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# Bioelements and Bioelementology in Pharmacology and Nutrition: Fundamental and Practical Aspects

#### Additional information is available at the end of the chapter

# 1. Introduction

A.V. Skalny

The development of bioelementological approach can open the new perspectives in creation of integrative diagnostics of the health status and provision by "blocks of life" of the humans and provide the real personalized nutrition and therapy of diseases at etiological niveau – imbalance of bioelements.

Despite the biological role of chemical elements has come under intensive studying in the last decades, the "lack of multidisciplinary approach has been the Achilles heel of biological trace element research" [1]. The desire to integrate the "organic" and "inorganic" approach in studying the biological role of chemical elements is observed in a number of fundamental works. Since 2003 we put forward and develop the concept of bioelements and bioelementology as an integrative scientific direction [2, 3]. Bioelement is the elemental functioning unit of living matter, which is a biologically active complex of chemical elements as atoms, ions and nanoparticles with organic compounds of exogenous (primary) or biogenous (secondary) origin. Bioelements include any chemical structures found in living nature, but which do not have a set of fundamental properties of living things: metabolism, variability, reproduction and heredity. The assembly of bioelements can be called "bioelementome". We propose to subdivide bioelements into simple (atoms, ions, among them structural elements C, H, N, O, P, S, Si, Ca, electrolytic K, Na, Ca, Cl, Mg, enzymatic Mg, Fe, Zn, Cu, Mn, Co, Cr, Mo, Se, Sn, F, I, Ni, V, B, and water as the universal solvent), and complicated ones, consisting of the abovementioned 68 molecules (8 of them are nucleosides, which compose DNA and RNA, 20 are natural amino acids necessary for protein synthesis, at least 32 glycans, 8 types of lipids). Also, bioelements can be subdivided into primary, i.e. those which could exist before the origin of life, and secondary, i.e. those which have formed as production of living organisms.



In principle, bioelements include any chemical structures found in living nature, but which do not have a set of fundamental properties of living things: metabolism, variability, reproduction and heredity. Primarily, these are organogens (C, H, N, O), P, S and representatives of four classes of small organic molecules which compose the cells: amino acids, nucleotides, sugars, fatty acids, - and coordination structures, aquated ions of vital macro and trace elements and water as well. Bioelements can continuously form from ionic compounds when they enter the cell. Inside the cell, biopolymers and their complexes create a complicated, coordinated and regulated system for transformation of substances. Cell is the main place of natural birth of secondary bioelements and their destruction. Biosphere is an assembly of bioelements and living organisms existing under permanent regulatory influence of physico-chemical factors of terrestrial and cosmic origin. The evolution of living organisms on Earth was accompanied by a broadening and deepening of the utilization of chemical elements and their compounds, i.e., in fact, by diversification, improvement and complication of bioelements. This process continues today in both natural and artificial environment, if allowing for the development of biotechnology, genetic engineering and pharmacy. The scientific discipline, which study bioelements, is proposed to be called bioelementology. This discipline could lay the foundation for the integration of bioorganic chemistry, bioinorganic chemistry, biophysics, molecular biology and other parts of life sciences.

### 2. Terminology and classification of bioelements and bioelementology

It is known that the chemical element exists in the organism not by itself, but in close interaction with other components. There are no any particular elements in cell, which are typical of only living nature. On the level of atom, there are no differences between chemical composition of organic and inorganic matter. The differences are found on higher, molecular level of organization.

Thus, the position and classification of the chemical elements in the Periodic System of Elements (PSE) does not permit any statement to be made about their functional essentiality or their acute or chronic toxicity for living organisms. This is due to the fact that the Periodic System is based on purely physicochemical aspects [4]. Therefore B.Markert developed an idea about a Biological System of Elements (BSE), which primarily considers aspects of basic biochemical and physiological research. As the author said, "Biological processes on the molecular level are frequently based on physical and chemical conditions... However, these physical and chemical regularities are frequently modified in biological systems". The BSE of B.Markert is obtained from data on correlation analysis, physiological function of individual elements in the living organism, evolutional development out of the inorganic environment and with respect to their uptake by the living organism as a neutral molecule or charged ion.

Atoms, atomic nuclei, elementary particles and fields that bind them, which have independent significance at the physicochemical stage of evolution, after being included in biological molecules lose this self-importance and play their role in the ensemble, called by me bioelement, where everything is interdependent, more complicated and at the same time more

vulnerable to external influence. Since the general conditions of biological evolution (the composition of biosphere), are continuously changing, a set of bioelements in a living organism can also change. This distinguishes them from chemical elements as objects of physicochemical stage, which remain identical to themselves along the course of evolution. So, bioelement is the elemental functioning unit of living matter, which is a biologically active complex of chemical elements as atoms, ions and nanoparticles with organic compounds of exogenous (primary) or biogenous (secondary) origin [3].

In principle, bioelements include any chemical structures found in living nature, but which do not have a set of fundamental properties of living things: metabolism, variability, reproduction and heredity. Primarily, these are organogens (C, H, N, O), P, S and representatives of four classes of small organic molecules which compose the cells: amino acids, nucleotides, sugars, fatty acids, – and coordination structures, aquated ions of vital macro and trace elements and water as well.

Bioelement is not a chemical element inside a molecular compound, but it is temporarily formed biocomplex, where the chemical element is bound by covalent (chelate) bond to the organic molecule. They should not be considered separately, because, interacting, together they produce biological effect of new quality [5].

If chemical element is a physicochemical unit of the matter's evolution, then bioelement – is a precursor of a biological unit, which has physicochemical nature. Fundamental differences between chemical elements and their compounds in abiogenic media and bioelements are described in Table 1.

Bioelements can continuously form from ionic compounds when they enter the cell. Inside the cell, biopolymers and their complexes create a complicated, coordinated and regulated system for transformation of substances. Cell is the main place of natural birth of secondary bioelements and their destruction.

According to modern views, the life processes cannot occur outside the cell. Therefore, the cell is considered as the smallest quantum of life, which, for managing its internal parameters and performing cell-cell interactions, use information, energy and substances, including bioelements, obtaining them from the environment. Bioelement is yet a substance. Cell (organism) is already a being. In our opinion (Figure 1), bioelements are precursors of living matter, a successful combination of which, particularly of polymer-ion reactions running autocatalytically, led to the formation of cells.

We proposed to call the assembly of bioelements "bioelementome" unlike elementome as an assembly of chemical elements and their compounds. Bioelementome is a particular continuum of molecules for the maintenance of biological units of evolution, possessing the ability to control the process, and biological objects [3].

However, when considering the biological role of bioelements, we should clearly distinguish two questions. The first is a question of initial formation and participation of bioelements in the origin of life. The second is a question concerning the role of bioelements in the modern

Chemical element	Bioelement
There in the biosphere and beyond. Weight is virtually unlimited.	There is mainly in biosphere. Outside biosphere, existence is temporary or impossible. Weight limited.
No quantitative limits.	The quantitative limit exists (depends on the space of the biosphere), as space available for organisms is limited.
	Limit of bioelements in the "mass of life" is constant in the course of geological time.
Exists in 2000-3000 species of minerals and corresponding chemical compounds.	Exists in millions of biological compounds.
Involved in formation of biologically inert natural objects by physico-chemical and geological processes, regardless of the previously existed natural objects.	Like a living organism is born only from another living organism, the new bioelement appears in biochemical transformations of the previous compounds (living objects, containing bioelements). In the course of geological time, some qualitative changes in forms of bioelements happen, which lead to the evolution of species or loss of some of them.
Its formation may occur in living bodies, varying in its manifestations and giving inert natural bodies elements incorporated in living natural body (e.g., concretions in kidneys).	Bioelements are formed not only during natural biochemical transformations of other living bodies, containing bioelements, but also can be created as a result of human activities (industrial synthesis of bioelements, biotech processes) from abiotic substances or other bioelements (from simple to complicated).
The process of turning abioelements in inorganic matter, as the processes that created the inert natural object, is reversible in time.	Formation of bioelement (i.e., form of existence of a chemical element in the biosphere), as well as the creation of a natural living body, is process irreversible in time.
Number of elements as components of inert natural objects, does not depend on size of the planet, but is determined by the properties of planetary matter – by energy.	Number of bioelements and number of living natural bodies are limited by the size of the biosphere (Earth).

**Table 1.** The fundamental main characteristics of chemical elements and bioelements (modified from ideas ofV.I.Vernadsky [5] about abiotic and botic matter) [3]

biosphere, at the anthropogenic stage of its development. I.e., one should separate the role of bioelements during early formation of the biosphere, and the modern role of bioelements.

On our opinion, as a result of chemical evolution on the Earth there appeared the "prebiological organic world" [7], a variety of living systems, which consists of the same set of molecules (bioelements), work by the same laws, have the metabolism based on the same principles, and the system of homeostasis that can control the flows of food, energy and information.

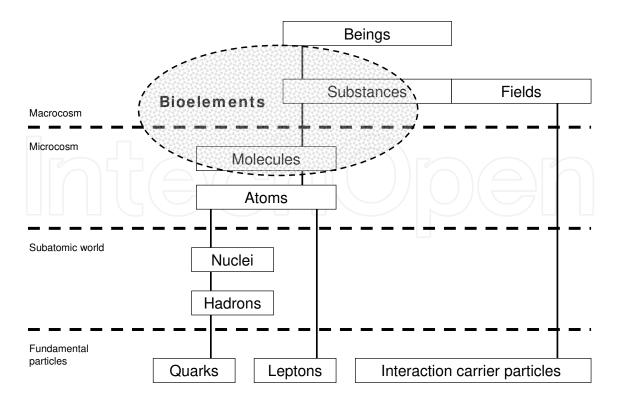


Figure 1. Structural levels of the matter (by Yu.N.Orlov [6], expanded by A.V.Skalny)

The biological evolution has led to a sharp increase in mass and diversity of the living substance on the planet, including formation of new chemical compounds and molecules, the novel (secondary) bioelements (in cells) [3].

So called "simple bioelements" produced four fundamental components of cellular life, which, according to J.D.Marth [8], divided into 68 molecular building blocks ("building blocks of life"). I.e., the simplest bioelements formed more complicated, macromolecular bioelements.

We proposed to subdivide bioelements into simple (atoms, ions and water as the universal solvent), and complicated ones, consisting of the above-mentioned 68 molecules (8 of them are nucleosides, which compose DNA and RNA, 20 are natural amino acids necessary for protein synthesis, at least 32 glycans, 8 types of lipids, see Table 2) [8].

Thus, bioelements can be subdivided into primary, i.e. those which could exist before the origin of life, and secondary, i.e. those which have formed as production of living organisms. This division is necessary for us to better understand the nature and role of bioelements. For example, the fact that life is a self-sustaining process that can produce "raw material" for new living structures. This agrees with the theory of natural self-organization of pre-biological processes by M.Eigen [9] and ideas of I.Prigogine [10] about self-organization in open systems.

In recent years, along with the evolution of our knowledge and understanding of bioelements, the definitions of bioelementology evolved [2, 11-12]. Currently, we guess the most appropriate definition of bioelementology is the following:

		C, H, N, O, P, S, Si, Ca (structural)
	Simple	K, Na, Ca, Cl, Mg (electrolytic)
		Mg, Fe, Zn, Cu, Mn, Co, Cr, Mo, Se*, Sn*, F*, I*, Ni*, V*, B** (enzymatic
Primary Complicated		H <sub>2</sub> O, O <sub>2</sub> , N <sub>2</sub> etc.
	Complicated	Nucleic acids (deoxyadenosine, deoxycytidine, deoxyguanosine, deoxythymidine, adenosine, cytidine, guanosine, uridine)
		Glycans (Fucose, galactose, glucose, glucuronic acid, mannose, N- acetylgalactosamine, N-acetylglucosamine, neuraminic acid, xylose, nononic acid, octulosonic acid, arabinose, arabinofuranose, colitose, fructose, galactofuranose, galacturonic acid, glucolactilic acid, heptose, legionaminic acid, mannuronic acid, N-acetylfucosamine, N- acetylgalacturonic acid, N-acetylmannosamine, N- acetylmannosaminuronic acid, N-acetylmuramic acid, N- acetylperosamine, N-acetylquinovosamine, perosamine, pseudaminic acid, rhamnose, talose)
		Proteins (Alanine, arginine, aspartic acid, asparagine, cysteine, glutamic acid, glutamine, glycine, histidine, isoleucine, leucine, lysine, methionine, phenylalanine, proline, serine, threonine, tryptophan, tyrosine, valine)
	Lipids (Fatty acyls, glycerolipids, glycerophospholipids, polyketides, prenol lipids, saccharolipids, sphingolipids, sterol lipids)	
Secondary of bio		Metabolome (components)
		Metallome
	Complicated (components	Lipidome
	of bioelemental systems,	Proteome
	"omes")	Genome
		Transcriptome
		(?)

Bioelementology is a science, which can unite all the "omics", probably including genomics. Authors of the term "genomics", V.A.McKusick and F.H.Riddle, in the editorial article to the first issue of the journal "Genomics" have explained introduction of the new term as follows: "...logies" are very academic, while "...omics" are more aggressive and democratic [13] in style of live matter studying.

Thus, bioelementology is a part of biology (and of the "life science" in terms of V.I.Vernadsky), a science about biological role of substances, important for building and existence of the living matter [3].

Bioelementology is a direction of fundamental science studying the transition state of the matter (evolution from biologically inert to living), formation and change of bioelements, which are vital or conditionally essential for the living matter, under influence of various physical interactions and matrix effect of water.

Bioelementology as an integrative science, based on the ideas of V.I.Vernadsky, will bring us closer to understanding the origin of life. Unlike the currently prevailing molecular approach, which unfortunately does not solve the problem of the life origin despite the involvement in consideration of new biochemical factors – nucleic acids, matrix mechanisms of continuity and biochemical memory [14], – bioelementology, in our view, will help to consider the conditions of life more holistically as the presence of bioelements is already the most important condition for its maintenance. The planetary environment, which surrounds the living substance, and the extraplanetary space environment which influence it, together provide the necessary material and energy flows for the proper functioning and continual renewal of the structure of living matter.

The ideas of autotrophy of the mankind and noosphere, suggested by V.I.Vernadsky in 1923 [5], have fostered the epoch of nanobiology, the living matter of Universe. We believe that bioelementology can help to solve the main problem of the mankind – achievement of the autotrophy – through solving the problem of essence of the living matter of Earth and identification of this essence with wider principle of life existence in Universe [15].

The bioelementology combines the systemic and integrative approaches in life science and is a possible precursor to systemic biology.

# 3. Practical aspects

The materials above illustrates that the evolution of living organisms on Earth was accompanied by a broadening and deepening of the utilization of chemical elements and their compounds, i.e., in fact, by diversification, improvement and complication of bioelements. This process continues today in both natural and artificial environment, if allowing for the development of biotechnology, genetic engineering and pharmacy.

Diversification of bioelements is a natural tool of the evolution aimed at adaptation of living organisms to the changing conditions of their existence. The emergence of new bioelements accompanies the process of evolution from simple prokaryotic cells (universal) to specialized cells within multicellular organisms with longer duration of individual life at a deceleration of reproduction rate. Changing the composition of the extracellular environment, such as the concentration of key ions or gases, it is possible to cause a cascade of formation of new bioelements. More diverse set of bioelements is observed in organisms with relatively low reproduction rates, but with a longer individual life.

It must be remembered that a set of bioelements is a necessary but not sufficient condition for the formation of life. In many cases in medicine, in our opinion, it is possible to use bioelements for maintaining organs and tissues instead of using cell cultures and tissues, because it is not always necessary or possible (including for financial reasons) to recover the function by a substance, organ or tissue, completely identical to the living one (e.g., in transplantology, orthopedics, in treatment of osteoporosis, diseases of skin, hair, etc.).

The development of bioelementology may lead to appearance of modified cells or technologies for creation of new cells which can be used for medical purposes. Without going into details, we only note that this tale may sooner become a reality with the correct formulation of tasks, based on the correct understanding of the hierarchy of "pre-living" processes and of the life itself, on the formation of new methodological approaches on its basis, on the proper division of essential substances in necessary and sufficient, primary and secondary, with a better understanding of the boundary between "pre-living" and "living", between the set of bioelements and life.

It is reasonable that the deficiency of only one primary bioelement can due to the extinction of living organism in Earth. According to US Department of Energy (2010), in not far future chemical (elemental) diversity may be sacrified (Table 3). The lack of rare earths can stop the "Clean green future", but deficiency f only one trace element (cobalt) can have the dramatic effect on a lot of species, for which this element and the vitabin B12 are essential.

Level	Elements
Critical	Y, Nd, Eu, Tb, Dy, In
Near-critical	La, Ce, Te
Non-critical (but not far future)	Co, Li, Ga

Table 3. Risk of supply disruption by 2015 (US Department of Energy, 2010)

This is why the mankind needs to plan and realize the emergent actions. Below we present our point of view on the strategy of survival.

Strategy of survival:

- 1. Reducing of resources consumption (?)
- 2. Free redistribution of resources between countries (nations) (?)
- 3. Restoring of resources:
  - **a.** Conservation of nature (±)
  - **b.** Biotechnological (microbial etc.) production of resources (+)
- 4. Artificial life technology developing (protocells etc.) (±)

Of course, today the mankind is not ready to reduce its resource consumptions, which leads to decreasing of number of bioelements. Also, on a pity, the nations are not ready to agree with free redistribution of resources between them. The conservation of nature has also a lot of limitations because of decreasing of forests and desertization intensive use of more and more soils and water for agriculture etc. Only the biotechnological (or pharmaceutical) production of secondary bioelements which are more effective, better available and safe is a fruitful direction toward provision of humans and animals by "blocks of life". The developing of so-called artificial life technologies is a controversial way for accumulation of bioelements, because such experiments can produce undesirable effects from unknown protocells and other modified organisms.

An example of technology for enlargement of food density for future use is enrichment of algae (Spirulina, Nostoc) [16]. We have managed to obtain the greatest possible accumulation of some essential trace elements by cell cultures of S. platensis and S. maxima. This could considerably increase the value and applicability of spirulina biomass in human health care nutrition. The work has begun from registering a patent [17] for a method of obtaining selenium-containing preparation of spirulina biomass enriched with selenium in organic form with pronounced antioxidant properties. The content of selenium in the cells was determined by atomic-adsorption and fluorometric methods, the total elemental composition of the cell – by developed complex of ICP-AES methods [18].

The possibility to obtain spirulina biomass enriched with selenium in organic form, which has increased bioavailability, has promptly caused the appearance of works extending this direction. In some works a spirulina preparation enriched with bioavailable selenium in combination with reduced glutathione was administered to rats, allowing normalization of intestinal permeability, impaired after systemic anaphylaxis. In other studies it was shown that effective regulation of homeostasis was possible by addition of selenium-rich spirulina to rats' feed. Also there were reports about successful use of selenium-enriched spirulina and yeast as a dietary supplement for patients with non-specific ulcerative colitis and for patients with coronary heart disease [19-20].

The material demonstrates that electromagnetic radiation of millimeter range (EHF) at low non-thermal intensity, which can be characterized as extremely weak and possibly even superweak physical influence, can affect various aspects of metabolism of phototrophic cyanobacteria and microalgae, stimulate growth and yield of biomass of the cultures etc. It can also influence the accumulation of some essential trace elements in cells of cyanobacteria. It is shown that EHF radiation can reduce the toxicity of trace elements introduced into the medium. And, for the first time, it is established that the entering of elevated concentrations of certain trace elements into cultural medium causes shifts in general mineral profile of the cyanobacterial cells.

# 4. Novel paradigm of the nutrition and pharmacology

As it is ahown in Figure 2, for the effective prevention and treatment of human disease it is essential to control and correct the initial imbalances of bioelements, caused by suboptimal nutrition, ecological influence, stress etc. We can do this for relatively healthy people that to prevent their disease. If we missed the possibility of the correction of human health by bioelements in stages I-II, we need to start the treatment but also with the restoration of basic defects of metabolism (stable deficiency of bioelements).

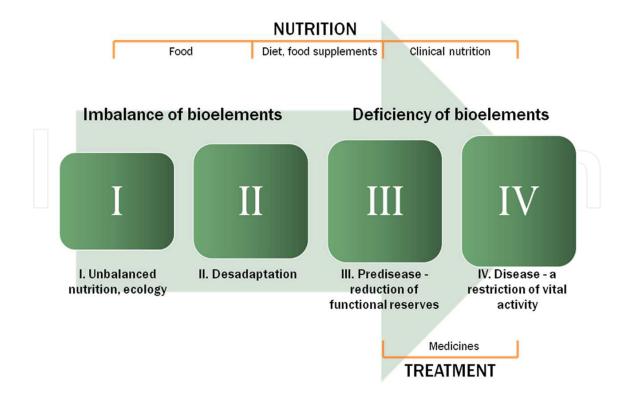


Figure 2. Levels of bioelement imbalances and their correction

Medical and pharmaceutical strategy	<ul> <li>«+» Personalized medicine - individual observation and treatment.</li> <li>«+» Innovations in laboratory diagnostics and pharmaceutical industry.</li> <li>«-» Expensive: the equipment, personnel, education of specialists and population takes time (from 5-10 years for the country).</li> </ul>
Nutritional strategy	<ul> <li>«+» A natural way to provide the population with nutrients.</li> <li>«+» Industrialization, massive involvement (Implementation - from 2- 5 years at the national level).</li> <li>«+» Modernization of food industry.</li> <li>«-» No individual approach, only group approach is possible - regional, sectoral, social nutrition.</li> <li>«-» It is necessary to observe population of regions and specific groups.</li> </ul>
Agricultural strategy	<ul> <li>«+» Involvement of farmers.</li> <li>«+» Formation of the market of organic food and products of regional demand.</li> <li>«+» Innovations in agricultural chemistry, animal and plant farming.</li> <li>«-» Changing the mindset of farmers</li> <li>«-» Governmental support is needed.</li> <li>«-» Takes time (5-10 years for the country).</li> </ul>

Figure 3. Approaches to solving the problem of bioelements provision for human health

So, there are few directions to serve and develop the "life set" of bioelements. As demonstrated in Figure 3, the mankind can use medical and pharmacological therapy for detection of individual and populational provision by bioelements (primary and secondary). This is the most expensive way, but realistic for rich countries, which needs to develop the technological diagnostics ("omics"), personalized healthy nutrition and treatment.

The second direction is more natural – improvement of nutrition on the basis of fortified foods, "high food density" products. It is appreciable for almost all countries and layers of population, if the governments and international organizations (FAO, IMF, UNIDO etc.) will support the development of food industry and support authorities to manage the social nutrition, for example. The last strategy is most natural, but needs a lot of efforts in agricultural sector of industry and science. More detailed description of the strategies is presented below.

- 1. Medical and pharmaceutical strategy
  - Development of personalized medicine and medical geography, epidemiology and ecology
  - Improving methods of laboratory and clinical diagnostics of micronutrient deficiencies and intoxications
  - Creation (reconstruction and development) of resource base for food and pharmaceutical industry
  - Creation and production of adapted means for nutraceutical and pharmaceutical correction of deficiency/surplus of micronutrients (based on physiological, regional and professional needs)
  - Creation and production of new drugs for treatment of genetic and other rare diseases related to metabolic disorders of micronutrient exchange
- 2. Nutritional strategy
  - Fortification (enrichment) of food with micronutrients at the production stage focused and strictly bound to the elemental status of the population (massive involvement)
  - Choice among existing products the required (enriched) ones to complete rations
  - Exchange of products between the regions
  - Dietary supplements an individual approach 10% of the population, in developed countries up to 80%
  - Functional food
  - Forming assortment of food products information policy
  - Creation of functional beverages, artificial water mineralization
  - Exchange of products between regions according to regional needs in micronutrient
  - Improving the quality of tap water

• Social nutrition (water consumption) on the basis of physiological and professional groups of the population

Food fortification as a long-term regional program "Development of a regional system for detection and prevention of natural and technogenic deficiencies and surpluses of macro and trace elements in the population"

Project

• Formation of scientific and methodological basis for monitoring of elemental status of the population and correction of deviations

Regional program for monitoring elemental status of the population

- Determination of deficiencies and surpluses of macro and trace elements
- Development of recommendations for correction of deviations

Formation of regional regulations based on governmental policy in the field of healthy nutrition

• Increasing the proportion of production for mass consumption, rich in vitamins and minerals, including mass varieties of bakery products, and dairy products - up to 40% of total production

Consolidated ordering of fortification ingredients for the regional food producers

• Formation of joint supply of fortification ingredients for the regional producers of products for social and mass feeding in accordance with results of the monitoring

Sectoral nutrition

- Scientific and methodological support of diets for different groups of people in the region: pupils, students, workers etc.
- Regional standards for food products
- System of targeted subsidies for fortification (enrichment of food with micronutrients)
- **3.** Agricultural strategy
  - Agrochemical service: targeted introduction of *microfertilizers*
  - Variety zonation
  - Breeding
  - Specialized mixed feeds, premixes for animals, mineralized water
  - Development of industry: fertilizers, animal feed, etc.

Before the realization of the presented strategies it is needed to estimate the balance of bioelements in population or individuals. Below we present an example of evaluation of bioelement (macro and trace elements) status of population.

- **1.** Screening of the region
  - Screening (assessment of the current state)
    - Organizational period (1-3 months)
    - Collection of biological material (2 months)
    - Investigations (3-6 months)
    - Data processing, development of recommendations (1-2 months): factor analysis, identification of basic dependencies
    - Preliminary report (1-2 months): organizational policy

In the result of the screening we get the identification of factors and control parameters, forming mineral profile of the region. Further step is analysis of obtained data and creation of database for public health, agriculture, social services of a region.

- 2. Creation of database on directions:
  - Updatable database on physical media
  - Medical information
  - Epidemiological information
  - Database of technologies, measures, activities, management decisions
  - Regional standards of the consumer basket (nutrients)

The efforts of correction of bioelement status can be insufficient if medical doctors, social workers in population do not understand the aims of such studies and do not participate actively in the prophylactic activity. So, we need organize an information campaign in the region with a support of local medical, public health and social organizations and authorities.

- 3. Information policy in the field of healthy living
  - Educational lectures
  - Declaration of human responsibility
  - Creation of an independent "guild" of doctors
  - Lack of proper information policy exit to informational diseases
  - Training program for students on nutriciology
  - Organization of club structure (stimulation of involvement)

#### Feedback

- Control of elemental status of the population influence on medical and demographic indices
- Quality of life: formation of focus groups for continuous monitoring of the life quality

- Analysis of statistical data (demography, health, employment, etc.)
- Monitoring (repeated screening every 3-5 years) of a representative sample of the population.
- · Update of data banks and databases with identification of trends and forecasting
- One-time studies connected to emergencies, disease outbreaks of unknown etiology, etc. Determination of non-obvious causes of emergencies.

## 5. Conclusion

So, the evolution of living organisms on Earth was accompanied by a broadening and deepening of the utilization of chemical elements and their compounds, i.e., in fact, by diversification, improvement and complication of bioelements. This process continues today in both natural and artificial environment, if allowing for the development of biotechnology, genetic engineering and pharmacy.

In many cases in medicine, it is possible to use bioelements for maintaining organs and tissues instead of using cell cultures and tissues, because it is not always necessary or possible (including for financial reasons) to recover the function by a substance, organ or tissue, completely identical to the living one (e.g., in transplantology, orthopedics, in treatment of osteoporosis, diseases of skin, hair, etc.).

The development of bioelementology may lead to appearance of modified cells or technologies for creation of new cells which can be used for medical purposes.

On our opinion, the progress in trace element research will be due to interdisciplinary approach such as bioelementology. It needs change in educational programs for high school students of biological, chemical and physical specialties, creation of special programs for biotechnologists, medical researchers, ecologists and pharmacists. And this will demand united efforts of scientists and specialists from adjacent fields. Integration of scientific researches without division into separate parts, studied by only one of the "omics", though this will demand deeper and more global planning of scientific investigations on the basis of the multidisciplinary concept. Also, it is necessary to change the paradigm of diseases' prevention and treatment from mainly symptomatic to basics to prevent and normalize the balance of bioelements by nutrition and use of sources of bioelements in pharmacotherapy.

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