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The alternative use of medicinal plants in the treatment of depression caused by pesticide: A literature review

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Abstract— *In the last decade, Brazil has expanded the pesticide market by 190%, becoming to be the first place in the world ranking of consumption since 2008. This way, the negative impacts for the environment and human health, because of the exposure to chemical inputs, are diverse. Among the disorders caused, depression stands out, due to the exposure of field workers to pesticides. As a possibility to an alternative treatment there is the use of plants to control depression. Therefore, the objective of this study was to evaluate the profile of publications in the last five years about plants that can be used in the alternative treatment of depression. This is a bibliographic search, in the integrative review modality. Thus, nine papers were selected from scientific studies with medicinal plants used to control depression. Among the mentioned plants that were used in the antidepressant treatment there is the Hypericum perforatum, Crocus sativus, Valeriana officinalis, Lavandula officinalis e Rosmarinus officinalis. Given to the exposure of farmers and the surrounding populations to agrochemicals and also to the repercussion, such as depression, the alternative use of medicinal plants in the treatment of this disease, it is shown as an important alternative. Therefore, this review brought the knowledge of a diversity of plants with mediated antidepressant activity.*

I. INTRODUCTION

In the last decade, Brazil has expanded the pesticide market by 190%, becoming to be the first place in the world ranking of consumption since 2008. In the 2010 and 2011 harvest alone, 936 thousand tons of pesticides were consumed (RIGOTTO et. al., 2014). The agri-food system has been one of the biggest factors of environmental imbalance, and the discussion that permeates health and environment must consider this fact, expanding the discussions related to the pesticides use (AZEVEDO & PELICIONI, 2011). According to the Program for Analysis of Pesticide Residues in Food (Programa de Análise de Resíduos de Agrotóxicos em Alimentos - PARA) of the Brazilian Health Regulatory Agency - ANVISA (2011) 1/3 of the food consumed daily by Brazilians is contaminated by pesticides, according to the

analysis of samples collected in all 26 states of Brazil (CARNEIRO, 2015). Still according to ANVISA, the use of one or more than one pesticides in crops, for which they are not authorized, especially those in reassessment or scheduled discontinuity phase due to its high toxicity, shows negative consequences on human health and to the environment. One of the consequences is the increase of food insecurity to the consumers who eat contaminated food with Active Ingredients (AI).

Conforming to ANVISA (2011) the AI with high degree of proven acute toxicity may be triggers of health problems, like for example: neurological, reproductive, hormonal dysregulation and even cancer.

Therefore, the negative impacts of the exposure to the chemical inputs are diverse to the environment, animals, ecosystems as well as for human health. Theses repercussions affects, directly, farmers, rural workers and the population surrounding the crops, especially pregnant women and children who are part of the most vulnerable risk group to the harmful effects of these chemicals (CARNEIRO, 2015). This exposure is justified by the fact that only 30% of the pesticides are sprayed in the "target", the remnant is disseminated in the ecosystem, contaminating, for example, soil and rivers (PIGNATI et. al., 2014). Regarding the environmental aspects, it also can be highlighted the soil degradation, waste and excessive use of water, environmental pollution, dependence on external inputs and loss of genetic diversity. About the factors involving human health, it is associated with the emergence of imbalances such as infertility, hormonal disorders, depression, suicide, cancer, among others (COSTA et. al., 2017; JOO & ROH, 2016; STROPARO & BRAGUINI, 2011).

Among the disorders caused by the chronic exposure of pesticides to rural workers, depression stands out with a high incidence and important repercussion, as it is associated with suicide. Depression is a severe mood disorder, with significant loss of mental function and distortion of the way the person experiences and understands reality (BARBOSA, 2016). It is understood as a mood disorder with a decline, to varying degrees, of interest in everyday facts, lowering of attention, impairment of memory and suicidal ideation. Depression compromises daily activities in such a way that it results in a lower quality of life, which may lead the affected person to withdraw from work (ELY, 2014).

In this context, the medicinal plants have been widely used as an alternative for the treatment of various diseases and this practice is also known as phytotherapy or herbal medicine often symbolizing the only therapeutic resources of many communities and ethnic groups, even with the encouragement of pharmaceutical industry and use of industrialized drugs (LACERDA, 2013). Based on this, it is justified the relevance of this study, which aimed to discuss the objective of evaluating the profile of publications in the last five years about plants that can be used in the alternative treatment of depression, from the perspective of the authors Qin et. al. (2017), Chen et. al. (2019), Perviz et. al. (2016), Rabiei & Rabiei, (2017), Lopes-Rubalcava & Estrada-Camarena, (2016), Kourosh Saki et. al., (2014), Lee & Bae (2017), Jeanette Martins (2018), Hosseini & Hosseini (2018).

This is a bibliographic research, based on the integrative review modality, where it was selected 09 scientific papers about medicine plants used to control depression. From these nine, seven had the profile of literature review of plants used in the treatment of this pathology and two were experimental studies with models of depression in rats testing an herbal formula and an active ingredient.

Lastly, knowing the strong association between pesticides and the development of depression in rural workers and exposed populations and that herbal medicine is a possibility in the treatment of depression, the main results analyzed point to the mechanism of action proposed for the antidepressant activity that involves antioxidant action of the nervous system, inhibition of apoptosis through ROCK/Akt, synaptic regulation of serotonin, noradrenaline, dopamine, regulatory activity by the hypothalamus-hypophysis-adrenal axis.

II. METHOD

This study is a bibliographic research, based on the integrative review modality of the developed literature, respecting the following phases: elaboration of a guiding question, sampling the literature, data collection, critical analysis of the included studies, discussion of results and presentation of the integrative. So, according to Marconi & Lakatos (2011) the bibliographic research, or secondary research source, resumes all scientific production that has already been made public in related to the topic of the study.

The integrative literature review is one of the research methods that allows the evidences' incorporations in clinical practice. It consists in the construction of a broad analysis of the literature, contributing to discussions about research methods and results, as well as reflections about the realization of future studies. The initial purpose of this research method is to gain a deep understanding of a particular phenomenon based on previous studies. (BROOME, 2000).

So, the guiding question was: What is the profile of publications in the last five years about plants that can be used in the alternative treatment of depression? The study was carried out in the databases Science Direct, Coordination for the improvement of Higher Education Personnel (CAPES), Latin-American and Caribbean Literature in Health Sciences (LILACS), Publisher Medline (PubMed), Scientific Electronic Library Online (SciELO). From the association between terms, in English: Depression, phytotherapy, plants selected as Descriptor in Health Science (DeCS) of the BVS portal. The terms were crossed as subject descriptors following Boolean logic in the following ways: ((Depression) AND (phytoterapy) AND plants). After reading the titles and abstracts, it was included the papers that fitted in the proposed theme and discussed about medicinal plants used in the alternative treatment of depression during the last five years.

An average of 195 papers were found at the first search, which after applying the selection criteria were restricted to 09 papers. The inclusion criteria were publications that treated directly about medicinal plants or active principles focused on the treatment of depression (both review, clinical and experimental studies) in the last five years. Given to the great number of publications, editorials, letters to the editor, books and duplicated publications were excluded from the study.

III. RESULTS AND DISCUSSION

Thus, it was selected 09 scientific papers about medicine plants used to control depression. From these 09, seven had the profile of literature review of plants used in the treatment of this pathology and 02 were experimental studies with models of depression in rats testing an herbal formula and an active ingredient. The publications are concentrated on countries such as Chine, India, Bangladesh, Iran, Pakistan, and Mexico, between the years 2014 to 2019.

Several plants used on the treatment of depression have been mentioned in publications among them there is the Hypericum perforatum (popularly known as erva-de-são-joão), Crocus sativus (real Saffron), Valeriana officinalis (minor valeriana, wild valeriana), Lavandula officinalis (Alfazema) e Rosmarinus officinalis (Rosemary) present in almost all studies. It is important to highlight that some of these plants acted in the treatment of depression as well as anxiety.

So, given the side effects that the conventional medications have provided, there is an increase in the consumption of drugs of phytotherapeutic origin and medicinal plants. According to Hosseini & Hosseini (2018) it has been seen that many phytochemicals, such as saponins, alkaloids, polyphenols, triterpenoids, essential oils, fatty acids and flavonoids, have anxiolytic and antidepressant effects.

In Perviz's et. al. (2016) work it was seen the antidepressant effect of several isolated alkaloids plants, such as Psychotria myriantha, which has as active ingredient the stridosidinic acid, by the serotonergic system (5-HT) in the hippocampus of rats. There is also the Beberis aristata (berberina) which significantly decreased the immobility of rats and increased the climbing behavior in the forced swim test. However, there was no effect on swimming time, while increased the exploration of open arms in the elevated plus maze test that confirmed the activity similar to depression medication. Just like the alkaloids from Annona cherimolia, including 1,2-dimethoxy-5,6,6a, 7-tetra-hydro-4H-dibenzoquinoline-3,8,9,10-tetraol, anonain, liriodenine e nornuciferin and the β-carboline, such as harmana, norharmana e harmine produced an effect similar to an antidepressant (PERVIZ et. al., 2016).

Also, in the previous study, it was seen that the acute administration of lyophilized extract of Rhazya stricta, (active ingredient: akuammidine, rhaziminin and tetrahydrosecamine) resulted in an antidepressant effect in experimental animals. Such activity was also seen in the following species: Mitagyna spicosa, Peganum harmala, Ziziphus apétala, Aconitum baicalense, Boerhaavia diffusa, Evodia fructus, Sceletrium tortuosum, Piper nigrum, Piper laetispicum e Dactylicapnos scanens. The mechanism of action of these plants was due to the monoaminergic system (serotoninergic, noradrenergic and dopaminergic), inhibitory action on monoanine oxidase, decrease in plasma levels of corticosterone and inhibitory of the 11-β-hidroxisteroid deshydrogenase.

The Hipérico, scientific name, Hypericum perforatum is a plant which has antioxidant property, anxiolytic activity and it is very used in the treatment of depression. Its extract is used both in the therapy of this syndrome and also to prevent its recurrence. Thus, its action is longer drawn out than the citalopram. Given its wide dissemination as an antidepressant, many studies have been developed to identify its active principles and mechanisms of action (HOSSEINI & HOSSEINI, 2018; SINGER et. al., 2011; BUTTERWECK, 2003).

The H. perforatum is a weak inhibitory of monoamine oxidase, but it acts on synaptosomal reabsorption of serotonin, dopamine, and norepinephrine. As it also has a little effect on beta- adrenergic and it is more potent on serotonin receptors (BUTTERWECK, 2003). Its antidepressant activity is as effective as the medication imipramine (SABZHAH et. al., 2009).

A follow-up study of Sabzhah et. al. (2009), in long term, recruited 426 patients and subjected them to administration of extract of H. perforatum (3 × 300 mg / day) to be evaluated for remission rates of depression. The results showed a beneficial effect of the extract in preventing relapse, while long-term maintenance and tolerability was comparable to placebo (SABZHAH et. al., 2009).

Crocus sativus is a spice better known as Saffron, which is produced from parts of the flower, rich in secondary metabolites such as flavonoids, anthocyanins and tannins (BABAEI et. al., 2013). The bitter taste is due to the presence of a substance called picocrocina. Other carotenoids, such as beta-carotene, lycopene and zeaxanthin, and vitamins, especially riboflavina and tiamine, are found in the Saffron. Crocetin, crocetin and Saffron are active principle of Saffron (ASISHIRAZI et. al., 2017).

In two randomized clinical trials using the saffron (30mg/day), patients showed a significant improvement from depression compared to placebo. As well, in three independent randomized clinical trials using the Hamilton Rating Scale for Depression protocol, it was observed equivalent effects when comparing saffron to imipramine or fluoxetine (LEE & BAE, 2017). In a limited meta-analysis, it was possible to conclude that the saffron supplementation may improve the symptoms of depressive patients and other literature review indicated thar it helps in mild or moderate depression (HAUSENBLAS et. al., 2013; LOPRESTI & DRUMMOND, 2014). The authors propose that the saffron action mechanisms occur by serotonergic, antioxidant, anti-inflammatory, neuroendocrine and neuroprotective pathways.

The valerian, scientifically known as Valeriana officinalis, belongs to the Family of Valerianaceas and acts in diseases of central nervous system, such as insomnia and anxiety (ROOZBEHI et. al., 2015). In studies with valerian, sedative, hypnotic and antidepressant effects were noticed, with isovaltractin, valproate and didrovaltro as active ingredients (REZVANI et. al., 2010). Its antidepressant activity occurs through serotonin, GABAergic and adenosine systems (CARRETTIERO et. al., 2009). Besides, the results of a study show that this effect occurs by acting on the biosynthesis of serotonin neurotransmitters in the brain (DIETZ et. al., 2005).

The lavender, scientifically called by Lavandula officinalis, is a plant from the Lamiaceae family. It is one of the most used herbs in traditional medicine that is effective in the treatment against diseases related to the central nervous system, helping to better reconcile sleep and in the treatment of anxiety (AKHONDZADEH et. al., 2003). Researchers attribute that its anxiolytic effect is similar to the benzodiazepines and is also due to the increased amount of neurotransmitter GABA (CAVANAGH & WILKINSIN, 2002). In Rezaei's et. al. (2010) work, the sedative and anxiolytic effects of lavender have been attributed to the binding to GABAA and it is believed that this effect is superior to the effects of diazepam. Studies have revealed the antidepressant effects of this plant and that the association with the medication imipramine improves the action of it (AKHONDZADEH et. al., 2003). Hritcu et. al. (2012) reported that the chronic exposure to lavender oil markedly inhibited depressive behaviors in rats when evaluated in the forced swim and elevated plus maze tests.

The rosemary, scientifically known as Rosmarinus officinalis, is from the Labiatae Family and it has uncountable pharmacological effects, including hepatoprotective, antibacterial, antiulcer, anticoagulant, diuretic, antidiabetic, antioxidant e antidepressant (RABIE et. al., 2016). The antidepressant activity is justified by the monoaminergic system (MACHADO et. al., 2009). It was noticed in Machado's (2013) studies that the ursulic acid, an important compound of rosemary, s an antidepressant effect at a concentration of 0,1 mg / kg in rats. This activity is increased in the presence of agonists from the dopamine receptors and impeded in the presence of their antagonists (MACHADO et. al., 2013).

The polyphenols effects of R. officinalis, constituted by carnosic acid, rosmarinic acid and luteolin, on depression and on PC12 cells, in studies of in vitro, were observed in mice. In the proteomic analysis of PC12 cells, it was seen that the extract caused a positive regulation on the tyrosine, hydroxylase and pyruvato carboxylase (the genes involved in the GABAergic, serotonergic, and dopaminergic systems). These polyphenols also protected the nerve cells against the toxicity introduced by the corticosterone (SASAKI et. al., 2013).

The plant Danggui-Shaoyao-San exerts therapeutic effects on depression induced by chronic stress. In a study Kou et. al. (2005) this herb caused an increase in the monoamine neurotransmitters on the brain of elderly mice40. Chamaemelun nobile is from the Asteraceae/Compositae family. It has diuretic, transpiratory, gastrotonic, carminative, stomach, digestive, anti-inflammatory, antipasmodic, and calming properties. An experimental study demonstrated antidepressant effects on the extract of the C. nobile on the progesterone induced major depressive disorder. The Mexican Cristactinia is used on the treatment of fever, rheumatism, diuretic, sexual stimulant, and anticonvulsant. On the pharmacological antidepressant activity of the aqueous extract of the Mexican C., it was seen in mice applying the

forced swim test and the tail suspension test; it was found out that these activities were similar to a conventional antidepressant like clomipramine (RABIEI & RABIEI, 2017; JÄGER & SAABY, 2011; CASSANI et. al., 2015).

Magnolia officinalis is a plant in the Magnoliacea family which is used to treat neurological disorders such as convulsions, depression, and anxiety. It also can be used as sedative and analgesic. Magnolol and honokiol are two active principles identified in these vegetables. It was related that these compounds cause antidepressant effects because they activate the serotoninergic system. The oral use of magnolol e honokiol (20 and 40 mg / kg) caused a decrease in the duration of immobility on the forced swim test and an increase on the preference for sucrose (RABIEI & RABIEI, 2017).

Sálvia Sclarea, the sálvia, is considered the most important genus of the Lamiaceae family. The antidepressant effects of several species of this genus have been confirmed. An experimental study showed that the activity of S. sclarea was sharper than the Rosmarinus officinalis, L. angustifolia and Anthemis nobilis. And the action mechanism of S. sclarea is exerted through the dopaminergic system (SEOL et. al., 2010).

The ginger scientific-named Zingiber officinale, from the Zingiberaceae family, is one of the plants very used in traditional medicine, in addition to food supplementation. Its pharmacological activities are antioxidants, antitumor, anti-apoptotic, anti-inflammatory, anti-hyperglycemia, antitussive and anti-flu. It has been reported in diabetic patients an increase in insulin secretion and a reduction of glucose levels in blood after the administration of ginger extract and that such mechanisms are justified by the serotonin, receptor 5HT-3. For these reasons, the ginger extract can improve symptoms of diabetes and associated depression (HOSSEINI & HOSSEINI, 2018).

Schinus molle, from Anacardiaceae family, exerts certain pharmacological properties, including anti-inflammatory, antitumor, antifungal, anticonvulsant and analgesic (MACHADO et. al., 2007). The injection with extract of n-hexano S. molle (3-600 mg / kg) significantly decreased the duration of immobility in the tail suspension test in mice with comparable efficacy to fluoxetine (10 mg/kg). The antidepressant effects of the extract of n-hexano S. molle can be exerted by the serotonergic, dopaminergic, and noradrenergic (HOSSEINI & HOSSEINI, 2018).

Beside the mentioned plants at this work, it was seen in the review mexican herbs such as Annona sp; Byrsonima crassifolia (L.) Kunth; Casimiroa edulisLa; Annona cherimola, Justicia spicigera which have antidepressant actions. Still in the data search, it was seen that Rhodiola rosea, Echium amoenum (borage), Albizia julibrissin (mimosa), Nelumbo nucifera e Papaver rhoeas also present such action and mediated by monoaminergic systems.

In a study by Neto et al. (2018) it was discussed the association between pesticide poisoning and the emergence of depression in agricultural workers in a clinical case study with a rural worker with a history of absence from work by depression. It was seen that the exposure of the rural worker was to the pesticides Deltametrina, Pendimetalina and Metalaxil-M. Although, in the pesticides directions there was no association with chronic exposure to these and to emergence of mental disorders. However, in the worker's family history, he states that there was suicide in his family members and that they worked in the same activity he did, dealing with the same chemicals. When asked if in the absence periods from work his depressive symptoms underwent any change, the respondent stated that after a few months of leave, he felt an improvement in his mood, slept better and did not feel suicidal ideation that had previously disturbed him (FILHO NETO & FÉLDEN, 2018).

Malekirad et. al. (2013) studied the anxiety/insomnia and severe depression indices and noticed that these were much higher in rural workers when compared to control groups ($p=0,015$; $p<0,001$) (MALEKIRAD et. al., 2013). Thus, the conclusion of this last study was that farmers exposed organophosphorates are prone to neuropsychological disorders and that the longer the exposure time, the greater clinical symptoms.

In Brazil a study of Beseler et. al. (2008) reported that the exposure in high acute intensity as well as cumulative pesticides may contribute to depression in pesticide applicators. In a work with 229 elderlies who lived in the urban and rural zones in Cachoeira do Sul (RS) city, it was identified a high prevalence of the use of pesticides 35,8%, being significantly higher ($p<0,001$) among elderly people living in rural areas (60,2%) (SILVA et. al., 2013).

Thus, given the link between chemical inputs and depression in rural workers and exposed populations, these plants mentioned in the review are seen as a possibility of alternative treatment for depression caused by chronic pesticide poisoning.

In the analyzed Works it was observed that plants are used in the treatment of depression as well as anxiety, like some studies reported. Among these, active ingredient s already isolated could be seen, such as umbelliferone, herbal formulas, plants rich in alkaloides, H. perforatum, C. sativus, V. officinalis, L. officinalis e R. officinalis, as also other herbs mentioned in the text. As it was seen that the main action mechanisms that were elucidated were due to the antioxidant action of the nervous system, inhibition

of apoptosis by the ROCK/Akt pathway, synaptic regulation of serotonin, noradrenaline, dopamine, regulatory activity by the hypothalamic-pituitary-adrenal axis.

Through the specific analysis of the chosen papers to compose this study, it was understood the importance of the medicinal plants in drugs production for the treatment of depression, especially because of its efficiency, potence and security, since the conventional treatment present a percentage of the therapeutic failure and side effects . As well as it was noticed the necessity to elaborate new researches about this thematic (medicinal plants) used on the treatment of depression, since there is too little studies about it; by this way it is possible to have a better understanding of effectiveness of these active principles.

IV. FIGURES AND TABLES

Table 1 – Studies of plant species with antidepressant pharmacological activities.

Species Vegetabçe/ chemical compounds	Results	Origin Country	Authors
Daucus carota, Coriandrum sativum e Angelica archangelica(umbeliferona.)	The treatment with umbelliferona (15mg/kb) Significantly improves depressive behaviours Induced by CUMS (experimental model).	China	Qin et. al.,2017.
Panax ginseng Angelica sinensis Polygala tenuifoliaZiziphi spinosa (PAPZ)	Together, the PAPZ has therapeutic effects in a depression model of rats, increasing the proteic expresson of the brain-derived neutrofic factor (BDNF) and improving the brain anti-oxidance	China	Chen et. al.,2019.
Berberis aristata (Beberina) Psychotria myriantha (Ácido estrictosidina) Annona cherimolia (Anonaina e Liriodenina) Rhazya stricta (Akuammina) Mitagyna speciosa (Mitaginina) Peganum harmala (Norharmana,Harmana e Harmina) Ziziphus apétala (Mauritina A) Aconitum baicalense (Songorina) Boerhaavia difusa (Punarnavina E) Evodia fructus (Evodiamina)Sceletrium tortuosum (Mesembrina) Piper nigrum (Piperina) Piper laetispicum (Leatispicina e Leatispiamida A) Dactylicapnos scanens (protopina)	Strong potential of plants rich in alkaloid for the formulation of new medications for treatment of depression	Pakistan	Perviz et. Al., 2016.
Danggui-Shaoyao-San Epimedium brevicornum Chrystactinia mexicana Chamaemelun nobile Magnolia officinalis Hypericum perforatum Lavandula officinal Salvia sclarea Rosmarinus officinalis Schinus molle	Antidepressant effects through synaptic regulation of serotonin, norepinephrine and dopamine, regulatory activity of the hypothalamic-pituitary-adrenal axis, antioxidant activity and by decreasing inflammatory mediators.	Bandaglas h	Rabiei & Rabiei, 2017.
Annona sp Byrsonima crassifólia Casimiroa edulis Matricaria chamomilla Annona cherimola Justicia spicigera	Species used on the treatment of anxiety and depression disorders.	Mexico	Lopes-Rubalcava & Estrada-Camarena, 2016.
Hypericum perforatum Crocus sativus Rhodiola rósea Lavandula spp. Echium amoenum Panax ginseng Albizia julibrissin	Possible to use in the treatment of anxiety and depression.	Iran	Kourosh Sakiet al., 2014.
Croças sativus Camellia sinensis Echium amoenumPiper methysticum Rhofiola rósea Lavandula angustifólia Nelum bo nucifera	Anti-depressant effect by action mechanisms acting in the hypothalamic-pituitary adrenal (HPA) axis. Monoamine neurotransmitters and mechanisms of neurogenesis/neurotrophic factors (such as inhibition of apoptosis and neuronal cells)	Republic of Korea	Lee & Bae, 2017.
Albizzia julibriss in Canavalia brasiliensis	Antidepressant ation mechanisms	India	Janette Martins, 2018

V. CONCLUSION

Given the exposure of farmers and populations around agrochemicals and its repercussions, such as depression, and the alternative of medicinal herbs in the treatment of this disease, this study is a very important contribution, especial for the social vulnerable communities who do not Always have access to conventional treatment. Based on the literature reviewed it was possible to know various mechanisms of action, as mentioned in the context of this study. Being potential candidates to be used in alternative therapy for this disease. However more preclinical and clinical studies are necessary.

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REFERENCES

[1] AKHONDZADEH, S. H.; KASHANI, L.; FOTOUHI, A.; JARVANDI, S.; MOBASHERI, M. Comparison of lavandula angastifolia mill tincture and imipramine in the treatment of mild to moderate depression, a double -blind randomized trial. Prog Neuropsychopharmacol Biol Psychiat. 2003; 27: 7-123. Disponível em: file:///C:/Users/Usuario/Downloads/CMS%20(1).pdf Acesso em: 25 de outubro de 2019.

[2] ASISHIRAZI, E.; HOSSEINI, S. A.; KEIKHOSRAVI, F. The hypoglycemic interactional effect of saffron aqua extract and swimming training in streptozotocin induced diabetic rats. J Sabzevar Med Sci Univ. 2017; 24 (4): 273-279. Disponível em: https://www.sid.ir/en/journal/ViewPaper.aspx?id=561591 Acesso em: 21 de outubro de 2019.

[3] AZEVEDO, E.; PELICIONI, M. C. F. Promoção da Saúde, Sustentabilidade e Agroecologia: uma discussão intersetorial. Saúde Soc São Paulo. 2011, v.20, n.3, p.715-729. Disponível em: https://www.scielo.br/pdf/sausoc/v20n3/16.pdf Acesso em: 08 de outubro de 2019.

[4] BABAEI, A.; ARSHAMI, J.; HAGHPARAST, A. R.; DANESH MESGARAN, M. Effects of crocus sativus petals extract on blood parameters in rat. J Arak Uni Med Sci. 2013; 16 (6): 14- 21. Disponível em: http://jams.arakmu.ac.ir/article-1-2195-en.pdf Acesso em: 21 de outubro de 2019.

[5] BARBOSA, D. G. et. al. Sintomas depressivos em adolescentes em situação de vulnerabilidade social. Cad Saúde Colet. 2016; 24(2): 221-27. Disponível em: https://www.scielo.br/pdf/cadsc/v24n2/1414-462X-cadsc-1414-462X201600020195.pdf Acesso em: 14 de outubro de 2019.

[6] BESELER, C. L. et al. Depression and pesticide exposures among private pesticide applicators enrolled in the Agricultural Health Study. Environ Health Perspect. 2008;116(12):1713-9. Disponível em:

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2599768/ Acesso em: 29 de outubro de 2019.

[7] BESELER, C. et al. Depression and pesticide expousures in female apouses of licensed applicators in the agricutural health studu cohort. J Occup Environ Med, 2006 v. 48, n. 10, p. 1005–1013. Disponível em: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1626656/ Acesso em: 15 de setembro de 2019.

[8] BROOME, M. E. Integrative literature reviews for the development of concepts. In: Rodgers BL, Knafl KA, editors. Concept development in nursing: foundations, techniques and applications. Philadelphia (USA): W.B Saunders Company; 2000. p.231-50. Disponível em: <https://www.scielo.br/scielo.php?script=sci_nlinks&ref=000112&pid=S0104-07072008000400018000014&lng=en>. Acesso em: 13 de jun. 2020.

[9] BUTTERWECK, V. Mechanism of action of St John's wort in depression. CNS Drugs. 2003; 17: 539-62. Disponível em: https://link.springer.com/article/10.2165/00023210-200317080-00001 Acesso em: 05 de outubro de 2019.

[10] CARNEIRO, F. F. (Org.) Dossiê ABRASCO: um alerta sobre os impactos dos agrotóxicos na saúde / Organização de Fernando Ferreira Carneiro, Lia Giraldo da Silva Augusto, Raquel Maria Rigotto, Karen Friedrich e André Campos Búrigo. - Rio de Janeiro: EPSJV; 2015 São Paulo: Expressão Popular. Disponível em: https://www.abrasco.org.br/dossieagrotoxicos/wpcontent/uploads/2013/10/DossieAbrasco_2015_web.pdf Acesso em: 09 de outubro de 2019.

[11] CARRETTIERO, D. C.; DA SILVA, S. M.;, FIOR-CHADI, D. R. Adenosine modulates alpha2- adrenergic receptors through a phospholipase C pathway in brainstem cell culture of rats. Auton Neurosci. 2009; 151 (2): 174-177. Disponível em: https://www.sciencedirect.com/science/article/abs/pii/S1566070209003750 Acesso em: 15 de outubro de 2019.

[12] CASSANI, J.; ALBERTO FERREYRA-CRUZ, O.; MARIA DORANTES-BARRÓN, A.; VIGUERAS VILLASEÑOR, R. M.; ARRIETA-BAEZ, D.; ESTRADA-REYES, R. Antidepressant-like and toxicological effects of a standardized aqueous extract of Chrysactinia mexicana A. Gray (Asteraceae) in mice. J Ethnopharmacol. 2015; 171: 295- 306. Disponível em: http://repositorio.inprf.gob.mx/handle/123456789/4390 Acesso em: 29 de outubro de 2019.

[13] CAVANAGH, H. M.; WILKINSIN, J. M. Biological activities of lavender essential oil. Phytother Res. 2002; 16: 301- 308. Disponível em: http://naturalingredient.org/wp/wp-content/uploads/Biological-Activities-of-Lavender-Essential-Oil.pdf Acesso em: 20 de setembro de 2019.

[14] COSTA, V. I. B.; MELLO, M. S. C.; FRIEDRICH, K. Exposição ambiental e ocupacional a agrotóxicos e o linfoma não Hodgkin. Saúde Debate, 2017 v. 41, n. 112, p. 49–62, mar. Disponível em:< http://www.scielo.br/scielo.php?pid=S010311042017000100049&script=sci_abstract&tlng=pt>. Acesso em: 07 de outubro de 2019.

[15] DIETZ, B. M.; MAHADY, G. B.; PAULI, G. F.; FARNWORTH, N. R. Valerian extract and valerenic acid are partial agonists of the 5-HT5a receptor in vitro. Brain Res Mol Brain Res. 2005; 138 (2): 191- 197. Disponível em: https://www.sciencedirect.com/science/article/abs/pii/S0169328X0500197X?via%3Dihub Acesso em: 25 de setembro de 2019.

[16] ELY, P.; et. al. Avaliação psicológica da depressão: levantamento de testes expressivos e autorrelato no Brasil. Aval Psicol. 2014 v. 13, n. 3, p. 419–426. Disponível em:< http://pepsic.bvsalud.org/scielo.php?script=sci_abstract&pid=S1677-83047120140003000014&lng=en&nrm=iso&tlng=pt>. Acesso em: 12 de setembro de 2019.

[17] FILHO NETO, M. G.; ANDRADE, R. D.; FELDEN, É. P. G. Trabalho na agricultura: possível associação entre intoxicação por agrotóxicos e depressão. R Perspect Ci e Saúde 2018;3(1):69-82. Disponível em: file:///C:/Users/Usuario/Downloads/192-852-1-PB.pdf Acesso em: 30 de outubro de 2019.

[18] FIRMO, W. C. A. et. al. Contexto histórico, uso popular e concepção científica sobre plantas medicinais. Cad pesqui. 2012; 18 (Especial): 90-95. Disponível em: file:///C:/Users/Usuario/Downloads/746-14638-1-PB.pdf Acesso em: 21 de outubro de 2019.

[19] GUTIÉRREZ, W. et. al. Caracterización de las exposiciones a plaguicidas entre los años 2006 y 2013 reportadas al Centro de Información Toxicológica de la Pontificia Universidad Católica de Chile. Rev méd Chile. Out 2015, v. 143, n.10, p. 1269-127. Disponível em:<https://scielo.conicyt.cl/scielo.php?script=sci_arttext&pid=S0034-98872015001000009>. Acesso em: 04 de outubro de 2019.

[20] HAUSENBLAS, H. A.; SAHA, D.; DUBYAK, P. J.; ANTON, S. D. "Saffron (Crocus sativus L.) and major depressive disorder: a meta-analysis of randomized clinical trials" J of Integr Med, vol. 11, no. 6, pp. 377–383, 2013. Disponível em: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4643654/ Acesso em: 25 de setembro de 2019.

[21] HRICTU, L.; CIOANCA, O.; HANCIANU, M. Effects of lavender oil inhalation on improving scopolamine-induced spatial memory impairment in laboratory rats. Phytomedicine, vol. 19, no. 6, pp. 529–534, 2012. Disponível em: https://pubmed.ncbi.nlm.nih.gov/22402245/ Acesso em: 15 de outubro de 2019.

[22] HOSSEINI, S. E.; HOSSEINI, S. A. The Therapeutic Effects of Medicinal Plants on Depression and Anxiety Disorders. Report of Health Care. 2018; 1 (1): 67- 80. Disponível em: http://jrhc.miau.ac.ir/article_2941_64e1e77bd5c495f3f6bc79f821fcf39e.pdf Acesso em: 17 de setembro de 2019.

[23] JÄGER, A.; SAABY, L. Flavonoids and the CNS. Molecules 2011; 16: 1471-85. Disponível em: https://www.researchgate.net/publication/49826957_Flavon

oids_and_the_CNS/link/561763a208ae1a88800370d6/download Acesso em: 23 de setembro de 2019.

[24] JOO, Y.; ROH, S. Risk factors associated with depression and suicidal ideation in a rural population. J. toxicol environ health. 2016 v. 31, p. e2016018, 26 ago. Disponível em:< https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5080792/>. Acesso em: 10 de outubro de 2019.

[25] LACERDA, J. R. C. et. al. Conhecimento popular sobre plantas medicinais e sua aplicabilidade em três segmentos da sociedade no município de Pombal-PB. Rev. ACSA, jan./mar, 2013, v. 9, n.1, p.14-23. Disponível em: file:///C:/Users/Usuario/Downloads/250-997-1-PB.pdf Acesso em: 20 de setembro de 2019.

[26] LEE, G.; BAE, H. Therapeutic Effects of Phytochemicals and Medicinal Herbs on Depression. BioMed Research International, volume 2017, Article ID 6596241, 11 pages. Disponivel em: https://doi.org/10.1155/2017/6596241. Acesso em: 10 de outubro de 2019.

[27] LOPRESTI, A. L.; DRUMMOND, P. D. "Saffron (Crocus sativus) for depression: a systematic review of clinical studies and exam- ination of underlying antidepressant mechanisms of action". H Psychopharmacol, vol. 29, no. 6, pp. 517–527, 2014. Disponível em: https://onlinelibrary.wiley.com/doi/epdf/10.1002/hup.2434 Acesso em: 25 de setembro de 2019.

[28] MACHADO, D. G.; BETTIO, L. E.; CUNHA, M. P.; CAPRA, J. C.; DALMARCO, J. B.; PIZZOLATTI, M. G.; RODRIGUES, A. L. Antidepressant-like effect of the extrat of Rosmarinus officinalis in mice: Involvement of the monoaminergic system. Neuropsychopharmaol Biol Psychiatry. 2009; 33: 642-50. Disponível em: https://www.sciencedirect.com/science/article/abs/pii/S0278584609000633 Acesso em: 20 de outubro de 2019.

[29] MACHADO, D. G.; CUNHA, M. P.; NEIS, V. B.; BALEN, G. O.; COLLA, A.; BETTIO, L. E.; OLIVEIRA, A.; PAZINI, F. L.; DALMARCO, J. B.; SIMIONATTO, E. L.; PIZZOLATTI, M. G.; RODRIGUES, A. L. Antidepressant-like effects of fractions, essential oil, carnosol and betulinic acid isolated from Rosmarinus officinalis L. Food Chem. 2013; 136: 999- 1005. Disponível em: https://www.sciencedirect.com/science/article/pii/S0308814612014306?via%3Dihub Acesso em: 20 de outubro de 2019.

[30] MACHADO, D. G.; KASTER,M. P.; BINFARÉ, R. W.; DIAS, M.; SANTOS, A. R. S.; PIZZOLATTI, M. G. Antidepressant-like effect of the extract from leaves of Schinus molle L. in mice: Evidence for the involve- ment of the monoaminergic system. Prog Neuropsycho-pharmacol Biol Psychiatry. 2007; 31: 421-28. Disponível em: https://www.sciencedirect.com/science/article/abs/pii/S027858460600399X?via%3Dihub Acesso em: 29 de outubro de 2019.

[31] MALEKIRAD, A. A. et al. Neurocognitive, mental health, and glucose disorders in farmers exposed to organophosphorus pesticides. Arh Hig Rada Toksikol. 2013;64(1):1-8. Disponível em: file:///C:/Users/Usuario/Downloads/[Archives%20of%20Industrial%20Hygiene%20and%20Toxicology]%20Neurocognitive,%20Me Acesso em: 29 de outubro de 2019.

[32] MARCONI, M. A; LAKATOS, E. M. Técnicas de pesquisa: planejamento e execução de pesquisas, amostragens e técnicas de pesquisas, elaboração, análise e interpretação de dados. 7 ed. São Paulo: Atlas, 2008.

[33] MEYER, T.; RESENDE, I.; ABREU, J. Incidência de suicídios e uso de agrotóxicos por tra- Métodos. Rev Bras saúde ocup. 2007 v. 32, n. 116, p. 24–30. Disponível em:<http://www.scielo.br/scielophp?pid=S0303765720070 00200004&script=sci_abstract&tlng=pt>. Acesso em: 10 de setembro de 2019.

[34] PERVIZ, S.; KHAN, H.; PERVAIZ, A. Plant Alkaloids as an Emerging Therapeutic Alternative. Front Pharmacol. 2016 7:28. doi: 10.3389/fphar.2016.00028. Disponível em: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4753303/pdf/fphar-07-00028.pdf Acesso em: 15 de outubro de 2019.

[35] PIGNATI, W. A.; OLIVEIRA, N. P.; SILVA, A. M. C. Vigilância aos agrotóxicos: quantificação do uso e previsão de impactos na saúde-trabalho-ambiente para os municípios brasileiros. Ciênc Saúde Colet., 2014, v. 19, n. 12, p. 4669–4678, dez. Disponível em: https://www.scielo.br/pdf/csc/v19n12/1413-8123-csc-19-12-04669.pdf Acesso em: 10 de outubro de 2019.

[36] QUANDT, S. A. et. al. Cholinesterase Depression and Its Association with Pesticide Exposure across the Agricultural Season among Latino Farmworkers in North Carolina. Environ health perspect. 2010 v. 118, n. 5, p. 635–639. Disponível em:< https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2866678/>. Acesso em: 10 de outubro de 2019.

[37] RABIEI, Z.; RABIEI, S. A review on antidepressant effect of medicinal plants. Bangladesh J Pharmacol 2017; 12: 1-11. Disponível em: https://www.researchgate.net/publication/314163884_A_review_on_antidepressant_effect_of_medicinal_plants Acesso em: 25 de setembro de 2019.

[38] RABIE, Z.; RABIE, S.; LORIGOIENI, Z. A review on antidepressant effects medicinal plants with emphasis on their mechanisms of action. JMP. 2016; 4 (60): 24- 38. Disponível em: https://core.ac.uk/download/pdf/143840256.pdf Acesso em: 21 de outubro de 2019.

[39] REZAEI, A.; JAFARI, B.; JALILZADEH, H. M. Study of sedative, preanaesthetic and anxiolytic effect of herbal extract of lavandula stoechas in comparison with diazepam. J Tabriz Med Sci Univ. 2010; 3: 899- 905. Disponível em: file:///C:/Users/Usuario/Downloads/611-614.pdf Acesso em: 19 de setembro de 2019.

[40] REZVANI, M. E.; ROOHBAKHSH, A.;, ALLAHTAVAKOLI, M.; SHAMSIZADEH, A. Anticonvulsant effect of aqueous extract of valeriana officinalis in amygdala- kindled rats: possible involvement of adenosine. J Ethnopharmacol. 2010; 127 (2): 313- 318. Disponível em: https://www.sciencedirect.com/science/article/abs/pii/S037

8874109006977?via%3Dihub Acesso em: 15 de outubro de 2019.

[41] RIGOTTO, RM; VASCONCELOS, DP; ROCHA, MM. Uso de agrotóxicos no Brasil e problemas para a saúde pública. Cad Saúde Publica. 2014; 30(7): 1-3. Disponível em: https://www.scielo.br/pdf/csp/v30n7/pt_0102-311X-csp-30-7-1360.pdf Acesso em: 03 setembro de 2019.

[42] ROOZBEHI, A.; DELAVIZ, H.; HEIDARIAN, A.; MOHAMADI, J. The effect of hydroalcohlic extract of Valeriana officinalis on the astrocytes of hippocampus in rats. Yasouj Med Sci Unic J. 2015; 20 (4): 298- 308. Disponível em: https://www.sid.ir/en/journal/ViewPaper.aspx?id=482108 Acesso em: 20 de setembro de 2019

[43] SABZHAH, S.; VAEZI, G. H.;BAKTIARIAN, A.; SALARIAN, A.; ZARE HAGHIGHI, M. The effect of D2 agonist versus D2 antagonist on the fear behavior in the male rats using plus-maze method: the prospective study. Tehran Univ Med Sci J. 2009; 67 (8): 535- 541. Disponível em: http://tumj.tums.ac.ir/article-1-421-en.html Acesso em: 03 de outubro de 2019.

[44] SASAKI, K.; EL OMRI, A.; KONDO, S.; HAN, J.; ISODA, H. Rosmarinus officinalis polyphenols produce anti-depressant like effect through monoaminergic and cholinergic functions modulation. Behav Brain Res. 2013; 238: 86-94. Disponível em: https://www.sciencedirect.com/science/article/abs/pii/S0166432812006572 Acesso em: 05 de outubro de 2019.

[45] SEOL, G. H.; SHIM, H. S.; KIM, P. J.; MOON, H. K.; LEE, K. H.; SHIM, I.; SUH, S. H.; MIN, S. S. Antidepressant-like effect of Salvia sclarea is explained by modulation of dopamine activities in rats. J Ethnopharmacol. 2010; 130: 187-90. Disponível em: https://www.sciencedirect.com/science/article/abs/pii/S0378874110002667?via%3Dihub Acesso em: 30 de outubro de 2019.

[46] SILVA, E. F. D. et al. Prevalência de morbidades e sintomas em idosos: um estudo comparativo entre zonas rural e urbana. Ciên Saúde Colet. 2013;18(4):1029-40. Disponível em: https://www.scielo.br/pdf/csc/v18n4/16.pdf Acesso em: 30 de outubro de 2019.

[47] SINGER, A.; SCHMIDT, M.; HAUKE, W.; STADE, K. Duration of response after treatment of mild to moderate depression with Hypericum extract STW 3-VI, citalopram and placebo: A reanalysis of data from a controlled clinical trial. Phytomedicine 2011; 18: 739-42. Disponível em: ??? Acesso em: colocar a data que acessou o artigo para consulta.

[48] STROPARO, L. F.; BRAGUINI, W. L. Avaliação da exposição à organofosforados entre produtores de tabaco de uma localidade do município de Irati – Paraná. Publicatio UEPG - Ciencias Exatas e da Terra, Agrarias e Engenharias, 2011. Disponível em: <https://www.researchgate.net/publication/274051393_A>. Acesso em: 04 de setembro de 2019.

[49] VEIGA JÚNIOR, V. F.; PINTO, A. C.; MACIEL, M. A. M. Plantas Medicinais: Cura Segura? Revista Quim. Nova. May-jun, 2005, v. 28, n. 3, p. 519-528. Disponível em: https://www.scielo.br/scielo.php?script=sci_arttext&pid=S0100-40422005000300026 Acesso em: 03 de outubro de 2019.

[50] ZHANG, X. et al. Pesticide poisoning and neurobehavioral function among farm workers in Jiangsu, People's Republic of China. Cortex, 2016, v. 74, p. 396–404, jan. Disponível em:<https://www.ncbi.nlm.nih.gov/pubmed/26475098>. Acesso em: 10 de outubro de 2019.