

## **Herbal remedies in depression – state of the art**

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### **Summary**

Recent decades have seen development of research and an increased interest in the psychopharmacology of natural remedies. More than 20 herbal remedies have been identified that may potentially be applied in medicine as antidepressive, anxiety relieving or sleep-inducing agents. Patients often prefer to take herbal remedies and often take them on their own, without consulting a physician. The aim of the study is to present the state of the art concerning the use of natural remedies in the treatment of depression.

Following a literature review, 7 herbal remedies for which preclinical and clinical trials suggest their antidepressive influence have been identified: hypericum, lavender, borage, roseroot, chamomile, saffron and ginseng. For two of these, i.e. hypericum and saffron extracts, antidepressive effect in subjects with mild or moderate depression has been confirmed in controlled randomized clinical trials.

**Key words:** depression, herbal medicine, saffron

### **Introduction**

Depression is one of the most common diseases, and according to WHO it may become a primary cause of disability in the future. Although there is a wide range of depression treatment strategies, both pharmacological and psychotherapeutic, they are not effective with all patients. Moreover, in many countries of the world, natural medicine remains the most available and sometimes the only form of medical care, also as far as mental health is concerned [1].

According to some studies, post-industrial societies reveal an increasing interest in alternative medicine, including herbal therapy, despite the achievements of conventional medicine. It seems that for many people the „natural” model best meets their expectations concerning effective and safe treatment [2-3]. Using herbal remedies is perceived by patients as safe, not excessively invasive and having a „holistic” effect on the whole body. Herbal remedies are usually available over the counter and it is not as stigmatising to take them as to take synthetic psychotropic drugs. Studies conducted on subjects with anxiety disorder or mood changes indicate that as many as half of those subjects turn to so called complementary medicine [1-9]. Yet physicians often do not understand the underlying cause of such behaviour and the choices of the patients. Also, they are often unaware of the effects caused by the preparations used by the patients [1, 3, 9].

### **Towards evidence-based herbal medicine**

The practice of using plant-derived remedies is the feature of Complementary and Alternative Medicine (CAM). Within CAM, the more and more frequently used term is nutraceuticals, which refers to various dietary supplements, herbal products or ready-made food products that are intended to provide health benefits [3,7].

The market of dietary supplements and phytomedicines may be attractive for the pharmaceutical industry. Accordingly, progress in scientific standardisation of research into herbal remedies can be observed. This refers both to the quality of the active substance, as well as to the research into the mechanism of action, composition, pharmacokinetics and the toxicology of the preparations [10].

A lot of physicians claim that herbal preparations are completely ineffective and their use is only a delay to proper treatment and is not rationally grounded. However, these critics forget about the origins of medicines which play a very important role in modern medicine, i.e. aspirin, opiates, digoxin or paclitaxel [2]. Also, the fact that there is a list of herbal intoxicants does not raise any controversies [11]. The existence of this kind of „double standards” in the interpretation of placebo-controlled trials on synthetic drugs and herbal remedies was indicated by Kirsh [12]. On the one hand, there is no reason to apply different standards to trials concerning natural remedies and synthetic drugs. On the other hand, such trials should comply with the standards of Evidence Based Medicine.

Sarris (2011) states that the number of publications presenting the results of trials concerning the influence of plant-derived substances on various mental disorders has increased by as much as 50% in the last few years [6]. For example, several randomized clinical trials concerning the assessment of the antidepressive effect of herbal substances have been published in this period.

### **Objective**

The aim of this study is to present the state of the art concerning the use of natural remedies in treating depression and to answer the question whether apart from hypericum extract there is some more evidence that other natural remedies may be effective against the symptoms of depression.

The literature review was based on the review of Medline/Pubmed database (depression, herbal medicine/nutraceuticals/phytomedicines/natural, double-blind, randomized). The study includes those phytomedicines for which pre-clinical in vitro and in vivo trials revealed a potential antidepressive effect and for which the clinical activity against the symptoms of depression was the subject of a clinical trial on humans. The emphasis was placed on randomized controlled trials (RCT).

### **The mechanism of action of plant-derived medicines**

Studies show that the effect of plant-derived medicines on health may result from their antioxidant properties and potential influence on the processes of cell metabolism.

They may modulate neurotransmission through direct impact on receptors and they may also influence neurotransmitter synthesis or distribution. Activity through modulating immunological processes is also possible [13]. Sarris notices that the activity of phyto-medicines may be based on synergy (i.e. the intensification of the pharmacological effect of one substance by another substance contained in the given plant). Another possibility is polyvalent activity, i.e. causing different pharmacological effects by particular components. One component may have a particular pharmacological effect but another may influence its absorption and distribution. Herbonomics is a concept whose aim is to analyse the psychopharmacological effects of plant-derived medicines by means of complex genetic technologies, such as pharmacogenomics, epigenetics and metabolomics. If we take hypericum preparations, for example, it was discovered that similarly to imipramine they may influence the expression of certain protein-coding genes responsible for synaptic functions and energy metabolism [1,6].

Table 1 presents mechanisms of antidepressive activity of herbal remedies that were identified by in vitro and in vivo trials.

Table 1. **Herbal remedies with potential antidepressive effect**

Name	Active components	Possible mechanism of antidepressive effect (Pre-clinical trials)	Antidepressive efficacy (Clinical trials)
Hypericum (Hypericum L.)	Hyperforin Hypericin	Modulation of monoamine transmission – affecting through sodium channels Non-selective inhibition of monoamine reuptake Effect on the 5HT1 receptor function Effect on dopaminergic activity Neuroendocrine modulation	Confirmed Meta-analysis of RCT (n=>5000) - antidepressive effect greater than for placebo and comparable to SSRI and TLPD (non-inferiority)
Lavender (Lavandula L.)	Linalool Linalool acetate	GABA modulation	Unconfirmed (not enough data)
Borage (Borago officinalis, Echium amoenum)	Rosmarinic acid γ-linoleic acid	Inhibition of 5HT reuptake Immunomodulation?	Unconfirmed (not enough data)
Roseroot (Rhodiola rosea L.)	Salidroside Tyrosol Rosavin	Inhibition of monoamine oxidase A Modulation of monoamine transmission Normalization of serotonergic transmission	Unconfirmed (not enough data)
Chamomile (Matricaria chamomilla)	Apigenine Bisabolol	GABA modulation Modulation of monoamine transmission Neuroendocrine modulation	Unconfirmed (not enough data)

*table continued on next page*

Saffron ( <i>Crocus sativus</i> )	Crocin Crocetin Safranal	Inhibition of monoamine NA, DA (crocin) Inhibition of 5HT reuptake (safranal) NMDA antagonism GABA $\alpha$ agonism BDNF activation? (neurotrophic influence)	Possible, Efficacy of saffron for symptoms of mild to moderate depression was shown in 2 RCT with placebo (n=80) and 4 RCT (n=154) with fluoxetine 20 mg daily or imipramine 100 mg daily (non-inferiority)
Ginseng ( <i>Panax ginseng</i> )	Ginsenosides	Modulation of the hypothalamic-pituitary axis Modulation of monoamine (DA and 5HT) transmission Antioxidant and anti-inflammatory effect Inhibition of nitric oxide synthase 5HT $2A$ agonist (?) BDNF activation and up-regulation of neurogenesis in the hippocampus	Unconfirmed (not enough data)

RCT – randomized controlled clinical trial, DA – dopamine, NA – noradrenalin, 5HT – serotonin, 5HT $2A$  – type 2A serotonin receptor, 5HT $1$  – type 1 serotonin receptor, NMDA – receptor for glutamate, activated by N-methyl-D-aspartic acid, GABA $\alpha$  – type A GABA receptor, BDNF Brain Derived Neurotrophic Factor SSRI – serotonin reuptake inhibitors, TLPD – tricyclic antidepressants

Some of these mechanisms are equal to those of registered antidepressants: inhibition of monoamine reuptake (hypericum, borage, saffron), inhibition of monoamine oxidase (roseroot, chamomile), effect on serotonin receptors (hypericum, ginseng) and GABAergic receptors (lavender, chamomile, saffron). However, the discovered effects included also the neurotrophic effect, e.g. by BDNF activation (saffron, ginseng), and neuroendocrine effect (hypericum, chamomile, ginseng). Saffron has turned out to be the antagonist of postsynaptic NMDA receptors [14]. According to the glutamatergic hypothesis of depression, substances that inhibit glutamatergic transmission may have an antidepressive effect [15]. Low affinity to the NMDA receptor is an essential feature, since the use of strong antagonists (such as ketamine) is related to poor tolerance and potential neurotoxic activity [14].

### Clinical trials in herbal remedies for depression

#### *Hypericum (St John's wort)*

Hypericum is the best researched herb with regard to the antidepressive activity. Meta-analysis involving 29 RCT (n=5489) showed that hypericum preparations as compared to placebo revealed efficacy towards depression symptoms (RR = 1.28 (95% CI 1.10-1.49), their effect was not worse than SSRI (RR = 1.00 (95% CI 0.90-1.11). Hypericum extracts were also compared with TLPD (RR = 1.02 (95% CI 0.9-1.15).

It should be noted that more recent and methodologically better trials have usually revealed a lesser effect of a standardised hypericum extract [12,16,17]. Kasper et al. published a study showing that hypericum may be effective in long-term prevention of depression recurrence [18].

Hypericum has a low profile of adverse reactions. The number of subjects dropping out of the trial due to adverse reactions ranged from 0% to 5.7% and was not significantly different from placebo. As compared to serotonin reuptake inhibitors, hypericum preparations were slightly better tolerated. However, phototoxic reactions, serotonin syndromes or cases of inducing mania during the use of the preparations were described [17,19,20].

An important limitation of hypericum is the fact that its use (especially at high doses) may trigger CYP3A and p-glycoprotein induction. In polytherapy, this may lead to a decrease in serum levels of numerous agents, such as oral contraceptives, digoxin or warfarin. Metabolism and elimination of xenobiotics may be increased. What is important, hypericum preparations interact with numerous psychotropic drugs: clomipramine, citalopram, alprazolam, clozapine, sertindole, aripiprazole, zopiclone, diazepam [19,20].

A separate problem is the bad quality of certain preparations and the lack of adequate information concerning safety, especially of the above-mentioned interactions. This is a deeper problem concerning numerous natural remedies. In some preparations from India or China, the presence of heavy metal ions was discovered at levels exceeding permissible standards [21].

To sum up, hypericum extracts used at doses of 900-1800 mg/daily may be used as second- or third-line therapy in subjects with mild or moderate depression who do not want to take synthetic drugs or do not tolerate them.

Due to the risk of interaction, it is not recommended to combine hypericum preparations with other medicines.

### *Saffron*

Saffron is a substance obtained from saffron crocus (*Crocus sativus*). As early as at the beginning of the 11th century the Canon of Medicine drawn up by Avicenna presented numerous uses of saffron in treatment of melancholy and insomnia.

Over the last decade there has been a series of clinical trials in which standardized water-alcohol extract of saffron (30 mg contained about 0.6-0.7 mg of safranal) was used in subjects with mild or moderate depression [22-28].

As compared to placebo, the group receiving saffron revealed significantly better results - a decrease in symptoms in the HDRS-17 Hamilton scale after 6 weeks was  $12.2 \pm 4.7$  points, while in the placebo group only  $5 \pm 4.7$  points. Saffron tolerance was similar to that of placebo. In the group treated with saffron there was one drop-out, while in the placebo group there were 4 drop-outs [24]. In another placebo-controlled trial lasting 6 weeks, saffron confirmed its efficacy by lowering depression symptoms by  $14 \pm 5.5$  points Hamilton scale, while in the placebo groups they were lowered by

$5 \pm 4.6$  points. 1 subject dropped out in the saffron group and 3 in the placebo group. There were no significant differences in the frequency of side effects [27].

A trial with imipramine revealed comparable results for the group treated with saffron and the group treated with imipramine 100 mg/daily. Within 6 weeks, the improvement was about 10 points on the HDRS-17 scale. Saffron caused dry mouth and sleepiness less frequently than imipramine [23]. In a trial with fluoxetine at the dose of 20 mg/daily, the results after 6 weeks also revealed similar improvement in both treated groups – ( $-12.2 \pm 4.7$  vs  $-15 \pm 5.9$ ; saffron and fluoxetine respectively). There were no statistically significant differences with regard to side effects [28]. The comparison of saffron (30 mg/daily) obtained from petals of *Crocus sativus* and fluoxetine used at the dose of 20 mg/daily for 8 weeks did not reveal significant differences between the groups. Remission (HDRS < 8) in both groups involved 25% subjects. Reduction in the intensity of the symptoms in HDRS by 50% involved 75% in the saffron group and 85% in the fluoxetine group. There were no differences as for tolerance and there was one drop-out in each group [25].

In the first trials on saffron, the extract was obtained from the stigma of the flowers. However, it is the petals which are more available and economic on industrial scale. A comparison of saffron preparations obtained from stigma and petals did not reveal differences after 6 weeks of treatment. Remission was reported in 18% of subjects in both groups, whereas significant (50%) decrease in symptom intensity HDRS was observed in 68% of one group (petals) and 77% of the other group (stigmas) [26].

Recently, results of a randomized, double-blinded, clinical trial comparing the efficacy and safety of saffron 30mg/d with fluoxetine 40mg/d for improving depressive symptoms in post percutaneous coronary intervention patients. Saffron extract - SaffroMood®, capsules containing 15 mg of saffron extract standardized to 0.13–0.15 mg of safranal and 1.65–1.75 mg of crocin were used. Short term therapy showed similar antidepressant efficacy and tolerance. These results are interesting with regard to saffron's potential greater acceptance and cardioprotective properties [29].

All the above trials were of good quality, with a score of 4 or 5 on the 5-point Jadad scale. The summary of the results is presented in table 2 – *next page*.

The limitations of the presented trials include small count of the groups, short observation time, no assessment of efficacy and tolerance of various saffron doses, and also the fact that the trials come from only one centre and have not been replicated outside Iran so far.

Apart from the presented trials, in which saffron efficacy was assessed, there were two other randomized clinical trials in subjects with recognised depression. Their results indicated that 30 mg saffron combined with fluoxetine may to a small extent mitigate certain sexual dysfunctions caused by the use of serotonin reuptake inhibitor, both in women and men:

Modabbernia et al. [30] assessed the use of saffron in men with sexual dysfunctions resulting from the use of fluoxetine. The trial was randomized and lasted 4 weeks. It was based on the use of saffron 30 mg/daily (n=18) or placebo (n=18). Sexual dysfunctions were assessed by the IIEF questionnaire. The subjects included in the trial were already free of intense symptoms of depression (HDRS < 10). In the saffron group, an

Table 2. Randomized, double-blind clinical trial concerning the use of saffron extract in the treatment of depression

Author, (year of publication)	Indication	Size of the groups (women %)	Quality of the trial (Jadad)	Saffron (dose)	Control (dose)	Trial duration	Assessment of depression intensity	Efficacy	Tolerance
S.Akhondzadeh 2004	Major depression (DSM-IV)	30 (15/15) (57%) 35 years	5	30 mg daily (stigma)	Imipramine 100 mg daily	6 weeks	HDRS-17	Saffron non-inferior to IMI (non-inferiority)	SZA<IMI less frequently dry mouth and sleepiness
A.A.Noorbala 2004	Major depression (DSM-IV)	40 (20/20) (50%) 37 years	4	30 mg daily (stigma)	Fluoxetine 20 mg daily	6 weeks	HDRS-17	Saffron non-inferior to FLU (non-inferiority)	SZA=FLU No significant differences
S.Akhondzadeh 2005	Major depression (DSM-IV)	40 (20/20) (45%) 36 years	4	30 mg daily (stigma)	Placebo	6 weeks	HDRS-17	Saffron significantly better than placebo	SZA=PLA No significant differences
E.Moshri 2006	Major depression (DSM-IV)	40 (20/20) (42.5%) 35 years	4	30 mg daily (petals)	Placebo	6 weeks	HDRS-17	Saffron significantly better than placebo	SZA=PLA No significant differences
A.Akhondzadeh Basti 2007	Major depression (DSM-IV)	40 (20/20) (52.5%) 35 years	5	30 mg daily (petals)	Fluoxetine 20 mg daily	8 weeks	HDRS-17	Saffron non-inferior to FLU (non-inferiority)	SZA=FLU No significant differences
A.Akhondzadeh Basti 2008	(DSM-IV)	44 (19/25) (50%) 35 years	5	30 mg daily (saffron petals)	30 mg daily (saffron stigma)	6 weeks	HDRS-17	Saffron from petals non-inferior to saffron from stigma	No significant differences
N.Shahmansouri 2013	Major depression (DSM-IV-TR)	44 (22/22) (56.8%) 52-53 years	5	30mg/dz (extract)	Fluoxetine 40mg daily	6 tyg	HDRS-17	Saffron non-inferior to FLU (non-inferiority)	SZA=FLU No significant differences

HDRS-17 – Hamilton depression rating scale, 17-point version,  
 IMI- imipramine, FLU- fluoxetine, SZA- saffron, PLA- placebo

improvement in erection and satisfaction with the intercourse was obtained, although it was slight. There were no differences as to orgasm, desire and general satisfaction.

Kashani et al [31] assessed the effect of saffron on women with sexual dysfunctions during the fluoxetine treatment 40 mg/daily. This randomized placebo-controlled trial also lasted 4 weeks. Sexual functions were assessed by means of the FSFI questionnaire (Female Sexual Function Index). 34 women were included in the trial. After 4 weeks of using saffron, improvement was observed in the total FSFI score ( $p < 0.001$ ), as well as in particular domains assessing arousal and vaginal lubrication. Similarly to the group of men, there was no improvement as to the feeling of desire, orgasm and sexual satisfaction.

Agha-Hosseini [32] assessed the effect of saffron in a group of 50 women with symptoms of PMS (Premenstrual Syndrome, according to criteria of the American College of Obstetrics and Gynecology) persisting for at least 6 months. Saffron at the dose of 30 mg/daily or placebo were used in two monthly cycles. In the group of women receiving saffron, the clinical response defined as 50% decrease in PMS symptoms was observed in 76% of women. In the group receiving placebo, the response was 8%. A reduction in symptoms on the Hamilton depression scale was also observed.

On the basis of available literature data, it may be stated that saffron is usually well tolerated [22, 33, 34]. In placebo-controlled trials, no statistically significant differences in the incidence of adverse reactions were observed. In the group of subjects receiving saffron, there was a tendency towards frequent occurrence of nausea, dyspepsia, appetite changes (including both increase and decrease in appetite), tachycardia and anxiety [22,33]. Cases of allergy and one case of anaphylactic shock after receiving saffron were reported. Taking into account the frequency of saffron usage as a seasoning, the risk is very low [35].

As for potential interactions, there is no data concerning saffron influence on hepatic CYP enzymes. There is no data on interactions with food or alcohol. One must remember about possible pharmacological interactions (intensification of the effect of antihypertensive, antiasthmatic and antidiabetic drugs, as well as medicines influencing coagulation and aggregation of platelets). Therefore, caution is recommended for subjects using saffron together with such drugs as aspirin, warfarin, klopidogrel and nonsteroidal anti-inflammatory drugs [22, 34].

### *Lavender*

The antidepressive effect of the alcohol solution of lavender was assessed in a small (n=45) randomized trial lasting 4 weeks, which used lavender tincture and imipramine in monotherapy or lavender tincture combined with imipramine. The greatest reduction in depressive symptoms assessed with the Hamilton scale was observed in the group using the tincture and imipramine jointly. The tincture alone was less effective than imipramine in monotherapy. The suggested synergistic effect may depend on the postulated effect of lavender on the GABAergic system and its anxiolytic effect [36]. Currently, there is no evidence from clinical trials that lavender in monotherapy is

effective against depression symptoms. No significant pharmacokinetic interactions have been described

### *Borage*

Pre-clinical trials show that the borage extract has a similar effect to that of serotonin reuptake inhibitors. In a small (n=35) randomized placebo-controlled trial, a significant improvement in depressive symptoms was observed after 4 weeks of treatment. However, after the trial completion after 6 weeks, the difference between the groups receiving borage and the placebo group was not statistically significant [37]. Borage oil is a source of gamma-linolenic acid and is sometimes used in the treatment of atopic dermatitis and rheumatic disease. A case of staticus epilepticus was reported for a female subject receiving high doses of borage oil for a week [38]. The use of borage in treating depression would require further studies, but according to some researchers it is not advisable due to potential problems with its toxicity at higher doses.

### *Roseroot (arctic root).*

Authors from Armenia assessed the effect of two doses of roseroot extract (SHR-5, Swedish Herbal Institute: 340 mg and 680 mg) in comparison with placebo. Eighty nine subjects with depression symptoms took part in this six-week randomized trial, which revealed only a slight effect on depression symptoms assessed with the use of Hamilton scale. The tolerance of treatment was good. The quality of the trial, however, raises some doubts and it does not allow for drawing conclusions on roseroot antidepressive efficacy [39].

Apart from the trial on depression, we also have trials suggesting mild stimulating activity of roseroot and its positive influence on the physical capacity and decreased fatigue in healthy subjects. 2/6 of RCT revealed a positive influence of *R. rosea* on physical fatigue, whereas 3/6 of RCT indicated a positive influence on the symptoms of mental fatigue. In general however, the quality of these trials was described as poor and biased [40].

Roseroot has no addictive potential. Tolerance of roseroot is rather good. No significant adverse reactions were reported in trials. Possible reactions include irritability, insomnia, vivid dreams, headaches, and a decrease in platelet aggregation at high doses. No influence on CYP enzymes was revealed in vivo. The doses used in the trials ranged from 50 mg to 1500 mg daily. In trials with positive results, for mental fatigue, the doses of 100-600mg were used and for physical fatigue they amounted to 200-700 mg daily. The preparations should be taken on empty stomach, and due to the risk of insomnia they should not be taken late in the evenings. It was revealed that the roseroot extract may bind to oestrogen receptor. Thus, it should not be used by women with a family history of breast cancer [40-41].

In order to confirm the antidepressive effect of *Rhodiola rosea*, it is necessary to conduct further trials.

### *Chamomile*

In 2009, Amsterdam et al. conducted a trial in which they showed an anxiolytic effect of chamomile extract (220mg-1100mg, standardised to 1.2% apigenine) in comparison to placebo after 8 weeks of treatment [42].

Out of 57 subjects enrolled in the trial, 19 had depressive and anxiety disorders, 16 had anxiety disorders and a history of depression and 22 had just anxiety disorders. The analysis of results performed with the use of the Hamilton scale revealed that a decrease in depression symptoms was more significant in the chamomile group than in the placebo group ( $P < .05$ ). The same tendency was observed in the group with concurrent anxiety and depression symptoms, but it was not statistically significant. According to the authors, the results suggest not only an anxiolytic effect of the chamomile extract, but also an antidepressive effect. Generally, chamomile is well tolerated. Possible interactions with warfarin, statins and oral contraceptives were described in literature. Due to its anxiolytic effect, chamomile may intensify the activity of benzodiazepines. It is a promising plant-derived medicine. However, at the present stage of research, its antidepressive effect has not been proven [43].

### *Ginseng*

No randomized clinical trials for ginseng have been conducted so far among subjects with depression. However, the alternative medicine section of the Swedish Research Council published a large randomized clinical trial in 1999, in which they presented the results of the use of ginseng in women during menopause. They were based on the following questionnaires: Psychological General Well-Being (PGWB) and Women's Health Questionnaire (WHQ). It was a randomized, double-blind, placebo-controlled trial lasting 16 weeks. The assessed parameters included FHS, estradiol levels and endometrial thickness. 384 women at the average age of 53.5 were enrolled in the study. No differences were reported neither in the PGWB scale nor in physiological parameters between the group receiving ginseng ( $n=193$ ) and the group receiving placebo. However, a statistically significant improvement was observed in the group of women treated with ginseng with regard to depression [44]. The results await replication. In 2004, Hartley et al. conducted a small randomized placebo-controlled trial, in which both ginseng and ginkgo-biloba were used, but no positive influence on the mood and cognitive functions of women after menopause was observed [45].

Traditional medicine associates ginseng preparations with a stimulating effect. In an 8-week trial involving young and healthy volunteers, Reay et al. found that 400mg/day of ginseng had a significant influence on the reaction time and abstract thinking, as compared to placebo [46]. As far as tolerance of ginseng preparations is concerned, the most frequent adverse reactions include agitation, insomnia, anxiety, gastro-intestinal disorders. Also, decreased platelet aggregation was reported, which leads to a higher risk of bleeding in subjects receiving anticoagulants. A glycemia reducing effect was also reported. Ginseng at high doses may also affect CYP3A4 activity and inhibit

p-glycoprotein activity. It was also stated that ginseng reduces the analgesic effect of morphine [44-49].

Summing up, the existing data suggests that ginseng may have an antidepressive effect. However, it requires further confirmation by randomized placebo-controlled trials.

### Conclusions

Hypericum extracts remain the best documented natural remedies for treatment of mild and moderate depression. It has good tolerance, but the most important aspect in terms of safety issues are its pharmacokinetic and pharmacodynamic interactions.

In a few controlled clinical trials it was shown that saffron was more effective than placebo and no worse than standard medicines for mild and moderate depression [6,22,50]. Saffron therapy is now the second best documented herbal therapy for the symptoms of depression [6, 22, 50]. As compared to hypericum extracts, saffron did not pose significant safety threats, especially with regard to the risk of interactions.

Trials concerning other herbal remedies, such as lavender, borage, chamomile and ginseng suggest their antidepressive effect, but it must be emphasised that this effect has not been proven at this stage yet.

### Растительные лекарства при лечении депрессии – актуальные данные

#### Содержание

В последние десятилетия опубликованы многочисленные исследования и увеличенная заинтересованность психофармакологией лекарствами растительного происхождения. Идентифицировано более 20 растительных препаратов, которые могут иметь потенциальное применение ввиду своего антидепрессивного действия, также и противобоязненного, или же как снотворные лекарства. Такие препараты охотно используются пациентами, нередко принимаемые по собственному желанию, без консультации с врачом.

Заданием работы является представление настоящего уровня знаний на тему применения лекарств натурального происхождения при лечении депрессии. На основании литературного обзора выделено 7 растительных лекарств, в случае которых предклинические, или и клинические исследования, указывают на антидепрессивное действие. К ним относятся: зверобой, лаванда, огуречник, ромашка, шафран и жень-шень. В случае двух из них – экстрактов из зверобоя и шафрана – эффективность антидепрессивного действия у больных легкой или умеренной депрессией были подтверждены при контрольных рандомизованных клинических исследованиях

**Ключевые слова:** депрессия, растительные препараты, шафран

### Heilpflanzen in der Behandlung von Depression – aktueller Wissensstand

#### Zusammenfassung

Die letzten Jahrzehnte förderten die Entwicklung der Untersuchungen und dann stieg das Interesse an Psychopharmakologie der Mittel pflanzlicher Herkunft. Es wurden mehr als 20 Heilpflanzenmittel identifiziert, die eine potentielle Anwendung als Antidepressiva, Mittel gegen Angst oder Schlafmittel finden können. Sie werden oft von den Patienten bevorzugt, nicht selten werden sie ohne Beratung mit dem Arzt eingenommen. Das Ziel der Studie ist es den jetzigen Wissensstand zur Anwendung der Heilpflanzenmittel bei der Behandlung von Depression zu besprechen.

Aufgrund des durchgeführten Literaturreviews wurden 7 Heilpflanzenmittel identifiziert, bei denen die präklinischen oder/und klinischen Untersuchungen einen antidepressiven Einfluss vermuten: echtes Johanniskraut, Lavendel, Borretsch, Rosenwurz, Kamille, Safran, Ginseng. Bei zwei von ihnen – Tinktur vom Johanniskraut und Safran – wurde die Wirksamkeit der antidepressiven Wirkung bei den Kranken mit der mäßigen oder leichten Depression in den kontrollierten randomisierten klinischen Studien nachgewiesen.

**Schlüsselwörter:** Depression, Heilpflanzenmittel, Safran

### Les remèdes à base des plantes dans le traitement de la dépression – état actuel du savoir

#### Résumé

Les dernières décennies apportent le développement des recherches et l'intérêt augmenté de la psychopharmacologie des remèdes à base des plantes.

On a identifié plus de 20 remèdes à base des plantes qui, à cause de leur effet antidépresseur, anti anxieux ou soporifique, peuvent être les médicaments potentiels. Ils sont préférés souvent par les patients, parfois usés sans prescription ni consultation du médecin. Ce travail vise à présenter l'état actuel du savoir concernant l'usage des remèdes à base des plantes dans le traitement de la dépression.

En basant sur la revue de la littérature en question on identifie 7 remèdes naturels pour lesquels les examens cliniques et précliniques suggèrent l'effet antidépresseur : millepertuis, lavande, bourrache, orpin rose (*Rhodiola rosea*), camomille, safran, ginseng. Pour les extraits de millepertuis et de safran on atteste leur activité antidépresseur dans le traitement de la dépression moyenne et modérée dans les recherches cliniques randomisées.

**Mots clés :** dépression, remèdes à base des plantes, safran

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