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Review

From Bioactive Molecules to Their Nutritional Effect, Biodynamic Interpretation Between Productional and Functional Aspects of Nutrients

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Abstract

In this article, the long journey from the production of food ingredients to their transformation into nutrients was described. The essential function of nutrients is to satisfy the primary needs of living organisms, namely energy, morphology and reproduction, through the consumption of food. Fulfilling its primary role, food must contain nutrients that are essential for the well-being of the living, along with others that are not essential but are still important for proper metabolism. These substances are known as bioactive substances. The subject of this article is to describe the main bioactive substances, their extraction and purification processes, their biological role and the technologies used to enhance their absorption and bioavailability. In addition, their application in natural foods is described, where they are added to transform them into functional foods. A holistic description of nutrition cannot be achieved without providing information about additives and preservatives that are added to foods, to enhance their organoleptic characteristics and extend their shelf life, but compromise food safety. In addition to altering the properties of food, these substances are responsible for emerging metabolic pathologies that are rampant worldwide.

Keywords
Active substances; extraction and purification; nutrients; absorption and bioavailability; delivery systems; functional foods; food additives

1. Introduction

Before addressing the description of bioactive substances, it is necessary to introduce the main preliminary information about the food. Food is the primary source of the fundamental substances that perform energetic and plastic functions in all living beings. Regardless of its nature and origin, whether animal or plant, the food contains essentially the same substances, called nutrients, represented by proteins, carbohydrates, fats and minerals, and many more other substances that do not directly perform the energetic and morphogenetic functions of the former, but have an essential role in proper metabolism. Therefore food is indispensable for a healthy life and the survival of living organisms.

In fact, all organisms require an energy supply that comes from the direct use of solar energy, water and carbon dioxide, as in the case of autotrophs, bacteria and plants, or by catching animal prey and ingesting plants, as in the case of heterotrophs, or finally by the direct use of nutrients provided by other organisms in various forms of commensalism, symbiosis and parasitism. The energy thus obtained from food is used to perform all the metabolic functions required by the organisms, from the simplest to the most complex, depending on whether it is a simple organism or a complex one. The former obtains nutrients directly from the external environment or, in the case of commensalism, from the host organism, while the latter must obtain nutrients by eating other organisms.

The consumption of food resources must maintain the close connection and balance between all organisms and the environment that hosts them and from which they obtain the food they need to survive. Unfortunately, the relationship between organisms and their environment and food sources has changed profoundly, especially with the industrial revolution, creating an imbalance between natural food and artificial food, and an imbalance in the availability of food products among the populations present on the planet.

Hunger is today an endemic problem in underdeveloped countries and is the cause of the death of thousands of children, while in industrialized areas, on the contrary, there is a surplus of food and overeating [1]. The spread of metabolic diseases has reached uncontrollable planetary dimensions and is currently a global health problem, and bulimia and anorexia, which are direct consequences of the reckless use of food to satisfy the growing demand for food, have produced and continue to produce a complete disruption of environmental balances [2].

The concept of the nutritional value of food has been around for miles of years, and the importance of food was first recognized by Hippocrates (460-337 B.C.) in ancient Greece, who coined the famous proverb "Let food be your medicine", which expresses comprehensively not only the nutritional value of food but also its essential "therapeutic" value. The current diet is the result of millions of years of evolution, where the relationship between the available food resources and their use for nutritional purposes was altered, which has been completely disrupted in the industrialized countries, where food is considered a commodity rather than a resource

indispensable for well-being [1-3]. And the industrial production of food has also introduced new standards and new habits for the consumption and intensive production of food, but the nutritional value of these industrially produced foods is low and unsafe.

In the last period of the century, Nutraceutica, the modern science of nutrition, has allowed a better knowledge of the close link between food and health conditions. And it has also selected and identified particular substances that, when added to food, have important functional properties in addition to their high nutritional content, the so-called "functional foods". In addition, several specialized branches have brought new knowledge to this field and generated specialized methods of investigation, namely nutrigenomics, microbiomics, and metabolomics. These disciplines have contributed to a deeper knowledge of the intimate mechanisms of nutritional processes, but at the same time have neglected to provide a holistic view of phenomena, often leading to opposing and conflicting interpretations between different research fields [4].

In this paper, the fundamental properties that must be present for nutrients to exert their healthy nutritional effect are described, including bioactivity, bioavailability and nutritional index [5, 6].

2. Definitions

Bioactivity refers to the effect of a natural substance on a biological system. Bioactive components are substances that positively affect biological systems, determining a physiological benefit and/or playing a preventive role in chronic-degenerative diseases. These substances are called "bioactive" because of their ability to modulate some important biological functions. For this effect to occur, the following conditions must be met:

- Bioactive substances, also known as "active substances", are produced by an animal or plant organism, and have nutraceutical activity;
- They must act on organic organs and systems of living organisms to produce a biologically important metabolism or behavior.

Therefore, to produce the biological effect, they must come into direct or indirect contact with the target structures. Bioactive substances by direct contact include enzymes and coenzymes (enzyme-substrate), hormones (hormone-receptor), antigens or antibodies (antigen-antibody), neurotransmitters (neurotransmitter-receptor), etc. Remote actions of biologically active events include quantum mechanics of electromagnetic radiation, sound waves, gravitational fields, etc.

That is, to describe bioactive substances, we must know their origin, properties and the effects that they produce at the biological level. All bioactive substances are predominantly (but not exclusively) extractive, and must undergo an extraction and purification process to eliminate foreign substances and to select the purified active components. Figure 1 shows a schematic representation of the extraction and purification process [7, 8].

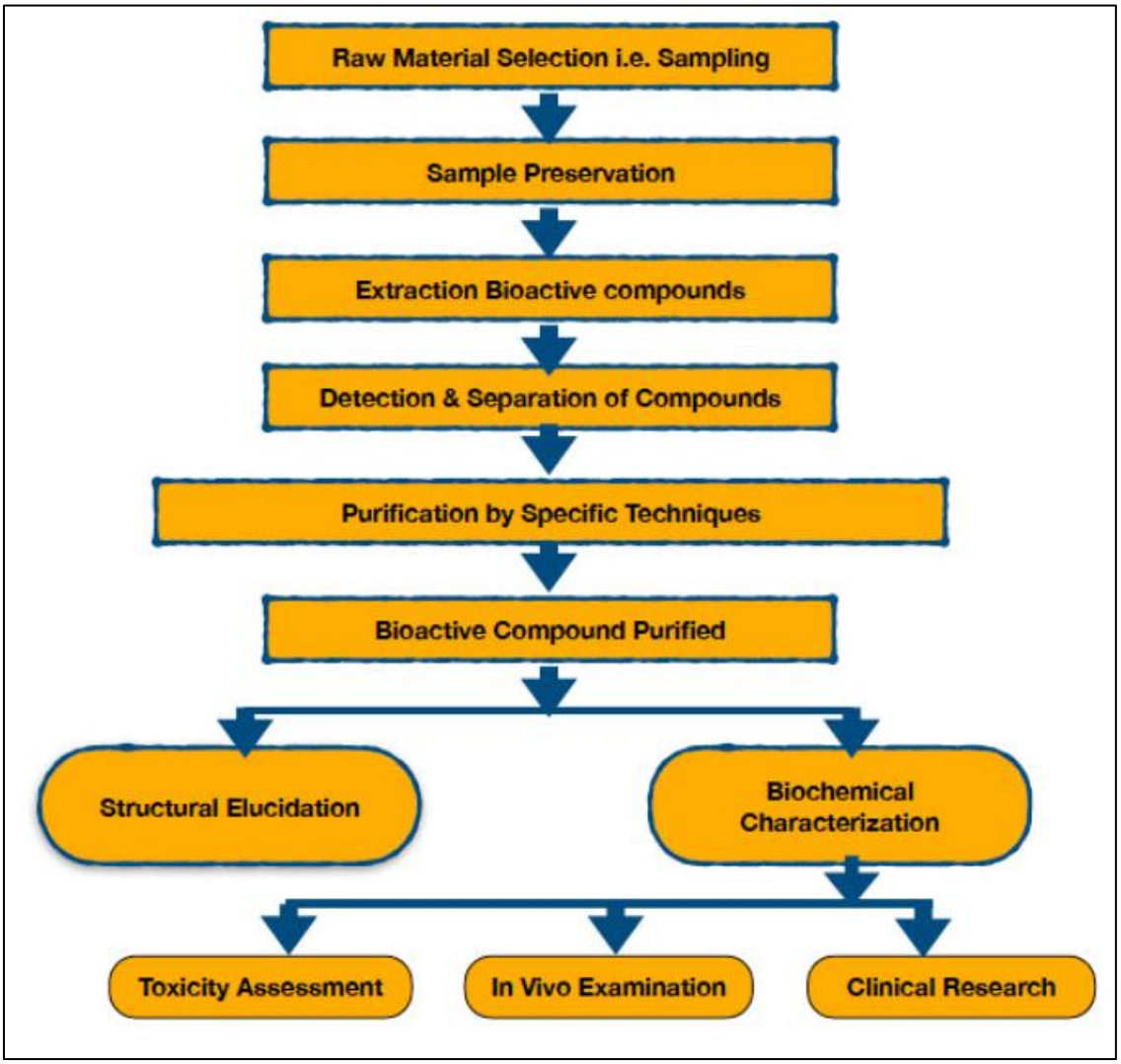
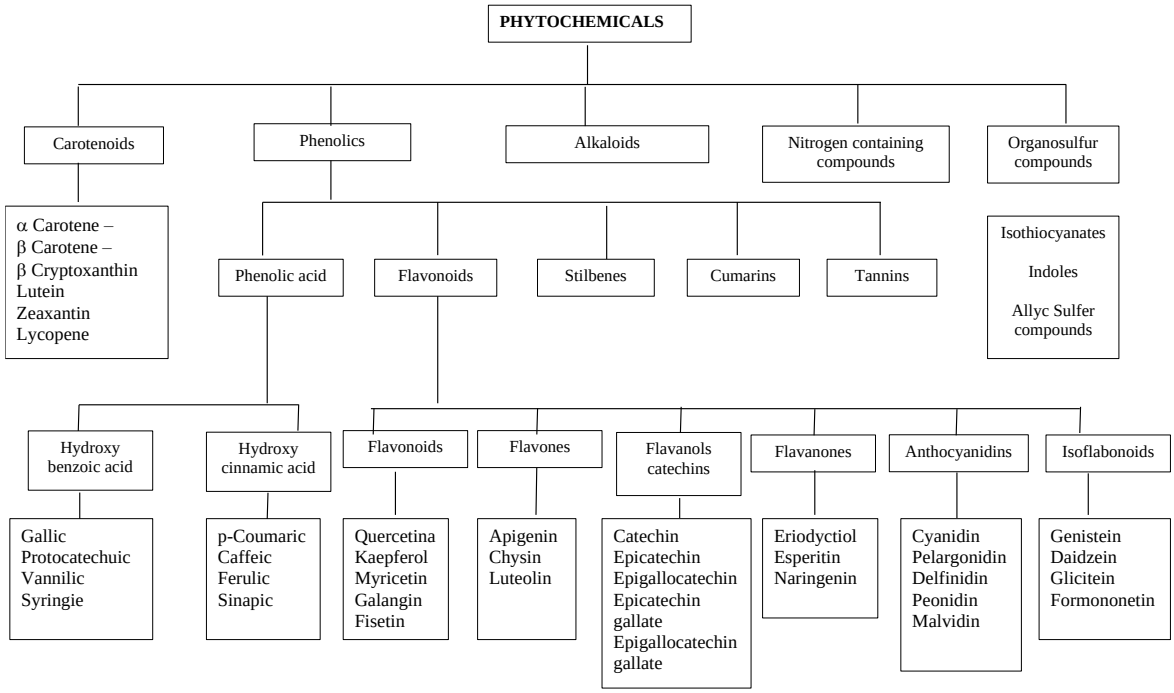


Figure 1 Flow diagram of the extraction and purification process of bioactive substances (drawn by the author).

Since it is impossible to provide an exhaustive list of the infinite number of bioactive substances known so far and the biological effects they produce, this paper only indicates the main chemical classes to which they belong and the biological effects related to these. The first classification collects foods in six groups of macro- and microelements with high nutritional value, including proteins, glycosides, lipids, minerals, vitamins and water. In addition to these substances, other food ingredients are not essential but play an equally important function in the modulation of metabolism and protection of general well-being. These bioactive substances, as we have mentioned, are mainly extracted from plants, hence they are also called phytochemicals, where the prefix FITO expresses the plant origin, and is the most important bioactive substance Tabe 1.

Table 1 Main phytochemicals extracted from plants. From: Bioactive Food Components, Changing the Scientific Basis for Intake Recommendations – The International Alliance of Dietary/Food Supplement Associations (IADSA) -October 2011. The main bioactive substances extracted from plants include carotenoids, flavonoids, proanthocyanidins, glucosinolates, isothiocyanates, lignanes, monophenols, monoterpenoids, organosilicon compounds, phenolic acids, phytosterol saponins, stilbenes, and tannins.



3. Main Methods of Extraction

There are many extraction methods currently available. The various extraction techniques depend on the starting material and the type of extracts to be obtained, and Figure 1 represents only the main extraction methods [9, 10].

4. Traditional Extraction Methods

Traditional extraction includes the following procedures: maceration, digestion, infusion, lixiviation (elution), decoction, tincture, steam distillation and hydrodistillation, etc.

5. Among the Innovative Methods

Innovative methods include microwave-assisted extraction (MAE), ultrasound-assisted extraction (UAE) or sonication extraction, pressurized liquid extraction (PLE) or accelerated solvent extraction (ASE), etc.

As mentioned, the number of known bioactive substances is a very large one, and for each substance or class of substances, thousands of specialized articles have been published. Some important international organizations and institutions regularly publish up-to-date information on individual substances. the most important of which are:

CODEX ALIMENTARIUS: https://www.fao.org/fao-who-codexalimentarius/resources/inf-doc/de/;

FAO Food and Agriculture Organisation: https://www.fao.org/home/en/;

WHO: World Health Organisation https://www.who.int/en/;

ePlantLIBRA: https://www.eurofir.org/our-tools/eplantlibra/;

EFSA: https://www.efsa.europa.eu/it;

FDA: Food and Drug Administration: An official US government website;

EUROPEAN MEDICINES AGENCY: https://www.ema.europa.eu/en;

International Life Sciences Institute of North America (ILSI): https://ilsi.org/about/;

International Food Information Council (IFIC): https://ific.org/ (*) [11].

(*) With regard to this organization, a number of documents were presented related to collusion with food multinationals, and the lack of objectivity.

The most relevant therapeutic activities exerted by bioactive substances include [12, 13]:

- antioxidant and anti-inflammatory activity;
- stimulation of the immune system;
- modulation of detoxification enzymes;
- modulation of hormonal metabolism;
- antibacterial and antiviral activity;
- anti-proliferative and pro-apoptotic activity;
- reduction of platelet aggregation.

Table 2 reported the cardioprotective activities of some bioactive substances in polyphenols for therapeutic use.

Table 2 Cardioprotective effects of bioactive substances in polyphenols. From, José S. Câmara, Bianca R. Albuquerque, Joselin Aguiar, Rúbia C. G. Corrêa, João L. Gonçalves, Daniel Granato, Jorge A. M. Pereira, Lillian Barros, and Isabel C. F. R. Ferreira; Food Bioactive Compounds and Emerging Techniques for Their Extraction: Polyphenols as a Case Study-Foods 2021, 10, 37.

Polyphenols		Main Cardioprotective Effects	Type of Assay
Classes	Compounds		
Phenolic acids	Gallic acid	↑Glucose tolerance	Animal model
	p-Coumaric acid	↑Glucose tolerance	Animal model
Anthocyanins		↓Platelet chemokines; ↓LDL-C	Clinical trial
		↓TC; ↓LDL-C	Clinical trial
Flavan-3-ols	Catechins	↓CK; ↓CK-MB; ↓LDH; ↓TnT; ↑LVEF; ↓LVIDs	Animal model
Flavanones	Hesperidin	↓CK; ↓ cTnT; ↓oxidative stress; ↓cardiac tissue lesions	Animal model
Flavones	Apigenin	Anti-cardiac fibrosis	In vitro
Flavonols	Quercetin	Anti-platelet properties;	In vitro
		↑Vasodilatation	Clinical trial
	Kaempferol	Anti-platelet properties	In vitro
		↓LDL-C	Clinical trial

Isoflavones		↓Blood pressure	Clinical trial
		↑Antioxidant activity in the blood; ↓Diabetic body weight	Clinical trial
Stilbenes	Resveratrol	↓TC; ↓blood pressure; ↓glucose	Clinical trial
		↓Blood glucose; ↓body weight; ↑plasma insulin; ↓inflammation factors; ↓oxidative stress; ↑eNOS	Animal model
Curcuminoids	Curcumin	↓Inflammation factors; ↓LDL-C; ↑Nrf2, ↓At1R; ↓NF-κB	Clinical trial

Legend: At1R—Angiotensin II type 1 receptor; CK—creatine kinase; cTnT—cardiac troponin; eNOS—Endothelial nitric oxide synthase; LDH—lactate dehydrogenase; LDL-C low-density lipoprotein cholesterol; LVEF—ventricular ejection fraction; LVIDs—systolic internal diameter; NF-κB—Nuclear factor kappa B; Nrf2—Nuclear factor (erythroid-derived 2)-like 2; TC—Total cholesterol.

As shown in Table 2, the mechanism of action is not specific to a particular substance, or a class of substances, normally several substances produce the same result, although they use a molecular target and a different mechanism of action. To better perform their functions, for example, the polyphenols act synergistically with carotenoids, which are found both in the plant and animal kingdoms and whose chemical structure is very different from polyphenols. Carotenoids belong to:

- carotenes, precursors of vitamin A, typical of carrot roots;
- lycopene from tomato;
- the xanthophyll or lutein spread in all green plants.

Some non-specific characteristics are typical of all polyphenols, others are typical of one or more families, and still others are still attributable to precise molecules of interest. The non-specific characteristic shared by polyphenols is the antioxidant activity that protects cells from free radicals generated by normal cell metabolism or environmental events, such as radiation, pollutants, or physical stress, etc. In this way, polyphenols help to slow down the speed of cellular aging. And their antioxidant effect can be always ascribed to other benefits, a feature common to all polyphenols:

- protecting the skin from UV damage;
- reducing inflammation by modulating enzymes such as cyclooxygenase and lipoxygenase;
- reducing the risk of cardiovascular disease;
- helping regulate blood pressure;
- inhibiting the growth of cancer cells and the development of microcirculation that feeds the tumor;
- protecting against the development of some forms of dementia or other neurological diseases;
- helping to reduce postprandial lipemia, that is, the presence of fats in the blood after meals.

Table 3 and Table 4 [14] have shown the properties of some polyphenols, the characteristics of which are synthesized below.

Table 3 Mechanism of actions of flavone and flavonol. From: Sivapragasam Gothai, Palanivel Ganesan, Shin-Young Park, Sharida Fakurazi, Dong-Kug Choi and Palanisamy Arulselvan; Natural Phyto-Bioactive Compounds for the Treatment of Type 2 Diabetes: Nutrients 2016, 8, 461 Inflammation as a Target.

Class	Compounds	Plant Sources	Mechanism of Actions
Flavone	Apigenin	Parsley, Celery, Rosemary Oregano, Thyme, Basil Coriander, Chamomile Cloves	1. Activation of ERK1/2 2. Attenuates the production of pro-inflammatory cytokines such as IL-6, IL-1β, and TNF-α
	Diosmin	Lemon, Orange Buddha fingers	1. Deactivation of NF-κB targets 2. Suppression of monocyte chemoattractant protein-1 (MCP-1), tumor necrosis factor (TNF-α), and interleukins (IL-1β and 6)
Flavonol	Quercetin	Capers, Onions Cranberries, Blueberrie Chokeberris	1. Inhibition of NF-κB system 2. Reduction in serum level of both TNF-α and CRP
	Kaempferol	Tomatoes, Onions Cranberries, Blueberrie Chokeberris	1. AMPK activation 2. Decrease the fasting blood glucose, and improved insulin resistance
	Eriodictyol	Lemons Mountain balm	1. Suppress the activation of NF-κB system 2. Reduce TNF-α, intercellular adhesion molecule 1 (ICAM-1), vascular endothelial growth factor (VEGF), and endothelial NOS (eNOS)

Table 4 Various bioactive food components, common food resources and biological functions. From Joy Emilie Swanson; Bioactive Food Components-Encyclopedia of Food and Culture – Encyclopedia.com.

Bioactive component	**Food source**	**Function**
Glucosinolates, diallylsulfides, isothiocyanates	Broccoli, cauliflower, brussels sprouts, garlic, onions	Induction of detoxifying enzyme systems, antimicrobial, immunomodulator, anticancer
Tocopherols and tocotrienols	Vegetable oil, nuts, seeds	Antioxidant, immunomodulator
Isoflavonoids and polyphenols	Grapes, red wine, tea, fresh fruit, and vegetables	Antioxidant, lipid- lowering, immunomodulator, antiosteoporotic, anticancer
Phytoestrogens (genistein, daidzein)	Soybean and other soy-based products, flaxseed, cabbage, legumes, tea	Antiestrogen, anti-osteoporotic, antiproliferative
Phytosterols	Vegetable oils, nuts	Lipid-lowering

Dietary fiber	Whole grains, oats, fresh fruit with skin	Lipid-lowering
γ-linolenic acid, α-linolenic acid, andomega-3 fattyacids	Evening primrose or borage oil, walnuts, rapeseed, flaxseed, fish, microalgae	Anti-inflammatory, lipid-lowering
Lutein	Green leafy vegetables	Reduction in age- related macular degeneration

6. Quercetin

Quercetin induces peripheral vasodilation by activating the enzyme protein kinase C, which is one of the molecular mechanisms of its antihypertensive effect. In addition, studies have also shown quercetin inhibits some oncogenic factors and increases apoptosis (i.e. programmed cell death).

7. Resveratrol

Resveratrol, present in red wine, grape skins and some legumes (peanuts), inhibits platelet aggregation and combines antioxidant properties with low cholesterol properties (it counteracts the oxidation of LDL), suggesting its possible benefits in the prevention of cardiovascular diseases.

8. Isoflavones

Isoflavones are polyphenols endemic to soy and red clover that mimic and modulate estrogen metabolism (hence the definition of phytoestrogens). They compete for the same estrogen receptors, even if they are less specific and perform a mild agonism/antagonism effect. They are used as post-menopause dietary supplements to combat osteoporosis, and hot flashes, but also appear to have a preventive effect against breast cancer and prostate cancer.

9. Phytosterols

In nature, 250 phytosterols have already been identified, and over the years they have entered the diet of many supplements, acting as cholesterol-lowering agents. The best-known of these substances are beta-sitosterol, campesterol, and stigmasterol, whose known mechanism of action is to compete with cholesterol for absorption.

The fundamental phase that food must overcome to become nourishment is digestion, a complex process that transforms natural foods into assimilated substances. The digestive process is different according to the animal species concerned, but it goes through the same fundamental physiological stages, in the various traits of the digestive system, as shown in Figure 2.

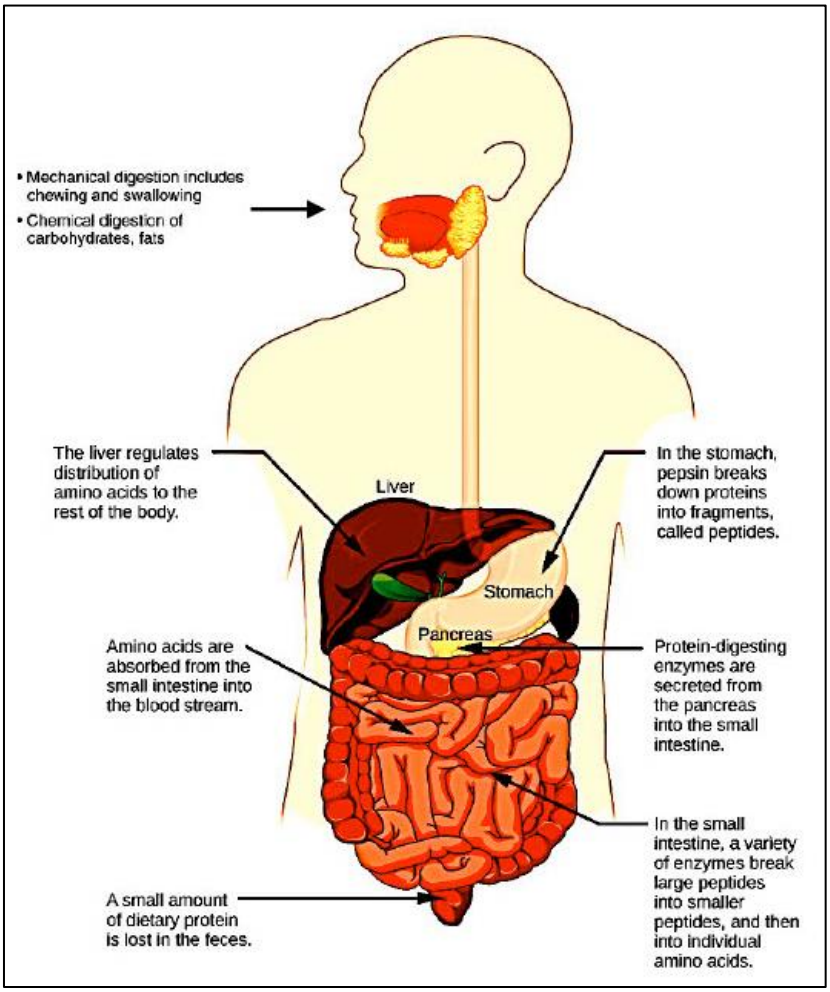


Figure 2 Scheme of the digestive process: Nutrient Acquisition by Animals by Georgia Tech Biological Sciences https://organismalbio.biosci.gatech.edu/.

Understanding how the interactions between bioactive substances and molecular targets are achieved requires first understanding all the phases of the metabolic pathway, from absorption to tissue distribution and bioavailability, as well as the fundamental properties that produce the biologically relevant effect, as shown in Figure 3 [15, 16].

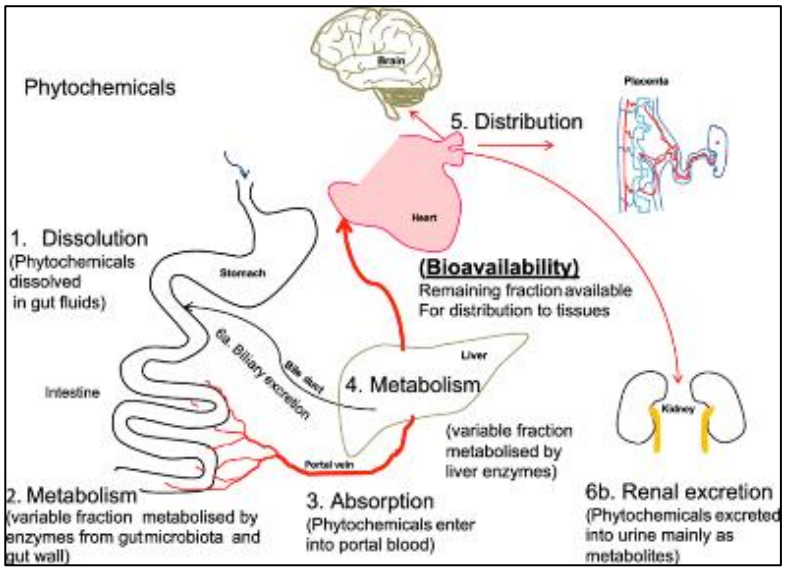


Figure 3 Scheme of oral bioavailability and disposition of phytochemicals. Absorption and disposition of phytochemicals in humans. - From: Yan Li and James W. Paxton ResearchGate-21 January 2015.

- **Absorption**: Describes how the substances move from the site of administration to the site of action.
- **Distribution**: Describes the flow of active substances through the bloodstream to various tissues of the body.
- **Metabolism**: Describes the process that breaks down substances.
- **Excretion**: Describes the excretion of substances from the body.
- Many factors influence the absorption and bioavailability of bioactive substances, including [17]:
- type of chemical compound and its form;
- whether there is a selective tropism;
- binding to other molecules (e.g. by esterification or glycosylation);
- interaction with other components;
- the nature of the food matrix (e.g. solid, liquid);
- the presence of factors in food that increase or counteract its absorption;
- the processing process the food undergoes (thermal, homogenization, etc.);
- intrinsic factors of absorbing biological structures, presence of transport systems, presence of specific channels, etc.;
- particular physiological or pathological conditions.

10. Absorption from the Gastrointestinal (GI) Tract

To achieve their beneficial effects, these bioactive molecules must overcome several absorption barriers in the GI tract before they can be delivered to the target tissues and organs. First of all, they must dissolve in the GI tract and survive at different pH intervals from the stomach to slightly basic in the small intestine. They may also undergo degradation and metabolism by intestinal enzymes, such as glycosidases, esterases, oxidases and hydrolases, which are derived from the host and the microbiota residing in the GI tract.

11. Distribution

Once the substance is absorbed, it is transported through the body. It flows from blood to intracellular tissues and fluids and binds to receptors. And its distribution can be reversible, meaning that molecules that are not absorbed and released by receptors can return to the bloodstream. This step may be partially responsible for the side effects of a phytochemical. Because the substance is transported throughout the body, it can affect one or more organs, and some organs may not be the target organ for the substance to reach (Figure 3).

12. Metabolism

After the substance has been systemically distributed, the next stage is metabolism, which is the stage where phytochemicals are broken down. Metabolism occurs mainly in the liver, and although the liver is the primary site of the metabolism of active substances, other organs such as the kidneys, gastrointestinal tract, and lungs may also perform metabolic functions. During this phase, enzymes break down the Phyto complex to create metabolites.

13. Excretion

The final phase in the pathway of the bioactive substance within the body is excretion, the process by which the substance and its metabolites are eliminated from the body, mainly through urine or feces. Some substances can also be excreted through breast milk or expired air. A substance can be excreted in its altered form, either metabolized or excreted intact.

14. Bioavailability

Bioavailability refers to the active fraction of a nutrient that reaches the systemic circulation and the specific sites where it can exercise its biological activity.

15. Nutritional Quality Index (NQI)

The NQI expresses the property of a nutrient to completely meet a specific requirement or functional need and is calculated as the ratio between the nutrient need coverage and the caloric need coverage, which is described for each portion of food administered.

16. Use of Bioactive Substances

Among the bioactive substances available today, plant extracts are the most widely used, both because of the long tradition and experience in their use passed down through the years and because of the wide range of available products [14, 18]. Incidentally, many drugs of current use are derived from standardized plant extracts. The active component of plant extracts is called Phyto complex, which includes:

- **one or more active ingredients**: one or more substances having a biological nutritional effect;
- **secondary metabolites:** substances other than the active substance, which have synergistic activity with the active substance by modulating its pharmacokinetics, absorption, metabolism, elimination, and consequently the pharmacological profile.

So there is a difference between the active ingredient and the Phyto complex.

- The "Phyto complex" is the set of substances (active ingredient + secondary metabolites) that gives a plant a specific healing power;
- The "active ingredient" generally means any substance with specific biological activity, which can be either toxic (e.g. in poisons) or therapeutic (e.g. in drugs).

Then, it is possible to make a comparison between the Phyto complex and the drug:

Phyto complex (obtained from the plant) ⟹ active ingredient + secondary metabolites

Drug (*) ⟹ active ingredient + excipients (* often obtained synthetically, or extracted from the Phyto complex obtained from the plant).

Of all the values described so far, the most important for nutritional purposes is the amount of substance that reaches the molecular target in bioavailable active form, to become a "bioactive substance".

The minimum effective dose (M.E.D.) is defined as the lowest dose producing a blood concentration at which the substance takes effect. Similarly, a sub-toxic dose is defined as a dose that produces a blood concentration below which secondary and/or toxic effects occur (Figure 4).

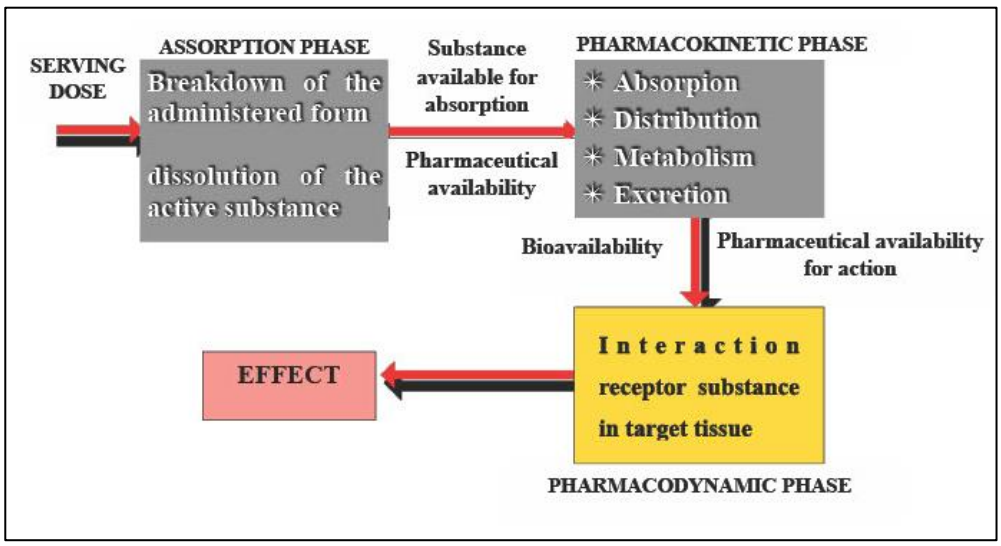


Figure 4 The absorption, pharmacokinetic and pharmacodynamic phases of phytochemicals in humans. From: Yan Li and James W. Paxton; Oral Bioavailability and Disposition of Phytochemicals Absorption and disposition of phytochemicals in humans. - ResearchGate-21 January 2015.

17. Dose Ratio Administered and Efficacy

The nutritional value of many bioactive substances currently in use has been widely confirmed in numerous literature monographs. Nutraceutical substances have entered the scope of treatment therapeutic by general practitioners and specialists, who are increasingly using them either as an adjuvant to drug therapy, or as a primary treatment in the prevention of chronic pathologies-degenerative under particular conditions, or as a dietary supplement in deficiency forms. Another use favored by nutritionists is the addition of specific nutrients to food, therefore defined as "functional foods", which play an irreplaceable role in the prevention of large-scale endemic nutritional deficiencies.

There is no unanimous agreement on the definition of nutraceuticals and functional foods among dietetic operators. According to the International Food Information Council (IFIC), (*) functional foods are "or dietary components that may provide a health benefit beyond basic nutrition". While the International Life Sciences Institute of North America (ILSI) has defined functional foods as "foods that by virtue of physiologically active dietary components provide health benefits beyond basic nutrition".

Functional foods include fortified cereals, bread, sports drinks, bars, fortified snacks, baby food, prepared meals, and more. Despite their high nutritional value, bioactive substances that become part of functional food or supplements tend to have reduced bioavailability or lower nutritional index, and often also reduced absorption. So that to achieve their optimal nutritional effect, they must be administered in massive doses.

In addition, in many cases, bioactive substances form complexes with the food matrix containing these substances and are poorly usable for nutritional purposes. This occurs in many plant foods, where bioactive substances bind with the so-called anti-nutrients, represented by structural components of plants, which is not always possible to eliminate with the process of purification of active substances [19, 20]. The best-known are:

Lecithins, oxalates, phytates, saponins, haemagglutins, tannins.

These substances form insoluble complexes with true nutrients and are poorly digestible and therefore have reduced nutritional value.

When nutrients are essential for diet and health, such as many vitamins and minerals, methods of extraction from other food sources or chemical synthesis are used. Examples include iron, the B complex vitamins, vitamin D, Omega 3, etc. But even when obtained by synthesis, many of these substances, those mentioned in particular, are still poorly absorbed or with unpleasant organoleptic properties, or still with reduced therapeutic index. Fortunately, new technologies provide us with a way to overcome these limits, using substances of various chemical composition, which include nutrients and act as carriers to facilitate their absorption and assimilation, or to overcome organoleptic defects, for which they are called delivery systems [21-23]. These carriers have the ability to contain the active substances in them and overcome the barriers that prevent their absorption, represented by the endothelial cellular membranes. This is because their chemical structure has considerable affinity with cell membranes that can easily cross, as shown in the example of liposomes in Figure 5.

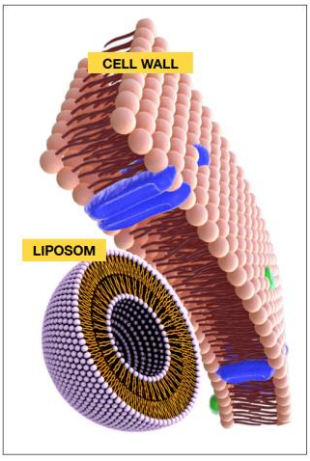


Figure 5 Structural affinity of liposome ssswith cell wall-From Autor’s data on file.

Liposomes are among the most widely used delivery systems, because of their simplicity of production and versatility compared to the other available carriers in Figure 6, in particular in the case of drugs with low therapeutic indexes such as antitumor or gene therapy. However, due to the high cost of liposomes, they are poorly used for the production of nutraceuticals or functional foods, and they are used only in selected cases or for particular nutrients with high biological value, or with reduced therapeutic index.

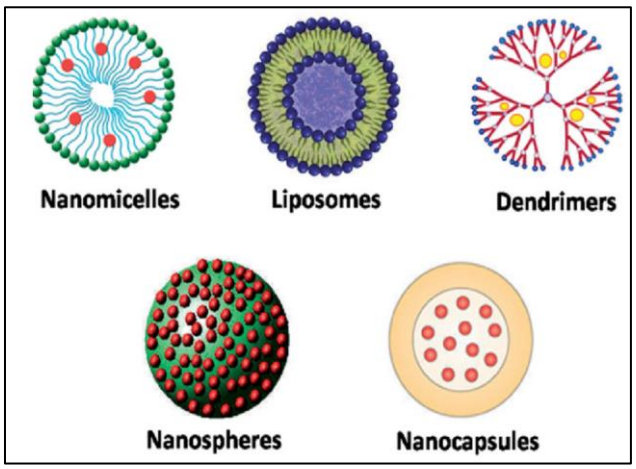


Figure 6 The most widely used delivery systems. From Riccardi B.; The Added Value of Technology in Food Integration-Holistic Approach, *J. Nutrition and Food Processing*, 5(4)-August 31, 2022.

18. The Use of Delivery Systems in Functional Foods and Supplements

There are very few examples on the market of the use of delivery systems in functional foods and supplements. But in no case is such products provided with strict documentation on their production technology, but they only emphasiz the obtained clinical results with exaggerated claims. Such a lack of correct information may rise legitimate doubts about the quality standards of producers. Special mention should be made of the products obtained by LIPOTECH S.A. (www.lipotech.com.ar), an Argentinian company that has patented, in an impeccable way, cutting-edge technology used for the production of liposomes and has documented the clinical results obtained with these liposomes. The company produces bioactive substances including:

- Biofer (Patented): Iron solphate and vitamin C in liposomes;
- Iron-Folic (Nutraceutical product): Iron solphate and vitamin C + B vitamins in liposomes;
- Lifervit (Patented): Iron solphate, vitamin C, folic acid, vitamin B6, and vitamin B12 contained in the single liposomes;
- Ferric Pyrophosphate microencapsulated: Iron pyrophosphate microencapsulate.

Confirming the high technological content achieved by Lipotech, Figure 7 showed the micrographs obtained from the work of Biofer and Lifervit of Lipotech S.A. [24-29], who documented in an incontrovertible way the morphological and uptake of liposomes he produced on the cell cultures.

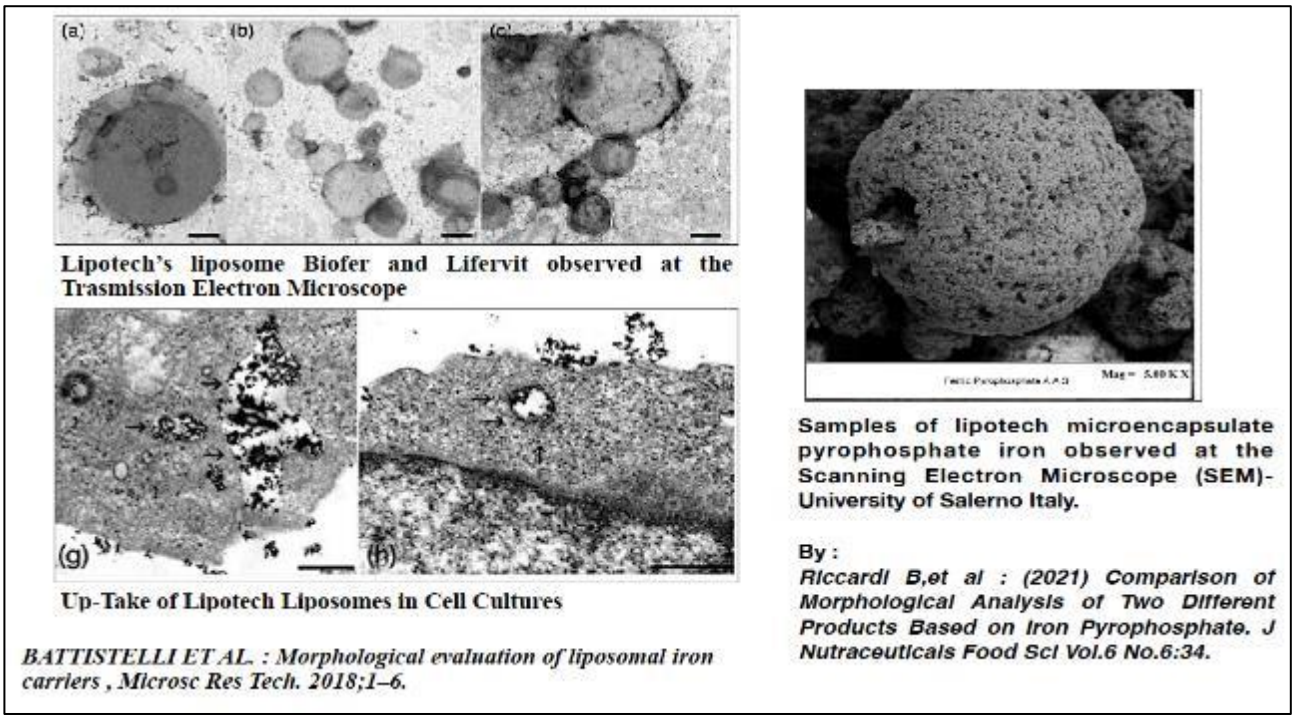


Figure 7 Morphology and uptake of liposomes produced on cell cultures. From Riccardi B.; The Added Value of Technology in Food Integration-Holistic Approach, *J. Nutrition and Food Processing*, 5(4)-August 31, 2022.

19. The Problem of Additives, Preservatives and Pesticides

A synthetic description of active substances and their use in supplements and functional foods, could not neglect a critical examination of the production processes adopted by the food industry. The need for intensive production of raw materials, cereals, wheat, milk and dairy products, vegetables, oil, etc., and their preservation in the food distribution chain for mass distribution has led to the increasingly widespread and indiscriminate use of pesticides, preservatives, sweeteners, flavor modifiers, and antibiotics, which irretrievably compromise the nutritional qualities of food and pose risks to consumer health [30-33].

In the advanced industrial society, food, like other products, is increasingly characterized as a consumer good, suitable to meet the needs of consumers artificially and scientifically induced using advertising, which is completely indifferent to the real nutritional and welfare needs. Even the increasing number of beverages on the market is not exempt from the same problems. In particular, in so-called functional beverages, the information provided by manufacturers is misleading as regards the health properties claimed. Whenever nutrients are found to be present in trace amounts and are often improperly indicated, for example, manufacturers declare the presence of vitamins and fat-soluble substances in water-based beverages. The level of food adulteration and sophistication has reached and surpassed guard levels, many consumer associations have long denounced the scale of the problem.

It is no coincidence that food diseases have taken on a real pandemic scale, with an exponential increase in obesity, dysmetabolic diseases, celiac diseases, diabetes, etc [34-37]. The categorical imperative of food needs in the consumer society has gone from Hippocrates' recommendation of "makes food a medicine", to the most unscrupulous consumer conditioning. In the consumer

society, food is not used not to satisfy physiological needs, but to fill the "consumerist" appetites that are induced by unrestricted or unregulated urgent advertising, and destined to fill the stomachs and the existential emptiness of the new generations.

A key part of global food misinformation lies with international organizations that have been created to confuse and confuse consumers about the mystified value of unsafe food. This is the word from the HTTPS organization: Pursuing Truth and Transparency for Public Health (HTTPS://USRTK.ORG/). This organization denounces and documents the numerous violations of the safety standards by multinational food companies in normal production processes for the sole purpose of maximum profit.

20. Conclusion

From food as a consumer good to responsible nutrition. The industrialized production of food has had negative consequences throughout the food chain, from the extraction, production and distribution of nutrients, and to their unregulated consumption. We are witnessing the limitless exploitation of natural and energy resources, and the production of polluting waste with consequent distortion and environmental degradation. The sophistication and adulteration of food products have the sole purpose of satisfying the growing needs of consumers artificially induced by advertising pressure. The only institutions that benefit from this type of approach are the food multinationals, dedicated to the industrial production of artificial food and junk food. I am convinced that the study and knowledge of bioactive substances and functional foods cannot be an end in itself, but the well-being of the recipients and end users (consumers) of these products must first be considered.

In fact, it is the physiological interaction between food and the biological apparatus of consumers that determines the nutritional result of well-being or food imbalance. The nutritional effect produced by foods, no matter how healthy and controlled they may and should be, also inherently depends on the condition of the consumer. Therefore, the sex, age, health status, etc. of the recipients must also be taken into account to evaluate the effect that the type of nutritional interaction can determine. Therefore, modern nutrition science must take a holistic approach, and consider all the factors that intervene in the food-patient relationship when determining the final nutritional result. In fact, it is the study of food-consumer interaction that has shown the increasing incidence of food intolerances in recent years, which compromise or nullify all efforts dedicated to the production of healthy nutraceuticals. There are various forms of congenital or acquired food intolerance that have taken on global proportions and represent a major health policy problem. Those most frequent are lactose and gluten intolerance, in these cases intolerant subjects should not consume foods that contain these substances.

Effective health policy requires full cooperation between dieticians and primary care professionals who treat patients. If we really want to restore the nutritional and therapeutic value of food, according to the teaching of Hippocrates, we must first completely change the method of food production, which must be sustainable and aimed primarily at meeting the biological needs and social well-being, and must also assess the impact of food on the individual subject, in accordance with the requirements of individualized nutrition. This priority need must be the basis of the founding value, and of the guidelines that inspire the science of nutrition in respect of human needs and balance with nature. This discipline cannot and should not be limited to the study of

nutrients and the effects they produce, in isolation from the production context and the end user, because these elements play a fundamental role in the resulting state of health. If the fundamental goal of nutrition is general well-being, then the correct information about the use of nutrients and a healthy lifestyle must be an integral part of nutrition science, and this cannot be negotiated and replaced by the study of nutrients and their mechanism of action.

Author Contributions

The author did all the research work of this study.

Competing Interests

The author has no conflict of interest in this manuscript.

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