

PHYTOTHERAPICS USE IN MOOD DISORDERS: MYTH OR REALITY?

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ABSTRACT

In search of medicinal products that presented minor side effects for the treatment of mood disorders some experts have pointed out use of herbal medicines in cases of anxiety and mild depression. What caused a large increase in the marketing of herbal medicines with indications in affective disorders. However, some experts if they show indifferent or resistant to this practice. In this context, this manuscript aims a systematic evaluation of herbal medicines used pharmacologically in clinical medicine for the treatment of mood disorders, raising the discussion on the efficacy and safety of this pharmacotherapeutic approach.

KEYWORDS: Phytotherapics, medicinal plants, herbal medicine, mood disorders, depression.

1. INTRODUCTION

The knowledge of plants always followed human evolution. At first, the earliest civilizations observed the animals sought in herbal cures for their ailments. They realized that alongside edible plants, had other endowed with greater or lesser toxicity, and these to be experienced in combating the disease, showed, though, empirically, its healing potential¹.

Records dating from the year 5000 b.C., in China, there were lists of plant medicines used in therapy of that time. Chinese Sheuing in the year 3000. b.C., applied to the cultivation of medicinal plants. Cho-Chin-Kei, the great emperor, known as the "Chinese Hippocrates" had the most complete work of pharmacognosy of Ancient China. In it was described the medicinal properties of Ginseng and Camphor², used in therapy until the present day.

In Brazil, the use of medicinal plants has its base in the indigenous practice, and under the influence of African and European cultures, generated the popular use of many plant species, native and/ or acclimatized to our climate³.

The Phytotherapy is used worldwide and is recommended by the World Health Organization (WHO) and widely used by the medical community¹.

According Tomazzoni *et al.* (2006)⁴, increased consumption of medicinal plants and herbal medicines are

due to the fact that people are questioning the dangers of abusive and irrational use of pharmaceuticals, seeking to replace them with therapies with fewer side effects. In addition, proof of therapeutic action of many plants used popularly has favored this dynamic. Another related factor is the dissatisfaction of the population before the official health system and the need to be able to control your own body and regain their health, taking health practices for you and / or your family.

Given the numerous literature reports describing the use of herbal medicines for mood disorders, especially in cases of anxiety depression 5-8, this manuscript aims a systematic evaluation of herbal medicines that are covered pharmacologically in clinical medicine for the treatment of disorders humor, raising the discussion on the effectiveness and safety of pharmacotherapy approach.

2. MATERIAL AND METHODS

The research was conducted through literature review with national and international articles obtained from BIREME databases (Virtual Health Library), PubMed (US National Library of Medicine), LILACS (Latin American and Caribbean Health Sciences) and SCIELO (Scientific Electronic Library), in order to perform an interpretative analysis of the rational use of herbal medicines in mood disorders.

3. LITERATURE REVIEW

Depression: a mood disorder

Mood disorders are characterized by affective manifestations considered inadequate in terms of intensity, frequency and duration. These manifestations, the most common is generically called depression and involves severe pain, which may include feelings of sadness, anxiety and hopelessness; low self-esteem; inability to experience pleasure; ideas of guilt, worthlessness and ruin; pessimistic views of the future and recurrent thoughts of death, accompanied by somatic alterations including sleep, appetite, psychomotor activity and sexual function. At the other extreme of mood disorders, are the manic episodes,

determined by an expansive affection, elated and irritable, as well as acceleration of thought with flight of ideas; inflated self-esteem and decreased need for sleep, among other changes⁹.

Depression is an affective or mood disorder that accompanies mankind throughout its history. It is considered the Century XXI disease, despite not having origin in modern life, having been described by Hippocrates there are approximately 400 BC, and however, it is increasingly common¹⁰.

According to WHO, 121 million people suffer from depression worldwide. Brazil ranks first in the ranking of prevalence of the disease among developing countries. Projections by the World Health Organization (WHO) indicate that by 2030 depression will be the most prevalent evil in the world, ahead of cancer and some infectious diseases¹¹.

Depression is a common medical condition, chronic and recurrent. It is frequently associated with functional disability and impaired physical health, generating great impact on the lives of patients and their family, especially by losses in various fields such as financial, personal and professional, often making it impossible to carry out their daily activities normally, the being fourth leading cause of disability throughout the world. Given its high prevalence and social costs, is a major problem for public health in the Americas¹².

Its cause is not fully understood but it is known that is linked to genetic, biological and psychosocial factors, and genetic factors of great importance, since the pathology involves a biochemical imbalance of the neurotransmitters responsible for maintaining the humor, which can be family origin¹³.

The treatment of depression consists of medication and psychotherapy. Pharmacological treatment is based on different classes of drugs such as tricyclic antidepressants (TCA), monoamine oxidase inhibitors (MAOIs) and selective serotonin reuptake inhibitors (SSRIs). Although these drugs are already consolidated as effective in treating depression, side effects, are presented as the main variable related to non-adherence of patients to drug treatment¹⁴. Therefore, the reduction of side effects is fundamental to the success of treatment. In addition, studies on the incidence of mood disorders have shown that people at risk for depression has changed a lot in recent years¹¹.

Today depression affects children, adolescents and workers of working age. Thus, the expansion of the class of substances with antidepressant activity is of utmost importance, being one of the alternatives in the search for new molecules with the natural source.

In the search for treatments that have fewer side effects, some experts point to use of herbal medicines for mood disorders. Thus, there was a large increase in the marketing of herbal medicines with indications for affective disorders.

Nonetheless, some experts have proved indifferent or resistant to this practice.

In this context, this article aims, a systematic evaluation of herbal medicines that are covered pharmacologically in clinical medicine for the treatment of mood disorders, as well as the development of a theoretical framework on the issue.

Phytotherapies in psychiatry

Valerian

Valeriana officinalis L. It is a medicinal plant of the Caprifoliaceae family (Figure 1), popularly known as valerian-of-pharmacy, or herb valerian wild cats, are very common in Europe and northern Asia. It is an herb of wet places, growing in abundance along the banks of rivers. It was widely used in the sixteenth century in Europe as perfume, despite the unpleasant odor. Its dye is today used as a sedative for presenting properties which facilitate and induce sleep¹⁵.



Figure 1. *Valeriana officinalis* L. (Valerianaceae), vegetable drug that gives rise to herbal medicine registered with the National Health Surveillance Agency (ANVISA) as simple anxiolytic (Registries: 1.2009.0004; 1.5423.0196; 1.4493.0042; 1.1861.0004; 1.1860.0032).

It is a species that has documented clinical efficacy¹⁵⁻¹⁷. The parts used this medicinal plant are the roots and rhizomes. Its extract is presented as a mixture of complex chemical constitution, but its therapeutic effect is related to the presence of: sesquiterpenes the volatile oil such as valerenic acid and its derivatives, and iridoids the valepotriates type, such as: valtrate, diacevaltrate and 11-acevaltrate¹⁸.

Valerian has several indications, but of greater importance to this article is related to its potential in treating nerve disorders such as anxiety and anxiety¹⁷⁻¹⁹. Due to its soporific potential, this plant is widely used as a mild sedative, tranquilizer in all cases of nervousness, even in cases of epilepsy and neurasthenia, and treating sleep disorders associated with anxiety.

Several clinical studies have proven the effectiveness of valerian as a sleep inducing agent, being correlated to valepotriates, which stimulate the release of gam-

ma-aminobutyric acid (GABA), increasing its concentration in the synaptic cleft, leading to the sedative effect. Another factor in the studies is the inhibition of the enzyme GABA transaminase valerenic acid, indicating that this inhibition increases the inhibitory effect of GABA in the CNS, thereby contributing to the sedative properties of valerian¹⁸.

Hiperico

Hypericum perforatum L. (Figure 2), is a perennial herbaceous plant belonging to the Hypericaceae family, frequently found in European countries, Asia, North Africa and acclimatized in the United States. In Brazil it is popularly known as St. John's wort. From their aerial parts, obtain an extract popularly used to treat depression²¹. The chemical content evaluated to date points to the presence of essential oil, tannins, resins, pectin, naphtho-diantrones, floroglucinois (hyperphoria), flavonoids (quercetin, quercetrin, isoquercetina, rutin), procyanidins (procyanidin, catechin), phytosterols, vitamins C, carotenoids, amino acids, and saponins.

The hiperico is known since antiquity for its anti-inflammatory properties²⁰. Nowadays, its use is related to the treatment of mild to moderate depression as well as treatment of associated symptoms such as anxiety, tension and muscle pain^{23,24}.

Butterweck (2003)²⁵ suggests that hypericins are responsible for the antidepressant activity. Already Kirakosyan *et al.* (2000)²⁶ attribute this activity to the group of hyperforin. However, the mechanism of action is not fully known. Nevertheless, numerous studies have reported the potential of this plant drug for the treatment of mood disorders²³⁻²⁶.



Figure 2. *Hypericum perforatum* L. (Hypericaceae), vegetal drug which led to herbal medicine registered at ANVISA as an antidepressant (Registry: 1.0155.0206; 1.1717.0055; 1.1860.0003).

Kava kava

Piper methysticum G. Forst. (Piperaceae), also known as kava-kava kava, intoxicating pepper, kava-root, kava

pepper among other denominations. It is a natural plant of Pacific Ocean islands²⁷.

This plant was used for hundreds of years for various purposes at least curious. Women of the time chewed the roots and leaves of kava-kava in order to form dough, which spit into a container and mix together the various drinks thus preparing a cocktail that, would be served on occasions such as weddings, births and funerals. The plant was also used for religious rituals and ceremonial dances, as generated in these relaxing effect, decreased fatigue and anxiety and hence the welfare of these people²⁸.

Studies on the chemical composition indicate the presence of various substances, such as tannins, benzoic acid, cinnamic acid, sugars, bornyl-cinnamate, stigmastrol, flavocavaines, mucilages, pyrones, tetra-hydroianganones and some mineral salts, particularly potassium. The substances primarily responsible for the pharmacological activity of kava-kava are the -pyrones named kavalactones²⁹.



Figure 3. *Piper methysticum* G. Forst. (Piperaceae), vegetable drug that gives rise to herbal medicine registered at ANVISA as simple anxiolytic (Registry: 1.1861.0089; 1.0235.0572)

The kava-kava is considered a drug alternative to the use of benzodiazepines because of its characteristic of not induce dependence in its users and not develop the adverse effects of benzodiazepines as loss of cognitive functions, drowsiness, reduced motor coordination³⁰.

In the years 1999 to 2002 this plant was in the top 10 best-selling herbal medicines in Brazil. It is indicated for the treatment of insomnia and anxiety, acting as soothing⁵.

Nowadays the kava-kava has been widely used for treating anxiety, stress, insomnia, agitation, epilepsy, psychosis and depression. No information on the use of kava-kava for other pathologies. However, it is used in folk medicine to promote wound healing, treating migraines, colds and respiratory tract infections, tuberculosis, rheumatism, urogenital infections, including chronic cystitis, venereal diseases, uterine inflammation, intestinal problems, ear infections and abscesses³¹.

The kava-kava has several effects on the central nervous system, related activities anxiolytic, sedative, anti-convulsants, local anesthetic, spasmolytic and analgesic; but still unknown the exact mechanism of these effects^{32,33}.

The consumption of kava in recommended doses and for a short period causes no adverse effects but their widespread use may cause hepatotoxicity, it is responsible for a large number of cases in Europe⁵.

Maracuja or Passion fruit

Passiflora incarnata L., also known as flower-of-passion, maracuja guaçu, wild maracuja/ passion fruit, is a perennial, fast growing bindweed, belongs to Passifloraceae (Figure 4).

Plant native to the Americas, known in Brazil as "maracujá" whose origin is indigenous and means "food prepared in bowl"; worldwide known as passion fruit to have a mystical relationship with Christ's passion. Some writers consider symbolic the parts of the passion flower. For them the female part of the flower consists of a tripartite stigma representing the three persons of the Holy Trinity Father, Son and Holy Spirit; since the male part, which was composed of five stamens symbolized the wounds of Christ; the part called corolla represented the crown of thorns; as the tendril represented whip. Thus it is considered mystique that plan was sent to Paul V, who sent cultivate it in Rome³⁴.

The Passion fruit is being popularly used throughout the world for its sedative, soothing, antispasmodic effects, beyond combat stress among other utilities²⁰.

The part used this species are the leaves that have soothing properties, diuretic, emmenagogue, contraceptive and antifebris. The roots have anthelmintic and anti-inflammatory activities. Its leaves consist mainly of: flavonoids (apigenin, luteolin, quercetin, chrysin, kaempferol, isovitexin, orientin, among others); alkaloids (harmana, harmol, harmine, and harmaline harmalol); cyanogenic glycosides, essential oil etc³⁵.

Studies over the decades have shown that passion fruit is indicated for the treatment of neuralgia, generalized convulsions, hysteria, insomnia, nervousness and agitation^{35,36}.

According to the National Health Surveillance Agency (ANVISA), through the publication of Resolution No. 95 of December 11, 2008, the indication of *P. incarnata* is as a sedative, and its mechanism of action is related to the induction sleep, which causes sedation and reduces anxiety³⁷.

Their depressant activity is primarily related to the harmana and harmaline alkaloids, which are beta-carbolines (derived serotonin and tryptophan). Acting as inhibitors of mono-aminoxidase enzyme (MAO), and exhibit agonist action on GABA receptors and benzodiazepine^{38,39}.

It is unclear the intensity and frequency of adverse reactions and contraindications of this plant⁴⁰. However, in the case of an overdose, it can cause sedation and potentiate MAOI therapy (inhibitor of monoamine oxidase). As for the side effects were not found evidence associated with passion fruit³⁹.

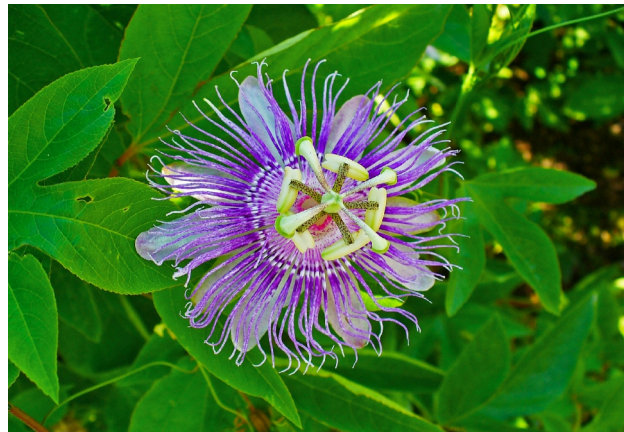


Figure 4. *Passiflora incarnata* L. (Passifloraceae), vegetable drug that gives rise to herbal medicine registered at ANVISA as simple anxiolytic (Registries: 1.0155.0098; 1.6773.0202; 1.0974.0168).

Cratogeomys

Crataegus oxyacantha L., also known as hawthorn albar (Portugal), spino albar, cratogeomys, majuelo, hawthorn (England), Biancospino (Italy), aubépine or epine blanche (France); is a tree of the family Rosaceae, its height varies from 2 to 7 meters (Figure 5). It is found in almost all of Europe, from the Mediterranean to southern Scandinavia, and the Atlantic coast to the west of Asia, and Siberia, North America and North Africa⁴¹.



Figure 5. *Crataegus oxyacantha* L. (Rosaceae) vegetable drug that gives rise to herbal medicine registered at ANVISA as simple anxiolytic (Registries: 1.0155.0098; 1.7287.0051; 1.0974.0168)

Cratogeomys has been used since immemorial times, but it was in ancient Greece, it was used to relieve heavy menstrual flow and relief of menstrual cramps. However, it is in the late nineteenth century in America, this plant gained notoriety being used in the treatment of atherosclerosis and angina pectoris⁴¹.

The extract obtained from the aerial parts of cratego's main chemical components: procyanidins; flavonoids, derivatives of quercetol, such as hyperoside, rutin, quercetin, kaempferol, and apigenol; vitexin and derivatives, vincenina; carboxylic acid (oleanolic, ursolic, crategolic, besides essential oils and tannins. Pharmacological studies suggest that compounds related to the therapeutic uses described so far are the flavonoids and procyanidins⁴².

The main uses involving mood disorders are as a sedative in cases of irritability, insomnia, anxiety, feeling dizzy, headaches and menopausal disorders; acts on the central nervous system producing an inhibitory action of the sympathetic tone improving symptoms of sentiment⁴³⁻⁴⁵.

Mulungu

Erythrina mulungu Mart. ex Benth. (Fabaceae), It is popularly known as mulungu, immortal stick, Jewish slipper, parrot's beak. It is widely used in healing and african-Brazilian religious rituals. Of their shells were isolated and identified the alkaloids; erythrina, erythrocoraloidine, erisopine, erisodine, eritramine, eritratine, erisovine, compounds that are related to its sedative action⁴⁶ (Figure 6).



Figure 6. *Erythrina mulungu* Mart. ex Benth. (Fabaceae), vegetable drug that gives rise to herbal medicine registered at ANVISA as simple anxiolytic (Registries: 1.7287.0051; 1.0066.0043).

Rodrigues *et al.* (2008)⁴⁶ reported the use of traditional mulungu for its soothing properties, sedative, hypotensive, tranquilizing, anxiolytic and atinociceptivo. Its use is through infusions, decoctions, dry extract, tincture and syrup.

According Faggion *et al.* (2011)⁴⁷, the erythrina alkaloid acts on the central nervous system (CNS), leading to a neuromuscular blocking smooth muscle relaxation and of significant anticonvulsant action.

Many literature reports suggest soothing action in cases of nervous agitation; used with sedative and hypnotic action and mild tranquilizer⁴⁸⁻⁵³.

No interaction was found in the literature; however

mulungu may potentiate the effect of some antianxiety drugs and antihypertensive.

Because it has hypotensive effect, it is recommended that patients who use herbal medicine to Mulungu base associated with antihypertensive medication, have your pressure controlled and monitored in accordance with proper precautions.

4. CONCLUSION

Currently, there are about 146 herbal medicines used in mood disorders registered with ANVISA, approximately 80 simple herbal medicines, and 66 herbal compounds. This figure is frequent changes, because the reality of the record is very dynamic, since the position of products and constantly modified. Every day, new drug are registered, while others lose their registration, either by rejecting the renewal request or cancellation of registration.

Among the herbal medicines registered for the treatment of anxiety and depression, the largest number of records in recent years, was awarded to Valeriana, with the total number of records with 47 products, followed by Cratego with 31; Passiflora 25; Hypericum 17; Mulungu with 15 and with 11 Kava products commercialized in Brazil.

It must be emphasized that the drug registration in Brazil is governed by specific legislation, which requires compliance with numerous protocols to ensure the safety, effectiveness and quality of the pharmaceutical product. In this context, the use of herbal medicines for the treatment of mood disorders has grown tremendously in recent years. Currently, there are health professionals with diverse opinions on the subject, supporters and tough, but we can conclude, before reports here exposed, that the herbal medicine, is still great ally of man for the treatment of mood disorders.

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