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Nutraceuticals in cardiovascular disease: a new opportunity for a better health

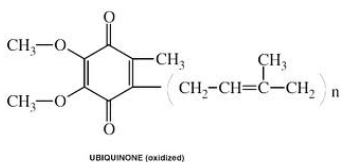
The term "nutraceutical" was coined in 1989 from "nutrition" and "pharmaceutical" by Stephen DeFelice, MD, founder and chairman of the Foundation for Innovation in Medicine from Cranford, New Jersey (USA). Today, as commonly used in marketing, this term is extensively used to describe **any product derived from food sources that provides extra health benefits in addition to the basic nutritional value found in foods** (1). These products typically claim to prevent chronic diseases, improve health, delay the aging process, and increase life expectancy.

Nutraceutical category

Because of a minimal international regulation over which nutraceuticals are allowed in the market we can find multiple different types of products that fall under the nutraceutical category. Because of this some of them have overlapping definitions. The most usual are herbals, dietary supplements, functional food, nutraceutical specifically said.

Herbals

Herbalism is a traditional medicinal or folk medicine practice based on the use of plants and plant extracts. Herbalism is also known as botanical medicine, medical herbalism, herbal medicine, herbology, and phytotherapy. An herbal is "a collection of descriptions of plants put together for medicinal purposes." (2) It is more than 100 years that doctors currently use herbals such as: digitalis lanata and atropa belladonna in clinical practice. Today the most of herbals being marketed as heart healthy, include CoQ10, garlic, fenugreek, magnesium, ginger, grape seed extract, l-carnitine, extract vitamins, flax seed oil, and ginkgo bilobe. But herbals are drugs too hence, all herbal supplements can have side effects too, ranging from mild to severe.



Digitalis lanata

They also interact with other herbs, drugs and food.

Dietary supplements

According to Dietary Supplement Health and Education Act of 1994 (DSHEA) (3) a dietary supplement is :

1. **a product** (other than tobacco) that is **intended to supplement the diet that bears or contains one or more of the following dietary ingredients**: a vitamin, an amino acid, a mineral, an herb or other botanical, ,
2. **a dietary substance** for use by man to supplement the diet by increasing the total daily intake, or a concentrate, metabolite, constituent, extract, or combinations of these ingredients.

Moreover a dietary supplement:

1. is intended for ingestion in pill, capsule, tablet, or liquid form
2. is not represented for use as a conventional food or as the sole item of a meal or diet
3. is labeled as a "dietary supplement"

The "dietary ingredients" in these products may include: vitamins, minerals, herbs or other botanicals, amino acids, and substances such as enzymes, organ tissues, glandulars, and metabolites. Dietary supplements can also be extracts or concentrates, and may be found in many forms such as tablets, capsules, softgels, gelcaps, liquids, or powders

Under the DSHEA rules, the dietary supplement manufacturer is responsible for ensuring that a dietary supplement is safe before it is marketed. FDA is responsible for taking action against any unsafe dietary supplement product after it reaches the market. Generally, manufacturers do not need to register their products with FDA.

Functional food

It is intended **a food cooked or prepared using "scientific intelligence" with or without knowledge of how or why it is being used.** It provides the body with the required amount of vitamins, fats, proteins, carbohydrates, etc, needed for its healthy survival. Functional foods are designed to allow consumers to eat enriched foods close to their natural state, rather than by taking dietary supplements manufactured in liquid or capsule form. They have been either enriched or fortified by a process called nutrification. Functional foods definitively are and must be foods and not drugs (Roberfroid, 2000).

Nutraceuticals specifically said

When functional food aids in the prevention and/or treatment of disease(s) and/or disorder(s) other than anemia, it is called a nutraceutical. Firstly they were defined by dr DeFelice as "a food (or part of a food) that provides medical or health benefits, including the prevention and/or treatment of a disease." Recently nutraceuticals, according to Health Canada, **must not only supplement the diet but should also aid in the prevention and/or treatment of a disease and/or a disorder.** Since most of the functional foods act in some way or the other as antianemic, the exception to anemia is considered so as to have a clear distinction between the two terms, functional food and nutraceutical. Thus, a functional food for one consumer can act as a nutraceutical for another consumer. Examples of nutraceuticals include fortified dairy products (eg, milk) and citrus fruits (eg, orange juice).

Nutraceutical and cardiovascular disease

As highlighted before nutraceutical affect chronic disease. Is than inevitable a large (favourable claimed) impact on cardiovascular disease such as:: heart attack/ischemia, stroke, coronary artery

disease, corpulmonale, hypertension or deep vein thrombosis, and atherosclerosis is than inevitable.

Nutraceuticals can follow several ways to take their effect on cardiovascular disease. First of all **they tend to reduce circulating levels of LDL-cholesterol**. This is achieved by modulating cholesterol production in the liver (i.e. monacolin, policosanol, red yeast rice, etc.), binding cholesterol within the intestines and/or increasing LDL-c receptor uptake in the liver (i.e berberina, phytosterols, etc.). In a 2003 research review from the UK's Peninsula Medical School, 11 nutraceuticals were found among 25 clinical studies to reduce cholesterol. The second strategy is to **reduce the possibility of oxidation by neutralizing radicals with antioxidants** (i.e. resveratrol, bioflavonoids, ubiquinone, phenols, flavones, etc) . The third strategy ends to reduce artery plaque through **fibrinolytic activity and to reduce blood pressure** (i.e. dietary peptides derived from milk protein mediated by ACE inhibition). Nutraceuticals are told to execute all three strategies.

Nutritional genomics

A new powerful and troubled market come from nutritional genomics that is the application of high skilled functional genomic technologies in nutrition. It means new or modified food for human and animal nutrition, but also the definition of gene polymorphisms that predispose individuals to disease and modify nutritional requirements. (4) Furthermore another interesting opportunity comes from the effect of certain nutraceuticals on stem cell growth and proliferation. (5)

Cardiological approach to nutraceutical

According to a recent review most cardiologists overlook the use of dietary supplements nutraceuticals and over-the-counter (OTC) drugs by heart patients because they consider them innocuous; lump them with dietary measures and lifestyle interventions; or consider them to be 'natural' and, therefore, safe and effective. In other words clinical providers "largely ignore" the use of nutraceuticals and OTC drugs in their patients. The study concluded that "clinicians should use a structured approach for identifying patient use of nutraceuticals and OTC drugs." (6)

Marketing and regulation

If herbals, dietary supplement and functional food are sold in many different places outside pharmacies (eg, supermarkets, herbalist's shop, etc...) on the contrary nutraceuticals are essentially sold in pharmacies and parapharmacies in form of drug and they claim drug properties.

Furthermore one bigger, attractive, and, sometimes dangerous, increasing market is on Internet. Here some companies looking to create a wide profit margin may create unregulated products with low-quality or ineffective ingredients.

Many reasons have increased in the last years the consumption of this products. Some of them are: society medicalization and alleged good outcomes with low side effects. Moreover the high cost of prescription of pharmaceuticals and reluctance of some insurance companies and health national systems to cover the costs of drugs help nutraceuticals to solidify their presence in the global market of therapies and therapeutic agents. According to CORDIS -the information service of the European Commission for research and development of science- nutraceuticals had a European turnover of about 1.4 billion euros in 2008 with 11% growth compared to 2007.

Many pharmaceutical and biotechnology companies have smelt the business and have invested heavily in nutraceutical sector to create a market that aims to cover 5% of the value of food sales worldwide

USA regulation

The FDA considers medical foods “to be formulated, consumed or administered internally under the supervision of a physician, and which is intended for the specific dietary management of a disease or condition for which distinctive nutritional requirements, on the basis of recognized scientific principles, are established by medical evaluation.”

In the private area from January 2007 the Nutraceutical Research & Education Act (NREA) proposed by the Foundation for Innovation in Medicine (supported by Dr DeFelice) to establish a new mechanism for exclusivity in nutraceutical area that is essential for the creation of a responsible, industry-funded, primarily clinical research-based industry. It also required the creation of appropriate channels for the review, approval, and regulation of new products and claims. (7)

EU regulation

The harmonization of EU food and food derived products law has been in progress for forty years. In 1985 a White Paper from European Commission to the European Council recommended a new legislation. **In 2000 the European Commission published five horizontal framework directives** which identified requirements of public health and safety, consumer information and general food control measurements. The five directives are on:

1. Food labelling and presentation
2. Food additives
3. Materials and articles in contact with food
4. Official control of food staffs
5. Food for particular nutritional uses (PARNUTS)

Since then, more than 90% of the White Paper proposals have been implemented. The ILSI Europe Report Series has published the “Application of the margin of exposure approach to compounds in food which are both genotoxic and carcinogenic”. The EFSA (European Food Safety Authority) controls the safety assessment of botanicals and “botanical preparations” intended for use as ingredients in food supplements (Guidance document of scientific committee. Question no EFSA-Q-2005-233). The rules of the general food law regulation are applicable to all foods. **In other words, there are a lot of regulations and, there is not, as such, a regulatory framework for ‘functional foods’ or ‘nutraceuticals’ in EU food law.**

This is why doctors and members of the medical community desire that the nutraceutical term be more clearly established in order to distinguish between the wide varieties of products out there.

However, with all of the aforementioned positive points, nutraceuticals still need support of an extensive scientific study to prove “their effects with reduced side effects.” Issues of study quality and bias, true efficacy, and toxicity continue to cause uncertainty.

The accumulated knowledge about nutraceuticals need to be validated and represents a great challenge for many professionals such as nutritionists, physicians, food technologists and food chemists. Only after this process public health authorities could consider prevention and treatment with nutraceuticals as a powerful, natural, and cheap instrument in preventing and maintaining health.



In conclusion we think we need first of all more attention to nutraceuticals from doctors, than a better taxonomy, more regulation, and the activation of some registers and national surveys to acquire the present consumption and indications. More controlled studies will give the scientific evidence essential to nutraceutical somministration both in prevention and therapy of cardiovascular disease. Finally the study and regulation of nutritional genomics can enable to use of nutraceuticals as an alternative to stem cells transplantation, targeting of nutritional advice and the development of food derived treatments by new nutraceutical for the best treatment at the level of population, particular group at cardiovascular risk, and individuals with cardiovascular disease.

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