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Scientific Evidence of Ethnobotanical and Mediterranean Knowledge of Food- and Well-Being Plants

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Abstract:
The scientific evidence of ethnobotany related to health-food plants use, is an urgent request referring to the botanical-based food supplements. The necessity to verify its scientific validity springs from the fact that plants produce thousands of active metabolites, not always quantifiable one by one. From this complex picture, it is clear that we need to define some criteria to be used in the studies of biologically active plants. One criterion, valid and effective, implies the statistical elaboration of data obtained from an ethnobotany survey, derived from traditional use as a starting point in experiments for the proof of biological activity. About three-quarters of the biologically active compounds presently in use worldwide, have been discovered through follow-up research to verify the authenticity of the data based on folk and ethnobotanical use. Over hundreds of years, man acquired a great knowledge on the use of plants, knowledge which must be safeguarded and considered scientifically valid.
Keywords: traditional use, quantitative ethnobotany, scientific evidence, health claims

INTRODUCTION

The traditional use and knowledge regarding food and health plants are determining factors to support and validate the physiological effects of a plant and/or its extract. Cultural food heritage must be preserved because it is a crucial factor which allows such knowledge to be handed over from one generation to another. The starting point for a serious ethnobotanic survey is a scientific approach. Before searching for information about a plant it is vital that a correctly spelt and up-to-date plant name is used, as suggested by the Kew Royal Botanic Gardens [1]. The next step is to continue the study with a methodological procedure, using only official scientific literature and reliable textbooks [2]. Only by examining such sources, we can understand the scientific basis related to traditional plant use. The ethnobotanic knowledge has recently been evaluated by many researchers and it is possible to find a great quantity of scientific papers, meta-analysis and epidemiologic data linking the traditional use with the scientific approach [3-9]. Roman and Greek heritages were a reference point for the Mediterranean area and Charlemagne's (742-814) edict *Capitulare de villis vel curtis imperii Caroli Magni* defined (among other things) a large number of agricultural laws and made a list of 89 food and health plants that had to be grown in the *Hortus simplicium* of all the monasteries of his empire (in the more Northern parts of Central and West Europe). It was actually the first case of knowledge sharing in European countries [10]. In Europe it is estimated that about 2,000 plants are traded commercially, of which 60-70 % are natives. Up to 90% of these species are still collected from the wild. These plants constitute an important market and an important genetic base for many essential drugs [11]. The renewed interest which emerged in European ethnobotany and ethnobiology in the last few years, has also thrown light on the actual situation and convinced UNESCO to officially recognize the Mediterranean diet.

Unesco Intangible Cultural Heritage of Humanity: Mediterranean diet and Ethnobotanic knowledge

The discovery of the Mediterranean diet is attributed to the American nutritionist Ancel Keys, who landed in Salerno in 1945. Stationed in the Cilento area, Keys noticed that cardio-vascular illnesses, which were widespread in his own country, were quite rare. In fact, among the population of Cilento there was a particular low incidence of the so called "diseases of affluence" (arteriosclerosis, hypertension, diabetes). These observations were the basis for an investigational scientific program (more than 12.000 subjects were observed). The results showed that the more they moved away from the Mediterranean areas, the higher the incidence of the above illnesses was recognised. A discovery that led American scientists to set up in the 70s a widespread program of preventive medicine based on the studies conducted by Keys in Cilento. The basic elements of such program are cereals (bread, pasta, polenta), legumes, vegetables, fruit and olive oil [12-14]. Recently, the Mediterranean diet has been recognized by UNESCO as an Oral and Intangible Heritage of Humanity, due to its historical importance and its positive effects which maintain and improve human health [15]. In 2007 the process of recognition by UNESCO started from Pioppi a small town (Salerno province), Cilento area, in Italy, soon followed by Soria in Spain, and then by Koroni in Greece and Chefchaouen in Morocco. The Mediterranean diet has been officially included in the UNESCO Cultural Heritage List on 16th November 2010. Point N° 3 of the UNESCO document states that "The nomination describes a series of safeguarding efforts undertaken in each country, together with a plan for transnational measures aimed at ensuring transmission to younger generations and promoting awareness of the Mediterranean diet." The Mediterranean diet (from the Greek □□□□□□ that means "way of life") is not simply based on food but is made up of other aspects such as knowledge, practices, skills, and traditions which range from landscape to table, including crops, harvesting, fishing, preservation, processing, preparation and, particularly, consumption of food. The Mediterranean diet is characterized by a nutritional model that remained constant over time and space, consisting mainly of olive oil, cereals, fresh or dried fruit and vegetables, a moderate amount of fish, dairy products and meat, and many condiments and spices, all accompanied by wine or infusions.

Many scientific studies have been carried out in order to evaluate the effectiveness of the Mediterranean diet, and the discovery of the health-promoting properties of the Mediterranean diet is one of the great successes of epidemiologic research in the second half of the 20th century [16].

The Mediterranean diet is often cited as beneficial for being low in saturated fat and high in monounsaturated fat and dietary fiber. One of the main explanations is thought to be the health effects of olive oil included in the Mediterranean diet [17].

The Mediterranean diet is high in salt content. Foods such as olives, salt-cured cheeses, anchovies, capers, salted fish roe, and salads dressed with olive oil all contain high levels of salt [18].

A psychiatric assessment conducted in the Mediterranean area, has showed that people who followed the Mediterranean diet were less likely to develop depression [19]. In addition, the moderate consumption of red wine improves antioxidant defenses, as it contains flavonoids with powerful antioxidant properties [20]. A 10-year study published in the Journal of American Medical Association (JAMA) found that adherence to a Mediterranean diet and healthy lifestyle can lower death rates by more than 50% [21]. Dietary factors are only part of the reason for health benefits enjoyed by certain Mediterranean cultures. A healthy lifestyle (notably a physically active lifestyle or job) is also beneficial [22, 23]. There is an inverse association between adherence to the Mediterranean diet and the incidence of fatal and non fatal heart disease in initially healthy middle aged adults in the Mediterranean region [24]. Interestingly, residents of the Mediterranean area present also very low rates of skin cancer (which is widely believed to be caused by over-exposure to solar UV radiation). The incidence of melanomas in the Mediterranean countries is lower than in Northern Europe and significantly lower than in other hot countries such as Australia and New Zealand. It has been hypothesized that some components of the Mediterranean diet may provide protection against skin cancer [25].

Another important and interesting approved document is the *Convention for Safeguarding Intangible Cultural Heritage* adopted in Paris by UNESCO: 17 October 2003 [26].

In this Convention, for the first time, it was stated that *knowledge and practices concerning nature and the universe* are part of our cultural heritage. This means that ethnobotany, ethnobiology, traditional environmental knowledge, ethnoveterinary, folk medical, and pharmaceutical knowledge are now recognized as being inextricable components of culture, and therefore worthy of being protected and sustained. The Convention's statement also represents an important shift in the political approach to scientific research concerning *ethnobiology* and *traditional knowledge*, which in ethnobotany represent the focus or the starting point of a lot of research and analysis.

Ethnobotany: History and Methods for a Quantitative Ethnobotany

For anthropologists, ethnobotany can be defined as an anthropological and historical approach to botany. Anthropological ethnobotany focuses, in the literal ethimological sense, on the human knowledge and practice of plants used as food, venoms, medicine, psychotropic or religious effects, etc. That means that this discipline studies how the evolutionary past of *Homo sapiens* has influenced his social organization and culture within the local socio-cultural context. The term "anthropology" was first used in 1501 by the German philosopher Magnus Hundt [27] and the anthropological interpretation of botany does not coincide with the "ethnobotany" first used by the botanist J. W. Harshberger in 1896 [28]. Ethnobotanists aim to document, describe and explain complex relationships between cultures and uses of plants, focusing, primarily, on how plants are used, managed and perceived across human societies (e.g. as foods; as medicines; in divination; in cosmetics; in dyeing; as textiles; in construction; as tools; as currency; as clothing; in literature; in rituals; and in social life).

Although the term ethnobotany was not used until 1896, practical interests in it go back to the beginning of civilization when people relied on plants for their survival. In European countries, ethnobotany started from the Roman and Greek cultures, and the herbal medicine of ancient Greece laid the foundations for our Western medicine [10]. Ethnobotany, the largest subdiscipline of ethnobiology, is generally defined as the "science of people's interaction with plants" [29]. Ethnobotanical research is a complex field that combines concepts derived from many disciplines including botany, anthropology, ecology, agriculture, genetics, evolution, economics, conservation biology and biochemistry. It has many fields that have helped to update and prove its usefulness in medicine, pharmacy, pharmacognosy, chemistry, archaeology, *etc.*

In the past, most ethnobotanical studies recorded vernacular names and uses of plant species with little emphasis on quantitative studies. In order to enhance the indicative value of ethnobotanical studies, in recent years there have been attempts to improve the traditional compilation-style approach via the incorporation of suitable quantitative methods of research in ethnobotanical data collection, processing and interpretation. Such quantitative approaches aim to describe the variables quantitatively, and analyze the observed patterns in the study, besides testing the hypotheses statistically. The concept of quantitative ethnobotany is relatively new and the term itself was coined only in 1987 by Prance and co-workers [30]. Quantitative ethnobotany is the elaboration of raw ethnobotanical data, and it may be defined as "the application of quantitative techniques to the direct analysis of contemporary plant use data" [31, 32]. Different approaches are taken to collect and analyse quantitative and qualitative ethnobotanical data. Some are suggested by the researchers of the Kew Royal Botanic Gardens [1, 2]. Other Authors presented their opinion in order to quantify and scientifically explain the ethnobotanical data [33 - 36].

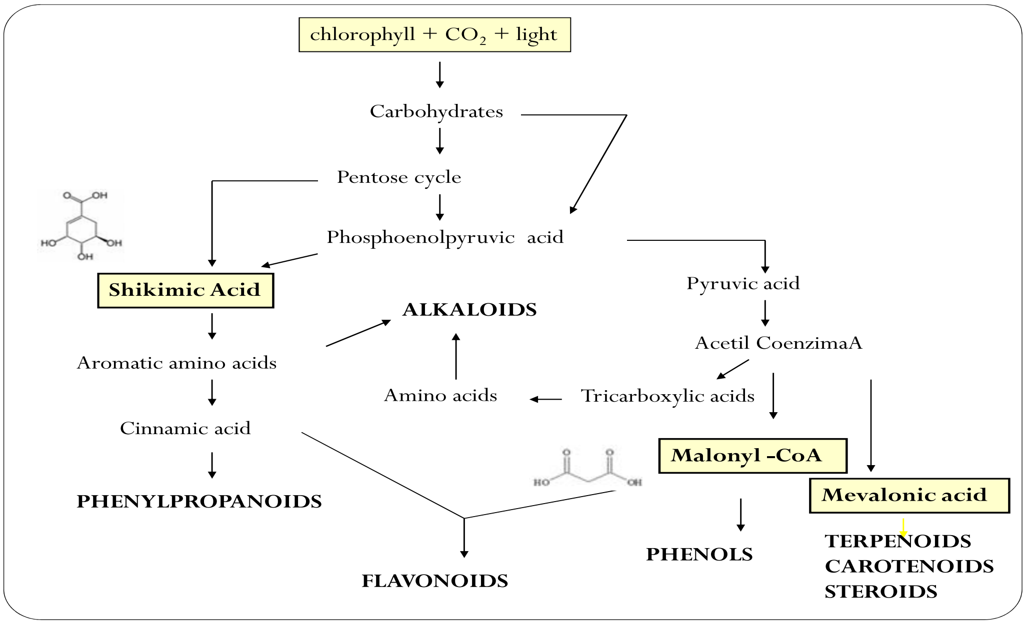
Hoffman and Gallaher focused his research statistically quantified by means of the Relative Cultural Importance (RCI) [37]. The "Ethnobotanical Index" gives more precise information on useful plants: it is the ratio between the used wild plants and the number the vascular plants known to occur in the region where people live, expressed as a percentage [38]. The degree of plant exploitation was determined by evaluating the number of medicinal plants used in a specific area, hence, the "Exploitation Index" . In general if within a community only few wild plants are used for well-being purposes, then that means that these few plants are well known and their safety and efficacy is equally well known to people [39].

In order to compare two different regions and evaluate the use of wild medicinal plants, it is possible to apply the Jaccard Index. The Jaccard's index (Jaccard's coefficient) is a simple measure of how similar two sets can be. A higher Jaccard Index value corresponds to higher affinity level among medicinal plants used in two compared regions [40]. The Quotation Index QI is another value that can help to elaborate the raw ethnobotanical data [41]. The ratio between the number of used plants (U) and the number of species referred to by people is a very important and interesting one (C). Such Index is important because it is independent from the true use of plants [42]. Different multivariate and statistical methods particularly applicable to the analysis of ethnobotanical field data can be applied. Data suitable for cluster analysis in ethnobotany could be: similarity/dissimilarity of people's responses to well defined questions, similarity/dissimilarity of plant utilization patterns among different ethnic, social or gender groups, similarity/dissimilarity of species based on people's indication of use values, similarity/dissimilarity of phenotypic characteristics (e.g. seeds) in different varieties of food plants, similarity/dissimilarity of the pattern of secondary compounds (e.g. essential oils) in different varieties of medicinal or aromatic plants [43]. An alternative method for the elaboration of ethnobotanical data is an approach with Statistical Package for Social Science SPSS Program, a software for predictive analytics used by health researchers in epidemiology, government, education researchers for sociological purposes, and others [44].

Interpretation and meaning of plant secondary metabolism

Estimates of the number of Higher Plants that have been found around the world vary greatly, from about 250,000 to 750,000 [5, 45]. Recently (December 2010) the collaboration between the Royal Botanic Gardens, Kew and Missouri Botanical Garden enabled the creation of "The Plant List" by combining multiple checklist data sets. This database contains 620 plant families, 16,167 plant genera, and 298,900 accepted species [46]. How many of these plants have been studied as a source of new compounds ? It is not possible

Figure 1 Primary and secondary metabolism reactions



to give an answer. In addition, a special feature of higher plants is to be found in their capacity to produce a large number of organic chemicals of high structural diversity (secondary metabolites): many thousands have been identified in several major chemical classes (Fig.1). Many of the currently available edible, pharmaceutical and health products are derived from the secondary metabolites. Plants use them to protect themselves from herbivores, insects, *etc*. [47]. Lead compounds can be identified in every plant. However, researchers need to discover them according to a specific approach. Such approaches can be listed either according to a careful evaluation of past as well as current claims of the effectiveness of plants as drugs in people culture [47, 48, 49], or production of toxic compounds, or selection based on chemical composition (plants producing diterpene alkaloids, or glucosinolate, *etc.*), or screening for a specific biological activity [49].

Living plants are solar-powered biochemical as well as biosynthetic laboratory which manufacture both primary and secondary metabolites from air, water, minerals and sunlight. Primary metabolites such as sugars, amino acids and fatty acids that are needed for the general growth and physiological development of plants are widely distributed in nature and are also utilized as food by people. The secondary metabolites such as alkaloids, glycosides, flavonoids, volatile oils *etc* are biosynthetically derived from primary metabolites (Fig.1).

Typical primary metabolites are found across all species within broad phylogenetic groupings, and are produced using the same pathway (or nearly the same pathway) in all plant species. Secondary metabolites, by contrast, are often species-specific (or found in only a small number of species in a narrow phylogenetic group), and without these compounds the organism suffers from mild impairment, lowered survivability/fecundity, *etc.* Secondary metabolites are those chemical compounds in organisms that are not directly involved in the normal growth, development or reproduction of organisms [4].

Secondary metabolites represent chemical adaptations to environmental stresses, or serve as defensive, protective or offensive chemicals against microorganisms, insects and higher herbivorous predators. They are sometimes considered as waste or secretory products of plant metabolism. Plants produce secondary metabolites as a response to adverse environmental conditions or in particular developmental stages. However, the exposure of plant to strong UV radiation (Mediterranean area, alpine zone) will also induce the biosynthesis of UV-absorbing compounds [50, 51].

These chemicals can affect not only herbivorous and/or insects metabolism, but also human biochemistry. One question that is not often taken into much account in the vast literature surrounding the effects of plant chemicals is: *why can the secondary metabolites (plant chemicals) affect human life ?*

Some chemists and biologists have attempted to explain why so many compounds in nature have biological effects on humans and other species. One explanation, which has been widely accepted, is that it is the result of long-term co-evolution within biological communities: interacting organisms that evolved in close proximity to one another developed compounds that could influence the biological processes of neighbouring species. Nowadays, we "could learn a lot from the historical record of using natural products to fight diseases . . . this knowledge represents the cumulative experience of thousands of years of . . . practice" [52]. Research in the science of stress has established that the ability of organisms to respond to physical, chemical, and social stressors is a fundamental process in life. It seems that low levels of stress can improve the health of an organism, their well-being, adaptability, and fitness through stimulation of the cellular stress response, a phenomenon known as hormesis [53, 54]. The hypothesis, called xenohormesis, was proposed to explain the origin of beneficial natural products. According to such theory, the common ancestor of plants and animals was able to synthesize a large number of stress-induced secondary metabolites (poliphenols, resveratrol, curcumin, *etc.*). Animals and fungi feeding on plants gradually lost the capacity to synthesize low-weight molecular compounds. However, they retained the ability to be sensitive to such substances present in plants and therefore react to them [55].

The concept of xenohormesis is the process by which one organism benefits from the stress response of another organism. The term "xenohormesis" is composed by "xeno", that means "foreign to the body" and "hormesis" which derived from the Greek verb □ρμάω : to set in motion, impel, urge on. The word "hormesis" has the same etymology as "hormone", but in the xenohormesis phenomenon the involved chemicals are not classical hormones, but on the contrary the chemicals are plant secondary metabolites (polyphenols, reseveratrol, curcumin, phytoestrogens, caffeine, *etc.*) which nevertheless stimulate and awake the human body which is to say, they have a biological function. Xenohormesis is a biological principle that explains how environmentally stressed plants produce bioactive compounds that can confer stress resistance and survival benefits to animals that eat them. Factors eliciting the plant stress response can judiciously be employed to maximize yield of health promoting plant compounds. Xenohormetic plant compounds can, when ingested, improve longevity and fitness by activating the animal's cellular stress response and can be applied in drug discovery, drug production, and nutritional enhancement of diet [53].

The hormetic reaction can be induced either by Direct Stimulation Hormesis (DSH) or can be the result of biological processes of compensation inherent to an initial Over Compensation Stimulation Hormesis (OCSH). The consumption of secondary metabolites can therefore help man to balance homeostasis [56].

In 2008, the Council of Europe published a document in which homeostasis was presented as a model to distinguish between foods (including food supplements) and medicinal products [57]. Especially when it comes to plant products these model can be of value as botanicals (crude plant extracts) and some of the active principles thereof are used in food and food supplements as well as in medicines. The EU document can be considered an interesting link to the xenohormesis interpretation.

The reverse pharmacology: a new approach on the basis of ethnobotanical data

Many modern drugs find their origins in ethnopharmacology and ethnobotany knowledge. We can here remember some important drugs deriving from plants, and discovered applying the method of reverse pharmacology. Traditional medicinal plants have provided the source of the two major families of anti-malarial drugs still in use today, artemisinin and quinine. A lot of researchers are yet screening different plants to identify new lead compounds to be used as anti-malarial drugs [58]. Another example is the experimental work of William Withering (1741-1799), a physician, chemist and botanist, working at Birmingham General Hospital, UK. He noticed a person with edema, formerly known as dropsy or hydropsy, improve remarkably after taking a traditional herbal remedy, containing, among other substances, purple foxglove leaves *Digitalis purpurea*, Plantaginaceae family (formerly Scrophulariaceae family). Withering's interest in this rose, he studied the folk remedy and published his related paper *An Account of the Foxglove and some of its Medical Uses*, which contained reports on clinical trials and notes on foxglove effects and toxicity. His studies on foxglove activity have opened the way for the pharmaceutical chemistry [59]. Another highly illuminating example is the discovery of the biological activity of galanthamine: an acetylcholine-esterase inhibitor. It is a natural product present in several members of the Amaryllidaceae and the idea for developing a natural product from these species seems to be based on ethnobotanical information [4]. *Galanthus* and other genera of the Amaryllidaceae were not particularly commonly used as medicinal plants. In 1950s, a Bulgarian physician noticed the use of the common snowdrop growing in the wild, which people rubbed on their foreheads to ease nerve pain. Also, some of the earlier publications indicate extensive use of snowdrop, Galanthus sp., in Eastern Europe, such as in Romania, Ukraine, Balkan Peninsula and Eastern Mediterranean countries. Galanthamine is today used to improve global and cognitive symptoms, in people with mild to moderate Alzheimer's disease.

The reverse pharmacological approach starts from empirical observations, the study proceeds by means of biochemical and molecular biological tools that permit the identification of new compounds [60, 61]. This is a different way of understanding pharmacology, different from classical or conventional pharmacology. Reverse pharmacology is an academic discipline able to reduce three major critical points in classical drug development: costs, time and toxicity. Reverse pharmacology shows that a standardized natural product can be developed faster and at a lower cost than conventional pharmacology. Before starting with a reverse pharmacogical study, the first step is to know which biological activity we would like to test on the basis of ethnobotanic data, and the second one to have validated and technologically standardized botanical extracts (authenticated plant identity, optimized extraction method, GC or HPLC profile, primary and secondary metabolites content, *etc.*). The reverse pharmacological approach can offer an alternative way to identify new molecules which are interesting for their biological activity on human health. The novelty of this approach is the basis of living traditional knowledge on food and health plant and the application of modern technology and processes to provide better and safer lead compounds.

Functional aspect of conventional food: innovative interpretation

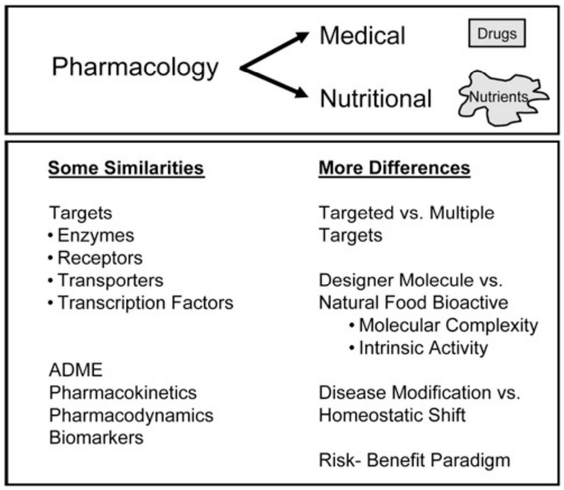
Recently, conventional food (fresh or cooked fruit and vegetables, dark chocolate bars, olive oil, *etc.*) has not simply been considered for its nutritional value, but also for other functional characteristics. The report of a Joint WHO/FAO Expert Consultation reviews the evidence of the effects of a diet and nutrition on chronic diseases and makes recommendations for public health policies and strategies that encompass social, behavioural and ecological dimensions. Although the primary aim of the Consultation was to set targets related to diets and nutrition, the importance of physical activity was also emphasized [62]. Nutrition is coming to the fore as a major modifiable determinant of chronic disease, with scientific evidence increasingly supporting the view that alterations in a diet have strong effects, both positive and negative, on health throughout one's life. For many years diets have been known to play a key role as a risk factor for chronic diseases. Traditional, largely plant-based diets have been swiftly replaced by high-fat, energy-dense diets with a substantial content of animal-based foods. Yet, notwithstanding the critical aspect of diets in prevention, one should not forget that they are only one of the risk factors. In the WHO-FAO publication, conventional food is presented as a determining factor for preventing cancer, dental problems, osteoporosis, obesity, type 2 diabetes and cardiovascular disease [62]. The WHO-FAO approach indicates that conventional food (fresh or cooked fruit and vegetables, dark chocolate bars, olive oil, wholemeal bread, *etc*.) has some innate physiological quality and exerts some functional claims on human health.

In recent years at world level, we have been observing a progressive loss in plant biological diversity (better known as "biodiversity") and this impoverishment influences our diet too. As a consequence, we do not get an adequate amount of micronutrients that we need to keep healthy. The term "micronutrients" includes mineral salts, vitamins, and phytochemicals (secondary metabolites), which do not bring calories to our diet, but they are indispensable for the correct functioning of our organism [63]. Among the ca. 300.000 Higher Plants till now identified [45], more or less 1% of them, which means 3,000 species ca., are used for food and feeding purposes. Within these 3,000 plant species, only 150 are intensively cultivated. In spite of that, the most important caloric contribution to our diet derives from only four species: wheat, rice, soya bean and maize. Given such basis, we can understand that our plant-based diet is qualitatively poor [64].

Inadequate dietary intakes of vitamins and minerals are widespread, most likely due to excessive consumption of energy-rich, micronutrient-poor, refined food. Inadequate intakes may result in chronic metabolic disruption, that can lead to DNA damage, mitochondrial decay, and other pathologies. Mitochondrial decay appears to be a major contributor to aging and its associated degenerative diseases, including cancer and neural decay. Oxidative damage of DNA, RNA, proteins, and lipids in mitochondrial membranes contributes to this decay and leads to functional decline of mitochondria, cells, tissues, and eventually organs such as the brain [65].

The functional characteristics of conventional plant-based food have been seen as an answer or a possible solution to the need to enrich our diet with micronutrients. The Nutritional Pharmacology is an interdisciplinary approach to evaluate the use of minerals, vitamins, plant- or herbal-derived extracts as food and/or nutritional supplements that affect specific functions or diseases [66]. There are many notable differences between drugs and nutrients in terms of how they elicit biological change in an organism (Figure 2).

Figure 2 Comparison between Medical and Nutritional Pharmacology (from Migrating principles of pharmacogenomics (PGx) to nutrigenomics (NGx) to enable the practice of preemptive nutrition. [from Gillies & Krul (83)]



One example may be represented by glucosinolates which are sulphur compounds prevalent in Brassica genus (mustards, cabbages, broccoli, cauliflowers, turnips, etc.). Since the 1970s glucosinolates and their breakdown products, have been widely studied for their beneficial and prejudicial biological effects on human and animal nutrition. More recently considerable attention has been paid to Brassica products for cancer prevention. The cancer-protective properties of Brassica intake are mediated through glucosinolates. Isothyocianate and indole products formed from glucosinolates may regulate cancer cell development by regulating target enzymes, controlling apoptosis and blocking the cell cycle [67]. Much remains to be learned regarding cruciferous vegetable consumption and cancer prevention, but the results of some prospective cohort studies suggest that adults should aim for at least 5 weekly servings of cruciferous vegetables [68].

Anthocyanins are another interesting group of natural occurring pigments responsible for the red-blue-violet colour, according to pH value, of many fruits and vegetables. Numerous studies indicate the potential effect that this family of compounds may have in reducing the incidence of cardiovascular diseases, cancer, hyperlipidemias and other chronic diseases through the intake of anthocyanin-rich foods [69, 70].

Carotenoids, identified by the orange colour, are another interesting group of phytochemicals present in oranges, carrots, red peppers, papayas, *etc*., which play an important role in the prevention of human diseases and in our wellness [71]. They are biosynthesized *de novo* by various plants, algae, and photosynthetic bacteria. Humans and animals are incapable of synthesizing carotenoids, and must intake them through their diet [72]. The most common carotenoids include lycopene (e.g. tomato, watermelon) [73] and the vitamin A precursor β-carotene. In addition to being potent antioxidants the carotenoids also contribute to dietary vitamin A intake. In green leaves vegetables, the xanthophyll lutein is the most abundant carotenoid, while in microalgae the most abundant xanthophyll is astaxanthin [74, 75].

Going back to the Mediterranean diet, in which olive oil is not only the primary source of fat, but it is also associated with a low mortality caused by cardiovascular disease, we can say that a diet rich in olive oil, or better virgin olive oil, decreases prothrombotic environment, by modifying platelet adhesion, coagulation and fibrinolysis [76]. In the last years olive oil, usually use alone as condiment or as an ingredient in salad dressing, has been considered, within the Mediterranean diet, as a protective factor against coronary heart disease (CHD), a main individual cause of death and morbidity in industrialized countries. However, myocardial infarction incidence rates, present a high regional variability, with lower rates in European Mediterranean countries than those reported in Northern European ones, the U.S.A, or Australia [77]. In 2004 the Food and Drug Administration announced the availability of a qualified health claim for monounsaturated fat from olive oil which reduces the risk of coronary heart disease (CHD): a qualified health claim on conventional food [78].

In the past 15 years there has been an increased interest in the potential health-related benefits of antioxidants and phytochemicals of dark chocolate and cocoa. Hundred of studies have been reported on bioactive compounds, chemical compositions, and health benefits of cocoa and cocoa products. Since cocoa products have greater antioxidant capacity and greater amounts of flavonoids per serving than all teas and red wines, it is important to underline the potential effects of chocolate on cardiovascular disease. Since ancient times, chocolate has been used as a medicinal remedy and has been proposed in medicine today for preventing various chronic diseases [79]. While chocolate has also sometimes been criticized for its saturated fat content, mostly in the form of long-chain stearic acid, dark chocolate has also been praised for its antioxidant potential [80]. A full range of health benefits can today be associated to the actions of flavanols and procyanidins on vascular function. These benefits are mainly ascribed to diets rich in flavanols and procyanidins. Chocolate and cocoa derivatives are among the most valuable components of such a diet [81].

Taking into consideration the biological effects of conventional food on human health, a European strategy for the prevention and control of noncommunicable diseases states that almost 60% of the disease burden in Europe, is accounted for by seven leading risk factors: high blood pressure (12.8%); tobacco (12.3%); alcohol (10.1%); high blood cholesterol (8.7%); overweight (7.8%); low fruit and vegetable intake (4.4%;) and physical inactivity(3.5%). The European legislator recommends to use fiscal measures to promote healthier choices, working with the agricultural and economic sectors at international, national and local levels to increase the availability of fruits, vegetables and other healthier foods at affordable prices [82]. In order to get the message through to children, the famous sentence "Fruit and Vegetables 5-a-day" was formulated.

Quite recently, with the advent of molecular nutrition, nutrition scientists have been offered a special opportunity to become major players in the health sciences and in the development of public health policy. The human genome project provides modern-day nutritionists with a basic knowledge and a set of tools to explore nutrient-gene interaction for an unprecedented level of inquiry. This new and molecular endeavor has been called "nutritional genomics". Initially the term "nutritional genomics" referred to the analysis of the effects of nutrients on gene expression. More recently the term has been expanded to include effects on proteins, metabolites, and pathways in a globally integrated model. As a subset of nutritional genomics, nutrigenetics focuses on the effect of structural variations in genes in an effort to understand the highly variable response of humans to diets. In an ideal scenario, it may be possible to leverage our understanding in nutritional genomics to tailor diets to the genetic background of an individual in order to optimize health and offset diseases. The integration of nutrigenetic information in the practice of nutritional pharmacology ultimately leads to preemptive nutrition [83].

CONCLUSIONS

The scientific evidence and proofs of ethnobotanic knowledge, related to aromatic and health-food plants use, is an urgent and important request mainly referring to the botanical-based food supplements. The necessity to verify its scientific validity springs from the fact that plants produce thousands of active chemical compounds, which are not always easily quantifiable one by one. We can therefore start from the fact that plants produce thousands of biologically active substances, with very precise functions, both for the plants themselves which produce them and for the animals which eat them. However, how comes that all these biologically active substances for plants are also effective for animals ? There have been numerous answers to that over the years, suggested by various researchers.

One of such answers maintains that the co-evolution man – plants, has caused them to interact, to the extend that man has been biologically influenced and has developed the ability to respond to the chemical stimuli produced by plants.

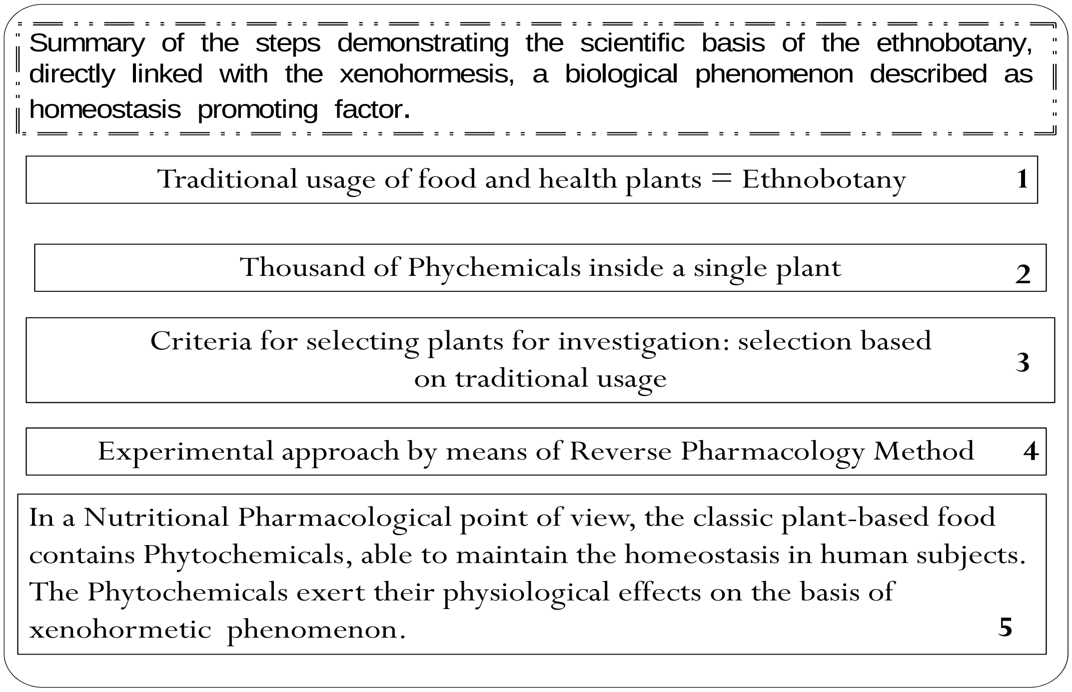
Another theory, named xenohormesis, is based on the assumption that there were common ancient organisms – both animals and plants – able to produce a lot of biologically active molecules (polyphenols, vitamins, resveratrol, etc.). According to such theory, both animals and fungi (given that they feed on plants and botanicals) lost the capacity to synthesize biologically active molecules over time, yet remaining sensitive to them. Animals and fungi are more inclined to take biologically active molecules when their organism is under stress (biotic and/or abiotic) and needs to reestablish a balance. In support to the hormetic theory, we find the concept of homeostasis linked to the intake by man of active secondary metabolites which favor the rebalance of homeostasis itself (when man is under stress). From this rather complex picture, it is quite clear that we need to define some criteria to be used in the studies of plants which have a biological effect on man and on animals.

One of the listed criteria, which is considered valid and effective, implies the use of ethnobotanical information, which is to say the use of knowledge derived from traditional use of plants as a starting point in experiments for the detection of biological activity.

About three-quarters of the biologically active derived compounds presently in use worldwide, have been discovered through follow-up research to verify the authenticity of the data based on folk and ethnobotanic use [84].

This type of research implies a different approach from the one used in 'classic' pharmacology, which is to say an application of reverse pharmacology.

Figure 3 The step-by-step scientific basis of ethnobotany



The possible conclusion, graphically reported in Fig. 3, is that the traditional use of plants is considered in the official scientific bibliography as a valid starting point to thoroughly study a plant and its specific biological activity (following the information given by the popular use of it). We can therefore say that the traditional use per se, is sufficient to validate and justify a specific physiological effect of a plant.

All that is supported by the fact that Farnsworth, one of the eminent researchers of Pharmacognosy, maintains that 74% of the plants which he had studied using such method, have had positive results over the follow on researches, on their biological activities and of reverse pharmacology [84].

The above illustrated points should make us ponder over the great knowledge acquired by man on the use of plants over hundreds of years. Knowledge which must be safeguarded and considered scientifically valid.

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