

The Added Value of Technology in Food Integration - Holistic Approach

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Abstract

The increasingly widespread consequences of globalization, and of an incongruous and unbalanced distribution of food, between geographical areas with reduced threshold of access to food, and industrialized areas where there is excess food and overeating, raise the urgent problem of proper regulation and management of all available food resources.

The emergence and expansion of diseases related to malnutrition and hypernutrition have reached pandemic and irreversible dimensions and, despite the excessive exploitation of water resources and primary food sources and the total depletion of natural resources, a positive solution has not yet been found yet.

Industrial food production, has been introducing new standards in the quality and consumption of nutrients, which are increasingly poor, with increasingly intensive and less controlled production systems.

The attempt to correct the wrong eating habits and inadequate lifestyle, with the intake of nutrients and active ingredients to fill dietary deficiencies, has not been producing the desired effects.

Nutraceuticals and the related sciences Nutrigenomics and Microbiomics, which should provide the basis for healthy nutrition and the correct information for the use of functional foods, too often are at the service of food multinationals, to promote the spread of an indiscriminate and massive use of supplements.

Key words: nutrigenomic; microbiomic; food supplements; liposomal technologies

Introduction

All living beings for their survival need energy supply that comes to them in different ways, or directly from sunlight, water and carbon dioxide, as in autotrophic organisms, or by the intake of food in the form of animal or vegetable food, as in heterotrophs, or finally directly using the nutrients provided by the guests, as in commensalism, symbiosis and parasitism.

To obtain the energy they need, the living use that provided by the breaking of chemical bonds from which food is formed. The energy thus obtained is used to perform all the metabolic functions they need, from the simplest to the most complex.

Metabolism takes on different aspects depending on whether they are simple organisms, prokaryotes, or more complex, eukaryotes. While the former assumes nutrients in the form of small molecules directly from the external environment, or from the host organism in the case of symbionts

and parasites, the latter must take nutrients from other organisms, which must be degraded and assimilated in the form of simple substances.

In any case, there is a very close link, which concerns transversally all living, between the nutritional needs, the type, quality and quantity of nutrients taken, and the preservation of a balanced relationship with the environment that hosts them, for the homeostatic maintenance of the general well-being.

Over the course of millions of years of biological evolution, this link has become more and more differentiated, assuming the infinite forms that we have known, in the different ecosystems present on our planet.

The current diet of every living being, from bacteria to man, is the result of millions of years of evolution, natural selection and mutual adaptation between the available food resources and their use for nutritional purposes.

As for our species, the eating habits have changed a lot, in relation to the different ways of obtaining food, from the Neolithic to our days. From the origins until the beginning of the Neolithic Age, about 10,000 years ago,

man lived on game, vegetables, dried fruit and, when it happened, fresh fruit. He was a hunter/gatherer and his daily life was based on a very high energy expenditure. Figure.1

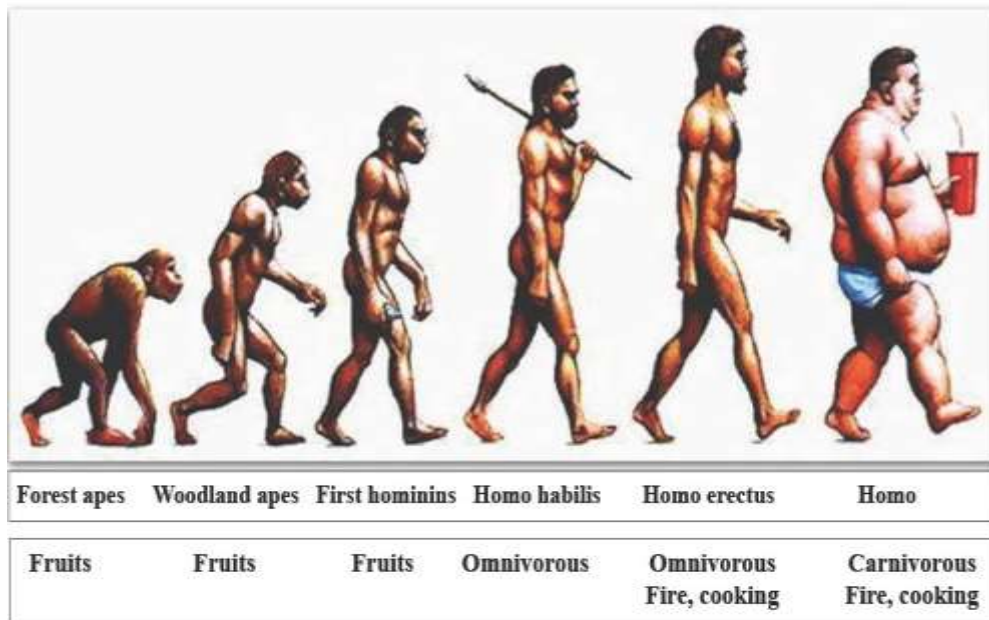


Figure 1: Evolution in Human diet

In the following centuries men learned to cultivate the land with the production of cereals and vegetables and to breed animals.

In the contemporary era the industrial production of food has been having an exponential development. The production of traditional foodstuffs (flour, oils, jams, butter, cheese...) that were once made by hand are now produced in large factories and the discovery of preservation procedures, of exaltation of the taste and then the freezing, have allowed to condition a large number of fresh foods in the form of canned or frozen (fruits, vegetables, meat, fish...). [1-3]

In parallel with the change in production methods, eating habits have degenerated, moving from a natural diet, to an artificial one, with production processes that modify and denature nutrients, to facilitate their

yield and storage and alter the organoleptic appearance to make it more attractive. This has negative repercussions on our well-being, with an extraordinary increase in obesity, diabetes and cardiovascular diseases, three of the major metabolic scourges that humanity is now facing.

A close look at many of the degenerative pathologies that has characterizes our century, are of food origin or rather are caused by the unnatural and poor quality of the food we eat daily.

The addition of pesticides, preservatives and dyes, flavor modifiers, can be the first cause of metabolic dysfunctions, which have taken pandemic proportions. Obesity, celiac disease, diabetes, metabolic syndrome, are the direct expression, as well as genetic defects, also of the incongruous food quality. [4] Figure. 2

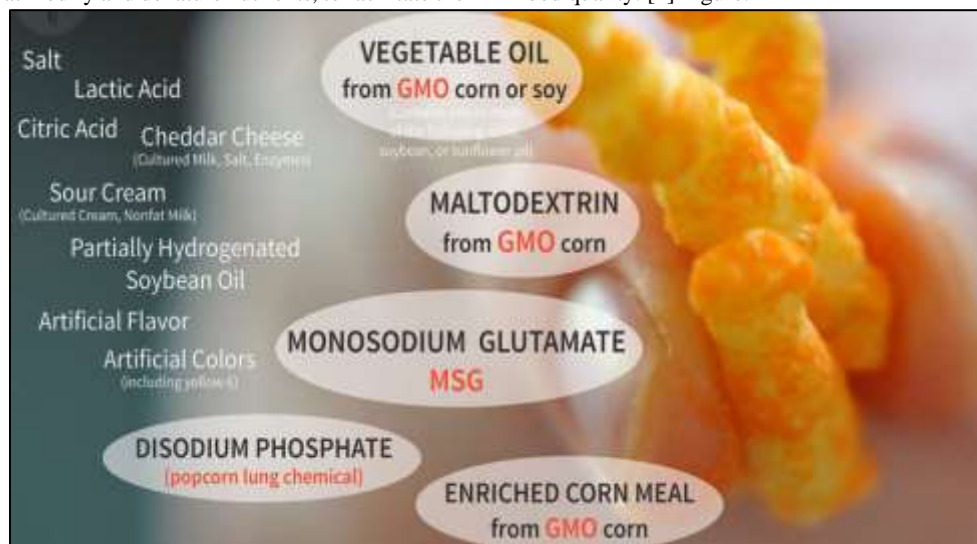


Figure 2: Presence of additives in food production

Dietology from antiquity to the present day

Until the most ancient observation the importance of food for our health was recognized, is famous the aphorism of Hippocrates: "Let Food be your Medicine and Medicine be your Food" - HIPPOCRATES OF COO (460-337 B.C.) which summarizes this ancient knowledge

In the last part of the century, the Nutraceutical, the modern Science of Nutrition has allowed a better knowledge of the close link between food and health conditions.

It has also selected and identified particular foods that in addition for having a high nutritional content have also been shown to possess important functional properties when added to foods ("Functional Foods")

A definition of functional food has been given by EUFIC (European Council Food Information):

"A food may be considered functional if it demonstrates positive effects on one or more specific functions of the body, in addition to normal nutritional effects, so as to improve the state of health and well-being and/or reduce the risk of disease. " <https://www.eufic.org/it>

Nutraceutical, specialized in different branches and with the use of different scientific disciplines, from genetics to microbiology, to

biochemistry, etc. has achieved results unthinkable, only in the last century.

The two research directions that have obtained the greatest results are Nutrigenomics and Microbiomics, followed by a whole series of "omics", which investigate individual aspects of nutritional metabolism.

Nutrigenomics, Epigenetics, Microbiomics

These three disciplines have definitively clarified the relationship between food intake and our state of well-being.

However, the excessive focus on individual aspects deemed responsible for degenerative diseases, such as SNP (Polymorphism of a Single Nucleotide) according to Nutrigenomics, led to paradoxical conclusions in the interpretation of their research.

For example, for many identical disease conditions different pathogenetic causes are assumed depending on the specific field of research. So, for example, regarding the predisposition for cardiovascular diseases CVD, the Nutrigenomica recognizes as the only determinant the polymorphism of the Single Nucleotide (SNP), Tab. 1, while according to the Microbiomica the real responsible is the imbalance in the composition of the intestinal microbiome. There are many similar examples in the literature [5-8]

CVD Risk Factor	Gene	SNPs	Genotype
Lipids	APOAI	-75G→A	GA
Lipids	APOC3	3175C→G	GG
Lipids	APOE	ε2, ε3, ε4	2, 3
Lipids	CETP	279G→A	GG
Blood pressure	ACE	Ins/Del	ID
Blood pressure	AGT	-6C→A	AA
Inflammation	IL1B	-511C→T	TT
Inflammation	IL6	-174G→C	GC
Methylation (folate)	MTHFR	677C→T	TT
Methylation (B12)	TCN2	776C→T	CT

Table 1: Nutrigenetic analysis of SNPs within some CVD-related genes, CVD – cardiovascular diseases

However, Nutrigenomica has reached important results in the knowledge of the effects that the food can have in the genetic expression and the existing relationships between genome and food Figure 3:

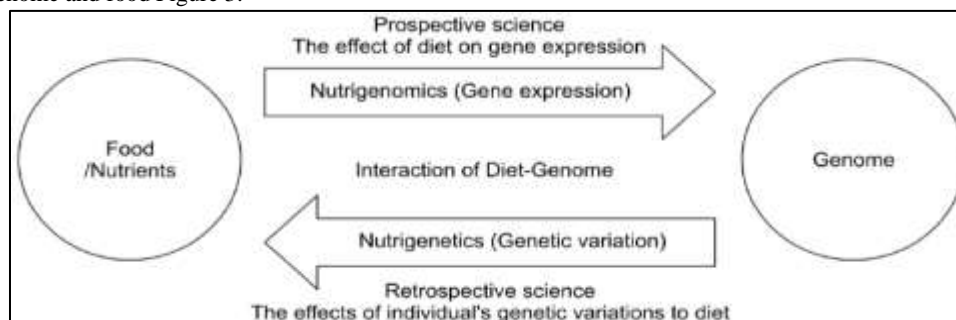


Figure 3: Interaction between food and gene expression

Nutrigenetics analyzes the effect of genetic variation on dietary response,

Nutrigenomics identify the genes that influence the risk of diet-related diseases on a genome -wide scale and to understand the mechanisms that underlie these genetic predispositions.

Mechanisms by which nutrients influence gene expression:

1. Regulation of transcription factors and transcription process

2. Regulation of chromatin structure and DNA susceptibility to transcriptional machinery, *how certain genes are switched on or switched off – nutri-epigenetics*

Personalized nutrition: a diet addressed to an individual and based upon her/his genotype, nutritional requirements and other factors (age and gender). It is expected that personalized nutrition will prevent diet-related chronic diseases: “*Food and nutrition in 21st century*”, Warsaw, 8-9.09.2011

Nevertheless, genetic analysis is not able to predict with certainty the effects of the Polymorphism of a Single Nucleotide, on metabolic expressions, because multiple epigenetic factors intervene that modify the final phenotype.

Microbiomic:

Microbiota or Microbiome?

It is necessary to make a distinction because when we are going to talk about Microbiota or Microbioma we refer to different contents.

Microbiota refers to the set of microbes (commensal bacteria, yeasts, viruses and very simple primitive animal organisms, such as protozoa) that coexist in our bodies.

Whereas Microbioma indicates the totality of the genetic patrimony possessed by the microbiota, that is the genes that the latter is able to express. [9-11]

The human gut microbiota consists of more than 50.000 billion microorganisms belonging to at least 1000 different species Figure 4.

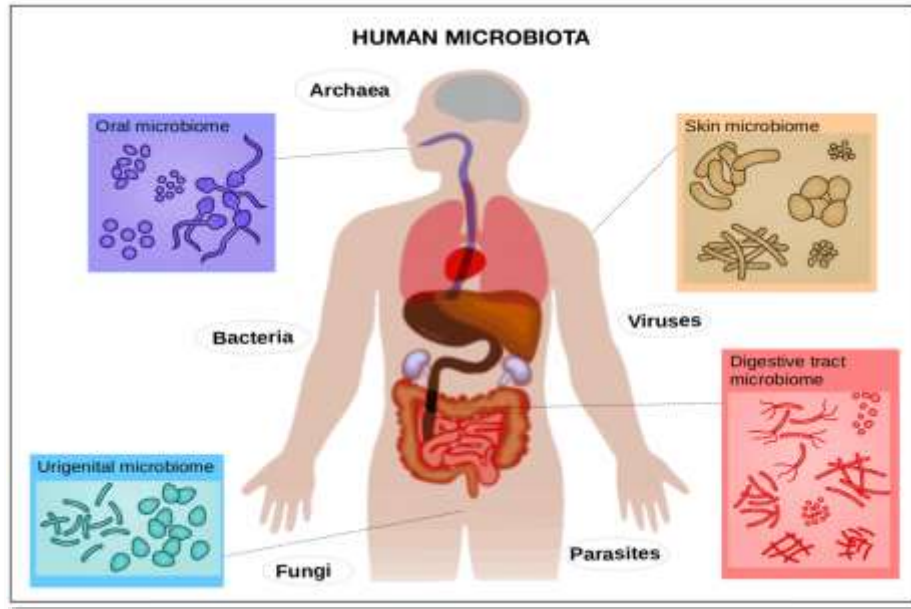


Figure 4: Human Microbiota

The Microbiomic has focused mainly on the intestinal microbiota, relating the intestinal dysbiosis and some pathologies Figure 5 .

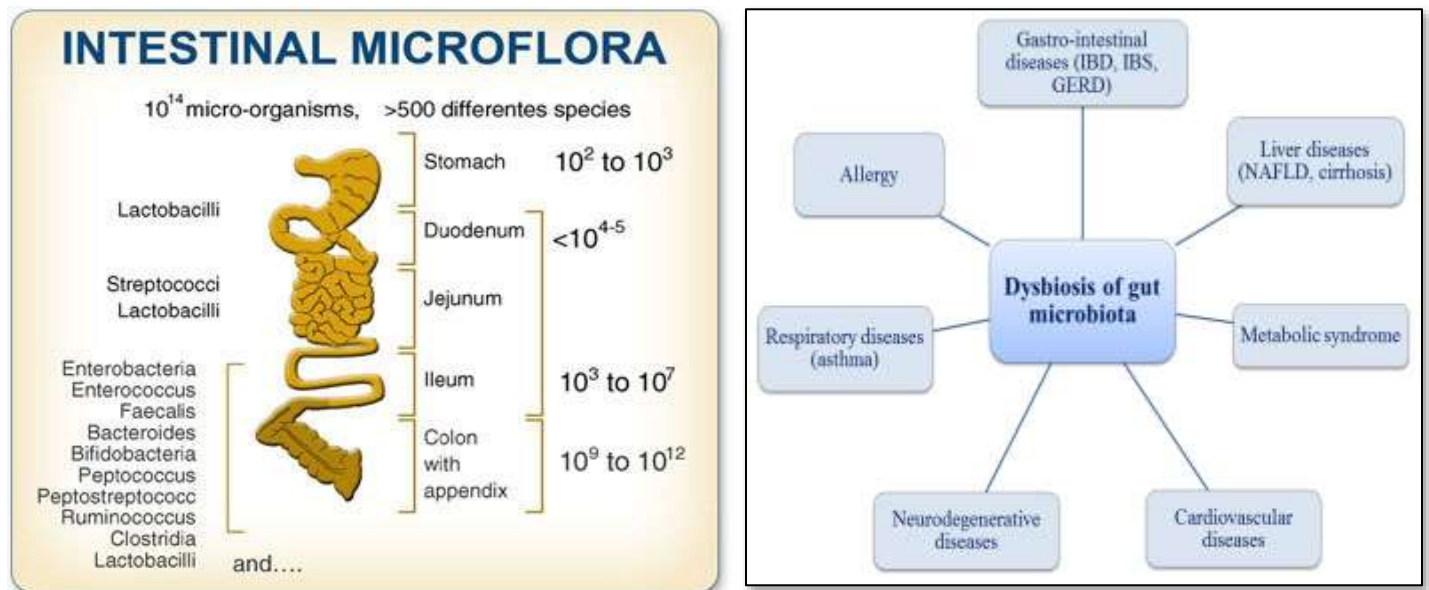


Figure 5: Composition of intestinal microflora and related pathologies

The excessive fragmentation of the two disciplines Nutrigenomics and Microbiomics, has focused on individual aspects of biological and pathogenic processes, has neglected the many variables that come into play in the determinism of the state of health or disease.

In particular, they have completely disregarded the harmful effects linked to the production chain of intensive crops and industrial food production,

which have introduced into the diet extremely harmful substances, which have been mentioned above.

This is how the idea spread in public opinion, that it was enough to change eating habits, with the intake of specific nutrients, to prevent or improve many degenerative pathologies.

In parallel with the development of Nutraceutical, and Microbiomic, the market for food supplements has developed exponentially Figure 6. [12]

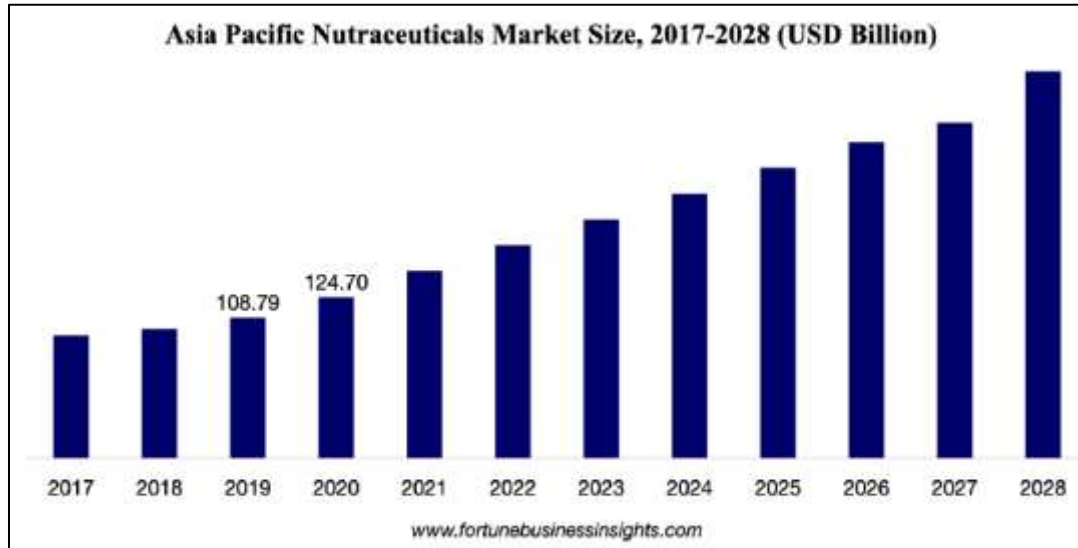


Figure 6: Nutraceuticals Market

The global nutraceuticals market is predicted to grow from \$352.92 billion in 2021 to \$658.11 billion in 2028 at a CAGR of 9.3% in forecast period 2021-2028. **Development Initiatives Poverty Research Ltd**, <https://www.fortunebusinessinsights.com/nutraceuticals-market-102530>

Today the most successful food supplements on the market today, are those based on minerals, vitamins, probiotics, immunostimulants, etc., which on the push of health claims unreliable, have reached huge sales volumes.

Food companies that have joined forces through the International Life Sciences Institute, an organization funded by the food and biotech industry, to which Coca-Cola adheres, have contributed to the success and growth of the supplement market, Nestlé, Basf, McDonald's, Monsanto, Pepsi and Syngenta among others, to shape the development of principles and theory of scientific integrity.

"The activities developed by ILSI on the principles of scientific integrity are part of a wider set of policy practices of stakeholders in the field to influence public health policy, research and practice. It is important to know and combat these practices as they risk shaping scientific standards to meet the interests of the sector rather than those of public health". [13]

The exponential development of the nutraceutical market has also been contributing to the absence of controls in the application of international guidelines for Good Industrial Production and has been compromising negatively both the origin and the quality of supplements and nutritional products.

Limits of Efficacy of Food Supplements

In addition to being qualitatively and quantitatively inadequate in compliance with LARN (is the acronym that means "Reference Nutrient

and Energy Intake Levels") classified according to sex, age and weight, or compared to RDA (Recommended Daily Allowance) indicating, the recommended amount of nutrients that a person should take every day [14], another aspect that contributes to limiting the effectiveness of nutraceuticals, is represented by the poor absorption and assimilation of many of the nutrients used for their production, such as Vitamins, Minerals, plant extracts, Probiotics, etc. when they are taken in their original standardized form.

In particular, some active ingredients and plant extracts have a reduced therapeutic margin and poor absorption, which compromises proper use for health purposes.

We are going to mention some trace elements or microelements.

These include minerals that, although present in our body only in small quantities or even in minimal traces, perform important biological functions. They can be divided into:

- essential, the deficiency of which compromises vital physiological functions (iron, copper, zinc, fluorine, iodine, selenium, chromium, cobalt).
- probably essential (manganese, silicon, nickel, vanadium).
- potentially toxic, as they can cause serious damage to the body if present at high concentrations.

Many essential vitamins and plant extracts also present the same problem.

Thanks to the development of new pharmaceutical technologies, which have produced systems of carriers and release of active ingredients, it has been possible to improve both the organoleptic properties, the absorption

and bioavailability of most of the active ingredients that are poorly endowed with them. [15-16]

Among the various methods of Delivery Systems produced by the new technologies available today, we are going to mention those most widely used, which include liposomes, polymer conjugates, micelles, dendrimers, carbon and metal based nanoparticles and other different carriers Figure 7.

However, the average modest cost of integrators discourages the adoption of such technologies that are generally neglected by the industry, compared to the more economical and profitable traditional technologies.

We have been adopting liposomal technology, because it is the most widespread and used and its ease of production and versatility of usage are known.

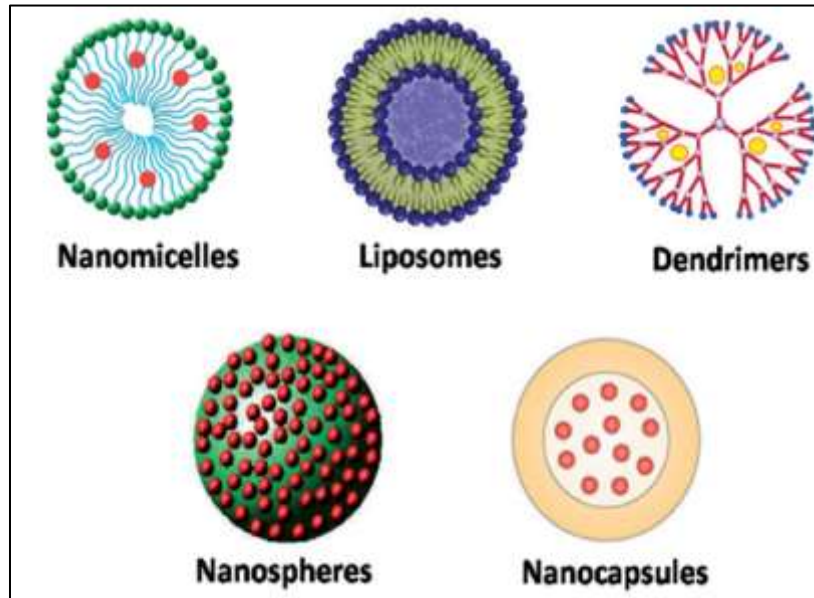


Figure 7: Different Nanocarriers

Liposomes consist of a double layer of phospholipids with an internal cavity that can contain and transport various substances in solution, such as drugs or active ingredients.

The use of liposomes as transporters is significant for pharmacologically active substances that have a low bioavailability index (such as some anticancer agents, antibiotics, etc.). They allow to reduce the concentration of drugs and improve their bioavailability with reduction of side effects.

The Argentine company Lipotech S.A. (www.lipotech.com.ar) has obtained and patented the most innovative results and has produced traditional and multifunctional liposomes, capable of carrying several substances simultaneously within the same liposomes, and also has produced some substances in microencapsulated form.

Multifunctional Liposomal Technology

The multifunctional liposomal technology of Lipotech has been providing products containing several active ingredients in liposomes, the morphological characteristics and the ability of cellular absorption and bioavailability of which, were documented with various instrumental examinations Figure 8, and clinical works. [17]

Some examples:

Biofer (Patented) : Iron sulphate and Vitamin C in liposomes;

Iron-Folic : Iron solfato and Vitamin C in Liposomi + Vitamine from Gruppo B;

Lifervit (Patented) : Iron solfato, Vitamin C, Folic Acid, Vitamin B6 ,Vitamin B12 In unico liposoma

Ferric Pyrophosphate microencapsulated: Iron Pyrophosphate microencapsulate

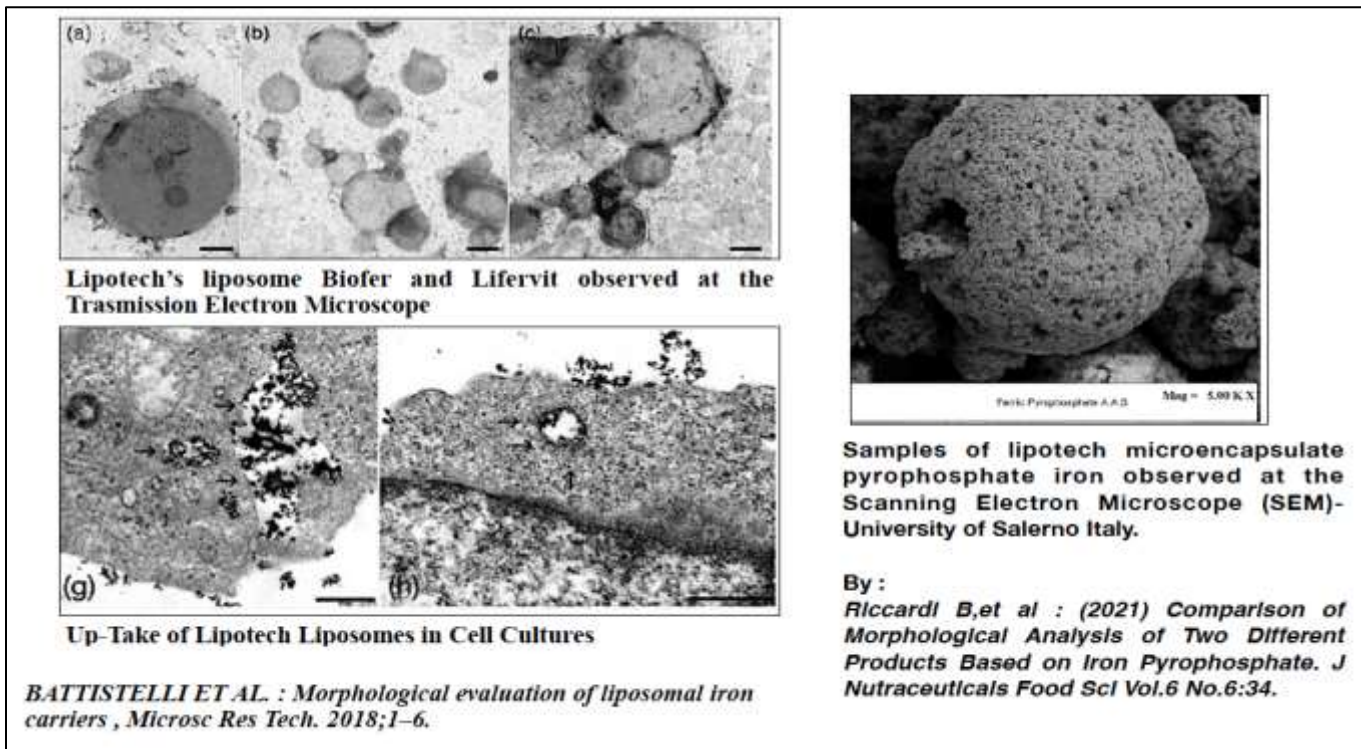


Figure 8: Micrography of liposome observed at Scanning and Transmission Electron Microscope.

Lipotech multipurpose liposomes have been used in the prevention of infectious diseases and in the treatment of different deficiencies, in large cases and with very good results. [18-21]

Thanks to the technology with multifunctional liposomes, it is possible to formulate supplements containing specific and selective active ingredients, able to solve individual nutritional deficiencies. Another advantage of this technology is the ability to overcome any impediments in the assimilation of necessary nutrients.

Use and abuse of food supplements

Food supplements are concentrated sources of nutrients (i.e., minerals, vitamins, probiotics, etc.) or other substances with a nutritional or physiological effect, marketed in the form of "dose" (e.g., pills, tablets, capsules, liquids at measured doses). Dietary supplements can contain a wide variety of nutrients and other ingredients, including vitamins, minerals, amino acids, essential fatty acids, fiber and various plants and herbal extracts.

Recently, the European Food Safety Authority (EFSA), produced a document in which the qualitative and quantitative nutritional characteristics of the nutrients that supplements must have, and the maximum permitted intake limits. [22-23]

According to international guidelines, the use of supplements should be restricted to three main situations:

- *Nutrient deficiencies important for proper metabolism, due to their insufficient intake or reduced absorption;*
- *Intake of nutrients essential for the prevention of morbid forms dependent on their absence in those at risk;*
- *Addition of specific elements to various foods, to compensate for endemic deficiencies of known nutrients (functional foods)*

It has been known for many years that diet in Western countries is not always able to provide adequate intake of various essential nutrients, in particular vitamins A, C, D and E, calcium, magnesium, iron, potassium, choline and fiber. [13]

This depends on many factors, such as eating habits (in vegans), the presence of numerous gastro-enteric diseases, consumption of technologically processed foods but depleted of nutritional value, etc.

In addition, the intensive industrial food production, offers on the market increasingly poor food from a nutritional point of view, and has enhanced the excessive processing of the organoleptic properties of food, and stressed advertising information conditioning the consumption of an incongruous diet, and compulsive eating behaviors, a real addiction to food.

A wide literature is informing us of the negative consequences for health, of the indiscriminate use of adulterations and manipulations and of the additives widely used with the industrial production, and the consumption of junk food. [24-26]

Conclusion

In recent decades we have been seeing the spread of many morbid forms resulting from wrong eating habits and lifestyles.

The current situation of malnutrition, and related diseases worldwide, presents a bleak picture.

We are faced with a worrying imbalance between people living below the minimum food threshold and industrialized countries, in which obesity and metabolic diseases linked to excessive food consumption are rampant. [27-29]

The need to produce more and more food to cope with the demographic increase has pushed the food industry to increasingly intensive production, consuming natural resources beyond those available and stressing the production cycles and the environmental balance.

The conditioning induced by the market of supplements to the consumption of health products, pushes consumers to assume increasing amounts of nutraceuticals, without any nutritional foundation, in the hope of preventing degenerative pathologies and correcting the incongruous diet resulting from the consumption of junk food.

The survey conducted by the Global Nutrition Report 2021, [30] edited by several authors, emerges a dramatic picture of food policies at the international level.

Despite the massive dissipation of natural resources, resulting from the intensive production of crops and food, we are still not able to meet the demand for healthy nutrition.

The solution of the food and health problem, must involve all operators in the common effort to improve production methods, to obtain nutrients qualitatively valid and technologically sustainable in the respect of nature, and better respond to the individual characteristics that modern surveys at our disposal allow us to diagnose.

To achieve this goal, it is necessary to change the methodological paradigm and adopt a holistic approach that takes into account all the variables that come into play in the complex food balance.

Such an approach requires the passing of surveys limited to individual scientific aspects, for example to Nutrigenomics and Microbiomics alone, formulation of diets; it also requires the renunciation of intensive food production, which prioritizes production efficiency, instead of food quality; and, above all, it requires the proper information of dieticians aimed at consumers for the adoption of a healthy diet and balanced lifestyles; overcoming the total dependence on the constraints and constraints imposed by the food multinationals.

In this article we have outlined some possible solutions offered by technology in production processes.

Disclosure

Neither Bruno Riccardi nor Sergio Resta and Giacomo Resta has any conflicts of interests related to this manuscript.

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