

Plants and humans: from tradition to the current scientific research.

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Humans have used plants as medicine since time immemorial. The oldest prescriptions date back to 3000 B.C., during the Chinese empire of Cho Chin Ken. Papyrus from ancient Egypt have been discovered with reference to over 1,700 medicinal plants. Other interesting findings come from Assyrians and Greeks.

Nowadays, the World Health Organization has recognized the use of medicinal plants for therapeutic purposes. For centuries, the knowledge of medicinal plants belonged to an ancient wisdom that has been transmitted from generation to generation. Thanks to an increasingly precise laboratory approach, efforts are now being made to learn about phytotherapeutic species in greater detail, identifying their pharmacological principles, their mechanisms of action and their efficacy. In fact, the number of scientific articles published in the last fifteen years has grown exponentially.

Plants produce numerous substances that are essential for their own metabolism, to defend themselves, to adapt to their environment and to survive the competitive presence of other living species. It is precisely these constituents, essential oils, flavonoids, alkaloids, and minerals that act as medicines in our bodies.

In 1976 the first European institution to catalogue, examine and support through scientific studies the therapeutic use of botanical species was born in Germany. Today, the German pharmacopoeia in phytotherapy remains the most up-to-date and the most reliable within the European community. The EMA (*European Medicines Agency n.d.r.*) has also made the database of medicinal plants accessible. Through this database, various information can be obtained, validated by scientific research and pre-clinical and clinical studies for their therapeutic use. At the same time there is also an attempt to standardise the use of plants by systematising and titrating their active ingredients. This allows therapeutic information to be easily compared with each other and with other pharmacological approaches. Thus, we speak of phytotherapeutic medicines, which require appropriate medical prescriptions. In fact, phytotherapy today is not only no longer the "little sister" of the broader pharmaceutical class. Instead, it has become an excellent support in relieving treatment plans and reducing exposure to side effects or toxicity to patients on polytherapy or in chronic patients. At the same time, it has also been possible to demonstrate how phytotherapeutic metabolites excreted from human or animal secretion are much less toxic than pharmacological metabolites. To date, the reasoned use of phytotherapy becomes a substantial ally for both human health and that of the environment in which we live.

However, it is not always easy to standardise the use of medicinal plants. They are in fact composed of numerous biologically active substances, which often act in combination or antagonism, modulating their therapeutic properties and possible toxic effects.

Despite the fact that even today the use of plants as medicine in health care is taken with suspicion for efficacy and safety, a large part of the population uses them either as a complementary support to drug therapy, for chronic disease management, or for prevention.

The production of a phytotherapeutic remedy undergoes strict quality controls, starting from the soil where it is grown, to the methods and time of harvesting, transportation and storage. In fact, heavy metals, pesticides, and residues of solvents and radioactivity must not be present. At every stage of phytotherapy processing, the absence of contaminants such as bacteria, viruses and fungi must be guaranteed.

In Italy, phytotherapeutic use is through the preparation of medicines, herbal or galenic products, or through dietary supplements. Phytotherapeutic medicine means drugs whose active ingredient is a plant; these are regularly controlled and selected by AIFA (*Agenzia Italiana del Farmaco - Italian Medicines Agency n.d.r.*) and a precise prescription is often required. The galenic preparation must also be prescribed by the doctor and prepared by properly trained pharmacists. In Italy, herbal medicine is also sold as a dietary supplement, so-called because its purpose is to supplement a diet and concentrate nutritionally important substances. Nevertheless, even this modality requires the support of scientific evidence. Phytotherapy is also present in cosmetics, where the usual quality and purity controls apply.

Due to the increasingly flourishing research in this field, the use of phytotherapy is being considered for moderate to medium severity conditions. to avoid major side effects from the continued use of drugs.

The best-selling medicinal plants are passionflower and lemon balm for their anxiolytic, relaxing and sedative properties and propolis for its antibacterial properties.

While these data highlight that, in Italy there is a greater sensitivity to the use of the plant as a therapeutic remedy, we understand that some of the main concerns are to manage anxiety, insomnia, concentration, and mental and physical recovery.

Thus, phytotherapeutic support becomes crucial to keep one's psycho-physical well-being in homeostatic balance, where psyche and body belong to the same unit.

It is simply no coincidence that we talk about psychophysical pathologies. Since the 1980s, a new discipline called *Psycho-Neuro-Endocrino-Immunology* (also called PNEI) came into being, identifying the connections between psyche and body. The founding father was Arder, a psychologist who in the 1970s, as a result of his observations in experimental animal models, had identified some correlation between behaviour and the immune system. To date, PNEI studies the intimate relationship between immune, physical, emotional and psychological aspects.

This discipline is not entirely new. As early as 1890 William James, a pioneer of psychology, wrote in his book "The Principles of Psychology" "no mental modification ever occurs which isn't accompanied or followed by a bodily change." In other words, it can be said that emotions and feelings influence biology, as well as the other way around. Later it was shown that this is also true in simpler organisms, such as invertebrates, where the neuroendocrine and immune systems communicate with each other. The psychological aspect is a further integration that occurs in the highest evolutionary levels of living species. From the most recent research, therefore, it can be said that the maintenance of the vital balance of the organism is ensured by three systems: the central nervous system and the autonomic nervous system, the endocrine system, and the immune system.

Communication between these systems is orchestrated by chemical messengers, through blood, lymph and nerves. The nervous system uses electrical signals and neurotransmitters. The endocrine system uses molecules, hormones, capable of reaching organs far from where they were produced. The immune system sends messages through cells that spread throughout the body inducing the production of antibodies and molecules, such as cytokines, capable of activating or shutting down the immune system.

The crucial organ in all this seems to be the hypothalamus, which performs strategic functions for survival and brain activity, regulating metabolism, hunger and satiety, body temperature, circadian rhythm, emotions, behaviours, and memory. Its function is not only a gateway but also a kind of gate for peripheral hormones.

It has been proved how emotional stress, loneliness, depression, social marginalisation are closely related to an increased inflammatory state. At the same time, the inflammatory state involves the central nervous system, altering nerve sensitivity and thus the same emotional experience towards the environment. In this way, the inflamed brain matrix itself becomes responsible for behavioural alterations and psychic suffering.

In addition to classical drug therapy, it has been shown that there are other valuable therapeutic approaches to rebalancing the psyche and body. Behavioural strategies such as meditation, yoga, tai chi, and nature walks, all of which are characterised by increased sedative activity by the parasympathetic nervous system and increased serotonin, also called the feel-good hormone, have proven useful.

There are numerous studies on the use of the medicinal plant to improve psyche-body balance. Over the past decade, the increasing number of scientific studies have explored the efficacy of phytotherapy in all its areas: from classical, European phytotherapy, to folk medicine, Chinese medicine and ayurveda, from simple inhalational use via essential oil, to the use of herbal teas, to complex preparations composed of single pharmacologically more active molecules.

In most of these studies, the results favour the efficacy of phytotherapy over placebo. In particular, encouraging results have been obtained in the treatment of stress, both psychological and physical in nature. It has been shown how it is possible to procrastinate or even avoid the use of anxiolytics or

hypnoinductives, how this approach has few side effects and is well manageable compared to classic medication. Not only are anxiety and insomnia from stress better controlled, but also quality of life is markedly improved, with increased resistance to fatigue, better concentration, less widespread pain. Such encouraging results were obtained not only on healthy volunteers, but also on patients with multiple diseases. Once again there is confirmation that psyche and body are not two separate entities.

Interestingly, this concept is well in place in nature, as if an ancient intelligence had foreseen this. In fact, each plant is composed of a myriad of pharmacologically active molecules. In the case of medicinal plants with anxiolytic and hypnoinductive action, not only are there molecules capable of interacting on GABA receptors as if they were drugs, or of being metabolised into serotonin, but there are other molecules capable of modulating the activity of the immune and endocrine systems, toward an anti-inflammatory and antioxidant reaction and thus protective for the whole organism.

Below are some of the latest and most significant scientific research in phytotherapy.

Mentha Piperita: The mint parts which are usually used are the leaves. They are composed mainly of essential oil (0.5-4%), the percentage of which varies according to origin, species and cultivation, tannins and flavonoids. Properties with spasmolytic, analgesic, carminative and choleric, and antiseptic actions have always been known. Hence, its field of use is the treatment of inflammation of the upper airways, gastro-intestinal tract and biliary tract. Recent studies have shown that olfactory exposure to mint essential oils reduces fatigue and improves both mood and sleep quality. Another interesting study conducted on healthy, volunteer students showed how drinking mint infusion strengthens memory and reduces anxiety, resulting in a better performance with respect to other students.

Hypericum Perforatum: *Hypericum* or St. John's Wort is one of the most studied plants. Nowadays, the pharmacologically active molecules found in large quantities in the flowering tops (hyperforin, hypericin and pseudohypericin and flavonoids), are well known. In 2009 EMA published a report on the effective uses of St. John's Wort, calling it an antidepressant, anxiolytic and neuroprotective. Its use is suggested for moderate forms of depression and it has been shown that the beneficial effect tends to appear after 4-6 weeks of therapy. From a biochemical point of view, its molecules act exactly like antidepressant drugs: they reduce the uptake of serotonin, dopamine, and norepinephrine by making them more active and also reduce the presence of beta-adrenergic receptors known for their depressive effect. If it is combined with serotonin-inhibiting drugs, it enhances their effect. However, it has severe contraindications: its use for internal use should always be supervised by the doctor, as it interacts with many drugs causing alterations in their metabolism, impairing their effectiveness.

Rosmarinus officinalis: The parts of rosemary which are used are leaves, flowers and young shoots. Through the action of its essential oils, it has antispasmodic, carminative, choleric, balsamic, diuretic, antiseptic, healing and neurostimulant actions. Recently, many studies have shown anti-inflammatory, antinociceptive, neuroprotective, and antidepressant properties that can improve physical fatigue and memory. One study conducted on healthy volunteers showed how simply inhaling essential oils improved performance by lowering cortisol levels. The hippocampus, which plays a pivotal role in mood regularisation memory and the stress response, is very sensitive to the action of free radicals. An antioxidant diet and the support of rosemary essential oil have been shown to be suitable for protecting against them. Rosemary hydroalcoholic extract and infusions have also been shown to be very useful in the management of neuropathic pain and in cases of *hyperalgesia* and *allodynia*, as well as in the management of mild forms of anxiety. Apparently, this is due to the presence of flavonoid diterpenes and rosmarinic acid.

Tilia tomentosa: The biochemically active compounds of linden are polyphenols and mucilage (10%).

Since ancient times, linden has always been valued for its sedative and antispasmodic activity. However, its main use is indicated for anxiety and sleep management. Thanks to recent studies, this has been shown to be due to its ability to promote elevation of plasma serotonin levels. Molecules with anti-inflammatory and anti-oxidant activity have recently been discovered.

Malva sylvestris: The flowers and leaves of Mallow are the richest part of the plant in healing substances because they are particularly rich in mucilage (8-10%), and molecules with antioxidant action. In herbal

medicine, Mallow is the main remedy for gastro-intestinal disorders due to its anti-inflammatory, antimicrobial and laxative properties. Mallow infusions have been shown to be important in counteracting gastrointestinal somatization and supporting the treatment of irritable bowel syndrome.

Salvia officinalis: Sage, commonly used in cooking, is an ancient medicinal plant whose essential oils account for 0.8-2.5 percent of the total. It has always been used for its eupeptic, antispasmodic and healing actions and is especially indicated for menstrual disorders as well as oral cavity and gastrointestinal inflammation. Baths with sage extract are useful for the treatment of skin dyshidrosis.

Sage has also recently been shown to have excellent anti-inflammatory properties for the mucous membranes of the gastro-intestinal tract, especially when sipped in infusions or drunk in drops with modest alcohol content. Finally, it has healing properties not only at the skin level, but also at the mucosal level (gingivitis, small ulcerative lesions of the gastrointestinal tract).

Betonica officinalis (*stachys officinalis*): In the past this plant was valued and used for its anti-diarrheal and febrifuge properties. It has an interesting anti-inflammatory action for the gastrointestinal mucous membranes. In Italy it was called the "herb of fear," because it was used to overcome moments of emotional distress. Many studies have confirmed its usefulness for treating stress, skin inflammation and digestive disorders. Thanks to its phytocomplexes, it not only has antioxidant properties but also has an analgesic effect.