes to use neural network technologies. A program in the high-level language Object Pascal was developed to design gerodietetic bread compositions [12]. M. A. Nikitina et al. (2018) pro-

posed to use the multi-criteria optimization method — the Pareto method [13].

A special place in modern biotechnology and food combinatorics is given to nutrition science research linked with the development of nutrition systems, diets and so on. The nutrigenetics field includes the genetic basis of different reactions of individuals to the same nutrients. Creation of an individual diet is based on analysis of genetic information, which needs a list of genes. Genes participating in gaining an excess weight take an important place in the nutrition research [14].

- **Genes responsible for carbohydrate and fat assimilation.** There are nine genes responsible for carbohydrate and fat assimilation: ADRB2 (polymorphisms rs1042714, rs1042713), TCF7L2 gene (rs12255372, rs7903146), FABP2 gene (rs1799883), PPARG gene (rs1801282), CETP gene (rs5882), ADRB3 gene (rs4994), ApoA5 gene (rs662799, rs3135506), LEPR gene (rs1137101) and ApoE gene (rs429358, rs7412).
- **Genes responsible for food intolerance.** The list includes the HLA-DQ and MCM6 (rs4988235) genes, which cause monogenic diseases. The HLA genes are part of the immune response mechanism; that is, they help the immune system to differentiate self-proteins of the body from foreign proteins — viruses and bacteria.
- **Genes responsible for vitamin metabolism.** They include BCMO1 (rs7501331, rs12934922, rs119478057), Alpl (rs1256335) and NBPf3 (rs4654748), MTNFR (rs1801133), FUT2 (rs602662), VDR (rs1544410) and GC (rs2282679), FI7ADS1 (RS14547).
- **Genes responsible for taste sensation.** GLUT2 (rs5400) is responsible for sweet taste sensitivity, TAS2R38 (rs1726866) for bitter taste, CD36 (rs1761667) is linked with taste sensitivity and preference for fat. ADD1 (rs4961) and CYP11B2 (rs1799998) are associated with salt sensitivity. The GLUT2 (or SLC2A2) gene encodes protein that transports glucose through the cell membrane; as a result, the gene is a good "sensor" of glucose sensitivity [15].
- **Genes responsible for metabolism of xenobiotics.** MnSOD (rs4880), GSTP1 (rs947894) and CYP1A2 (rs762551) take part in oxidation of xenobiotics entering the body with food.
- **Genes responsible for eating behavior.** The list of genes influencing food preferences includes FTO (rs9939609), MC4R (rs17782313), DRD2 (rs1800497). In this study, food preferences mean a tendency to overeat caused by genetic polymorphisms. The FTO gene encodes the protein that takes part in energy metabolism, oxidation reactions and metabolism of fatty acids.
- **Genes responsible for food addiction.** Genes responsible for the development of food addiction include ADH1B (rs1229984) and ALDH2 (rs671), CHRNA5 (rs16969968) and CHRNA3 (rs1051730). The ADH1B and ALDH2 genes are responsible for sensitivity to alcohol [16].

Definitely, available data are somewhat contradictory. It is impossible to give the decisive answer to the question about roles of genes, their polymorphisms in food preferences and several diseases. It is due to several reasons. The first one resides in the fact that a small number of people from different ethnic groups and different life conditions participated in the research [17, 18, 19, 20]. Sampling results are not fully relevant. The complex study of the human genome and use of population genetics data are necessary for system assessment. The second reason resides in the character of material under study. For analysis and assessment, we used data from already published papers and not from the initial data presented by authors. This focus of analysis significantly narrowed the review.

Today, it is possible to find databases that combine information for research in the field of nutrigenomics, for example, the studies of Oxford scientists NutriGenomeDB [21]. The authors' materials allow entering a gene or genes of interest and obtaining information about their expression. Comparatively recently, a model of a personalized diet has been developed, which includes individual restrictions (past medical history, DNA, habitat, climate, life style and energy expenditure), the purpose of a diet (to maintain health or physical fitness, longevity, taste preferences, a balanced diet that promotes fast saturation with a small portion) [22]. The presented model is based on the following criteria: information architecture, service technologies, production technology [23].

In addition, a method for the formation of personalized nutrition based on DNA analysis with an emphasis on excess weight and food intolerance was developed

[24]. The method includes the study of the polymorphic sites of the LCT, PPARG, ADRB2, FABP2, TCF7L2 genes and identification of the HLA-DQ haplotype. A corresponding diet is recommended depending on how the polymorphism influences the excess weight and/or food intolerance, and/or the presence of HLA-DQ haplotype. The examined method is effectively used by our national colleagues to select an individual diet. The authors believe that the method is well suited for the indicated genes (LCT, PPARG, ADRB2, FABP2, TCF7L2, HLA-DQ), but these are not the only genes that can influence excess weight and food intolerance.

T. Matsuo et al. [25] demonstrated that a diet with the high/low fat content influences the PPARG gene expression. It is noted that if there is a polymorphism in the gene, a body weight decreases. I. Arkadianos et al. [26] used a nutrigenetic test to optimize nutrients in a human diet. They performed genetic testing (one of gene analyses was PPARG) and modified the Mediterranean diet according to the individual requirements of the body according to the test results. Therefore, nutrigenetics is a tool for improvement and optimization of adequate nutrition. It is an effective means for long-term changes in the lifestyle.

Weaknesses of the available methods and apps for the development of personalized diets include the following:

- they do not take into account genetic data;
- they are difficult regarding adherence to a diet (both in a product choice and in a regime), therefore, a consumer often has to quit, which is harmful for the body;
- applications are not translated into a corresponding language;

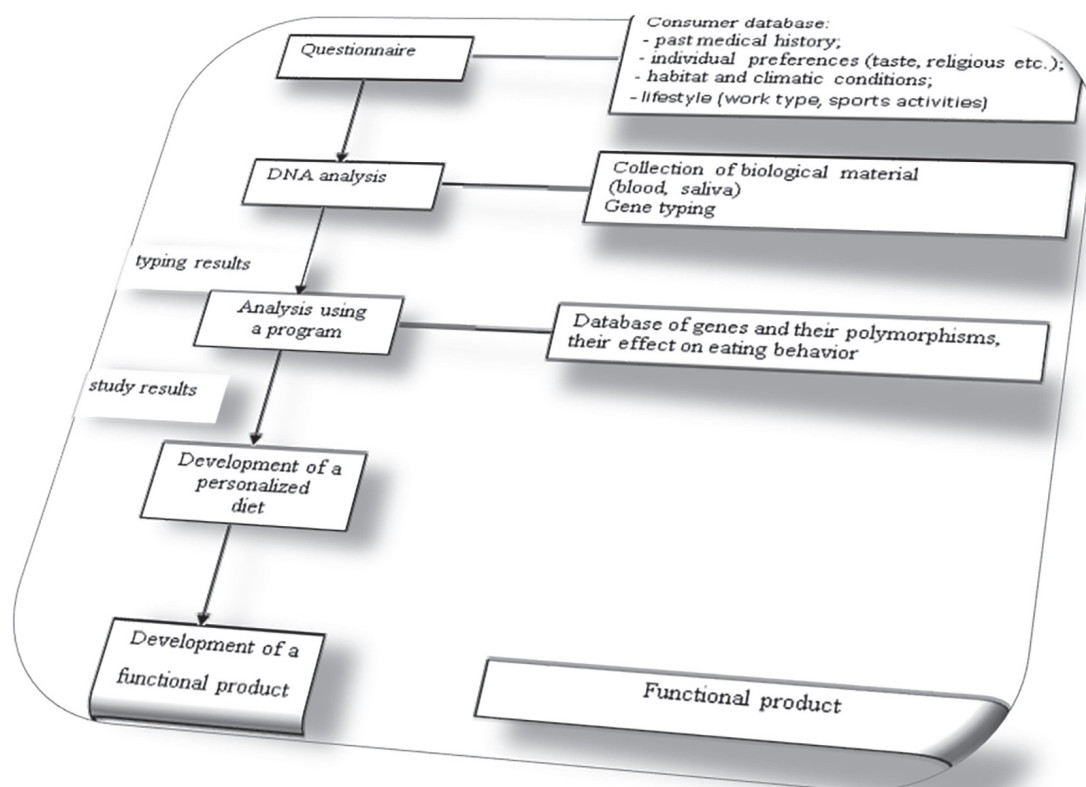


Figure 1. The model for the development of a personalized diet, which ultimate goal is production of a functional product [5,8].

- they should be paid for;
- information about a genetic predisposition is difficult to understand;
- population genetics is not taken into consideration.

Based on the presented weaknesses, a model for performing a nutrigenetic study was generated to create a personalized human diet (Figure 1).

The presented model consists of the following components. First, consumer survey questionnaire. It includes the past medical history, individual preferences (taste, religious), habitat, climatic zone of residence and lifestyle. All information should be entered into a protected database, which later on will be used for analysis of DNA testing results.

Second, DNA analysis (a gene or a set of genes that corresponds to the specified purpose is chosen with consideration for population genetics data). Materials (venous blood, buccal epithelium, saliva) are sampled, DNA is extracted and necessary polymorphisms are determined.

Third, analysis of data obtained using programs. A program analyzes data obtained upon extracted DNA typing, information from an individual questionnaire, data on genes and their influence on food behavior. In the end, the program gives a formed result;

Fourth, creation of personalized nutrition. An expert in nutrigenetics processes data obtained using a program and forms an individual diet for a consumer.

Fifth, development of a functional product. Based on obtained data and with a permission from consumers, optimal food components and nutrients are selected to develop a functional product of new quality based on genetic information and psycho-emotional preferences of a consumer [27].

Conclusion

The analyzed methods for formation of personalized diets have several weaknesses: some methods do not take into account genetic data; many diets are difficult regarding adherence (expensive products, tough regime), therefore, a consumer often quit a prescribed diet; the major-

ity of available programs are not adapted to foreign users; open access information about a genetic predisposition is difficult for understanding and interpretation of results; population genetics is not taken into consideration in designing diets. A significant drawback is analysis of a small number of genes. It is necessary to carry out complete analysis of the human genome for polymorphisms in different gene groups for complex consideration of eating behavior regularities, prescription of a corresponding diet. It is also important to take into account personal preferences of a consumer.

As a result of the analytical review, thirty eight genes responsible for food behavior were revealed. The obtained data indicate that the number of polymorphisms causing monogenic diseases is lower than the number of genes leading to appearance of polygenic diseases. It is possible to identify genes, which mutations can lead to the development of obesity (ADRB2, FABP2, PPARG, ADRB3, LEPR, FTO, MC4R); type 2 diabetes (ADRB2, TCF7L2, FABP2, PPARG, CETP, ADRB3, MTHFR, GLUT2, CD36); cardiovascular diseases (CETP, ApoA5, ApoE, MTHFR, GLUT2, CD36, ADD1, CYP11B2, MnSOD); oncology (MnSOD, GSTP1, CYP1A2, CHRNA5, CHRNA3); central nervous system diseases (CETP, ApoE, ALPL, NBPf3, MTHFR, TAS2R38, CD36).

Creation of a personalized diet envisages consideration for all genes influencing human eating behavior. It was established that substantiated dietetic recommendations based on a wide study of genes are not given in scientific literature despite the importance of nutrigenetic studies. It is linked with complexity of nutrigenetics as a science because there are many contradictory data about a role and effect of SNP genes responsible for eating behavior. In this sphere, there is a need for experts competent not only in genetics but also in dietetics. The future of the indicated multidisciplinary direction of studying methods for the development of personalized nutrition models resides in creation of qualitatively new technologies of functional food production that play an important part in human nutrition and life activity.

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