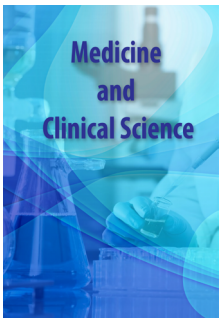
Medicine & Clinical Science

Short Communication



Pharmaceutical Care in Old Age For Patient Safety in Relation to The Interaction of Medicinal Plants With Drugs For Depression And Anxiety

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Mental disorders are very common pathologies in our population and their lifetime prevalence in Brazil is 45% (based on ICD-10 criteria). Depression is the most common of the affective disorders (of mood rather than disturbances of thinking or cognition); it can vary from a very mild alteration, bordering on normality, to severe depression (psychotic), accompanied by hallucinations and delusions. It is a heterogeneous disorder whose patients have one or more core symptoms, and is usually associated with other psychiatric conditions, including anxiety, eating disorders and drug addiction. Anxiety is the denomination attributed to a universal subjective experience of the human being in situations of danger or risk of negative outcomes of the most diverse natures, that is, it is a set of behavioral, physiological, cognitive reactions, perceived by the subject, who is in an aversive situation. Both, depression and anxiety need to be diagnosed and have medical follow-up for patient safety. People often think that it is something temporary and start to self-medicate with medicinal plants that act on these diseases without, however, having been diagnosed, which could aggravate the already present condition, in addition to compromising their safety and quality of life. Medicinal plants are very important when well used, but diagnosis, guidance and follow-up during the therapeutic proposal are necessary. Four medicinal plants and their characteristics are discussed below (*ANVISA. Memento phytoterapic. Farmacopeia Brasileira, 1.ed. 2016*) so that they can be used safely without compromising the individual's quality of life. With the knowledge of the patient, as well as his drug history, we can and should avoid numerous problems that are predictable, such as drug interactions.

Hypericum perforatum L. (St. John's Wort)

Recommendation: In mild to moderate depressive states.

Mechanism of action: In non-clinical tests, despite the inhibition of monoamine oxidase (MAO) and catechol-ortho-methyltransferase (COMT) enzymes have been demonstrated in in vitro tests with fractions of extracts, hypericin and flavones, the studies concluded that the antidepressant effect of *H. perforatum* could not be explained by MAO inhibition. Possible other mechanisms include the action of the extract in modulating the production of cytokines, the expression of serotonergic receptors and the hypothalamic-pituitary-adrenal axis. A meta-analysis study on clinical trials considering patients with mild to moderate depression concluded that the efficacy of *H. perforatum* was significantly superior to that of the placebo group, with few adverse effects compared to standard antidepressants.

Drug interactions: Interacts with: cyclosporine, coumarin anticoagulants, oral contraceptives, theophylline, digoxin, indinavir and possibly other non-nucleoside protease and reverse transcriptase inhibitors, impairing their effect, due to the induction by *H. perforatum* of the metabolic pathway involving cytochrome *P -450*. It may result in subtherapeutic concentrations of antiretroviral drugs, and the development of resistance. The administration of *H. perforatum* is contraindicated in situations: in association with MAO inhibitors, selective serotonin reuptake inhibitors. Combining *H. perforatum* with conventional antidepressants, such as tricyclic antidepressants or fluoxetine, is not recommended, except under medical supervision.

Passiflora incarnata L. (Passion fruit)

Recommendation: Anxiolytic and mild sedative.

Mechanism of action: An in vitro study concluded that the pharmacological effects of *Passiflora inca*rnata are mediated via modulation of the GABA system, including GABA A and GABA B receptor affinities, and on GABA uptake. In a clinical study

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with patients undergoing spinal anesthesia, treatment with *P. incarnata* suppressed anxiety before spinal anesthesia in a statistically significant way when compared to placebo, proving to be an effective and safe anxiolytic drug. In another study of clinical efficacy in patients with moderate, high and severe anxiety according to the VAS score, during a dental procedure, a significant difference was observed in the levels of anxiety before and after *P. incarnata* and the placebo group, indicating that the administration of passionflower, as premedication, is significantly effective in reducing anxiety.

Drug interactions: *P. incarnata* potentiates the sedative effects of pentobarbital and hexobarbital, increasing sleep time. There are indications that the coumarins present have potential anticoagulant action and possibly interact with warfarin. In addition, the use of *P. incarnata* associated with MAO inhibitor drugs (isocarboxazid, phenelzine and tranylcypromine) may potentiate the effect.

Piper methysticum G. Forst (Kava-kava)

Recommendation: Indicated for the symptomatic treatment of mild to moderate stages of anxiety and insomnia, in the short term (1-8 weeks). Note: Several cases of liver toxicity have been reported in Europe following the use of herbal products containing *P. methysticum* extracts.

Mechanism of action: In vitro studies did not significantly block serotonin reuptake by kavalactones, however, norepinephrine was blocked by three lactones, thus describing another possible mechanism of action. In animal models *P. methysticum* inhibits experimentally induced seizures, and this anticonvulsant effect may be mediated by local Na+ channel receptors, which are common targets of antiepileptic drugs. A meta-analysis study to demonstrate the therapeutic efficacy and safety of standardized extracts of Kava-kava in the treatment of anxiety suggested a significant reduction in the total score of the Hamilton anxiety scale, in patients treated with standardized extract of *P. methysticum*, in relation to those treated with placebo. Other studies have also shown that patients treated with Kava-kava have significantly reduced anxiety symptoms measured on the Hamilton Anxiety Scale.

Drug interactions: Interacts (may potentiate the effects) with medications and centrally acting drugs such as alcohol, barbiturates and other psych pharmaceuticals. There is also interaction with alprazolam, cimetidine and terazosin.

Valeriana officinalis L.

Recommendation: Used as a mild sedative, hypnotic and in the treatment of sleep disorders associated with anxiety.

Mechanism of action: In animal experiments, the following actions were observed: central depressant, sedative, anxiolytic, spasmolytic and muscle relaxant. In vitro, valerenic acids decreased the degradation of gamma aminobutyric acid (GABA). In addition, in animal experiments, there was an increase in GABA in the synaptic cleft via inhibition of reuptake and increased secretion of the neurotransmitter, which may be one of the effects that cause the sedative activity. Another mechanism is the presence of high levels of glutamine in the extract, which has the ability to cross the blood-brain barrier, being captured by the nerve terminal and converted into GABA.

Drug interactions: In general, it may potentiate the effect of other CNS depressants. In animal studies, *V. officinalis* has an additive effect when used in combination with barbiturates, anesthetics or benzodiazepines and other CNS depressant drugs. *V. officinalis* extracts containing valepotriates may help with withdrawal syndrome by withdrawing diazepam.

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