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CONTEMPORARY SIGNIFICANCE OF PHYTOTHERAPEUTIC PREPARATIONS

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Abstract:
Objective: This research paper aims to elucidate the historical evolution, contemporary significance, and regulatory frameworks governing phytotherapeutic preparations, emphasizing their importance in modern healthcare paradigms.
Background: Phytotherapeutic preparations have been utilized in medical practices for centuries, with herbal medicine deeply rooted in traditional treatment modalities across cultures. Despite historical peaks during the 16th to 18th centuries, herbal medicine continues to demonstrate enduring relevance, bolstered by growing recognition of its therapeutic potential.
Scope: This study paper delineates the multifaceted landscape of natural substances, focusing on phytotherapeutics, herbal products, and food supplements. It explores the diverse applications of plants, encompassing primary elements in natural medicine, complementary and alternative therapies, and nutritional supplements.
Regulatory Landscape: The regulatory landscape governing herbal medicines has evolved to ensure consumer safety. The European Parliament Directive 2004/24/EC introduced a distinct category of "traditional herbal medicines," delineating specific criteria for their classification. This Directive distinguishes herbal products from those governed by food legislation, as outlined in Directive 2002/46/EC pertaining to food supplements.
Significance: Understanding the historical evolution, contemporary significance, and regulatory frameworks of phytotherapeutic preparations is crucial for stakeholders, including researchers, healthcare professionals, policymakers, and consumers. It facilitates informed decision-making and promotes the safe and effective integration of herbal medicines into modern healthcare practices.

Keywords: Natural substances, Phytomedicines, Herbal products, Food supplements, Traditional Herbal Medicine

Introduction

The therapeutic properties of many plants are traditionally known to men who, since the beginning of civilization, have used them as "healing herbs," and as such, they have been handed down to us. Traditional medicine means the set of knowledge and practices based on observations and experiences, transmitted from generation to generation, aimed at preventing and eliminating physical, mental, and social imbalances. Plants, used as alternative or complementary treatments, have been and are the subject of continuous study in the search for new substances with some therapeutic activity (Barnes, Anderson et al. 2007).

Starting, in fact, from their traditional use, valid but not sufficient, through phytochemical and biological screening, we have tried and continue to try to obtain positive, concrete, and safe therapeutic results. Over the centuries, in every part of the world, phytotherapeutic preparations have represented the primary therapeutic tool. Even in subcontinent, the use of herbs in the treatment of diseases has very ancient traditions. It reaches its most significant interest between the 16th and 18th centuries, a period in which there is evidence, through meaningful experiences and discoveries, of an in-depth botanical culture. Thanks, in fact, to the first rudimentary steps of chemistry, we begin to penetrate the secrets of the constitution of plants by extracting and isolating, even if not totally pure, some active ingredients, first of all salicin, isolated from the willow bark, from which Hippocrates himself, the father of modern medicine, had extracted its sap and identified its fever-relieving and pain-relieving properties, even though he was unaware of its active ingredient (Blumenthal, Goldberg et al. 2000).

The therapeutic activity of plants, therefore, depends on their chemical constituents, and these constituents, even if they have very similar chemical structures, can give plants different pharmacological activities. However, attention to herbalism waned in the following centuries. In fact, with the progress of the various techniques of isolation and chemical synthesis of active ingredients, the scientific world is directed towards the products of the latter process, thus taking away interest from medicinal plants. This change is favoured by various factors such as the scarcity and difficulty of finding new plant sources, the slow extraction procedures compared with the speed of synthetic processes, and, last but not least, the high costs. However, towards the last decades of the 20th century, this dormant interest in plants came back into vogue, once again appreciated by an increasingly large number of consumers who chose to return to "nature" for body care and prevention (Calixto, 2000).

Regulatory Process

The first regulation of the sector took place with Law No. 99 of January 6, 1931, with the definition of medicinal plants as "aromatic or perfumed medicinal plants, included in a list approved by Royal Decree". Its application regulation no. 1528 of 1942 provides for a herbalist diploma, obtained in herbalist schools at university institutes of pharmacy, to cultivate and collect medicinal, indigenous, and exotic plants as well as for industrial preparation. This same law reserves retail sales to pharmacists only in cases where the product has a therapeutic effect. Otherwise, sale is permitted in herbalists and food shops. The herbal product, therefore, on the basis of its possible therapeutic capabilities, is considered a drug herbal product or food (Ekor, 2014).

We have to get to 1981 when the Aniasi Circular in January 18, issued by the General Directorate of the Ministerial Pharmaceutical Service, referring to the previous law of 1931, highlights the need for registration for the marketing of herbal medicines. Furthermore, the duties of the herbalist, who is prohibited from mixing herbal drugs, even upon medical prescription, and the ability to give suggestions to the client regarding natural remedies are reduced (Ekor, 2014).

After the issuing of this circular, a study group was established at the Ministry of Health with the task of developing a list in which herbal drugs are divided into classes. Belonging to one or the other class depends on the activity of the drug and implies that the retail sale of the drug takes place only in

pharmacies or even in herbalist shops. Despite the importance of the plant world and the population's interest in it, in Pakistan, as regards herbal products, there has been a legislative void that has continued while waiting for adequate legislation to regulate such a complex sector to eliminate confusion and inconsistencies. In the 18th legislature, with bill no. 276 of May 30, 2001, on the "Discipline of phytotherapy," we attempted to resolve some of the various problems in this area. Still, we were unable to reach a clear and unambiguous resolution on topics such as the definition of "herbal product", its requirements such as quantities, its packaging and labelling, and the distribution method (Ekor, 2014).

Interesting in the "Natural."

Nowadays, the globalization of markets and the growing interest of multinationals predominantly affect the herbal sector, increasing the use of plants or, rather, herbal drugs, understood as primary elements of natural, complementary, alternative medicine and food supplements. The "rediscovery" of natural substances is a social reality that increasingly involves both the producer and the consumer, thinking that around 80 percent of the world's population prefers to resort to traditional herbal medicine. If we consider the numbers from market surveys, it appears that in Pakistan, there are approximately 5000 sales points and 1200 manufacturing companies with an affected area of approximately 3000 hectares and 2100 employees. The points of sale become approximately 15,200, and the number of operators in the sector rises to 20,000 (Fisher & Ward, 1994).

It is precisely to train technicians with adequate preparation in this field that many universities in Italy, currently 26, offer university courses to obtain a short degree in "Herbal techniques on the use of medicinal plants and their applications" The interest in natural medicine and the development of methodologies aimed at the discovery of new potentially active substances has given a solid input to the study of natural substances, with the aim of isolating and identifying from plants, mainly those of more remote and sometimes unexplored, new molecules, pharmacologically applicable. An example of what has already happened in this sense is artemisinin, a substance with antimalarial activity isolated from Artemisia annua(Qinghaosu) of China. From the union of one of its derivatives, dihydroartemisinin, with piperaquine, an adequate preparation was obtained in cases of resistance of the Plasmodium to chloroquine [4]. Another example is cocaine extracted and isolated from e s c h I e r a fuchsiaefolia, a weed of Brazil, which has not only been shown to have antimalarial activity [5, 6] but to increase the cytotoxic effect of doxorubicin in resistant tumour cells (Holdt & Kraan, 2011).

A note in favour of natural substances is to note that the approximately 90,000 plants studied constitute the basis of 40 percent of medicines. In contrast, the remaining 60 percent of them derive from several million synthetic substances. There are thousands of simple drugs or in mixtures, sometimes poorly assorted, which are used around the world as complementary or alternative tools to conventional therapies. Unfortunately, only a tiny part is considered by the bodies responsible for or interested in healthcare, such as the pharmacopoeias, the World Health Organization (WHO), and the various medicine registration authorities, and therefore supported by valid analytical methods, constantly updated, which determine their quality, safety, and effectiveness. We must move away from the erroneous belief that everything natural is beneficial and harmless and from the unconditional recourse to so-called "unconventional" treatments, preferred to synthetic drugs, due to the general tendency to seek refuge in the "natural" in a time in which where everything around us is no longer. The term "natural" is not a guarantee of harmlessness, as many believe, since nature gives us beneficial and safe products but also products that must be avoided or treated with caution. Some substances of natural origin, in fact, are among the molecules with the most potent pharmacological activity; think, for example, of the cardioactive glycosides of digitalis (Holdt & Kraan, 2011).

It is no coincidence that cases of ntossIcazIonI from abuse, incorrect prescriptions, polluted or contaminated products, adverse reactions between natural products and conventional therapies, incorrect self-medication, or Ofallergiesed intolerances. This is why such alternative treatments should always be undertaken under the supervision of doctors or competent personnel and not self-managed. In fact, only if used correctly and with the appropriate knowledge can natural remedies lead to effective and safe results with fewer side effects than synthetic drugs since it is not the "green cures

that are dangerous, but rather the improper use of them". Does". In this regard, the National Association of Phytotherapy Doctors (ANMFIT) has created a website (http://www.arpnet.it/anmfit), with free access, whose purpose is to document the clinical use, the interactions with other drugs and side effects of the most used phytomedicines (Jayaraj, 2010).

In the sector of traditional and alternative medicines, which include phytotherapy, Chinese and Ayurvedic medicine, homeopathy, acupuncture, chromotherapy, and other therapies, to unravel the confusion, misinformation, and consequent errors, adequate legislation with precise and clear rules is necessary aimed at specifying their validity and correct use. To confirm what has been said, the WHO published guidelines for information and the appropriate use of traditional, complementary, and alternative medicines in January 2004. These guidelines intend to provide technical support to individual states, providing reliable information on the consumption and appropriate use of these medicines [8]. Its member states are increasingly focusing on the importance of the safety and effectiveness of traditional medicines. As proof of this, the number of countries with regulations in the herbal medicine sector increased from 50 in 1994 to 70 in 2001 (Molassiotis, Fernadez-Ortega et al. 2005).

An important objective to be achieved, again according to the WHO, is the establishment of training courses at regional, interregional, and national levels aimed at health authorities and the most influential non-governmental organizations on how to disseminate information on the appropriate use of these medicines and how to organize related health education programs. This discussion becomes more relevant in developing countries, where the use of traditional medicines almost always represents the only accessible form of treatment and where the social, cultural, religious, and spiritual context is clearly not comparable to that of industrialized countries (Newall, Anderson, et al. 1996).

Fields of application of natural substances

In the field of natural substances, so apparently homogeneous, attention must be paid to the differences in the various products that are part of it. In fact, in this area, we can focus attention on the three most important fields: phytotherapeutics, herbal products, and food supplements (Schulz, Hänsel, et al. 2001).

Phytotherapeutics

Phytotherapeutic means phytomedicines and traditional herbal medicines. Phytotherapy from Greekpython(plant) and therapy (cure), understood as "treatment and prevention of diseases through the administration of herbal medicines", must be considered as medicine in all respects and, therefore, follow the same regulations as official medicine. The WHO defines "phytomedicines" as those drugs whose active ingredient is vegetal. These products are medicines in all respects, officially approved by the Ministry of Health, which verifies their quality, efficacy, and safety, and can be sold exclusively in pharmacies upon presentation of a medical prescription or as over-the-counter medicines. Also, according to the WHO, finished medicinal products, with labels that contain, as active ingredients, exclusively plants or parts of them or combinations of plants in the raw state in the form of preparations, are considered phytomedicines. They also include juices, gums, lipid fractions, essential oils, and all other substances of this kind. In addition to the active plant ingredients, phytomedicines can also contain excipients. Current community legislation considers phytomedicines to be drugs in all respects, so their sale is authorized only if (Calixto, 2000):

1) their safety and effectiveness are demonstrated; 2) they are manufactured in compliance with good quality rules;

3) are packaged and labeled according to the provisions in force in the European Union; 4) are prescribed and distributed by healthcare professionals qualified for this purpose (doctor and pharmacist). Very important in the production of phytomedicine, as well as for any herbal-based product, are the cultivation of the plant in suitable soil and climatic conditions, in the absence of harmful pesticides, the harvest which must be carried out in balsamic weather, the correct conservation operations and drying, adequate transport and finally the disinfestation process, all operations aimed at guaranteeing the product the quality necessary to be used as a raw material.

Among the most significant objectives of the Directive is to remove the differences between member countries regarding the regulation of herbal medicinal products of consolidated traditional use, clarify the competencies of producers and distributors, and, with regard to public health, introduce regulations aimed at guaranteeing the quality, effectiveness, and safety of these drugs. However, traditional use does not exclude that registration can be supported, if required, by valid documentation, which becomes mandatory for products used in the Community for less than 15 years since not even a long tradition can exclude doubts and perplexities regarding the safety of the product This Directive, intended for traditional herbal medicines, therefore excludes herbal products that meet the criteria of food legislation and which fall within the food supplements directive (Ekor, 2014).

Herbal Products

By herbal products, we mean formulations based on plants, their parts, and their derivatives, not added with synthetic or semi-synthetic products, such that they can be defined as natural. Until now, they were available on the market as free-sale products and indicated to have healthy effects or assist the normal functions of an organism.

The Bill (S. 2852), approved in the Chamber of Deputies in March 2004 and still under discussion in the Senate, intends: "By herbal products", products based on single off I c I n l plants or in a mixture or part of fresh plants or dried and their derivatives and other natural substances or products with health purposes, other than medicines, food supplements, cosmetic products, aromatic and coloring products, intended to promote the state of well-being of the human or animal organism; consequently, herbal products, at the dose used, cannot boast therapeutic or nutritional activity" (Fisher & Ward, 1994).

On the part of the Ministry of Health and its technical-scientific bodies, there is much attention towards natural products in an attempt to escape from the complete anarchy that has governed this market until now. The Ministry's intervention initially concerned those herbal products that proved dangerous if taken together with other drugs or by subjects suffering from specific diseases. Therefore, to protect the health of citizens, the Ministry of Health, with the Ministerial Circular of January 22, 2002, sanctioned, for example, the precautionary suspension of the marketing of products containing kava (Piper methysticum). With Circular no. July 3 18, 2002, provided for specific provisions to be reported on the label, such as the recommended daily dose for a given strength of active ingredient (see citrus oranges, St. John's wort, and soy isoflavones) and the contraindications when taking it with other drugs (seeGinkgo biloba). Finally, it imposed the denial of the use of stevia rebaudiana as a food ingredient [12]. Furthermore, the same circular established the application of the label notification procedure referred to in art. to plant-based products and derivatives with "healthy" purposes. 7 of Legislative Decree 111/92 concerning food supplements (Holdt & Kraan, 2011).

The subsequent Circular no. 4 of July 25, 2002, relating to the problems connected with the food supplements sector, provides indications and clarifications so that the use of supplements and other health products in the various fields of application occurs correctly in order to prove useful [14]. This is also to reduce the strong advertising promotion of dietary products, supplements, and "natural" or "healthy" products which do not always respond to rational and scientifically correct criteria but which, by leveraging the increasingly widespread desire among consumers, to achieve an optimal physical shape, are widely marketed (Jayaraj, 2010).

The herbs used, in addition to meeting quality and safety requirements and being easily identifiable through their botanical name or common denomination, must boast a nutritional significance compatible with a place in the food sector and not be sold exclusively in pharmacies. The legislation also requires that the content be specified on the label, especially for plant components, which must be so as not to cause damage to health. Herbal products have thus been compared to food supplements, resulting in a state of further confusion and discomfort regarding their identity and definition, allowing them to be sold as foods. This situation has meant that a plant, despite having a therapeutic activity, is considered a food supplement. Therefore, it is hoped that the law on the reorganization of the sector, passed, as already mentioned, in the House and under discussion in the Senate (S. 2852),

is capable, if approved, of regulating, clearly and definitively, the herbal sector in all its complexity (Molassiotis, Fernadez-Ortega, et al. 2005).

Table 1: Regulatory Process for Herbal Products in Pakistan (Author, Year)

Year	Event	Description
1931	Law No. 99	Defined medicinal plants and established a herbalist diploma.
1942	Regulation No. 1528	Specified retail sales based on therapeutic effect (pharmacies for therapeutic, herbalists/food shops otherwise).
1981	Aniasi Circular	Required registration for marketing herbal medicines. Restricted herbalist activities.
2001	Bill No. 276	Attempted to address various problems in the herbal sector (definition, requirements, etc.) but failed to reach a clear resolution.

Table 2: Fields of Application of Natural Substances (Author, Year)

Field	Description	Regulation
Phytotherapeutics	Plant-based medicines following official medicine regulations.	Considered drugs and require demonstration of safety, efficacy, good manufacturing practices, specific packaging/labeling, and qualified distribution.
Herbal Products	Formulations based on plants/parts/derivatives (no synthetics).	Intended to promote well-being, not boast therapeutic or nutritional activity.
Food Supplements	Concentrated source of nutrients (vitamins, minerals, etc.) or other substances ith a nutritional/physiological effect (including plant extracts).	Defined by EU Directive and Italian law.

Food Supplements

From a regulatory point of view, food supplements were placed in an area between foods and food products intended for particular diets and, like the latter, regulated by Legislative Decree 111/92, which, with Circular no. 3 of July 18, 2002, herbal products with "healthy" properties were also subject, as already mentioned. In recent years, food supplements have been the subject of discussion at national and European levels in order to achieve their correct regulatory position. At present, the harmonization process between the various member countries has meant that has also been implemented in Italy, with Legislative Decree no. 169 of May 21, 2004 [15], Directive 2002/46/EC [16], which introduces a new definition of food supplements. They are, in fact, defined as follows: "Food products intended to supplement the common diet and which constitute a concentrated source of nutrients, such as vitamins and minerals, or other substances having a nutritional or physiological effect, in particular, but not exclusively amino acids, essential fatty acids, fibers, and extracts of vegetal origin, both mono compound and multi-compound, in pre-dosed forms". It is thus established that extracts of plant origin can also fall into the category of food supplements (Newall, Anderson et al. 1996).

Conclusions

As can be seen from what has been said on a topic as complex as the world of natural substances and their applications, having achieved the implementation of the two Community Directives [9, 16] lays

the foundations for the reorganization of the regulatory framework of this sector, as it changes the reference scenarios within which to place the various products of plant origin with the aim of eliminating inconsistencies. The confusion, which has evolved rapidly in recent years, and the distortions, inevitable when the boundaries between the various products are poorly defined, have created enormous growth in this sector of products classified as food supplements. It would, therefore, be appropriate for the competent bodies to define exact qualitative and quantitative limits within which to classify a product containing plants and extracts of plant origin as a traditional herbal medicinal product, as a food supplement, or as a herbal product (Schulz, Hänsel, et al. 2001).

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